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european academy of neurology

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Abstracts of the 11th Congress of the European Academy of Neurology

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Monday, June 23 2025

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European Journal of Neurology

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SPECIAL ISSUE Abstracts of the 11th Congress of the European Academy of Neurology, Helsinki, Finland

ABSTRACT

Plenary Symposium

Sunday, June 22 2025

Presidential Symposium

PLEN02_1 | How the Brain Represents the World

H. Sompolinsky[1,2]
[1]Harvard University, Cambridge, USA; [2]Hebrew University of Jerusalem, Jerusalem, Israel

One of the brain's most profound functions is to represent the world around us—transforming continuous, noisy streams of sensory input into stable internal models of the environment. These internal models support and guide perception, memory, cognition, and, most importantly, predictions about the state of the world. A leading hypothesis is that these internal representations correspond to stable patterns of activity in large populations of neurons. In this lecture, I will explain how such patterns emerge from the intrinsic dynamics and architecture of neuronal circuits. While the circuit dynamics constrain the repertoire of possible stable states, the specific state expressed at any given time is determined by ongoing sensory input. Disruptions in the balance between intrinsic dynamics and sensory-driven responses may underlie a range of neurological and psychiatric disorders. I will illustrate this principle using neuronal circuit models for memory, spatial navigation, object recognition, and language processing. This theory is supported and enriched by advances in artificial deep neural networks and generative AI, which provide powerful tools for testing hypotheses about brain function at realistic scales and levels of complexity.
Disclosure: Nothing to disclose.

PLEN02_3 | Multiple sclerosis, from biology to clinical translation. A focus on nodes of Ranvier and electrical activity

C. Lubetzki
Salpetriere Hospital, Paris, France

Multiple sclerosis (MS), an autoimmune demyelinating and degenerative disease of the CNS, remains only partly responsive to immunotherapies; despite reducing relapse rate, these immunomodulator/immunosuppressive drugs have not shown yet a convincing impact on disability progression. As remyelination might prevent axonal damage (although some controversies are ongoing...), finding new ways to promote remyelination and neuroprotection is now the next frontier for MS. Among innovative/disruptive perspectives from the recent years, we will here focus on the following steps necessary for CNS remyelination; and notably on the newly discovered neuron-glial interactions at the node of Ranvier, between node and oligodendrocyte precursors on the one hand, between node and microglia on the other hand. These studies led to the identification of clusters of nodal proteins detected prior to myelin deposition, structures that we named “pre-nodes”. These prenodes i) appear on axons prior to myelination onset, ii) participate to node of Ranvier formation, iii) accelerate propagation of axon electrical potential, leading to the new concept of increased conduction independent of myelin deposition, iv) are induced by a contactin-secreted oligodendroglial complex. In addition to these oligodendrocyte-node of Ranvier contacts, microglia have emerged as another major type of neuron glia interactions (for sake of time this field will be only alluded during the talk). Importantly, these interactions are both regulated by neuronal electrical activity, as shown using different techniques such as Dreadds and optogenetics. The established impact of electrical activity on (re)myelination prompted us to set up a small size study where trans-orbital electrical stimulation was used to favor remyelination after an episode of optic neuritis (Dr Beigneux, Pr Louapre, Paris, ICM; collaborations Prs Leocani (Milan), Sahel, Vignal and Touati (Paris). This controlled, recently completed study shows a tendency to reduced VEP latency between “stimulated” and “sham” group. A study assessing MEG latency and harmonics (N. George; B. Rossion, Paris) was added. Altogether, despite limitations, (small size of the study, MEG markers still pending...), human translation has suggested that stimulation of electrical activity might favor remyelination in the optic nerve opening novel perspectives of treatment for MS progression.
Disclosure: Nothing to disclose.

PLEN02_5 | Protein aggregation and its relevance for neurodegenerative diseases

M. Spillantini
Clifford Allbutt Building, Cambridge, UK

PLEN02_7 | Sleep by the brain, for the brain: Implications for neurology

C. Bassetti
University of Bern, Inselspital, Switzerland

PLEN02_9 | Myoclonus, you need to know it to see it

M. de Koning-Tijssen
Department of Neurology, University Medical Center Groningen, Groningen, The Netherlands

Myoclonus is a hyperkinetic movement disorder characterized by brief, sudden, shock-like jerks caused by hyperexcitable neurons, leading to either muscle activation (positive) or inhibition (negative). Myoclonus presents with a wide range of clinical manifestations and etiologies, including acquired causes such as medication side effects, metabolic or autoimmune conditions, and genetic disorders. This variability makes epidemiology unclear and contributes to under-recognition in clinical practice. Distinguishing myoclonus from other movement disorders, such as tics, tremor, or dystonia, relies heavily on clinical examination. However, phenotyping remains challenging, even among experts, due to overlapping features and subjective interpretation. Electromyography (EMG) can provide objective diagnostic support, as different movement disorders exhibit distinct EMG patterns. However, diagnostic accuracy remains limited as sensitivity and specificity of most electrophysiological tests are lacking. New machine learning tools hold promises in supporting more accurate classification. A structured diagnostic approach that integrates clinical features with neurophysiological data, supported by the new classification system, can aid in localizing the anatomical origin of myoclonus, including cortical, subcortical, brainstem, spinal, or peripheral myoclonus. Cortical myoclonus is the most common subtype. Functional jerky movements are also frequent and should be considered during evaluation. Generally, acute onset with rapid progression suggests an acquired etiology, while early-onset cases with slow progression point towards a genetic origin. Accurate identification of the underlying cause is important for guiding precision medicine-based treatment strategies, that may differ markedly depending on the anatomical and etiological classification.
Disclosure: Nothing to disclose.

Tuesday, June 24 2025

Highlights and breaking news

PLEN03_3 | Highlight: Dementia

S. Tomic
University Hospital Centre Osijek, Osijek, Croatia

PLEN03_4 | Highlight: Headache

P. Pozo-Rosich
Vall d'Hebron University Hospital, Barcelona, Spain

PLEN03_5 | Highlight: Movement disorders

A. Tessitore
University of Campania, "Luigi Vanvitelli", Naples, Italy

PLEN03_6 | Highlight: Cerebrovascular diseases

T. Truelsen
Rigshospitalet, Copenhagen, Denmark

PLEN03_7 | Highlight: Neuromuscular diseases

M. Filosto[1,2]
[1]Department of Clinical and Experimental Sciences, University of Brescia, Brescia, Italy; [2]NeMO-Brescia Clinical Center for Neuromuscular Diseases, Brescia, Italy

Neuromuscular disorders represent an increasingly dynamic field with profound implications for clinical neurology. Recent advancements have significantly reshaped both diagnostic and therapeutic paradigms, encompassing the expanded application of muscle imaging techniques, omics-based analyses, gene-targeted therapies, and emerging immunotherapies. This presentation aims to provide neurologists with a focused update on critical advancements across motor neuron diseases, neuropathies, myopathies, and neuromuscular junction disorders, with a particular emphasis on translating these innovations into clinical practice to enhance diagnostic precision and optimize patient management
Disclosure: MF has served as a participant in advisory boards for Sanofi, Amicus, Johnson and Johnson, Zambon and Biogen.

T. Emmenegger
Spinal Cord Injury Centre, Balgrist University Hospital, University of Zurich, Zurich, Switzerland

In spinal cord injury (SCI), magnetic resonance imaging (MRI) reveals tissue bridges and neurodegeneration for 2 years, while long-term effects remained unknown. This study aims to track initial lesion changes, subsequent neurodegeneration, and their impact on recovery over 5 years. Twenty-three acute SCI patients and 21 healthy controls were assessed clinically—and by MRI—regularly from 3 days up to 60 months post-injury. We employed histologically cross-validated quantitative MRI sequences sensitive to volume, myelin, and iron changes, reflecting indirect processes of neurodegeneration and neuroinflammation. General linear models tracked lesion and remote changes in volume, myelin-and iron-sensitive magnetic resonance indices over 5 years. Associations between lesion, degeneration, and recovery were assessed. Patients' motor scores improved by an average of 12.86 (95% confidence interval [CI]=6.70–19.00) points, and SCIM by 26.08 (95% CI=17.00–35.20) points. Within 3–28 days post-SCI, lesion size decreased by more than two-thirds (3 days: 302.52±185.80 mm^2, 28 days: 76.77±88.62 mm^2), revealing tissue bridges. Cervical cord and corticospinal tract volumes transiently increased in SCI patients by 5% and 3%, respectively, accompanied by cervical myelin decreases and iron increases. Over time, progressive atrophy was observed in both regions, which was linked to early lesion dynamics. Tissue bridges, reduced swelling, and myelin content decreases were predictive of long-term motor score recovery and improved SCIM score. Studying acute changes and their impact on longer follow-up provides insights into SCI trajectory, highlighting the importance of acute intervention while indicating the potential to influence outcomes in the later stages.

Disclosure: N.W. holds a patent on acquisition of MRI data during spoiler gradients (US 10,401,453 B2), which were parts of sequences used in this study. N.W. was a speaker at an event organized by Siemens Healthcare, which was the scanner brand used in this study, and was reimbursed for the travel expenses. The Max Planck Institute for Human Cognitive and Brain Sciences and Wellcome Centre for Human Neuroimaging have institutional research agreements with Siemens Healthcare, which as previously mentioned was the scanner brand used in this study.

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ABSTRACT

Symposia

Saturday, June 21 2025

EAN/MDS-ES: New and future treatments of Parkinson's disease and related disorders

SYMP01_1 | Update on management of early-stage Parkinson's disease

W. Meissner
Hôpital Pellegrin, CHU de Bordeaux, Bordeaux, France

SYMP01_2 | Update on management of advanced Parkinson's disease

M. Picillo
Largo Città di Ippocrate, Salerno, Italy

SYMP01_3 | Future therapeutic strategies in Parkinson's disease

J. Ferreira
Universidade de Lisboa, Lisbon School of Medicine, Lisbon, Portugal

SYMP01_4 | Update on disease modifying treatments for atypical parkinsonian disorders

I. Stankovic
Neurology Clinic, University Clinical Center of Serbia, School of Medicine, University of Belgrade, Belgrade, Serbia

Multiple system atrophy (MSA) and progressive supranuclear palsy (PSP) are prominent representatives of rapidly progressive neurodegenerative conditions termed atypical parkinsonian disorders. Development of disease modifying therapies (DMT) that would halt or slow disease progression is an urgent unmet need in these disorders. Numerous DMT targeting different key abnormalities of the neurodegenerative cascade are currently in various stages of clinical development. While alpha-synuclein and tau represent the most obvious therapeutic targets in MSA and PSP, other possible mechanisms underlying neurodegeneration have been targeted as well. In this talk, an update on the status of DMT in MSA and PSP will be provided, focusing ongoing phase 2 and phase 3 clinical trials.
Disclosure: Iva Stankovic received consultancy fee from Ferrer.

EAN/ECTRIMS: Advances for faster and improved diagnosis in Multiple sclerosis: New revised McDonald criteria

SYMP02_1 | Radiologically isolated syndrome: A new definition

C. Lebrun-frenay
Université Nice Côte d'Azur. CHU de Nice, Nice France

Recent advancements in understanding multiple sclerosis (MS) and the tools available for assessing its pathobiology have led to a comprehensive revision of the 2017 McDonald Criteria for MS. The updated 2024 McDonald Criteria offers a unified framework for diagnosing MS in individuals presenting with typical relapsing or progressive forms, from childhood to late adulthood. The optic nerve is now recognized as a fifth site in the central nervous system (CNS) for diagnosis. Additionally, new radiological indicators—specifically, the central vein sign (CVS) and paramagnetic rim lesions (PRLs)—can be employed to diagnose MS in specific contexts. Furthermore, the presence of cerebrospinal fluid (CSF) kappa-free light chains provides additional supportive evidence and can serve as an alternative to oligoclonal bands (OCBs). In some cases, radiologically isolated syndrome (RIS) also meets the criteria for preclinical MS. The guidelines include recommendations for diagnosing MS in individuals over 50, as well as those with significant comorbidities and headache disorders. This 2024 revision also applies to pediatric populations after excluding MOGAD and all forms of MS. The adaptability of the new diagnostic criteria aims to improve diagnosis while ensuring specificity, thereby enabling medical professionals, researchers, and students interested in neurology to better understand and identify MS.

Disclosure: No disclosure.

SYMP02_2 | Dissemination in time outdated? A paradigm shift

X. Montalban
Hospital General de la Vall d'Hebron, Barcelona, Spain

SYMP02_3 | Impact of new criteria on treatment and routine clinical practice

M. Moccia
Department of Molecular Medicine and Medical Biotechnology, Federico II University of Naples, Naples Italy

The implementation of new criteria for multiple sclerosis (MS) will not only allow earlier diagnosis, easier diagnosis and less misdiagnosis, than previous criteria, but will also focus the attention of MS specialists towards biological mechanisms of MS throughout the life span. While diagnostic criteria do not change local regulatory approvals of treatments and related prescription limitations, we expect that increased awareness on (and possibility of) early diagnosis will likely improve MS outcomes in the short and long term. Also, timproved he inclusion of new methodologies to assess specific disease mechanisms (such as the kFLC-index and PRLs) will improve our understanding of MS pathobiologies, likely with better prognostication and treatment allocation. Of course, the implementation of new criteria will require some efforts, with imaging protocols in people with suspected MS (e.g., brain MRI with susceptibility-based sequences for CVS and PRL, spinal cord MRI and multimodal imaging of the optic nerve) and new CSF measures (kFLC-index). More importantly, the implementation of new criteria will require MS specialists to make the most pragmatic decisions on how to make the diagnosis of MS in each case, without unnecessary complexity.
Disclosure: Nothing to disclose.

EAN/EuGMS: The impact of disease modifying therapies (DMTs) on dementia services: A forward view

SYMP03_1 | Transforming the diagnostic pathway in the era of DMTs

K. Frederiksen
Danish Dementia Research Centre, Copenhagen University Hospital – Rigshospitalet, Copenhagen, Denmark

The introduction of disease-modifying therapies for early Alzheimer´s disease heralds a new era in the diagnostic pathway for neurodegenerative diseases. Key to the implementation of DMTs which are aimed at patients at the early stage of disease is to further raise the awareness of the disease to enable earlier detection, implementation of biomarkers for the diagnosis of AD (e.g., blood based) and to ensure a faster pathway from early symptoms to assessment by a specialist. New technologies such as digital biomarkers will also be an important tool in reforming diagnostic pathways.
Disclosure: Advisor/Consultant Eisai, Novo Nordisk, Roche Diagnostics (re-numeration paid to institution) Speaking engagement Eisai/BioArctic, Novo Nordisk, Eli Lilly (re-numeration paid to institution) Principal investigator in clinical trials Biogen, Novo Nordisk, Roche, Roche Diagnostics (remuneration paid to institution) Editor-in-Chief Alzheimer's Research and Therapy (Springer) (personal remuneration) Research funding Aase og Ejner Danielsens Fond, Alzheimer Forskningsfonden, A.P. Møller fonden, Beckett fonden, C2N, DANMODIS, Ellen Mørch Fon-den, ERA-PERMED, Fonden for Neurologisk Forskning, Grosserer F.L.Foghts Fond, Harboefonden, Hertzfonden, IHI, Innovationsfon-den, Jascha Fonden, KID fonden, Kong Christian den Tiendes Minde-fond, Overretssagfører L. Zeuthens Mindefond, Parkinsonforeningen, Rigshospitalets Forskningspulje.

SYMP03_2 | Service delivery of DMTs for dementia: Challenges and solutions

Y. Saleh
John Radcliffe Hospital, Oxford, UK

SYMP03_3 | MRI for inclusion and monitoring into DMTs in Alzheimer's disease

T. Oliveira
Life and Health Sciences Research Institute (ICVS), School of Medicine, University of Minho, Braga, Portugal; Department of Neuroradiology, ULS/Hospital de Braga, Braga, Portugal

Anti-amyloid immunotherapies are the first class of disease-modifying therapies shown to slow cognitive decline by clearing amyloid plaques from the brains of AD patients. However, concerns have been raised due to the frequent occurrence of treatment-related MRI findings, known as amyloid-related imaging abnormalities (ARIA). Ranging in clinical outcomes from completely asymptomatic to severe impairment or death, ARIA represents the major side effect observed during clinical trials, occurring in up to 40% of individuals depending on the drug. ARIA can manifest in two forms: ARIA-E, characterized by hyperintense vasogenic edema and sulcal effusions on T2-FLAIR, and ARIA-H, associated with hypointense microhemorrhages and superficial siderosis on susceptibility-sensitive images. The occurrence of ARIA-E and ARIA-H depends on the dose and type of drug administered, as well as on APOE4 carriership. Microhemorrhages present at baseline prior to treatment increase the risk of developing ARIA-E, and data from trials indicate that extensive white matter hyperintensities and severe amyloid pathology are additional risk factors that should be considered. Further reports provide evidence linking ARIA to cerebral amyloid angiopathy pathology and the increased risk of intracerebral hemorrhage. Therefore, patient selection for anti-amyloid therapies significantly impacts the risk of developing ARIA. This text will discuss how brain MRI is used to identify patients eligible for anti-amyloid immunotherapies by assessing

baseline status, how it is employed to monitor ARIA throughout therapy, and its crucial role in differentiating ARIA from stroke in symptomatic acute presentations.
Disclosure: Consultant for Sonae, Guidepoint and Lilly. Fees as a speaker by Eisai and conference fees covered by Roche and Lilly.

SYMP03_4 | Applying lessons from MS to DMT delivery in dementia

A. Pröbstel
University Hospital of Basel, Basel, Switzerland

EAN/EFAS: Autonomic dysfunction and brain health: What is the impact for society?

SYMP04_1 | Autonomic dysfunction in aging populations

C. Falup-Pecurariu
Transilvania University Brasov, Brasov, Romania

SYMP04_2 | The involvement of autonomic dysfunction in neurodegenerative diseases

A. Fanciulli
Innsbruck Medical University, Innsbruck, Austria

SYMP04_3 | Societal impact of autonomic dysfunction and strategies for public health Improvement

R. Thijs
Leiden University Medical Centre, Leiden, The Netherlands

A healthy brain is a perfectly perfused brain. Although the dangers of ischemia are well known, the awareness of the broad spectrum of autonomic causes of cerebral hypopefusion is generally poor. Particularly the more subtle presentations of these highly prevalent conditions frequently go unrecognized hereby fueling unnecessary investigations. The prognosis may vary within the spectrum. While vasovagal syncope has an excellent prognosis, orthostatic hypotension may serve as a marker of a neurological condition. Regardless of the cause, all autonomic disorders predisposing to orthostatic intolerance and frequent syncope negatively affect quality of life and lead to traumatic falls. Early recognition of these common presentations is crucial as simple lifestyle interventions (e.g., hydration, physical countermanoeuvres) are effective in lowering the symptom burden. It is therefore time to raise public awareness and to promote autonomic education within the neurological community.
Disclosure: Lecture and consultancy fees from Medtronic, UCB, Angelini Pharma, Theravarance, Zogenix, Novartis, LivAssured, and Arvelle, as well as grants from Medtronic and NewLife Wearables.

SYMP04_4 | New technological innovations in the diagnosis and management of autonomic dysfunction in aging population

W. Struhal
Karl Landsteiner University of Health Sciences, Department of Neurology, Campus Tulln, Tulln, Austria

Autonomic dysfunction is quite common and present in a number of neurological conditions. Evaluation is often based on easy to measure biosignals including the ECG. A variety of equipment is already now available to pick up signals suitable for further processing and clinical evaluation, including providing "real world data." Equipment may however not always be suitable for measurements or is marketed as consumer electronics. The lecture provides an overview of current techniques employed, but also current challenges for clinicians, both for the use of equipment in clinical reasoning, as well as the legal framework for clinical use.
Disclosure: Nothing to disclose.

Neurorehabilitation during wars

SYMP05_1 | Challenges in neurorehabilitation in a war zone

T. Voloshyn
Iviv, Ukraine

Neurorehabilitation in war zones faces multifaceted challenges that significantly hinder the delivery of effective care. The high prevalence of traumatic brain injuries (TBI), spinal cord injuries, and post-traumatic stress disorders among combatants and civilians creates a pressing need for comprehensive rehabilitation services. However, these needs are often unmet due to the destruction of healthcare infrastructure, scarcity of specialized personnel, and limited access to advanced diagnostic and therapeutic technologies. The instability and security threats in conflict areas further impede the continuity of care, follow-up, and multidisciplinary coordination essential for neurorehabilitation. Moreover, psychological trauma, displacement, and stigma surrounding disability complicate patient engagement and long-term recovery. Innovative strategies—including mobile clinics, telemedicine, international collaboration, and culturally adapted therapeutic models—are critical for overcoming these barriers and improving outcomes for individuals with neurological impairments in war-affected regions.
Disclosure: Nothing to disclose.

SYMP05_2 | Receiving neurotrauma patients from war zones – the European experience

E. Hagen[1,2,3]
[1]*Spinal Cord Injury Centre of Western Denmark, Department of Neurology, Viborg Regional Hospital, Viborg, Denmark;* [2]*Department of Clinical Medicine, Aarhus University, Aarhus, Denmark;* [3]*Department of Brain Repair and Rehabilitation, UCL Queen Square Institute of Neurology, University College London, London, UK*

At the Spinal Cord Injury Centre of Western Denmark, we have rehabilitated several patients with spinal cord injury from war zones. Some of the patients were injured prior to the war, others during the war either as civilians or during combat. Language is a big challenge. We use translation apps on mobile phones and certified translators. The certified translators must be booked and cannot always be present during ward rounds and meetings. The patients often learn Danish words and small sentences during their stay. At times we have personnel at the unit coming from countries with similar languages, which is of great help. We give regular reports to the Ministry of Defense in their home country regarding patients injured during combat, to document the continuous need for rehabilitation. The patients are concerned about their colleagues still out in the field and want to get back to the front line as soon as possible. Some patents were transferred from hospitals in their home country as part of international agreements. Many of them have multi-resistant bacteria and must be isolated during their stay according to Danish Health Regulations. Many patients have developed PTSD prior to arrival. Some of the patients experienced being confined to a room, not able to get out, while bombs were falling close by. Concerns about family and friends back home add to their suffering during the rehabilitation. Both language barriers and cultural barriers make it challenging to give them sufficient help.
Disclosure: Nothing to disclose.

SYMP05_3 | Neurorehabilitation during wars: Challenges for policymakers and health care systems

M. Leonardi
Fondazione IRCCS Istituto Nazionale Neurologico Carlo Besta, Neurology Public Health Disability Unit & Coma Research Centre, Milan, Italy

SYMP05_4 | EAN's responsibilities and abilities to promote cross-border neurorehabilitation

K. Rauen
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Monday, June 23 2025

Neurology and society – how do they interact?

SYMP06_2 | The economic costs of neurological disorders

R. Dodel
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SYMP06_3 | Stigma and perception of neurological disorders in Europe

E. Ben-Menachem
Department of Clinical Neuroscience Sahlgrenska Academy, Gothenburg University, Gothenburg, Sweden

Stigma is a major cause of discrimination and exclusion in all societies: it affects self-esteem, disrupts family relationships and limits the ability to socialize and obtain housing and jobs. For centuries, stigma has been a well-known phenomenon for almost all who have or have had neurological disorders (ND). Murder, torture, ostracism have been just some of the punishments dealt out for people who cannot help the situation that they find themselves in. Some of the first to be murdered in Nazi Germany were people with ND. Since WW! II it has been recognized that there is a great need to change perceptions of ND with regards to stigma. Efforts have been increased to help people with ND and to educate about ND. In Europe there is now an organization especially formed to address stigma, the European Federation of Neurological Associations (EFNA), which is an organization comprised of several partners. They recently conducted a survey of people with ND. According to the EFNA, 92% of respondents report feeling affected by stigma. Lack of understanding in society is seen as the biggest cause of this, followed by myths/misconceptions about these disorders and their invisible nature. The majority of patients in the survey who experience stigma were those with epilepsy. What are people with ND and especially those with epilepsy dealing with in their daily lives and what are we as professionals doing about it? These questions will be the main topic of this presentation.
Disclosure: Consulting for. UCB pharma, Xenon Pharmaceuticals, Cogniguard, Angelini.

SYMP06_4 | Different approaches to neurological management in Europe (e.g., stroke)

M. Paciaroni
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Neurological diseases are highly prevalent, affecting millions of European residents. Worldwide, disorders affecting the nervous system have recently been estimated to be responsible for roughly 43%, affecting more than a third of the global population. Over the last 3 decades, progress in neurological care has led to the

formation of sub-specializations which have become established parts of contemporary healthcare. Arguably, the best example of this is acute neurology which is carried out for the treatment of stroke patients and the closely associated development of neurological emergency medicine. In fact, there is compelling evidence that stroke may be highly preventable, treatable and manageable. Moreover, the potential exists to drastically reduce the burden associated with stroke and its long-term consequences. However, the reported significant differences in stroke incidence, mortality, and disability rates differ throughout European countries. This is believed to reflect different degrees of delivery of evidence-based interventions in stroke prevention and care. In fact, the 2020 Stroke Alliance for Europe Report stated that only 30% of stroke patients across Europe currently have access to acute stroke unit care. Furthermore, the investigators also reported highly significant discrepancies in stroke burden rates across Europe. Specifically, reported age-standardized death rates in Bulgaria, Romania, Serbia, Latvia, Lithuania, Croatia, Hungary, and Slovakia were seven-fold higher than in France, Spain, Luxembourg, Italy, Austria, and Belgium. So, in light of this reality, a more uniform implementation of European guidelines for the management of stroke across all European countries would lead to a greater standardization of stroke care across Europe and therein align the poorer performing countries to those levels reported better performing nations.
Disclosure: Nothing to disclose.

EAN/ILAE-CEA: First seizure clinics – time matters in epilepsy, too

SYMP07_1 | First seizure management: The situation today

S. Rüegg
Department of Neurology, University Hospital, and Medical Faculty University of Basel, Switzerland

The management of a first seizure has changed over time. In the past, where stigma, misconception of the sequqelae of seizures, trivialization of seizures may have led to various kinds of suboptimal management of patients with a first epileptic seizure, it is increasingly acknowledged that a fast, comprehensive evaluation of a first seizure improves outcomes of patients regarding adherence to treatment, control of seizures, time to recurrence of seizures, and psychosocial factors. Such a fast comprehensive evaluation nowadays depends on various factors, including the amount of available health care resources in a specific country and health care politics. The current challenges to optimize first seizure management are presented.
Disclosure: Nothing to disclose.

SYMP07_2 | Inappropriate management of first seizures: Risks and pitfalls

R. McGinty
The Walton Centre NHS Foundation Trust, Liverpool, UK

SYMP07_3 | Missed first seizure diagnosis and poorer prognosis: What are the possible mechanisms?

S. Lattanzi
Department of Experimental and Clinical Medicine, Marche Polytechnic University, Ancona, Italy

Delay in the diagnosis of epilepsy occurs in up to 75–80% of people with epilepsy. Many factors can contribute to diagnostic delay, including missed or misdiagnosed signs or symptoms and barriers to accessing health care. The time from seizure occurrence to diagnosis and treatment initiation is a vulnerable period in which patients may experience potentially avoidable consequences. Potential consequences of delayed diagnosis include: injuries and motor vehicle collisions, death and SUDEP, negative effects on cognition, emotional well-being, and social functioning, reduced school/work productivity, increased health-care utilization (e.g., recurrent emergency department visits, hospital admissions, and redundant medical testing), higher burden of informal care needs (e.g., unpaid care provided by friends and family). A few studies also explored the impact of diagnostic delay on long-term seizure outcome in newly diagnosed patients. In summary, epilepsy diagnosis is often delayed. Diagnostic delay results in delayed treatment and potentially preventable morbidity and mortality. The impact of diagnostic delay per se on treatment outcome deserves further investigation.
Disclosure: Nothing to disclose.

SYMP07_4 | First seizure clinics: The benefits and challenges

M. Seeck
Hopitaux Universitaires de Genève-HUG, Geneva, Switzerland

Functional neurological symptoms: The interface of brain, mind and society

SYMP08_1 | The history of functional symptoms and society: From war neurosis to havana syndrome

J. Stone
Centre for Clinical Brain Sciences, University of Edinburgh, Edinburgh, UK

The history of FND can be traced back to Hippocrates. Since that time, it's been clear that societal influences can play an important role in shaping the nature of symptoms and the general public's response to them. In this lecture, I will trace the history of FND symptoms over time, looking especially at how they gained transient fame during the time of Charcot and then again as Shell Shock – also called "War Neurosis" during the First World War. I will look at what happened to FND in World War Two and ask why it became less visible in the press and the neurology curriculum in the 20th century. I will suggest that it has never really gone away – it's just our interest in it that waxes and wanes. In the 21st century, FND is interacting more visibly once again with societal factors, especially social media (in the example of functional

tics), vaccines and anti-vaxxers, and immigration (in the case of Resignation Syndrome). I will come back to a military example, with Havana syndrome. I will look at how difficult it is for journalists and the public to grasp a non-dualistic view of FND and how commonly we end up with a false narrative between a "real condition" and one perceived as "all in the mind." Finally, I will conclude that societal factors can be important for FND but note that this is true for ALL conditions in neurological practice.
Disclosure: Nothing to disclose.

SYMP08_2 | Localising Charcot's "dynamic lesion": Discovering where mind meets brain

S. Aybek
Science and Medicine Faculty, Fribourg University, Fribourg, Switzerland

Over a century ago, Jean-Martin Charcot envisioned a "powerful enough" microscope that would allow clinicians to observe the dynamic lesions underlying certain neurological symptoms, particularly those seen in Functional Neurological Disorder (FND), then known as Hysteria. Although his anatomo-clinical approach couldn't identify structural abnormalities, Charcot hypothesized that dynamic brain changes could explain such symptoms. His students, including Sigmund Freud, further proposed that psychological stressors might influence these processes through interactions between the brain and mind. Today, neuroimaging serves as that "microscope," providing insights into the neural underpinnings of FND. This talk reviews findings from structural and functional imaging studies, emphasizing disruptions in brain networks related to motor control, agency, and emotion regulation. Task-based fMRI has shown abnormal activation in regions such as the supplementary motor area (SMA), dorsolateral prefrontal cortex (DLPFC), and temporoparietal junction (TPJ), supporting theories of impaired volitional motor control. Dysregulation in limbic areas, including the amygdala and periaqueductal gray (PAG), points to emotion processing deficits. Structural imaging reveals gray and white matter differences that may reflect predispositions or consequences of FND. Resting-state connectivity analyses using machine learning suggest potential for diagnostic biomarkers. Emerging genetic and epigenetic research, particularly regarding the serotonergic and oxytocinergic systems, also hints at underlying biological vulnerabilities. These advances are reshaping our understanding of FND, reducing stigma, and bridging the gap between brain and mind through a biopsychosocial model that informs both clinical practice and patient care.
Disclosure: Nothing to disclose.

SYMP08_3 | The neuroscience of trauma: Risk and resilience in the brain

C. Heim
Charité Universitätsmedizin Berlin, Institute of Medical Psychology, Berlin, Germany

SYMP08_4 | The legacy of successful care for people with functional symptoms: Biopsychosocial integration for chronic neurological illness

M. Edwards
King's College London, Institute of Psychiatry, Psychology and Neuroscience, London, UK

EAN/ESO: Current and future treatment of acute ischemic stroke

SYMP09_1 | Intravenous thrombolysis in small and large artery occlusion

E. Sandset
Oslo University Hospital, Department of Neurology, Snarøya, Norway

SYMP09_2 | Mechanical thrombectomy and patient selection

A. Zini
IRCCS Istituto delle Scienze Neurologiche di Bologna, Department of Neurology and Stroke Center, Maggiore Hospital, Bologna, Italy

Mechanical thrombectomy (MT) has revolutionized acute ischemic stroke treatment and reperfusion therapies. In 2014-2015 RCTs in the 0–6h window (e.g., MR CLEAN, ESCAPE, SWIFT PRIME, EXTEND-IA, and REVASCAT) established MT plus intravenous thrombolysis as standard of care for large vessel occlusions (LVO). The best clinical outcomes (as mRS at 90 days) were obtained in patients who had undergone advanced neuroimaging (CTP, mCTA, or MRI). Subsequent studies (DAWN, DEFUSE 3) demonstrated benefit in selected patients up to 24h from onset, always due to selection with advanced neuroimaging. Recent trials targeting patients with large ischemic cores (SELECT2, ANGEL-ASPECT, RESCUE-Japan LIMIT, TENSION, TESLA, and LASTE) have further expanded indications, showing improved outcomes despite extensive infarction. However, strokologists' enthusiasm has been tempered by negative results treating large core patients in real world. In the end recent trials focusing MT on treating medium vessel occlusions (MeVO), such as DISTAL and ESCAPE-MeVO, but these trials currently fail to demonstrate significant clinical benefit. These findings highlight the importance of refining patient selection and device technology for distal occlusions. Following the experience of the CHOICE trial with rtPA, recent studies have begun to evaluate the efficacy of the use of intra-arterial TNK in patients who do not achieve complete recanalization (TICI>2b50-67%) While MT continues to evolve, future research must address optimal strategies for stroke patients and better integration of imaging biomarkers to guide individualized treatment and tailored treatments.
Disclosure: Andrea Zini reports consulting and speaker fees from Angels Initiative, Boehringer-Ingelheim, Alexion, Daiichi

Sankyo, Pfizer, fees for Advisory Board from Bayer, Daiichi Sankyo, and Astra Zeneca.

SYMP09_3 | Ensuring patients are treated – challenges and experiences across Europe

D. Aguiar de Sousa
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Equitable access to reperfusion therapies for acute ischaemic stroke remains a critical challenge in Europe. Despite major advances in clinical evidence and systems of care, wide inter- and intra-country disparities persist, not only in the delivery of intravenous thrombolysis (IVT) and endovascular thrombectomy (EVT), but also in the broader capacity to ensure timely and effective stroke care for all eligible patients. Barriers span the entire care pathway: from limited public awareness and delayed EMS activation, to underdiagnosis of stroke and large vessel occlusion, long distances to comprehensive stroke centres, workforce shortages, and in-hospital workflow inefficiencies. Systemic gaps in infrastructure, technology, policy prioritization, and reimbursement further contribute to the variability in access and outcomes. Drawing on data from the ESO/SAFE Stroke Action Plan and recent European audits, this talk will outline key implementation gaps and discuss strategies that have proven effective in overcoming them. These include the development of stroke networks, telestroke coverage, standardized care pathways, national stroke registries, and multi-stakeholder advocacy for system-level investment. We will also explore what proportion of ischaemic stroke patients could receive IVT or EVT if all potentially eligible individuals were reached, also in the context of recent expansion of treatment indications, and what such targets may require in terms of capacity. Emphasis will be placed on translating evidence into action and ensuring that all patients, regardless of geography or system capacity, have access to timely, effective stroke care.

Disclosure: Diana Aguiar de Sousa reports advisory board participation for Daiichi-Sankyo, Bayer, Organon and Johnson & Johnson, speaker fees from Astrazeneca and Bial, and grants from FCT, Astrazeneca foundation, MSD and European Society of Radiology.

SYMP09_4 | Optimizing the benefit of recanalization therapies

U. Fischer
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EAN/ERN EURO-NMD: New therapeutic roads for neuromuscular disease

SYMP10_1 | CAR-T-cell in myasthenia and beyond

K. Claeys
University Hospitals Leuven, Department of Neurology, Leuven, Belgium

SYMP10_2 | Gene therapy in neuromuscular disorders – what are the current caveats of antisense oligotherapeutics?

B. Schoser
Friedrich-Baur-Institute, Department of Neurology, LMU Clinics, Munich, Germany

Antisense oligotherapeutics (ASOs) offer precise gene modulation for neuromuscular disorders yet face key limitations. Efficient and targeted delivery to muscle tissue and across the blood-brain barrier remains challenging, often requiring invasive administration. While chemical modifications enhance stability, biodistribution and cellular uptake are hurdles. Off-target effects and potential toxicities necessitate careful monitoring. Variable efficacy across and within diseases highlights the need for personalized strategies and deeper disease understanding. Overcoming delivery limitations, minimizing off-target binding, and optimizing treatment regimens are crucial for broader applications. Dose-dependent off-target toxicities include hepatic transaminase elevation, thrombocytopenia via platelet surface protein interactions, and proximal tubular nephropathy through megalin-mediated endocytosis. Manufacturing complexities involve oligonucleotide synthesis scale-up challenges, including coupling efficiency optimization, chromatographic purification, and stringent quality control for impurity profiles and diastereoisomeric ratios. Manufacturing complexity and high costs also impact accessibility. Nevertheless, emerging advances in stereochemically pure synthesis, GalNAc-conjugation, peptide-mediated delivery, and exosome-based transport systems indicate potential resolution of current limitations, potentially enabling broader therapeutic application across the neuromuscular disease spectrum. Future research focusing on novel delivery methods, safer chemistries, and personalized approaches is essential to unlock the full potential of ASOs for a broader range of neuromuscular conditions.

Disclosure: I received unrestricted research grants from AMDA Foundation, Amicus Therapeutics, Inc., EU Horizon programs COMPASS and PaLaDIn, Marigold Foundation, and Roche Diagnostics; speakers' honoraria from Alexion Pharmaceuticals, Inc., Argenx, Kedrion, and Sanofi; and I have also been a scientific adviser for Amicus., Astellas, Avidity, Denali, Dyne, Pepgen, Sanofi, Takeda, and Taysha. He declares no stocks or shares.

SYMP10_3 | The advances in viral vector-mediated gene therapy

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San Raffaele Telethon Institute for Gene Therapy (SR-TIGET), IRCCS San Raffaele Scientific Institute, Milan, Italy

Over the past decade, gene therapy has opened new therapeutic options for several disorders, including different inherited neurological conditions. Advances in the development of viral vectors—particularly adeno-associated viruses (AAVs) and lentiviruses—have significantly enhanced our ability to deliver gene products effectively to target tissues. Two main strategies have emerged for treating neuromuscular and neurological conditions: in vivo and ex vivo gene therapy. These approaches enable gene replacement, silencing, addition, or editing. This talk will focus on gene therapies approved for clinical use in neurological diseases such as spinal muscular atrophy, leukodystrophies, and Aromatic l-amino acid decarboxylase (AADC) deficiency. These examples will highlight key challenges in targeting the central and peripheral nervous systems. These include crossing the blood-brain barrier, achieving precise delivery to specific brain regions, targeting skeletal and cardiac muscles in muscular dystrophies, and achieving a sustained effect outside the central nervous system. We will examine critical aspects of their clinical development, including trial design, definition of eligibility criteria, and selection of outcome measures. In addition, we will address ongoing post-marketing challenges, such as monitoring long-term safety and efficacy, and ensuring the sustainability of high-cost, transformative therapies. Finally, the availability of highly effective treatments—particularly when administered early in the disease course – underscores the urgent need to accelerate diagnosis and implement newborn screening programs for neurodegenerative conditions.

Disclosure: Francesca Fumagalli, have occasionally received consultant fees and reimbursement for travel costs and participation fees from Orchard Therapeutics. Francesca Fumagalli is an investigator or Principal investigator of MLD gene therapy clinical trials. MLD gene therapy (Atidarsagene autotemcel) was licensed to GlaxoSmithKline (GSK) in 2014 and GSK became the clinical trial sponsor. In 2018 MLD development rights were transferred to Orchard Therapeutics (OTL) and OTL became the clinical trial sponsor.

SYMP10_4 | Enzyme replacement therapies in neuromuscular disorders

N. van der Beek
Department of Neurology, Center for Lysosomal and Metabolic Diseases, Erasmus MC, University Medical Center Rotterdam, The Netherlands

Enzyme replacement therapy (ERT) is typically used to replace a missing or deficient enzyme in a person with an inherited enzyme deficiency syndrome. The identification of genes encoding various enzymes has facilitated the large-scale production of recombinant human proteins that are functionally similar to the native human protein. The missing enzyme is usually administered intravenously (or intrathecally for direct access to the CNS), to reduce substrate accumulation. I will use the example of Pompe disease, a rare inherited neuromuscular disorder, to illustrate the progress that has been made over the past few decades. Here, ERT has positively impacted the lives of many patients, but long-term treatment has revealed new disease patterns and large interindividual variations in efficacy. I will review the successes of ERT-based approaches and discuss the limitations and the challenges that lie ahead.

Disclosure: Dr. van der Beek has received consulting fees for advisory boards or speaker honoraria from Sanofi, Amicus Therapeutics, Shionogi and Bayer under agreements with Erasmus MC University Medical Center and the relevant industry.

Open science and medical informatics in neurology – an EAN-EBRAINS joint project

SYMP11_1 | Cytoarchitecture and brain atlases for a deeper understanding of brain organization and function

K. Amunts
Forschungszentrum Jülich GmbH, Jülich, Germany

Cytoarchitecture reveals the segregation of the cerebral cortex into distinct areas. More than 100 years ago, Brodmann used this concept to create his famous map, while working in the lab of the Vogts. They focused on myeloarchitecture to better understand brain organisation. Furthermore, Oskar Vogt compared his findings with those obtained by Förster, who stimulated the convexity of the brain during surgery. Now, neuroimaging provides insights into brain function in a much less invasive way for healthy subjects and patients, although its spatial resolution does not allow for histological detail. This was the motivation behind the creation of Julich-Brain, a multimodal 3D atlas of cortical and subcortical areas. It is based on an analysis of serial histological sections of 10 post-mortem brains. Cortical areas were identified across their entire extent based in a reproducible manner by using image analysis and statistical tools (Amunts, 2020). The individual cytoarchitectonic maps were then registered to a common reference space, and probabilistic maps were computed, to show the intersubject variability of the areas in each position of the space. Cytoarchitectonic maps serve as a reference to integrate data from different spatial scales, and various aspects of brain organization (e.g., connectivity, molecular and genetic maps) into a coherent system. This enables the use of maps to link MR-based patient study findings to the underlying microstructure and more precisely identify neuropathological networks, e.g., in Parkinson's disease. The Julich-Brain atlas is openly available through EBRAINS, a collaborative European digital research infrastructure. EBRAINS links atlas information to a broad range of other data, tools and services using the siibra tool suite. This tool suite provides an online viewer that intuitively accesses atlas data and a python interface that builds workflows and speeds up applications. The atlas helps to distinguish the different components of brain function, identify brain networks involved in neurological disorders more precisely, and gain a deeper understanding of the relationship between brain structure and function.

Disclosure: Nothing to disclose.

SYMP11_2 | Advancing connectomic research in clinical neurosciences

M. Corbetta
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SYMP11_3 | Uncovering the central autonomic network using human intra-cerebral EEG data

P. Ryvlin
Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland

SYMP11_4 | Epilepsy and decision making in the prefronto-insular circuit

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Univ. Grenoble Alpes, Inserm U1216, CHU Grenoble Alpes, Grenoble, France Grenoble Institute Neurosciences, GIN, Grenoble, France

In drug-resistant epilepsy, resective surgery remains a challenging intervention, with a substantial proportion of patients experiencing persistent seizures and post-operative cognitive deficits, despite extensive invasive electrophysiological mapping. One underexplored contributor to these outcomes may lie in alterations to decision-making processes, which rely on a distributed network including the anterior insula (aINS), dorsolateral (dlPFC), and ventromedial prefrontal cortex (vmPFC)—regions that can themselves be epileptogenic. In this study, we focus on aINS and vmPFC epilepsies, using intracranial EEG (iEEG) to investigate the interaction between spontaneous epileptic activity and physiological high-frequency responses (50–250 Hz), known biomarkers of both seizure activity and cognition. Twenty patients with pharmaco-resistant focal epilepsy performed a reinforcement learning task during iEEG monitoring. We identified spontaneous epileptic events (interictal spikes or pathological high-frequency oscillations) and outcome-locked physiological responses (broadband high-frequency activity). Critically, we found that physiological responses to outcomes were significantly reduced in cortical regions that also exhibited epileptic activity shortly before outcome presentation. This interference was observed in decision-making regions, extending previous findings from memory-related areas. Our results demonstrate that physiological responses can be detected in epileptic tissue but may be attenuated by temporally proximal epileptic activities. These findings suggest a functional overlap between epileptogenic and cognitive networks and propose a novel electrophysiological marker—transient interference between pathological and physiological signals—that could help anticipate post-operative cognitive deficits, particularly in patients with epilepsy involving decision-making circuits.
Disclosure: Nothing to disclose.

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ABSTRACT

Focused Workshop

Saturday, June 21, 2025

6 million years of evolution: Do we fit in today's society?

FW01_1 | Influence of sleep and chronotypes: Are we adapted for today's society?

A. Stefani
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The evolution of human sleep and chronotype patterns has been shaped by environmental pressures. Ancestral (and contemporary) hunter-gatherer societies exhibit polyphasic, flexible sleep patterns that are closely aligned with natural light cycles. In contrast, modern societies enforce rigid, monophasic sleep shaped by artificial lighting, screen exposure, and early work or school schedules. This phenomenon has resulted in pervasive circadian misalignment, particularly among evening chronotypes, manifesting as "social jetlag," a persistent dissonance between biological and societal clocks. This misalignment is increasingly recognized as a contributor to neurological and psychiatric morbidity, due to chronic sleep debt and circadian desynchrony. While light exposure, sleep hygiene, and behavioral interventions can shift circadian timing, structural changes, such as the implementation of flexible work schedules or delayed school start times, would likely be more effective in addressing systemic misalignment. The concept of chronotype as a biologically grounded trait with neurobehavioral implications underscores the necessity for chronotype-informed approaches in clinical neurology. Personalized sleep strategies and broader societal accommodations may offer novel pathways to improve brain and mental health, cognitive resilience, and quality of life across the lifespan.
Disclosure: Nothing to disclose.

FW01_2 | The social media/smartphone world: Effect on attention and memory

A. Weinstein
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The association between excessive smartphone use, Social Networking Sites (SNS), and mental health raises serious concerns among health and education professionals. Excessive smartphone use is associated with difficulties in cognitive-emotion regulation, impaired cognitive function, impulsivity, reduced cognitive control, and changes in the brain's gray matter volume. It is associated with impulsivity and involvement of frontal lobe circuits. We examined excessive smartphone use, impulsivity, and mental well-being in individuals with acquired brain injury (ABI) before and after treatment and healthy control participants. We studied 44 patients with acquired brain injury (ABI) (10 with orbito-frontal syndrome), and 69 healthy individuals at baseline and five months later. Participants used a smartphone application to track usage, computerized tasks to evaluate impulsivity (delay discounting DDT, and response inhibition). Excessive smartphone use correlated with impulsivity in all groups. At baseline, participants with ABI and OFC exhibited greater impulsivity (response inhibition and attention impulsivity) and excessive smartphone use compared with control participants. Patients with ABI showed improvement in delay discounting, but no longitudinal differences in smartphone use. Our findings suggest that brain injury, particularly in frontal regions, influences impulsivity and smartphone use. With the development of technology and the internet, social networks gained momentum quickly and play a central role in daily activities. Despite this, there is a public health concern over excessive use of social network sites (SNS). We studied 79 young participants, divided into two groups: 34 participants who excessively use social networks and 45 participants who do not excessively use social networks. Participants performed on computerized

cognitive tasks: GO/NO-GO (with Facebook and traffic signs pictures), Experimental Delay Discounting (EDT), and the Wisconsin Card Sorting Test (WCST). Excessive SNS users exhibited a lower ability to delay gratification on the EDT, indicating impulsivity. They made fewer non-perseverative errors on the WCST, which indicated high flexibility and working memory. Furthermore, on the GO/NO-GO task, excessive SNS users made more emission errors in response to the "Facebook" sign compared with traffic signs (GO condition), indicating impaired selective attention. Finally, they also showed higher subjective ratings of anxiety, depression, impulsivity, and compulsivity. The neurocognitive results provide evidence for impulsivity, lack of compulsivity, and impaired selective attention to social media stimuli ("Facebook" signs) in excessive SNS users. In conclusion, problematic SNS and smartphone use may have deleterious effects on attention and memory that should raise concerns by health and education professionals.
Disclosure: Nothing to disclose.

FW01_3 | Impact of lifestyle, nutrition, and pollution on the development of neurological disorders

B. Bloem
Radboud University Medical Centre, Donders Institute for Brain, Cognition and Behaviour, Department of Neurology, Centre of Expertise for Parkinson & Movement Disorders, Nijmegen, The Netherlands

In my lecture, I will use Parkinson's disease as an exemplary condition of how environmental factors can affect the development of neurological disorders. Parkinson's disease appears to be at least in part, if not to a large extent, man-made disease, the etiology of which can be ascribed in part to exposure to environmental chemicals such as pesticides. At the same time, there are protective factors, many of which relate to our lifestyle, including exercise and particular healthy diets. Recognizing these factors will be important for the development of future prevention strategies.
Disclosure: Prof. Bloem serves as the co-Editor-in-Chief for the Journal of Parkinson's disease, serves on the editorial board of Practical Neurology and Digital Biomarkers, has received fees from serving on the scientific advisory board for the Critical Path Institute, Gyenno Science, MedRhythms, UCB, Kyowa Kirin and Zambon (paid to the Institute), has received fees for speaking at conferences from AbbVie, Bial, Biogen, GE Healthcare, Oruen, Roche, UCB and Zambon (paid to the Institute), and has received research support from Biogen, Cure Parkinson's, Davis Phinney Foundation, Edmond J. Safra Foundation, Fred Foundation, Gatsby Foundation, Hersenstichting Nederland, Horizon 2020, IRLAB Therapeutics, Maag Lever Darm Stichting, Michael J Fox Foundation, Ministry of Agriculture, Ministry of Economic Affairs & Climate Policy, Ministry of Health, Welfare and Sport, Netherlands Organization for Scientific Research (ZonMw), Not Impossible, Parkinson Vereniging, Parkinson's Foundation, Parkinson's UK, Stichting Alkemade-Keuls, Stichting Parkinson NL, Stichting Woelse Waard, Topsector Life Sciences and Health, UCB, Verily Life Sciences, Roche and Zambon. Prof. Bloem does not hold any stocks or stock options with any companies that are connected to Parkinson's disease or to any of his clinical or research activities.

EAN/MDS-ES: Normal pressure hydrocephalus and neurodegeneration: Two sides of the same coin?

FW02_1 | Exploring the relationship between NPH and neurodegenerative diseases: Clinical insights

V. Leinonen
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Normal pressure hydrocephalus (NPH) may occur within a long time frame after severe brain insults like subarachnoid hemorrhage, traumatic brain injury or meningitis but is often idiopathic without obvious cause. The most frequent primary symptoms are gait difficulty with broad base and shortened step length followed by cognitive deficits and urinary urgency or incontinence. Cognitive symptoms are wide-ranging including psychomotor slowness, inattention, memory deficit and impaired executive functions. Differential diagnostic challenges and potential comorbidities are both memory diseases and movement disorders. Familial aggregation has been found in 15%–20% of iNPH patients and FinnGen GWAS study has identified several disease-associated loci. Selected patients benefit from CSF shunt surgery. After timely treatment, the final outcome is often determined by comorbid neurodegenerative diseases. Diagnostics and treatment of iNPH provide a unique ethical window into the living human brain. The frequent comorbid neurodegenerative pathologies of amyloid-β and neurofibrillary tau tangle accumulations indicate Alzheimer's disease and thus open a window for AD research. The heterogeneity across iNPH patients allows exploration and validation of disease phase dependent mechanisms and biomarkers.
Disclosure: Nothing to disclose.

FW02_2 | Exploring the relationship between NPH and neurodegenerative diseases: Laboratory markers

A. Bougea
National and Kapodistrian University of Athens, Athens, Greece

Given the prevalence of neurodegenerative comorbidities, it might be difficult to accurately diagnose normal pressure hydrocephalus (NPH) and predict how well these individuals would respond to therapy. Along with clinical and radiological symptoms typical of the illness, a thorough examination of cerebrospinal fluid (CSF) biomarkers that may be relevant in clinical practice may be very helpful in the NPH diagnostic battery. The findings on the potential applicability of Aβ42, NFL, P- and T-tau proteins, or LRG should be considered individually for prespecified iNPH patients. NPH's CSF profile appears to be easily distinguished from that of healthy individuals, although it is still difficult to distinguish it from other neurodegenerative diseases using these characteristics alone. When compared to iNPH, the comorbidities often have comparable (abnormally increased or abnormally lowered) levels of biomarkers in the CSF. The majority of studies reporting results on laboratory findings of NPH do not consider the ventricular volume in their calculations. Spinal Tap Test (STT)

is easy to perform and widely accepted to prove the diagnosis of NPH, however, negative STT does not completely rule out NPH. Even though current clinical practice does not use laboratory results for NPH, more study may be crucial for more accurately forecasting the evolution of NPH and, consequently, to enhance the therapeutic results and prognosis for individuals with NPH. In addition to providing pertinent data and summarizing current ideas on the subject, this workshop introduces and discusses NPH testing results.
Disclosure: Nothing to disclose.

FW02_3 | Exploring the relationship between NPH and neurodegenerative diseases: Imaging perspectives

G. Palermo
Center for Neurodegenerative Diseases—Parkinson's Disease and Movement Disorders, Unit of Neurology, Department of Neuroscience, University of Pisa, Pisa, Italy

Normal pressure hydrocephalus (NPH) is a potentially reversible cause of gait disturbance, cognitive impairment, and urinary incontinence in the elderly. However, its diagnosis remains challenging due to overlapping clinical and radiological features with neurodegenerative conditions, particularly parkinsonian syndromes and Alzheimer's disease. Neuroimaging plays a pivotal role in the diagnostic process and has traditionally been used to distinguish NPH from these disorders. Yet, recent evidence suggests that the boundaries are often blurred, pointing to shared or coexisting pathophysiological mechanisms. This presentation will focus on key structural imaging biomarkers of NPH, including the callosal angle, Evans' index, disproportionately enlarged subarachnoid space hydrocephalus (DESH), and periventricular white matter changes. Their diagnostic relevance and interpretative challenges will be discussed, particularly in the context of differential diagnosis with neurodegenerative disorders. Special attention will be given to the intersection between NPH and parkinsonism, and to the role of dopaminergic imaging in this context, where imaging findings may provide additional insights into the nature of NPH. By integrating classical markers and emerging neuroimaging tools with clinical judgment, this talk aims to shed light on the continuum between NPH and neurodegeneration, proposing a more nuanced framework that challenges the traditional dichotomy and supports personalized diagnostic and therapeutic strategies for these complex, often intertwined entities.
Disclosure: The author declares no conflicts of interest related to this presentation.

EAN/EANM: Translational imaging of epilepsy: What comes next?

FW03_1 | Updating the European intersocietal recommendations: Imaging from a clinical perspective

E. Pataraia
Department of Neurology, Medical University of Vienna, Vienna, Austria

FW03_2 | New MR techniques: Ready for practice?

R. Wiest
Inselspital, University of Bern, SCAN/Institute of Diagnostic and Interventional Neuroradiology/Neurocenter, Bern, Switzerland

FW03_3 | Nuclear imaging: Current and up and coming techniques

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Department of Radiology and Nuclear Medicine, UMC Utrecht, The Netherlands

Nuclear neuroimaging is a powerful tool in the clinical assessment of neurological disorders. This lecture will provide neurologists with a practical overview of key nuclear imaging modalities, focusing on HMPAO SPECT and FDG PET. Through case-based examples, we will explore the clinical applications, diagnostic value, and interpretation of these techniques, emphasizing their role in patient management. Additionally, the session will introduce promising emerging techniques, offering insights into future advancements in nuclear neuroimaging. Clinicians will gain a clear understanding of the "why, what, and how" of nuclear neuroimaging for epilepsy, enabling them to integrate this knowledge effectively into their clinical practice.
Disclosure: Advisory and consultancy for Telix Pharmaceuticals, in kind support Curium Pharma.

Autonomic nervous system and premature cerebrovascular aging

FW04_1 | Premature cerebrovascular aging in young patients with sickle cell disease with impaired cardiovascular autonomic nervous system

N. Nasr
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FW04_2 | Increased cardiovascular burden in hypertensive patients with impaired cardiovascular autonomic nervous system

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Neurology Department, University Hospital of Toulouse and ToNIC UMR 1214 Inserm, Toulouse, France

Hypertension is a risk factor for all-cause mortality and one of the most important prognostic factors for cardiovascular (CV) disease. Neurogenic orthostatic hypotension (nOH) is a main feature in patients with autonomic failure (AF). Supine hypertension (SH) is present in over 50% of patients with AF and nOH. Autonomic failure is common in synucleinopathies (Parkinson Disease, Multiple System Atrophy, Lewy Body Dementia, and Pure Autonomic Failure). Several studies have

shown that AF severity is a prognosis factor in these populations. The independent prognostic value of nocturnal hypertension is also well established both in the general population and in specific at-risk populations. OH is also known as a risk factor for CV morbi-mortality. However, the impact of the nOH itself is sometimes difficult to assess, so both nOH severity and SH are more frequently associated with small cerebral vessel disease. Autonomic failure has an impact on the BP level and increases BP variability. Several studies have shown that cardiac, vascular and renal organ damage are more prevalent and severe as BP variability increases for a given ambulatory BP mean value. The combination of nOH and SH makes the management of these patients more difficult. SH can worsen OH in the morning by promoting diuresis during the night, and treatment for nOH can worsen both SH and BP variability during the day ("short-life" treatment). Ambulatory 24-h BP recording of SBP is recommended to provide a better assessment of the BP profile in these patients, who will need regular CV monitoring.
Disclosure: Nothing to disclose.

FW04_3 | Premature cerebrovascular aging in elderly patients with orthostatic hypotension

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Orthostatic hypotension (OH) increases in prevalence with age, affecting up to 30% of older adults. A higher prevalence is seen in diseases that affect autonomic function, including diabetes, Parkinson's disease and multiple system atrophy. OH gives rise to symptoms such as dizziness, fatigue, visual disturbance, and coathanger distribution pain. It is associated with significant adverse health outcomes including falls, depression, cardiovascular morbidity, reduced quality of life, and all-cause mortality. OH, particularly if severe, prolonged and/or clinically manifest, is also associated with cognitive dysfunction. However, the mechanisms underlying this are unclear. Animal studies demonstrate links between cerebral hypoperfusion and increased deposition of tau and alpha-synuclein. In humans, varying links between OH and white matter hyperintensities (WMH), microbleeds, and lower brain parenchymal fraction have been reported. However, the evidence is inconsistent, and longitudinal studies do not demonstrate an association with WMH progression. There is therefore significant debate regarding optimal management of this challenging condition. Importantly, effective treatment of OH is hampered by limited numbers of pharmacological therapies, which lack a strong evidence base. The co-existence of marked blood pressure variability in many patients adds to the difficulty. In treating OH, it is important to consider symptoms, severity, duration, and chronotropic response. Co-morbidity is also important; patients with hypertension may be more vulnerable to cerebral hypoperfusion due to shifts in cerebral autoregulation boundaries. This session will explore these issues, and the surrounding evidence, in more detail.
Disclosure: In the past five years, Dr Haunton has received travel grants and/or speaker fees from the following companies: Bial Profile Pharma Ltd The Neurology Academy, UK.

Environmental impact on neurological disorders

FW05_1 | Air pollution and neuroinflammatory diseases

R. Bergamaschi
Multiple Sclerosis Center, IRCCS Mondino Foundation, Pavia, Italy

Neuroinflammatory diseases of the central nervous system, in particular multiple sclerosis (MS), are complex dysimmune diseases whose susceptibility risk results from the interplay between genetic, environmental and lifestyle related factors. Whereas some of them (infectious agents, vitamin D levels, smoke habit) have been extensively studied, data on the potential role of air pollutants are relatively few. Some ecological studies investigated the link between air pollution and MS prevalence, showing a positive association between levels of air pollutants and frequency of MS in different geographical areas. In addition, correlations between the risk of MS exacerbations and peaks of air pollutants were also reported. These relationships could be not causal, since there are some mechanisms through which MS might be triggered by air pollutants (a) their inhalation into the lower respiratory tract might induce a pro-inflammatory response in the lung, licensing auto-reactive lymphocytes to enter the central nervous system (b) they might sustain dysimmune inflammatory responses through oxidative stress, which leads to neuroinflammation and breakdown of the normal balance between immunity and self-tolerance (c) they might act as an atmospheric filter for ultraviolet light, that is the most important component for vitamin D synthesis, consequently causing vitamin D insufficiency in susceptible individuals (d) they might trigger epigenetic changes, especially DNA methylation alterations, resulting in pro-inflammatory cytokine production. To summarize, etiopathogenetic explanations and available epidemiological findings support the claim that air pollution might be one of the risk factors for MS onset and its unfavorable evolution.
Disclosure: Roberto Bergamaschi has served on scientific advisory boards for Biogen, Merck-Serono, Novartis, Sanofi-Genzyme, has had travel and congress expenses sustained by Biogen, Bristol Myers Squibb, Janssen, Novartis, Merck-Serono, Roche, Sanofi-Genzyme, received honoraria for speaking engagement from Biogen, Bristol Myers Squibb, Janssen, Merck-Serono, Novartis, Sanofi-Genzyme, received research support from Biogen, Merck-Serono, Novartis, Sanofi-Genzyme.

FW05_2 | Water pollution and neurodegeneration

E. Lagrange
Department of Neurology, CHU de Grenoble, Grenoble, France

As neurologists we are trained to focus on the molecular and clinical mechanisms of diseases affecting the brain and nervous system. But what if some of these mechanisms are being triggered or worsened by something as fundamental as the water that we drink? Growing evidence have pointed a link between environmental pollution and neurodegenerative diseases as Alzheimer disease, Parkinson and amyotrophic lateral sclerosis disease. We will see in this presentation the main types of water pollutants that pose a neurological risk and explore how they may contribute to

neurodegeneration, discuss the impacts on our clinical practice to provide the best prevention but also how to slow the progression of those three major diseases.
Disclosure: Nothing to disclose.

FW05_3 | Short-term exposure to air pollution and ischemic stroke

J. Verhoeven
Department of Neurology, Radboud University Medical Centre, Nijmegen, The Netherlands

According to the Global Burden of Disease study air pollution is the most pressing environmental risk-factor related to stroke and contributes to 16% of the global stroke burden. This burden is not equally distributed across the world and concerns mostly low- and middle-income countries. In these parts of the world the mean and peak exposure to pollutants is highest, and there is a clear association between the level of exposure and the risk of stroke. However, most studies carried out in high-income countries still show a small risk increase of ischemic stroke for lower exposure levels that are deemed safe by the World Health Organization. Short-term exposure to air pollutants is mostly linked to an increased risk of ischemic stroke due to atherosclerosis. Air pollutants seem act as an add-on risk factor or even trigger factor in patients with an increased cardiovascular risk profile. The effect of demographic factors such as age and sex on the occurrence of air pollution-associated stroke remains unclear. Several studies did demonstrate an interaction between socioeconomic status and the risk of air pollution-associated stroke. Overall, short-term increased exposure to air pollutants modestly increases the risk of stroke on an individual level but adds up to a significant risk-increase on a population level. Therefore, there may be a role for us as neurologists to contribute to the societal debate on the importance of governmental action regarding air pollution.
Disclosure: No disclosures.

Sunday, June 22, 2025

Interactions between brain and environment

FW06_1 | Neuropaedagogics—Linking brain function, teaching, and behavior

M. Spitzer
Universitätsklinikum Ulm, Ulm, Germany

FW06_2 | AI, neurotechnology, and society: A question of trust?

G. Starke
Institute of History and Ethics in Medicine, Technical University of Munich, Munich, Germany

The convergence of artificial intelligence (AI) and neurotechnology constitutes a key development in contemporary biotechnological innovation. The rise of a new generation of intelligent neural interfaces, including closed-loop and neuroadaptive technologies, hastens the clinical deployment of brain-computer interfaces (BCIs) to treat neurological and neuropsychiatric disorders and bridges the gap between clinical neuroscience and medical artificial intelligence. While offering promising applications in healthcare, these developments also raise numerous pressing ethical and societal challenges. Drawing on recent empirical work from neuroethics that engages with key stakeholders in Europe and North America, this talk will address these challenges by focussing on the role of trust in AI and neurotechnology. As the talk highlights, trust should not merely be considered as a prerequisite means for technology acceptance but as a normative and analytic lens that can inform policy-making, guide responsible innovation, and shape the development of patient-centric technologies. By critically reflecting on the specific contexts in which new technologies are introduced, the presentation highlights how trust can be fostered in ways that align with the ethical imperatives of neurological practice and improve clinical care.
Disclosure: Nothing to disclose.

FW06_3 | How do people with neurological disorders cope with global emergencies

O. Galvin
European Federation of Neurological Associations, Brussels, Belgium

Rare but treatable genetic neurological disorders with autonomic dysfunction

FW07_1 | Fabry disease—A treatable, diagnostic chameleon that often delays therapy

M. Hilz
University of Erlangen-Nuremberg, Erlangen, Germany

In Fabry disease, an X-linked recessive disorder, alpha-galactosidase A deficiency causes glycosphingolipid storage in body fluids and multiple tissues including vessel walls, the myocardium, the central, peripheral, and autonomic nervous system. Often, Fabry disease is identified only many years after symptom onset because symptoms are easily misdiagnosed. Individual symptoms may predominate, such as chronic or episodic pain, stroke at early age, small fiber neuropathy, autonomic dysfunction, gastrointestinal dysfunction, sudomotor dysfunction, chronic depression, fatigue, cardiac arrhythmia, hypertrophic cardiomyopathy, incipient or advanced renal failure. There are more than 1000 different mutations of the gene encoding alpha-galactosidase A. Apart from mutations causing the classical, early-onset Fabry disease, many mutations account for the 5–10 times more frequent but often less severe late-onset disease; there are genetic variants of unknown significance and benign polymorphisms without clinical relevance. Diagnostic difficulties will be demonstrated in the case of a woman with chronic pain and excessive use of nonsteroidal anti-inflammatory drugs and alcohol to mitigate

painful crises and depression. She was first misdiagnosed until one of her sons was diagnosed with hypertrophic Fabry cardiomyopathy. Further screening unveiled Fabry disease in several other family members all of whom presented with some of the clinical landmarks of Fabry disease. Subtle clinical, particularly neurological evaluation and assessment of diagnostic biomarkers facilitate the early diagnosis of Fabry disease and allow for adequate treatment which currently includes intravenous enzyme replacement or in patients with amenable mutations oral chaperone therapy. Early treatment is essential for slowing disease progression.

Disclosure: I received lecturing honoraria from Sanofi and travel support from Sanofi and Amicus Therapeutics.

FW07_2 | Hereditary transthyretin amyloidosis, a kaleidoscopic constellation of signs and symptoms: Clues from autonomic nervous system evaluation

P. Guaraldi
IRCCS Istituto delle Scienze Neurologiche di Bologna, Bologna, Italy

Introduction: Hereditary transthyretin amyloidosis (ATTRv) is a progressive multisystem disorder caused by mutations in the transthyretin (TTR) gene. It manifests with a broad and often misleading constellation of symptoms, among which autonomic nervous system (ANS) dysfunction frequently appears early and may offer valuable diagnostic clues.

Methods: This lecture synthesizes current evidence from the literature and personal data collected at a national referral center. The focus is on the diagnostic and prognostic significance of ANS involvement in ATTRv, alongside updates on clinical evaluation and therapeutic options.

Results: Autonomic disturbances—such as cardiovascular dysregulation, gastrointestinal dysmotility, urinary dysfunction, and sudomotor abnormalities—represent distinctive and disabling features across TTR variants. Despite their clinical relevance, these manifestations remain underrecognized. Standardized autonomic testing often reveals subclinical involvement, even in patients from non-endemic regions. Identifying early ANS impairment may serve as a practical biomarker, guiding timely therapeutic decisions and potentially altering disease trajectory.

Conclusion: A thorough clinical and instrumental assessment of ANS function enhances early detection and risk stratification in ATTRv. The expanding landscape of disease-modifying treatments, including TTR stabilizers and gene-silencing agents, highlights the need for prompt diagnosis. Incorporating ANS evaluation into routine diagnostic algorithms can improve clinical management and ultimately patient outcomes in this complex and evolving condition.

Disclosure: Dr P Guaraldi has been advisory board member of Alnylam and Sobi; Received speaker fees and honoraria from Alnylam, Astra Zeneca, Akcea Therapeutic, Biogen, Chiesi and Theravance Biopharma. Received congress and travel accommodation expense compensations from Abbvie, Alnylam, Bial and Zambon.

FW07_3 | Friedreich's Ataxia, new advancements: The role of the autonomic nervous system

E. Indelicato
Center for Rare Movement Disorders Innsbruck, Department of Neurology, Medical University Innsbruck, Innsbruck, Austria

Friedreich's Ataxia (FRDA) is a rare multisystem, life-limiting disease and the most common early-onset hereditary ataxia in populations of European ancestry. In recent years, significant progress has been made in elucidating the pathogenesis and natural history of the disease. The rapid translation of research advances has culminated in the completion of several clinical trials and the recent approval of the first disease-specific therapy, the NRF2 activator omaveloxolone. Several other trials, including gene therapy trials, are underway. In this workshop, we will focus on the role of the autonomic nervous system in FRDA. Although autonomic failure is not considered a primary feature of FRDA, clinical studies have shown frequent autonomic symptoms, particularly a high prevalence of pelvic symptoms (urinary, sexual, and lower gastrointestinal), decreased temperature perception, and vasomotor dysfunction in the lower extremities. Neuropathologic studies have shown marked small fiber involvement that correlates with the underlying genetic severity, such as several other disease milestones. More importantly, autonomic symptom burden shows a strong correlation with functional outcome scores, underscoring the importance of investigating autonomic involvement in FRDA.

Disclosure: Nothing to disclose.

The heat is on—Temperature and the brain

FW08_1 | Impact of early life temperature and climate on brain development

J. Paprocka
Department of Pediatric Neurology, Medical University of Silesia, Katowice, Poland

FW08_2 | Temperature regulation by and for sleep: From evolutionary biology to disorders of the brain

R. Fronczek[1,2]
[1]Department of Neurology, Leiden University Medical Centre, Leiden, The Netherlands; [2]Stichting Epilepsie Instellingen Nederland (SEIN), Sleep-Wake Centre, Heemstede, The Netherlands

Environmental factors have a major influence on the development or exacerbation of neurological diseases. Temperature extremes and rapid temperature fluctuations are also playing an increasingly important role in neurology due to climate change. In this part, the bilateral relationship between temperature and sleep-wake regulation and the associated functions of sleep are presented. Limits of thermoregulation and general effects of heat on brain health are also discussed.

Disclosure: Grant: ZonMw, Takeda, Medtronic. Consultant: Jazz Pharma, Lundbeck, Takeda. Speaker: Novartis, Pharmanovia. Advisory work: TEVA, Salvia.

FW08_3 | Risk and management of extreme temperatures and temperature changes in stroke and epilepsy

A. Arsovska
University Clinic of Neurology, University "Ss. Cyril and Methodius"-Faculty of Medicine, Skopje, North Macedonia

Extreme temperatures and rapid temperature fluctuations have been identified as significant environmental factors influencing the onset and exacerbation of neurological conditions such as stroke and epilepsy. Temperature extremes have impact on the pathophysiology, risk factors, and management of stroke and epilepsy, with a focus on both hyperthermic and hypothermic events. Elevated temperatures may increase the risk of stroke by promoting vascular dysregulation, thrombosis, and exacerbating metabolic stress, while rapid cooling or exposure to extreme cold can lead to ischemic events and seizures. Similarly, for individuals with epilepsy, both hyperthermia and hypothermia can act as seizure triggers, potentially leading to increased frequency and severity of seizures. The management of these conditions requires a multifaceted approach, including temperature regulation, pharmacological interventions, and environmental control strategies to minimize risks. Understanding the complex relationship between temperature changes and these neurological disorders is crucial for developing effective prevention and management protocols. There is a need for further research to refine therapeutic strategies, enhance patient care, and reduce the burden of stroke and epilepsy in the context of extreme environmental conditions.
Disclosure: Nothing to disclose.

EAN/ISNI: Underrecognized issues in females with demyelinating diseases

FW09_1 | Pregnancy related issues in demyelinating diseases

E. Koc
Department of Neurology, Faculty of Medicine, Bursa Uludag University, Bursa, Türkiye

Pregnancy in women with multiple sclerosis (MS) is generally safe when aligned with disease activity and reproductive goals. Fertility may be modestly reduced due to psychosocial and biological factors, but assisted reproductive technologies are effective without increasing relapse risk. Pregnancy, especially in the third trimester, exerts a protective effect, though relapse risk mildly increases postpartum. Early counseling is essential to coordinate disease-modifying therapy (DMT) with family planning. Misconceptions about DMT safety can delay treatment, but emerging evidence supports continuation of select therapies up to conception and even during pregnancy and breastfeeding, guided by placental drug transfer dynamics. Notably, monoclonal antibody transfer is limited in early pregnancy, increasing later, allowing clinicians to tailor treatment. Pregnancy does not accelerate MS disability progression, though peripartum mental health risks require attention. Early postpartum DMT resumption and breastfeeding-compatible treatments help reduce relapse risk. Multidisciplinary care and pregnancy registry participation enhance outcomes. In neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD), pregnancy poses greater challenges due to high relapse risk during and after pregnancy, risking cumulative disability. Pregnancy is not contraindicated but should follow at least 12 months of remission. Continued treatment during conception and pregnancy lowers relapse risk, with rituximab and IVIG being safer choices, while teratogens like mycophenolate are avoided. Understanding fetal IgG transfer timing helps balance maternal disease control and fetal safety. Early postpartum DMT re-initiation and breastfeeding-compatible therapies are crucial.
Disclosure: I declare that no honorarium was received for this presentation. Sanovel provided travel support to attend this congress. For unrelated scientific activities, I have previously received honoraria and travel support from Merc, Alexion, Teva, ARIS, Roche, and Biogen.

FW09_2 | Are sex hormones important for the course of demyelinating diseases?

S. Samadzadeh
Department of Neurology, Charité University Hospital/Southern Denmark University, Berlin, Germany

FW09_3 | Gynecological cancers and screening in demyelinating diseases

N. Szejko
Medical University of Warsaw, Warsaw, Poland

The purpose of this lecture is to review current evidence related to the complex association between gynecological cancers and multiple sclerosis (MS) in order to address the following questions: (1) the prevalence of gynecological cancers in MS; (2) the risk factors and symptoms of gynecological cancers in women with MS; (3) short and long-term effects of DMTs on the risk of gynecological cancers, particularly for high-efficacy DMTs and hematopoietic stem cell therapy; and related to it (4) recommendations for organization of cancer screening for gynecological cancer screening for women with MS using DMTs; (5) introduction and/or modification of DMTs in women with MS and with active gynecological cancer; (6) safety and efficacy of vaccines used for prevention of cervical cancer in women patients with MS. Additionally, barriers for women with MS to get cancer screening and treatment for gynecological cancers are discussed. Finally, currently available guidelines regarding oncological vigilance in MS are discussed.
Disclosure: Nothing to disclose.

EAN/EANO: CAR T cell therapy in neurology

FW10_1 | CAR T in neuro-oncology

M. Platten
Department of Neurology, Medical Faculty Mannheim, Mannheim Center for Translational Neuroscience (MCTN), Heidelberg University, Mannheim, Germany

Chimeric antigen receptor (CAR) T cell therapy have gained significant traction in the past years. In fact, brain tumors are the largest indication for CAR T cell development in solid tumors. Innovative designs of CAR T cells have been translated into phase 1 trials with remarkable efficacy in some cases. From these trials it has become clear, that both persistance and efficacy is increased with intrecerbroventricular rather than intravenous administration of CAR T cells. In this lecture I will highlight relevant target antigens and review available clinical trial data. I will discuss important factors impacting efficacy such as route of infiltration and immunosuppressive factors from the tumor microenvironment and present preclinical data subtantiating key mechanisms. I will also weigh CAR T cells against other modalities enabling target-specific T cell engagement such as T cell receptor (TCR)-transgenic T cells or bispecific T cell engagers (BiTEs). The current regulatory challenges associated with CAR T cell development will be highlighted and potential solutions will be discussed. Finally, I will discuss the implications for the use of CAR T cells in autoimmune neurological conditions.
Disclosure: Founder and managing director of Tcelltech. Inventor of technologies for T cell therapy. Research contributions by Pfizer, Roche, Merck, Bayer.

FW10_2 | The promise of CAR T cell therapy for neurological autoimmune conditions

Y. Morgado
Department of Neurology, Hospital Clinic Barcelona, Barcelona, Spain

FW10_3 | Neurotoxicity after CAR T cell treatment

A. Vogrig[1,2]
[1]Department of Medicine (DMED), University of Udine, Udine, Italy; [2]Clinical Neurology, Department of Head-Neck and Neuroscience, Azienda Sanitaria Universitaria Friuli Centrale (ASUFC), Udine, Italy

Chimeric antigen receptor (CAR) T-cell therapy is an effective immunotherapeutic approach that involves genetically modifying T cells to recognize and target-specific proteins on the surface of malignant cells. This method has shown significant efficacy in treating hematologic cancers, such as diffuse large B-cell lymphoma and multiple myeloma. However, the clinical use of CAR T cells is associated with specific toxicities, most notably cytokine release syndrome (CRS) and immune effector cell–associated neurotoxicity syndrome (ICANS). ICANS occurs in 10%–40% of patients and typically manifests as an encephalopathy with language difficulties, tremors, seizures, and intracranial hypertension. Diagnosis is primarily clinical after excluding other potential causes such as infection or hemorrhage, and treatment involves corticosteroids, anti-IL1R therapies, and supportive care. In addition to these known complications, recent reports have highlighted other neurological side effects, including ischemic stroke, peripheral neuropathy, and cerebellar toxicity. Of particular interest is movement and neurocognitive toxicity (MNT), which can develop with B cell maturation antigen (BCMA) targeting CAR T cells in multiple myeloma patients. MNT resembles parkinsonism and has been associated with T-cell infiltration and BCMA expression within the basal ganglia. Postmortem analysis revealed BCMA RNA expression in the caudate nucleus, offering insights into the pathophysiology of this toxicity. Further research is required to understand these neurological effects and develop strategies to mitigate their occurrence in CAR T-cell therapy for hematologic malignancies. This focused workshop will present how to correctly diagnose and manage ICANS and other neurological complications related to CAR-T cell therapy.
Disclosure: Alberto Vogrig has received personal compensation for serving on the Speakers Bureaus of Eisai and Angelini. The institution of Alberto Vogrig has received research support from the Italian Ministry of Health, specifically through the "Bando Ricerca Finalizzata" program.

FW10_4 | Challenges in translation of CAR T cell therapies from bench to bedside: From study designs to costs

B. Willekens
Department of Neurology, Antwerp University Hospital and University of Antwerp, Edegem, Belgium

CAR T cell therapies are considered as a ground-breaking approach in hematological malignancies. These personalized advanced therapy medicinal products (ATMP) are entering the neurooncological and neuroimmunological arena and provide hope for durable remission in treatment refractory patients.
Despite the unprecedented success of CD19 CAR T cell therapy in the treatment of B cell malignancies, several challenges need to be addressed to ensure successful translation from the bench to the bedside of neurological patients at a global level.
These challenges include patient selection and trial design, safety, selection of antigen and antigen-specificity, optimization of manufacturing process as well as development of cost-effective options.
Multi-stakeholder and cross-disciplinary collaborations are needed to drive innovation and to enable world-wide access to CAR T cell therapies.
Disclosure: Nothing to disclose.

EAN/MDS-ES: Update on genetic movement disorders

FW11_1 | Recent insights into the genetic architecture of Parkinson's disease

J. Trinh
Institute of Neurogenetics, University of Lübeck, Lübeck, Germany

Parkinson's disease (PD) is the fastest growing neurological disorder. The massive percentage increase of PD patients (60.7%) from 1990 to 2021, compared to a moderate increase for Alzheimer's disease (3.2%) is an unexplained phenomenon. Yet there are currently no disease-modifying interventions, and existing treatments only target the management of symptoms. More than 100 genes or genetic loci have been identified in familial and sporadic PD. In familial late-onset PD, dominantly inherited LRRK2 p.G2019S is the most common cause. On the other hand, PRKN and PINK1 variants cause early-onset disease. The prevalence of monogenic forms (when including GBA1 variants) in PD is much greater (~15%) than in other neurodegenerative diseases. The most recent monogenic finding is RAB32 in autosomal dominant PD, which presents with reduced penetrance. Thus, the genetic factors uncovered to date do not explain diversity in the manifestation of PD: there is variable age at onset and unaffected elderly individuals. Recent GWAS efforts in African cohorts have found an association in an intronic GBA1 variant. Besides monogenic forms and standard GWAS approaches, there is emerging field of polygenic risk scores. A polygenic risk score is a cumulative summary score built from a genome-wide association study of PD which estimates the effect of all genetic variants on an individual's risk of developing disease. Moreover, pathway-specific polygenic risk scores have been generated. Insights from genetic findings unify biological themes of mitochondrial, synaptic, lysosomal, and immunological mechanisms in PD.
Disclosure: Nothing to disclose.

FW11_2 | Update on hyperkinetic genetic movement disorders

F. Magrinelli
Department of Clinical and Movement Neurosciences, University College London, London, UK

FW11_3 | New repeat expansion disorders presenting with ataxia

E. Gustavsson
Department of Neurodegenerative Disease, University College London, London, UK

Clinical trials and biomarkers in ALS/FTD

FW12_1 | Role of neurofilaments and other wet biomarkers in ALS/FTD clinical trials: Implications for treatment

M. Synofzik
Hertie Institute for Clinical Brain Research, Tübingen, Germany

FW12_2 | Target engagement biomarkers in ALS/FTD clinical trials: Connecting biomarkers to treatment outcomes

I. Le Ber
GH Pitié Salpêtrière, Paris, France

FW12_3 | Neuroimaging biomarkers in ALS/FTD: Insights into treatment efficacy

F. Agosta
Neurology Unit, Neuroimaging Research Unit Division of Neuroscience, IRCCS San Raffaele Scientific Institute, Milan, Italy

Diagnosis and management of cerebral small vessel disease: Not so small matter

FW13_1 | Monogenic causes of cerebral small vessel disease, not a simple diagnosis

N. Rifino
Fondazione IRCCS Istituto Neurologico Besta, Milan, Italy

Monogenic forms of cerebral small vessel disease (cSVD), such as CADASIL, CARASIL, COL4A1/A2, and Fabry-related disorders, provide unique insights into the pathophysiology of cSVD, but their diagnosis remains complex and often delayed. These rare diseases can mimic sporadic forms of cSVD, and their clinical presentation is highly variable—even among carriers of the same mutation—ranging from migraine with aura and psychiatric symptoms to early-onset stroke and cognitive decline. Neuroimaging patterns, although suggestive, are not pathognomonic, and genetic testing poses interpretative challenges due to variants of uncertain significance. In this lecture, I will discuss key clinical, radiological, and genetic features that may guide the diagnostic process, highlight the role of multidisciplinary evaluation, and emphasize the importance of accurate diagnosis for prognosis, and family counseling. Emerging genotype–phenotype correlations and recent advances in risk stratification based on mutation location for CADASIL will also be addressed.
Disclosure: Nothing to disclose.

FW13_2 | The increasing impact of cerebral amyloid angiopathy as a cause of cerebral SVD

G. Banerjee
MRC Prion Unit at UCL, Institute of Prion Diseases, UCL, and the National Hospital for Neurology and Neurosurgery, Queen Square, London, UK

Cerebral amyloid angiopathy (CAA) is a recognized cause of recurrent intracerebral hemorrhage and vascular cognitive impairment, with well-established clinical and radiological criteria that allow diagnosis to be made with confidence in life. In this cerebral small vessel disease, amyloid-beta protein is deposited in small to medium sized cortical and leptomeningeal vessels. Recent clinical and research observations are providing fresh insights into the pathophysiology of CAA. This includes recognition of the new etiological category of iatrogenic CAA (i.e., CAA consequent to previous medical procedures), the temporal and spatial clustering of hemorrhagic events in CAA, and a growing appreciation for the role of inflammation as a trigger for CAA-related vasculopathy. Together, these suggest that CAA is a more dynamic disease than usually assumed and thus provides an alternative theoretical framework within which to consider potential strategies for disease modification; this points to the rather exciting possibility that CAA, as a model disease system, could have pathophysiological relevance and important implications for other cerebral small vessel diseases.

Disclosure: I receive research funding from Alzheimer's Research UK, the National Institute for Health and Care Research (NIHR) and the Stroke Association UK. I am a Board Member of the International CAA Association (unpaid committee role). I have received honoraria for teaching (ESO European Stroke Master Programme, University of Bern, Switzerland).

FW13_3 | Neuroimaging in cerebral small vessel disease: How much can it help in diagnosis?

M. Düring
Medical Image Analysis Center, Basel, Switzerland

Cerebral small vessel disease (cSVD) presents with various manifestations on magnetic resonance imaging (MRI), which support the diagnostic process. The recently revised STandards for ReportIng Vascular changes on nEuroimaging (STRIVE-2) provide a harmonized framework for the terminology associated with cSVD MRI features, thereby facilitating standardized assessments in clinical and research settings. Advancements in artificial intelligence enable the quantification of key MRI features, for example, for tracking disease progression. By analyzing spatial patterns, it becomes possible to differentiate among distinct forms of cSVD, including arteriolosclerosis, cerebral amyloid angiopathy, and hereditary variants. Emerging quantitative MRI biomarkers hold significant promise for enhancing the characterization of cSVD.

Disclosure: Nothing to disclose.

Tuesday, June 24, 2025

Novel therapeutic strategies for multiple sclerosis and other inflammatory demyelinating diseases

FW14_1 | Multiple sclerosis: New therapeutic targets and strategies

M. Filippi[1,2]
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Multiple sclerosis (MS) is a chronic, immune-mediated disorder of the central nervous system marked by early and ongoing neuroinflammation, demyelination, and neurodegeneration. Emerging evidence suggests that these pathological processes begin from the earliest phases of the disease, emphasizing the importance of early intervention to prevent irreversible damage and long-term disability. Over the past decade, high-efficacy disease-modifying therapies (HE-DMTs) have significantly reshaped the MS treatment landscape. These therapies consistently outperform moderate-efficacy agents by reducing relapse rates, delaying disability progression, and minimizing CNS tissue damage. Nevertheless, HE-DMTs are often reserved for use only after moderate therapies fail—a strategy that may compromise long-term outcomes. Increasing data now support initiating treatment with HE-DMTs early in the disease course to better control inflammation, preserve neurological function, and modify disease trajectory. Concurrently, innovative therapeutic strategies are being developed to target the chronic, compartmentalized inflammation and neurodegeneration that drive MS progression. Promising approaches include Bruton's tyrosine kinase inhibitors (BTKi), frexalimab, and CAR-T cell therapies. Additionally, neural stem cell therapy, and agents that promote remyelination and neuroprotection, are under active investigation with the goal of restoring function and halting disease progression. This presentation will review current evidence supporting early HE-DMT use and explore emerging therapeutic targets addressing both inflammatory and degenerative mechanisms. Collectively, these advances represent a shift toward more proactive, effective, and personalized treatment strategies for each MS patient.

Disclosure: M. Filippi is Editor-in-Chief of the Journal of Neurology, Associate Editor of Human Brain Mapping, Neurological Sciences, and Radiology; received compensation for consulting services from Alexion, Almirall, Biogen, Merck, Novartis, Roche, Sanofi; speaking activities from Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme. He receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and Fondazione Italiana Sclerosi Multipla.

FW14_2 | NMOSD: New therapeutic targets and strategies

J. Palace
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Neuromyelitis optica spectrum disorders (NMOSD) include those with serum AQP4-IgG, those with MOG-IgG and double seronegative patients (DN-NMOSD). Great progress has been made in the development of drugs for AQP4-NMOSD patients. Recently licensed therapies include those targeting complement C5, IL6 receptors and CD-19 (a broader target in the B cell maturation pathway than CD20). Improvements in treatments include longer acting formulations, the option of subcutaneous delivery allowing self-administration, along with good evidence of marked efficacy. No licensed therapies exist for DN-NMOSD and those with MOG-IgG who are managed empirically. The potential of repurposed treatments, HSCT, tolerising strategies and potential treatments from research data such as genetic studies will be discussed.

Disclosure: Jacqueline Palace has received support for scientific meetings and honorariums for advisory work From Merck Serono, Novartis, Chugai, Alexion, Roche, Medimmune, Amgen, Vitaccess, UCB, Mitsubishi, Amplo, Janssen. Grants from Alexion, Argenx, Clene, Roche, Medimmune, Amplo biotechnology. Patent ref P37347WO and licence agreement Numares multimarker MS diagnostics Shares in AstraZenica. Her group has been awarded an ECTRIMS fellowship and a Sumaira Foundation grant to start later this year. A Charcot fellow worked in Oxford 2019–2021. She acknowledges partial funding to the trust by Highly specialized services NHS England. She is on the medical advisory boards of the Sumaira Foundation and MOG project charities, is a member of the Guthy Jackon Foundation Charity and is on the Board of the European Charcot Foundation and a member of MAGNIMS and the UK NHSE IVIG Committee and chairman of the NHSE neuroimmunology patient pathway and ECTRIMS Council member on the educational committee since June 2023. Currently on the ABN advisory groups for MS and neuroinflammation and recently on neuromuscuscular diseases advisory group.

FW14_3 | MOGAD: New therapeutic targets and strategies

R. Marignier
Service Sclérose en plaques, pathologie de la myéline et neuro-inflammation, and Centre de référence des maladies inflammatoires rares du cerveau et de la moelle (MIRCEM), Hospices Civils de Lyon, Lyon, France

Myelin oligodendrocyte glycoprotein antibodies (MOG-Ab)-associated disease (MOGAD) is a recently identified neuroinflammatory demyelinating disorder of the central nervous system. MOGAD is affecting mainly children and young adults, with a sex-ratio around 1. MOGAD is a potential devastating condition, with an unpredictable risk of visual, motor, sphincter and cognitive disability. The clinical course is heterogeneous, and ranges from monophasic to chronic with relapses, with a proportion of patients with a relapsing disease and severe outcome or experiencing a single devastating attack. There is no evidence-based data regarding the management of MOGAD, neither for the treatment of acute episode, nor for the prevention of further attacks or long-term disability. The wide spectrum of disease course emphasizes the need for early stratification of patients to adjudicate who will benefit from maintenance immunotherapy. Though there is still some controversy to propose a preventive treatment after a first episode, there is a consensus to treat patients preventively with immunoactive drugs in case of a relapsing course. However, the choice of the best drug, and duration of the treatment is still debated. Finally, recent works suggest a spontaneous decrease of disease activity among time, supporting de-escalation to minimize the risk of chronic exposure to unnecessary treatment. In addition, biomarkers to monitor treatment response and optimization have not been deeply evaluated in MOGAD. We will first propose an overview of the current knowledge of MOGAD disease course and associated therapeutic strategies. Then, we will highlight the potential new therapeutic targets and strategies for the management of MOGAD.

Disclosure: RM serves as scientific advisor for UCB and Roche and is the PI of an academic trial on MOGAD treatment supported by the French Research Agency.

Advancements in migraine treatment: Exploring anti-CGRP and anti-PACAP pathway therapies

FW15_1 | Understanding the mechanisms: Anti-CGRP pathway therapies in migraine treatment

S. Sacco
Università degli Studi dell'Aquila, L'Aquila, Italy

FW15_2 | Beyond CGRP: Exploring emerging therapies targeting the PACAP pathway

M. Ashina
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Pituitary adenylate cyclase–activating polypeptide (PACAP) has emerged as a promising migraine target: intravenous PACAP38 reliably induces migraine-like attacks in susceptible individuals, highlighting its pivotal role in migraine pathophysiology. The development of monoclonal antibodies against PACAP marks a new era in migraine prevention, and ongoing trials will determine the optimal formulation, dosing, and safety profile of these agents. In this lecture, we will present the scientific rationale for targeting PACAP, including key human and animal studies of PACAP-induced migraine, and discuss the development and future potential of anti-PACAP pathway drugs.

Disclosure: MA is a consultant, speaker, or scientific advisor for AbbVie, Astra Zeneca, Eli Lilly, GlaxoSmithKline, Lundbeck, Pfizer, and Teva; a primary investigator for ongoing AbbVie, Lundbeck and Pfizer trials. MA reports research grants from Lundbeck Foundation and Novo Nordisk Foundation (all to institution). MA serves as associate editor of the Journal of Headache and Pain and associate editor of Brain.

FW15_3 | Future directions: Combination therapy and individualized approaches

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ABSTRACT

Special Session

Saturday, June 21 2025

The description of neurological disorders in the arts

SPS01_1 | Epilepsy and music

S. Evers
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A link between epilepsy and music has already been proposed in the work of William Shakespeare. Since then, several citations have been found in the history of medicine. The first link is the provocation of epileptic seizures by music, that is, musicogenic epilepsy. This is regarded as a part of the reflex epilepsies. Clinical cases will be presented. The second link is music as a symptom of epileptic seizures. Here, the phenomenon of ictal singing and of aura continua musicalis have been described. The third link regards music as a treatment of epilepsy. The so-called Mozart effect has been examined in this context: piano sonata KV 488 as a medicine against epilepsy in children. The fourth link is the influence of epilepsy and of the treatment of epilepsy on musical ability, It has been shown, for example, that untreated left temporal epilepsy impairs musical ability. The fifth link refers to epilepsy in famous composers and musicians. While in the history of music only little is known about composers with epilepsy (e.g., Mussorgsky, Gershwin), some famous artists in modern times use their epilepsy as a creative source for their music (e.g., Ian Curtis). Finally, a link between epilepsy and music can be seen in compositions. There are only examples of operas in which epileptic seizures are described such in Otello (Verdi) or Golem (d'Albert).
Disclosure: Nothing to disclose.

SPS01_2 | Migraine in literature

M. Weatherall
Ealing Hospital, Department of Neurology, Southall, UK

EAN/EPA: Brain and mental health across the lifespan: A neuropsychiatric perspective

SPS02_1 | Adolescent brain development and early onset of psychiatric disorders

U. Volpe
Unit of Clinical Psychiatry, Department of Clinical Neurosciences/DIMSC, Università Politecnica delle Marche, Ancona, Italy

Adolescence marks a critical window in neurodevelopment characterized by profound structural and functional brain changes, particularly in regions governing emotion regulation, executive function, and social cognition. These neurobiological transitions coincide with a heightened vulnerability to the onset of psychiatric disorders, including mood, anxiety, psychotic, and substance use disorders. The interplay between normative brain maturation and the emergence of adult psychopathology is crucial for understanding the key neurodevelopmental trajectories and risk factors—genetic, environmental, and psychosocial—that contribute to early disease onset. Neuroimaging findings and longitudinal cohort studies will be examined to explore the implications of early identification and intervention strategies. By framing adolescent mental health within a lifespan neuropsychiatric perspective, this presentation underscores the need for integrative approaches to prevention and care during this formative period.
Disclosure: Nothing to disclose.

SPS02_2 | Bridging neurology and psychiatry: The case for integrated brain health

P. Mohr
National Institute of Mental Health, Klecany, Czechia

SPS02_3 | Brain Health starting from the beginning: The role of child neurology

G. Gröppel
Kepler University Hospital, Department of Paediatrics and Adolescent Medicine and Department for Neurology, Linz, Austria

SPS02_4 | The Brain Health Mission, an inclusive platform for brain health advocacy and advancement in Europe

P. Boon
Ghent University Hospital, Department of Neurology, Ghent, Belgium

Neurological disorders in Europe: Impact, costs, and the road ahead

SPS12_1 | The burden of neurological diseases in Europe

M. Leone
IRCCS Casa Sollievo della Sofferenza, S. Giovanni Rotondo, Italy

Background: We estimate prevalence and health loss for 26 neurologic conditions across the WHO European Region from 2017 to 2021. Methods: We estimated mortality, prevalence, and disability-adjusted life-years (DALYs) by age and sex from the WHO Europe macroregion (East-Central-West Europe) for 2021, and for the 2017–2021 period. Findings: In 2021, an estimated 449.2 million (Mio) people in the WHO Europe had one or more diseases affecting the nervous system (50% of the population). The resulting disease burden was estimated to be 1.8 Mio deaths and 49.1 Mio DALYs. Globally, these 26 conditions were the most prevalent disease group the leading cause of death, and the second leading cause of for DALYs. Eight diseases accounted for more than 90% of DALYs in WHO Europe: stroke, Alzheimer's disease and other dementias, migraine, diabetic neuropathy, cancer of the nervous system, Parkinson's disease, epilepsy, and traumatic brain injury. The age-standardised prevalence rate of all neurological diseases remained relatively stable from 2017 to 2021 (52.4 to 52.7 per 100,000, a 0.54% increase). The prevalence rates increased more than 5% for five conditions (neurosyphilis, diabetic neuropathy, GBS, tetanus, and cystic echinococcosis). Conversely, central nervous system cancer showed the largest decline (-6.5%). In spite of a stable prevalence, age-standardized death and DALYs rates showed a remarkable reduction of 6.0%, and of 2.5%. Interpretations: Neurological disorders are the leading cause of overall disease burden in Europe. Health authorities should prioritize neurological disease prevention and care.
Disclosure: Nothing to disclose.

SPS12_2 | The cost of neurological disorders in Europe – COIN-Eu

M. Montes-Martinez[1], L. Welter[1], R. Dodel[1], P. Boon[2], C. Bassetti[3], T. Berger[4], E. Moro[5], C. Kruse[1], M. Lolich[6], M. Konti[6], M. Arvandi[7], N. Mühlberger[7], U. Siebert[7]
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Introduction: Neurological conditions are a leading global cause of health loss, accounting for 11.1 million deaths and 443 million disability-adjusted life years. We aimed to estimate their macroeconomic societal burden across 12 disease groups in 47 European countries. Methods: We applied a four-step approach: (1) epidemiological data were sourced from the Global Burden of Disease (GBD) Study 2021 and supplemented with literature reviews for selected conditions; (2) economic data were identified via systematic review; (3) data were extracted, pooled, and structured by country-economic parameters, which were also used to impute values for countries lacking primary data; and (4) neurology experts assessed the plausibility of country-level results. Costs were assessed from a societal perspective, including direct, indirect, and informal care, and reported at country and per-patient levels. Results: Our findings point to total costs of approximately €1,232 billion in Europe in 2019 (adjusted for purchasing power parity) associated with 10 neurological disease groups. For sleep disorders and polyneuropathies, based on alternative epidemiological sources, we suggest additional costs of around €423 billion and €39 billion, respectively. Costs ranged from €149 million (meningitis) to €815 billion (headache disorders). Indirect costs comprised 42% of the total burden, followed by direct costs (37%) and informal care (21%). Conclusion: Our results indicate a substantial economic burden from neurological diseases in Europe, highlighting the need for better understanding, research, and more effective strategies—including health promotion, prevention, treatment, and rehabilitation—and targeted policy action. Data scarcity limits current analyses, especially in middle-income regions.
Disclosure: Commissioned by the European Academy of Neurology, with additional support from the Lundbeck International Neuroscience Foundation.

SPS12_3 | Costs and epidemiology of sleep disorders in Europe

C. Bassetti
Department of Neurology, Inselspital, University of Bern, Bern, Switzerland

SPS12_4 | The future of general neurology

C. Bassetti
Department of Neurology, Inselspital, University of Bern, Bern, Switzerland

Sunday, June 22 2025

What's new on EAN guidelines?

SPS04_1 | From the oven to the table: A scoping review on the roadmap for implementation of neurological guidelines

K. Rukavina
Hospital for Movement Disorders Beelitz, Beelitz, Germany

The European Academy of Neurology (EAN) strives to harmonize neurological care across Europe through the development of high-quality clinical practice guidelines (CPGs), but their impact relies on effective implementation. We reviewed recent literature on CPG implementation in neurology and synthesized findings from 36 relevant studies. This lecture explores the challenges of CPG implementation, tackles common barriers and facilitators at the individual, organizational, and system levels, and proposes tailored planning approaches and targeted interventions to better translate EAN CPGs into everyday clinical practice.
Disclosure: Nothing to disclose.

SPS04_2 | EAN-MDS-ES guideline on Parkinson's disease—Part II: Pharmacological management of motor symptoms—Section 1: First-line treatment for initial monotherapy in early Parkinson's disease

K. Smilowska
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Background The treatment options for early Parkinson's disease (PD) continues to evolve. In response, the European Academy of Neurology (EAN) and the Movement Disorder Society European Section (MDS-ES) initiated a collaborative project to update clinical practice guidelines. Objective To provide updated, evidence-based guidance tailored to the European context on the initiation of pharmacological therapy for motor symptoms in individuals with early PD. Methods A multidisciplinary panel of 16 neurologists and two patient representatives was convened by EAN and MDS-ES. The panel adopted a methodology (GRADE-ADOLOPMENT), which integrates elements of adoption, adaptation, and de novo development of recommendations, structured through GRADE Evidence to Decision frameworks. Two key review questions were established: the comparative efficacy of initial drug therapies and the risk of impulse control disorders associated with these treatments. Existing guidelines were systematically evaluated, and an updated systematic literature search was performed in March 2023 to identify relevant new clinical trial data. Results Two foundational guidelines—NICE (2017) and AAN (2021)—were selected as the basis for the evidence review. The panel reviewed recent evidence and synthesized findings related to available pharmacological interventions for early PD treatment. Focus was given to the balance of benefits and harms, patient values and preferences, and the feasibility and acceptability of each treatment approach. Conclusions This guideline project provides an updated synthesis of the current evidence for initiating pharmacological treatment in early PD. It aims to support more consistent, evidence-based decision-making across Europe, enhance patient-clinician discussions, and improve overall care quality in the early Parkinson's disease.
Disclosure: KS has received honoraria from the European Academy of Neurology, International Parkinson and Movement Disorder Society, AbbVie and Pfizer.

SPS04_3 | EAN-ESCMID guidelines on the diagnosis and management of encephalitis in adults caused by infection

J. Sellner
Landesklinikum Mistelbach-Gänserndorf, affiliated with Karl Landsteiner University of Health Sciences, Krems, Austria

Background Encephalitis, a life-threatening condition associated with significant morbidity and mortality, is difficult to diagnose and manage. The latest European guidelines were published in 2010. Since this time, novel causes of encephalitis have emerged and diagnostic processes have evolved, which need to be reflected in updated guidelines. Objective We aimed to produce recommendations for the diagnosis and management of infectious encephalitis in adults based on current evidence and expert opinion to optimise diagnosis and treatment and improve patient outcome. Methods This guideline was developed by a multidisciplinary task force of 19 specialists, and recommendations were developed according to the GRADE approach. Where there was a lack of evidence or evidence was too indirect or heterogeneous, a good practice statement was made. Sixteen PICO questions were considered. Results The following two recommendations were reached: for initiation of intravenous acyclovir as soon as possible upon suspicion of encephalitis and against replacing pathogen-specific polymerase chain reaction (PCR) testing of cerebrospinal fluid (CSF) with multiplex CSF PCR panels for diagnosis of adult patients with suspected infectious encephalitis. A further 14 good practice statements regarding when to clinically suspect infectious encephalitis, microbiological investigations, additional investigations, treatment, and ongoing care and rehabilitation were agreed. Conclusions Given the lack of direct evidence identified by this review, future large-scale multi-centre studies of encephalitis are encouraged. In particular, research should focus on novel treatments and diagnostics and development of a core outcome set definition for use in future trials of interventions for acute care and post-encephalitis rehabilitation.
Disclosure: Nothing to disclose.

SPS04_4 | EAN CoCoCare Graduation 2024

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Academic Centre for Epileptology, Epilepsy Centre Kempenhaeghe & Maastricht University Medical Centre, Netherlands

EAN CoCoCare Graduation 2024: Building Guideline Development Skills for Cost-Conscious Neurological Care Clinical practice guidelines are essential tools in achieving high-quality, cost-efficient healthcare. Recognizing the need to strengthen competencies in this area, the Cost-Conscious Healthcare (CoCoCare) training programme was initiated in 2018 at Maastricht University (Netherlands) and later adopted by the European Academy of Neurology (EAN). Initially supported by an EU Erasmus grant, the programme became an official EAN initiative in 2023. CoCoCare is a structured, year-long educational programme aimed at neurology residents and early-career neurologists. It equips participants with the skills needed to develop and implement evidence-based, economically sound clinical guidelines. The training combines e-learning, an in-person kick-off workshop at the EAN Congress, monthly webinars, self-directed learning, and on-the-job practical guideline development. The course concludes with project presentations at the EAN Congress, providing both academic recognition and practical exposure. Since its launch, 114 participants from 23 countries have taken part. Feedback has highlighted the programme's impact on fostering critical reflection on cost-conscious decision-making and stimulating active involvement in guideline development. With its third edition launching at the EAN Congress 2025, CoCoCare continues to invest in the future of neurology by nurturing a new generation of experts capable of leading guideline development within the EAN framework. Graduates benefit from mentorship, congress participation grants, and enhanced professional visibility—contributing to the long-term quality and sustainability of neurological care across Europe.

Disclosure: Nothing to disclose.

Breakthroughs in treatment Neurology—Part 1

SPS05_1 | Directly isolated allogeneic virus-specific T cells in progressive multifocal leukoencephalopathy

L. Grote-Levi
Department of Neurology, Hannover Medical School, Hannover, Germany

Progressive multifocal leukoencephalopathy (PML) is a life-threatening viral brain infection that predominantly affects immunocompromised individuals. The primary therapeutic goal—reconstitution of the compromised immune system—is not always achievable, depending on the underlying condition. To date, no approved antiviral treatment is available. Treatment with directly isolated allogeneic virus-specific (DIAVIS) T cells demonstrated promising therapeutic effects in 28 patients treated monocentric at the Hannover Medical School, between March 2020 and February 2022. In this retrospective case series, patients with definite, progressive PML received DIAVIS T cells as a single fresh infusion containing up to 2×10^4 $CD3^+$ cells/kg body weight. Remaining T cells were cryopreserved in divided aliquots and administered in additional doses approximately 2 and 6 weeks later. DIAVIS T cells, directed against the BK polyomavirus, were isolated from healthy donors within 24 hours. Twenty-two patients (79%) showed a clinical response, characterized by stabilization or improvement of neurological symptoms and reduction in viral load. Six patients (21%) were classified as non-responders and experienced rapid deterioration leading to death; two additional patients died during the 12-month follow-up period. Older age emerged as the only predictor of poor treatment response. Survival analysis demonstrated improved 12-month survival rates for DIAVIS-treated patients (18 of 26 [69%]; hazard ratio 0.42, 95% CI 0.24–0.73, $p=0.02$) compared with historical controls receiving best supportive treatment (57 of 113 [50%]; 12-month survival including censored data: 45%). This case series provides first class IV evidence that DIAVIS T-cell therapy may reduce mortality and improve functional outcomes in patients with PML.

Disclosure: Lea Grote-Levi reported receiving financial support from Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) Young Academy – PRACTIS (Program of Hannover Medical School for Clinician Scientists; ID 413617135)

SPS05_2 | Cipaglucosidase alfa plus miglustat in adults with late-onset Pompe disease: A phase III open-label extension study

A. Toscano
Azienda Ospedaliera Universitaria Gaetano Martino, Department of Clinical and Experimental Medicine, University of Messina, Messina, Italy

SPS05_3 | Phase 2 proof-of-concept: Targeting PACAP pathway for migraine treatment

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Pituitary adenylate cyclase–activating polypeptide (PACAP) and its receptors are expressed in migraine-relevant structures, including the trigeminal ganglion, cranial vasculature, and sphenopalatine ganglion, underscoring PACAP's role in migraine initiation. Monoclonal antibodies against PACAP have been shown to block PACAP38-induced cranial artery dilation and reduce headache in healthy human subjects. In a phase II randomized, double-blind, placebo-controlled trial, a single 750 mg infusion of Lu AG09222, a humanized monoclonal antibody targeting PACAP, was administered to adults with migraine who had failed two to four prior preventive therapies. Over the first four weeks post-infusion, Lu AG09222 reduced mean monthly migraine days by 6.2 compared with 4.2 for placebo (difference, −2.0 days; 95% CI, −3.8 to −0.3; $p=0.02$). Treatment

was generally well tolerated, with adverse events occurring at rates similar to placebo. These data establish PACAP ligand neutralization as a compelling proof-of-concept approach for migraine prevention and support further evaluation in larger, longer-term studies.
Disclosure: MA is a consultant, speaker, or scientific advisor for AbbVie, Astra Zeneca, Eli Lilly, GlaxoSmithKline, Lundbeck, Pfizer, and Teva; a primary investigator for ongoing AbbVie, Lundbeck and Pfizer trials. MA reports research grants from Lundbeck Foundation and Novo Nordisk Foundation (all to institution). MA serves as associate editor of the Journal of Headache and Pain and associate editor of Brain.

SPS05_4 | CD19 CAR T therapy in myositis: Hype or hope?

M. de Visser
Academic Medical Centre Amsterdam, Department of Neurology, Amsterdam, The Netherlands

SPS05_5 | Safety and efficacy of ocrelizumab in treatment of pediatric Multiple sclerosis

L. Papetti
IRCSS Bambino Gesù, Rome, Italy

SPS05_6 | Efficacy and safety of elamipretide in individuals with Primary Mitochondrial Myopathy of nuclear origin

M. Mancuso
Azienda Ospedaliera Universitaria Pisana U.O.C. Neurologia, Pisa, Italy

Clinical Grand Round: Unravelling interesting neurological diagnoses

SPS06_1 | Severe progressive tetraparesis out of the blue

L. Väli
Tartu University Hospital, Tartu, Estonia

A 56-year-old male presented with progressive leg weakness, hypesthesia, and upper body pain. EMG indicated acute demyelinating polyneuropathy. Despite initial treatments (IVIG, plasma exchange, corticosteroids), the condition worsened to severe flaccid tetraplegia over three months. Rituximab proved more effective. The patient is now ambulant with some restrictions and weak to moderate tetraparesis.
Disclosure: Nothing to disclose.

SPS06_2 | Rare movement disorder, diagnosed by patient himself

K. Resik
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Abstract: An 18-year-old male patient presented to our epilepsy clinic with episodes of involuntary movements, which started at the age of four. These episodes were characterised by dancelike and writhing movements on one or both sides of the body and face. Episodes occurred 10 to 80 times a day with each lasting about 20 seconds. Awareness was fully retained. Episodes were triggered by voluntary activities, and he was able to induce an episode with sudden movements. The patient used Google and ChatGPT to find a diagnosis that explained his symptoms.
Disclosure: Nothing to disclose.

SPS06_3 | Paroxysmal visual symptoms

K. Orav
Neurology Department, North Estonia Medical Centre, Tallinn, Estonia

A 27-year-old female reports episodes of flickering in the right eye with a sensation of right eye lateral deviation. During these attacks, other people's speech fades away and she can experience nausea. Headache may follow. These episodes started when she was 10 years old and currently occur almost daily. They usually last a few seconds, but vision can be impaired for hours. The attacks can be provoked by stressful situations. Additionally, the patient has separate episodes of retrograde amnesia lasting 24 hours which occur every 3 months.
Disclosure: Nothing to disclose.

EAN/ESC: Neurology & cardiology meet epilepsy and critical care

SPS07_1 | Heart-brain-interaction in cardiovascular disease

T. Lüscher
Zurich Heart House, Zurich, Switzerland

The heart and the brain interact extensively within the body. The two organs are connected by neural pathways, such as the sympathetic nervous system and the vagal nerve, regulating heart rate and cardiac contractability as well as vasomotor tone of the coronary circulation via beta-and alpha-adrenergic receptors. Furthermore, the heart feeds back signal into the brain, particularly through pain pathways, reaching the thalamus and the frontal cortex during episodes of ischaemia, leading to the perception of angina. Thus, the neural pathways affecting the brain and the heart are closely interconnected, in particular with the midbrain, such as the amygdala and hippocampus, thalamus and other centres.

A classic example of a cardiac disease that is basically a neurological condition with the heart as a target organ is the Takotsubo syndrome, mainly effecting post-menopausal women. Our research has shown that appropriate processing of physical and psychological stimuli entering into the amygdala and hippocampus leads, due to inappropriate signal processing, to an overactivation of the sympathetic nervous system with a search of catecholamines and also endothelin leading to an increased vascular resistance, ischaemia with chest pain and eventually left ventricular dysfunction in the form of apical ballooning, mid-ventricular, basal or antero-lateral wall motion abnormalities. Although commonly transient in nature, the Takotsubo Syndrome is associated with significant complications, such as ventricular tachycardia and fibrillation, cardiogenic shock and cardiovascular death.
Similarly, the activity of the activity of the amygdala determines outcomes in patients with coronary artery disease. The activity of this mid-brain structure, as assessed by 18Flurodeoxyglucose positron emission tomography, is predictive of a major cardiovascular events during long-term following up suggesting that anxienty and other emotions do impact on the heart leading to increased major cardiovascular events.
Thus, neurophysiological research has markedly improved our understanding of the interaction of brain structures with the heart and the possible involvement of psychological and neurogenic factors in cardiovascular disease.
Disclosure: Nothing to disclose.

SPS07_2 | Sudden unexpected death in epilepsy (SUDEP)

P. Ryvlin
Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland

SPS07_4 | Hypothermia and brain protection after cardiac arrest - neurologic perspective

T. Cronberg
Lund University Hospital, Department of Neurology, Lund, Sweden

A cardiac arrest is typically caused by myocardial ischemia and it is a leading cause of death. Patients who are resuscitated usually remain unconscious on arrival and most will be transferred to an intensive care unit where approximately half will die during the coming week, most after a decision to withdraw intensive care based on a presumption of a poor neurological prognosis for meaningful recovery.
Whole body cooling before the onset of circulatory arrest will mitigate most pathological processes and has undisputable brain protective effects in experimental models and in numerous case reports of cold-water drowning where survival with good outcome has been reported after >2 hours cardiac arrest with body temperature as low as 13°C. This protective effect is still used in thoracic surgery.
In 2002, two clinical trials were published, presenting evidence that systemic hypothermia after a cardiac arrest lead to increased survival and neurological function. This started an era of optimism for a new treatment strategy with potential also in traumatic brain injury and stroke. Implementation was rapid as was the development of new invasive and non-invasive technology to cool. However, large trials with strictly controlled neuroprognostication and long-term follow-up have failed to show any difference in outcome between patients treated with 33 versus 36°C (TTM-trial) and 33°C versus normothermia with fever prevention (TTM2-trial). Accordingly, international guidelines have been updated to recommend fever prevention only.
This lecture will discuss current state of the art and remaining knowledge gaps for hypothermia as a treatment strategy for cardiac arrest victims.
Disclosure: Nothing to disclose.

SPS10_1 | Acute and chronic stress, its complications, and the benefits of relaxation methods

M. Hilz
University of Erlangen-Nuremberg, Germany, and Icahn School of Medicine at Mt. Sinai, New York, USA

Stress imperils physical and mental health. Hans Selye coined the term "Stress" and described it as "nonspecific response of an organism to any noxious or aversive event". He distinguished chronic stress responses from the acute stress response that was first described by Walter Cannon as "Fight-or-Flight-Response". Selye recognized that chronic stress induces a response pattern that he called "General-Adaptation-Syndrome": after an initial "alarm-phase", the organism tries to maintain homeostasis by activating coping strategies. After this "resistance-phase" follows the "exhaustion-phase". Now, the organism is prone to disease or death. In response to stress, the so-called "central stress system" mediates the "stress-syndrome", a range of responses that imply interactions of the central nervous system with endocrine pathways and the immune system. The "central stress system" is intertwined with the central autonomic network and activates the hypothalamic-pituitary-adrenocortical axis. Stress-induced adrenaline release stimulates the renin-angiotensin-aldosterone system. Arginine-vasopressin release increases renal water retention and affects blood pressure. The "stress-syndrome" further involves catecholamine-associated inflammasome upregulation. While sympathetic outflow increases, parasympathetic activity and its effects on organs as well as vagus-mediated anti-inflammatory effects decrease. Acute stressors may trigger syncope, arrhythmias, coronary artery occlusion, sudden death, Takotsubo syndrome, hypertensive crises, fear, panic attacks, etc. Chronic stress sequelae include obesity, diabetes, arterial hypertension, renal failure, stroke, myocardial infarction, pain syndromes, gastrointestinal, sexual, or cognitive dysfunction, depression, fatigue, burn-out syndrome, pseudo-dementia, etc. Endurance training, breathing techniques, Yoga, Tai-Chi, meditation, prayer, olfactory stimuli, music, progressive muscle-relaxation, functional relaxation, or autogenic training mitigate negative stress effects.
Disclosure: Related to this presentation I have nothing to disclose. I received honoraria for lecturing from Sanofi and travel support from Sanofi and Amicus Therapeutics.

SPS10_2 | What is autogenic training?

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Autogenic Training (AT) is a relaxation technique developed by the German psychiatrist Johannes Heinrich Schultz (1884–1970) and published in 1932. AT is widely used to counterbalance the negative effects of an acute or chronic "Stress-syndrome". In contrast to many relaxation techniques, AT yields "self-generated" relaxation. Different from mediation techniques that use and repeat mantras, or from Progressive Muscle Relaxation which induces relaxation indirectly via voluntary repetitive contractions and relaxation of specific muscle groups, AT generates relaxation via self- or auto-suggestion and passive, mental focusing on bodily perceptions, such as heaviness and warmth of a limb, sensations that in turn induce mental and physical relaxation with inner calm and tranquility. Persons practicing AT silently repeat a set of formulas that suggest and predict sensations that very likely occur regularly during AT, such as heaviness or warmth of a limb or perceiving free, automatic, slow respiration. Perceiving these sensations and breathing slowly and deeply augment parasympathetic and attenuate sympathetic outflow and thus mitigate or counterbalance the detrimental effects of acute or chronic stress. Electroencephalogram recordings during AT show increased alpha activity and reduced theta activity which indicates that the trainee is not dozing or sleeping but alert. Regularly practicing AT has shown beneficial effects in multiple somatic and mental disorders, including, for example, headaches, arterial hypertension, coronary artery disease, preeclampsia, asthma, pain disorders, functional sleep disorders, anxiety, depression, dysthymia, sexual arousal dysfunction, impaired memory or concentration. AT should not be used by psychotic persons.

Disclosure: I have nothing to disclose related to this presentation. I received lecturing honoraria from Sanofi and travel support from Sanofi and Amicus Therapeutics.

SPS10_3 | Condensed introductory course of autogenic training

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Autogenic Training (AT) uses formulas that suggest – and predict – sensations that subsequently manifest in most AT-trainees, such as heaviness or warmth of limbs. While the trainee mentally repeats phrases that predict a sensation, the incipient, actual perception of this sensation reinforces the prediction as factual experience and thus corroborates the trainee's expectation and confidence that the self-suggestions will indeed yield the predicted sensations that reflect and further relaxation. Hence, AT is based on observations of physiological phenomena and does not impose any external values, philosophies, or esoteric beliefs on trainees. The self-suggestive formulas aim at perceiving and enhancing sensations of muscular relaxation sensed as heaviness of limbs, improved limb perfusion sensed as perception of warmth, stable cardiac function and rhythm perceived as regular, calm, and stable heart-beat, enhanced, steady and unobstructed respiration perceived as automatic, free, and comforting regular breathing, increased splanchnic and bowel perfusion and function perceived as abdominal or epigastric warmth, and comfortable temperature or perfusion of the (fore)-head perceived as "comfortable coolness of the forehead". The very first self-suggestion seems difficult in stressful situations but is effective: the trainee self-suggests tranquility and calm to reach a state of focused silence and concentration. "I will be calm", "nothing will disturb me" help achieve a state that facilitates perceiving the sensations predicted and induced by the aforementioned self-suggestions. AT should be practiced regularly. Initially, two or three daily 20-minute sessions might be needed for several weeks to achieve all self-suggested effects of AT.

Disclosure: I have nothing to disclose related to this presentation. I received lecturing honoraria from Sanofi and travel support from Sanofi and Amicus Therapeutics.

Monday, June 23 2025

European Journal of Neurology: Clinical research that changed practice

SPS08_1 | Pathophysiological underpinnings of recanalization therapies

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Stroke is the second-leading cause of death and the third-leading cause of combined death and disability worldwide. Acute ischemic stroke results from the occlusion of cerebral arteries, leading to a cascade of events including energy failure, excitotoxicity, and oxidative stress. Recanalization therapies, such as intravenous thrombolysis (IVT) and endovascular thrombectomy (EVT), aim to restore blood flow and mitigate these deleterious processes. Alteplase was the first thrombolytic used in the treatment of acute ischemic stroke, but it is increasingly being replaced by tenecteplase, a genetically modified tissue plasminogen activator with potentially superior efficacy in large vessel recanalization and practical workflow advantages. EVT, in addition to IVT, has been proven beneficial over IVT alone in patients with large vessel occlusions. However, outcomes are not always favorable even when successful recanalization of the occluded blood vessel is achieved. While successful recanalization is necessary for reperfusion, it does not guarantee it. The underlying pathophysiological mechanisms for recanalization and reperfusion are complex and multifaceted, involving molecular and cellular processes. Several mechanisms can cause tissue damage even if successful reperfusion is achieved. These include incomplete reperfusion/microvascular obstruction, blood-brain barrier breakdown with resulting hemorrhagic complications and inflammatory changes, reperfusion- and excitotoxicity-related injury, and secondary changes post-infarction, including brain atrophy. Understanding these mechanisms is crucial for developing strategies to enhance the efficacy of recanalization

therapies. Several promising neuroprotectant candidates as adjunctive treatments to recanalization therapies have been identified to further improve patient outcomes by preventing post-recanalization tissue damage; however, none have been approved for clinical use yet.
Disclosure: Nothing to disclose.

SPS08_2 | Autoimmune nodopathies

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Autoimmune nodopathy (AN) is a rare neuromuscular disorder affecting the nodes of Ranvier of myelinated axons in peripheral nervous system. Insofar, four pathogenic autoantibodies have been associated with AN and are good diagnostic and prognostic biomarkers. These autoantibodies target cell adhesion molecules which play crucial role in the function and formation of the node of Ranvier and of the paranodal region: neurofascin-155 (Nfasc155), neurofascin-186 (Nfasc186), contactin-1 (CNTN1) and anti-contactin associated protein 1 (CASPR1). Autoantibodies in AN are mainly of the IgG4 isotype. Since 2021, AN has been recognized as a separate pathological entity from chronic inflammatory demyelinating polyneuropathy (CIDP) due to the presence of these well-described pathogenic antibodies and a specific response to therapeutic strategies. In this presentation, we will outline the clinical presentations and therapeutic responses of AN, and the specificities associated with each autoantibody. We will also recapitulate the knowledge on the pathogenic mechanisms responsible for AN, and particularly the implication of IgG4 autoantibodies in conduction slowing. Therapeutic anti-CD20 monoclonal antibodies and plasma exchange have been shown to be efficient in AN. The potential of novel therapeutic strategies will be approached as well as the strengths and limitations of available autoantibody diagnosis tools. Altogether, this should bring a broad overview of the current knowledge on AN diagnosis, treatment, and physiopathology.
Disclosure: Nothing to disclose.

SPS08_3 | CGRP in migraine pathophysiology

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Calcitonin gene–related peptide (CGRP) is now recognized as a key mediator of migraine. Released from activated trigeminal fibers, CGRP promotes vasodilation and neurogenic inflammation, setting the stage for migraine pain. The advent of oral "gepants" and monoclonal antibodies against CGRP or its receptor has revolutionized both acute and preventive migraine management, offering sustained reductions in attack frequency with favorable tolerability. This lecture will trace CGRP's journey from peptide discovery to the clinic, highlighting pivotal human models and the therapeutic breakthroughs that have reshaped migraine care.
Disclosure: MA is a consultant, speaker, or scientific advisor for AbbVie, Astra Zeneca, Eli Lilly, GlaxoSmithKline, Lundbeck, Pfizer, and Teva; a primary investigator for ongoing AbbVie, Lundbeck and Pfizer trials. MA reports research grants from Lundbeck Foundation and Novo Nordisk Foundation (all to institution). MA serves as associate editor of the Journal of Headache and Pain and associate editor of Brain.

Breakthroughs in treatment Neurology—Part 2

SPS09_1 | Rejection and approval: Lecanemab and the future of anti-amyloid treatments

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The advent of monoclonal antibodies targeting amyloid-beta represents a groundbreaking shift in Alzheimer's disease (AD) treatment, offering the first disease-modifying therapies for early-stage AD. While these treatments have demonstrated amyloid clearance and modest slowing of cognitive decline in clinical trials, their real-world impact remains uncertain. Strict eligibility criteria limit patient access, with studies indicating that only a fraction of individuals with modest cognitive involvement qualify for treatment (1, 2). The EMA initially rejected lecanemab due to concerns over its clinical significance, as its modest cognitive benefits did not outweigh the risks, particularly amyloid-related imaging abnormalities (ARIAs) (3). However, following further review and pressure from advocacy groups and clinicians, the EMA later granted approval, reflecting the ongoing debate over the balance between biological efficacy and meaningful clinical outcomes. Despite regulatory acceptance, the lack of long-term efficacy data and the challenges of implementation in routine clinical practice further complicate the widespread adoption of these therapies. As global regulatory agencies take divergent stances on approval, the discussion continues over whether anti-amyloid therapies truly alter the course of AD or merely offer biological rather than meaningful clinical benefits. Given the limitations of amyloid-targeting approaches, there is increasing attention toward alternative therapeutic targets, such as tau pathology, neuroinflammation, synaptic dysfunction, and metabolic pathways. Ongoing research into tau-targeting, anti-inflammatory, and neuroprotective agents may offer more comprehensive and effective treatment options in the future. Further real-world data and long-term studies are essential to determine the role of current and emerging therapies in AD management.
Disclosure: Nothing to disclose.

SPS09_2 | New concept to improve care: Rapid and early seizure termination

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SPS09_3 | Trial of N-Acetyl-L-Leucine in Niemann-Pick disease type C

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Introduction Niemann-Pick disease type C (NPC) is a rare, autosomal recessive neurodegenerative disorder. The IB1001-301 clinical trial was a Phase III, double-blind, randomized, placebo-controlled trial comparing N-acetyl-L-leucine (NALL) with placebo for treating neurological signs and symptoms in NPC after 12 weeks with a subsequent ongoing open-label extension phase. Methods Patients received treatment with orally administered NALL 2–3 times per day (patients 4-12 years receiving weight-based doses). The primary endpoint for the placebo-controlled parent study was the Scale for the Assessment and Rating of Ataxia (SARA). Following the parent study patients could enroll into an open-label extension phase. In the extension phase the primary endpoint was the modified 5-Domain NPC Clinical Severity Scale (5-Domain NPC-CSS); comparisons were made to the expected annual trajectory of disease decline established in published natural history studies. For both endpoints a lower score represents better neurological status. Results In the parent study a cohort of 60 NPC patients aged 5-67 years met its primary and all secondary end points. The mean (±SD) change from baseline in the SARA total score was −1.97±2.43 points after 12 weeks of receiving NALL and −0.60±2.39 points after 12 weeks of receiving placebo (least-squares mean difference, −1.28 points; 95% confidence interval, −1.91 to −0.65; P<0.001). The results for the secondary end points were supportive of the findings in the primary analysis. The incidence of adverse events was similar with NALL and placebo, and no treatment-related serious adverse events occurred. In the extension phase 54 patients aged 5–67 years were treated. The improvements in neurological status demonstrated in the parent study's primary SARA endpoint were sustained over the 24-month long-term follow-up: the mean (±SD) change from baseline on the 5-Domain NPC-CSS was -0.24 (±2.69) on NALL, compared to +3.0 (±6.32) in the historical cohort: mean difference -3.24 (95% Confidence Interval (CI) -5.59 to -0.89; $p = 0.009$). NALL was well-tolerated, and no treatment-related serious AEs occurred. Conclusion Treatment with NALL for 12 weeks led to a significant improvement in neurological status compared to placebo. The continued treatment with NALL over 24 months was associated with a statistically significant and clinically meaningful reduction in disease progression and consistent with a neuroprotective, disease-modifying effect.
Disclosure: Nothing to disclose.

SPS09_4 | Persistent remission from treatment refractory autoimmune neuropathies by autologous CD19-targeted CAR T cell therapy

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Objective: To demonstrate the efficacy of autologous anti-CD19 CAR T cell therapy in two severe cases of autoimmune neuropathies Methods: Two patients with a history of more than 12 months of severe tetraparesis with insufficient response to established immunotherapies were selected from our clinical cohort of autoimmune neuropathies. Patients' lymphocytes were collected by leukapheresis. CD3+ selected T cells were transduced with a second-generation anti-CD19 CAR construct (KYV-101, Kyverna Therapeutics, Inc., CA, USA) resulting in CAR/KYV-101 expression in 78 % (patient 1) and 66 % (patient 2) of T lymphocytes, respectively. Following standard lymphodepletion with fludarabine (30 mg/m^2) and cyclophosphamide (300 mg/m^2) CAR T cells were administered following established procedures. Results: Patients exhibited only moderate side effects after CAR T cell infusion and continuous improvement of neurological symptoms occurred starting at week 4 post CAR T cell transfer. Even without continuation of previous immunotherapies they stabilized. At 6 months post transfer they were already able to perform squats and pull-ups or walk independently over 200 meters respectively with subsequent continuous improvement. Conclusion: Even with the availability of modern treatment approaches via anti-FcRn antibodies or complement neutralization for chronic autoimmune neuropathies most severe disease courses still exist. CAR T cell-based therapy may be an alternative for those patients.
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SPS09_5 | Acetyl-DL-leucine in two individuals with REM sleep behavior disorder improves symptoms, reverses loss of striatal dopamine-transporter binding and stabilizes pathological metabolic brain pattern – case reports—3-year follow-up

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Introduction: Isolated REM Sleep Behavior Disorder (iRBD) is considered a prodrome of Parkinson's disease (PD). Methods: We investigate whether the potentially disease-modifying compound acetyl-DL-leucine (ADLL; 5g/d) has an effect on prodromal PD progression in 2 iRBD-patients. Outcome parameters are RBD-severity sum-score (RBD-SS-3), dopamine-transporter single-photon emission computerized tomography (DAT-SPECT) and metabolic "Parkinson-Disease-related-Pattern (PDRP)"-z-score in 18F-fluorodeoxyglucose positron emission tomography (FDG-PET). Results After 3 weeks ADLL-treatment, the RBD-SS-3 drops markedly in both patients and remains reduced for >18 months of ADLL-treatment. In patient 1 (female), the DAT-SPECT putaminal binding ratio (PBR) decreases in the 5 years pretreatment from normal (1.88) to pathological (1.22) and the patient's FDG-PET-PDRP-z-score rises from 1.72 to 3.28 (pathological). After 22 months of ADLL-treatment, the DAT-SPECT-PBR increases to 1.67 and the FDG-PET-PDRP-z-score

stabilizes at 3.18. Similar results are seen in patient 2 (male): his DAT-SPECT-PBR rises from a pretreatment value of 1.42 to 1.72 (close to normal) and the FDG-PET-PDRP-z-score decreases from 1.02 to 0.30 after 18 months of ADLL-treatment. We will present follow-up data of the 2 RBD patients after 2.5 to 3 years of ADLL-therapy on the patient-related subjective RBD-severity score and the two objective imaging procedures DAT-SPECT and FDG-PET. Conclusion The results support exploration of whether ADLL may have disease-modifying properties in prodromal PD. Oertel et al. Nature Communications 2014 Supported by ParkinsonFonds Deutschland.

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SPS09_6 | Parkinson's disease in Africa; from Genome wide association to novel genetic mechanism

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In Parkinson's disease (PD), large-scale genome-wide-association-studies (GWAS) in European, Asian, and Latin American populations have identified multiple risk-loci. One particular PD risk-gene of interest is GBA1 gene which encodes glucocerebrosidase (GCase).

Until recently, PD in African populations remain completely unexplored. We performed a comprehensive genome-wide-assessment of PD in 197,918 individuals (1,488 cases; 196,430 controls) of African (Nigerian) and African-admixed ancestry, characterizing population-specific risk, coding and structural genetic variation. We identified a novel common risk-factor for PD and age-at-onset at the GBA1 locus (risk, rs3115534T>G; OR = 1.58, 95% CI = 1.37-1.80, $p = 2.397E-14$). Sequencing did not reveal any coding/structural variation. However, we identified GBA1 rs3115534T/G signal mediates PD risk via expression quantitative-trait locus (eQTL) mechanisms, found to be extremely rare in non-African populations.

Using full-length RNA transcript sequencing, we identified partial intron-8 expression in risk variant carriers (G) but not in nonvariant carriers (T). Clustered regularly interspaced short palindromic repeats editing of the reported index variant (rs3115534) revealed that this sequence alteration is responsible for driving the production of transcripts containing intron-8. We showed the variant is a key intronic branchpoint sequence and measuring glucocerebrosidase activity, we identified a dose-dependent reduction in risk variant carriers, a potential therapeutic target in an underserved and underrepresented population.

Disclosure: Nothing to disclose.

Condensed Autogenic Training Session (Part 2)

SPS11_1 | Condensed autogenic training session

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This session recapitulates the Autogenic Training (AT) concept and practices AT. Participants in the first session can deepen their AT experiences, newcomers may start perceiving relaxing AT effects. AT is practiced in a quiet environment. Participants should join with “an empty bladder and an open mind”. They shall turn off phones, remove watches, glasses, wear comfortable clothes, and loosen tight clothing. AT is practiced in a comfortable, sitting, reclined, or lying position. AT-participants should internalize the trainer's hetero-suggestions and repeatedly self-suggest the proposed sensations. They can close their eyes but shall not fall asleep. The initial suggestion conveys calm and resilience against any disturbances. Then follow suggestions of heaviness and afterwards warmth of the arms and legs. The subsequent suggestion “the forehead is comfortably cool” helps avoid unpleasant sensations of a warm or hot head potentially associated with hotheadedness. Of note, cold-face stimulation induces parasympathetic activation. The next suggestion of a calm, comfortable, rhythmic, and regular heartbeat furthers relaxation. Then follows the self-suggestion of free, automatic, unrestricted, and comfortable breathing. Slow breathing again augments cardiovagal activity and thus relaxation. The so-called “solar plexus exercise” suggests that the upper abdominal or epigastric area with its large vasculature and autonomic nerve plexus is pleasantly warm and well-perfused. There are additional suggestions such as warmth and relaxation of the neck and shoulders, or individual formulas. Participants may end AT by actively reestablishing muscle tone and full alertness. Consequent AT reduces negative stress effects and mitigates somatic or mental complaints.

Disclosure: I have nothing to disclose related to this presentation. I received lecturing honoraria from Sanofi and travel support from Sanofi and Amicus Therapeutics.

ABSTRACT

Oral Presentation

Saturday, June 21 2025

Motor Neurone Diseases

OPR-001 | Glymphatic dysfunction in clinical phenotypes of motor neuron disease

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Background and Aims: Converging evidence supports a key pathogenic role of the glymphatic system in the accumulation of pathological aggregates in several proteinopathies, including amyotrophic lateral sclerosis (ALS) and other motor neuron diseases (MNDs). This study aimed to verify glymphatic function impairment calculating diffusion tensor imaging analysis along the perivascular space (DTI-ALPS) and explore its clinical correlations in MND phenotypes.

Methods: Fifty-seven MND patients (41 ALS, 7 with lower motor neuron, and 9 with upper motor neuron presentations) and 32 age- and sex-matched healthy controls underwent 3 Tesla brain MRI, including DTI sequences. We obtained DTI-ALPS index from each individual, evaluating its relationship with measures of motor and cognitive disability, site of symptom onset, cognitive status, and fractional anisotropy (FA) of white matter tracts. Comparisons between groups were evaluated using ANCOVA models, age- and sex-adjusted. Partial correlations with clinical and cognitive measures were also tested.

Results: MND patients exhibited significantly reduced DTI-ALPS index values compared to healthy controls ($p < 0.001$). Patients with bulbar onset had lower DTI-ALPS values than those with spinal onset ($p = 0.046$). Similar DTI-ALPS values were found across all MND phenotypes, with no effect of cognitive diagnosis or C9orf72 expansion status. Significant correlations were identified between DTI-ALPS and disease duration ($r = -0.30$, $p = 0.03$), as well as FA values in the anterior corona radiata ($r = 0.31$, $p = 0.02$) and body of the corpus callosum ($r = 0.37$, $p = 0.049$).

Conclusion: This study confirms glymphatic dysfunction across MND phenotypes, particularly in bulbar-onset cases, supporting a pathogenic involvement of this system for the accumulation of TDP-43 proteinopathy in MND.

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OPR-002 | Tofersen in the treatment of SOD1 ALS—experience from the Polish EAP

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Background and Aims: Tofersen is approved for the treatment of amyotrophic lateral sclerosis (ALS) caused by SOD1 mutations. We prospectively analyzed its effectiveness in participants of the expanded access programs (EAP) in Poland.
Methods: Twenty SOD1-ALS patients (11 FALS and 9 SALS, 65% males) qualified to EAP between 10.2023 and 08.2024. The analysis included the demographic and genetic data, ALS functional rating scale-revised (ALSFRS-R), delta ALSFRS-R, forced vital capacity (FVC), and NfL CSF concentration.
Results: Median age of disease onset was 51 years, age at tofersen administration - 53 years and the disease duration - 28 months. The mean duration of tofersen treatment was 11 months (5–15 months). Mean delta ALSFRS-R delta ranged from 0,19 prior to treatment to 0,14 at the last assessment. One patient withdrew after the first tofersen administration due to clinical state. Twelve patients (63%) showed an increase of ALSFRS-R by 1–2 points in the treatment period, 4 patients (21%) stabilized, while 3 patients (16%) showed further progression. The NfL concentration decreased in 6/7 of analyzed patients, while delta ALSFRS-R decreased in 80% of patients with stable/increased functional state and only 33% with decreasing ALSFRS-R. The treatment was well tolerated in 95% of patients. One patient experienced SAE after the 9th infusion – a transverse myelitis with fever, myalgia and gait disturbance (ALSFS-R drop from 40 to 39/48), which completely resolved within 8 weeks after iv methylprednisolone treatment and physical therapy.
Conclusion: the data supports the clinical andë molecular response to tofersen in SOD1-ALS.
Disclosure: Authors participated in the advisory boards for Biogen (MKK, MK) and Ferrer (MKK); MKK obtained financial compensations from Biogen and Ferrer for lectures on ALS.

OPR-003 | Predictors in late-stage amyotrophic lateral sclerosis

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Background and Aims: Prognostic factors in amyotrophic lateral sclerosis (ALS) are defined by clinical features, progression rate and physiological changes at first observation or over follow-up. The prognostic factors associated with late-stage disease are uncertain. We sought to identify factors predicting survival in advanced ALS.
Methods: We collected data from patients followed at our clinic and analysed a subgroup with late-stage ALS defined as ALSFRS-R≤24. We characterized this population by examining demographic and clinical variables, including phenotype, sex, age, disease duration at diagnosis, non-invasive ventilation (NIV), percutaneous endoscopic gastrostomy (PEG), early and late disease progression rates measured by ALSFRS-R score and survival. Multivariate analysis with Cox regression was performed to ascertain predictive factors for survival in late-stage.
Results: We included 704 late-stage ALS patients (Group A) with 260 having at least 6 more months of follow-up (Group B). Factors associated with short survival in late-stage were onset-age (age > 54 years, HR 2.15, 1.49–3.09), bulbar-onset (HR 1.67, 1.05–1.87), diagnostic delay (≥12 months, HR 0.61, 0.40–0.92) and progression rate until late-stage (ΔFS until late-stage> 0.55, HR 3.56, 2.25–5.64). PEG and NIV in the late-stage were not independent predictors of survival.
Conclusion: Independent predictors of late-stage ALS survival include onset-age, onset-region, diagnostic delay, and functional decline (ΔFS) until late-stages (but not at diagnosis). For this group, monitoring functional decline during follow-up is valuable for prognosis.
Disclosure: Nothing to disclose.

OPR-004 | Abstract withdrawn

OPR-005 | Identifying mild cognitive and behavioural dysfunction in amyotrophic lateral sclerosis provides key prognostic insights

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Background and Aims: Amyotrophic lateral sclerosis (ALS) is a multisystem neurodegenerative disease encompassing cognitive and behavioral impairments. The Revised Diagnostic Criteria for ALS-frontotemporal spectrum disorder (ALS-FTDS), while widely adopted, may overlook subtle impairments such as memory and visuospatial deficits, limiting their prognostic value. This study aimed to apply the Mild Neurocognitive-Behavioural Dysfunction (MiND) approach, adapted from other neurodegenerative diseases to ALS patients and assessed its prognostic utility for survival and disease progression.
Methods: A prospective cohort of 201 ALS patients was evaluated between January 2018 and July 2024. Participants underwent comprehensive cognitive and behavioral assessments. The MiND approach identified patients with mild cognitive impairment (MCI), mild behavioral impairment (MBI), or combined mild cognitive-behavioral impairment (MCBI). Prognostic value was analyzed using Kaplan-Meier survival curves, Cox proportional hazards models, and logistic regression for disease progression, adjusting for clinical covariates.

Results: MiND was identified in 67% of patients previously classified as cognitively normal by the Revised Diagnostic Criteria for ALS-FTDS. At a median follow-up of 15 months, these patients had shorter tracheostomy-free survival compared to those with normal cognition (all $p < 0.005$). Mild cognitive impairment (HR 5.7; CI 1.26–25.82; $p = 0.024$) and frontotemporal dementia (HR 4.7; CI 1.01–21.4; $p = 0.04$) independently predicted poor outcomes. Logistic regression showed mild cognitive-behavioral impairment and frontotemporal dementia were associated with rapid disease progression (both $p < 0.019$).

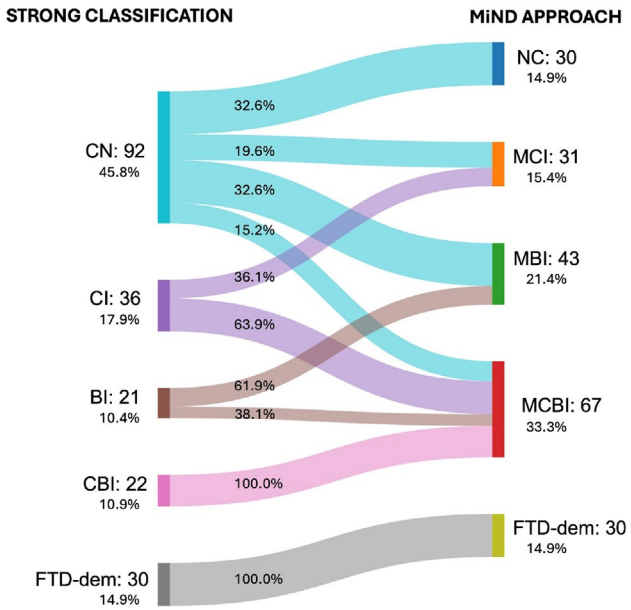

FIGURE 1 Sankey Diagram Comparing Patient Transitions Between Strong classification and MiND approach for Cognitive and Behavioral Impairments in ALS.

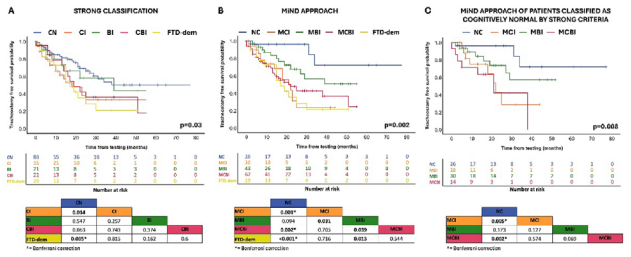

FIGURE 2 Survival analysis according to MiND approach, Strong criteria, and in the subgroup of patients classified as cognitively normal according to Strong criteria.

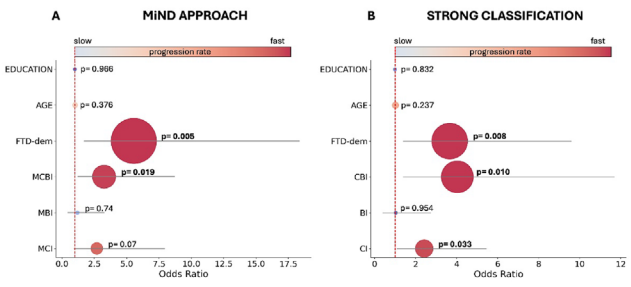

FIGURE 3 Binary logistic regression for disease progression rate

Conclusion: The MiND approach enhances detection of mild cognitive and behavioral impairments in ALS, providing prognostic insights and improving stratification over ALS-FTDS criteria. This supports personalized care and clinical trial design for early disease stages.
Disclosure: Nothing to disclose.

OPR-006 | The brain functional neural organization of apathy and depression in ALS: A connectome-based study

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Background and Aims: Apathy and depression are the most prevalent neuropsychiatric symptoms in Amyotrophic Lateral Sclerosis (ALS). Although insufficiently investigated, their distinction holds important clinical relevance for accurate diagnosis of ALS with behavioural impairment, and for patients' prognosis and management. In the present study, we aimed to assess both apathy and depressive symptoms in patients with ALS and whether they have similar or different functional neural correlates.
Methods: Using graph analysis and connectomics, global and lobar nodal properties and regional functional brain connectivity were assessed in ALS patients without apathy/depression (ALSn, $n = 42$), with apathy without depression (ALSa, $n = 14$), with depressive symptoms without apathy (ALSd, $n = 20$), with apathy and depressive symptoms (ALSad, $n = 6$) and 46 healthy controls. Correlations between brain functional properties, apathy and depressive symptoms were performed in all patients.
Results: Depressive symptoms were related with reduced path length within bilateral basal ganglia (BG) network, apathy was related with increased path length, decreased nodal strength

and local efficiency within left BG network. ALSa patients showed altered functional nodal properties within BG network compared to ALSn and ALSd. Compared to healthy controls and all non-apathetic patients (ALSn and ALSd), all apathetic patients (ALSa and ALSad) exhibited altered functional nodal properties within parietal, occipital and frontal networks. Non-apathetic patients, compared to apathetic patients, showed relatively preserved functional nodal properties in the BG network.
Conclusion: Our findings indicate differences in brain functional neural organization associated with apathy and depression, underscoring the importance of distinguishing these symptoms in ALS and highlighting the need for targeted interventions.
Disclosure: Funding: ERC (StG-2016_714388_NeuroTRACK); Next Generation EU, in the context of the National Recovery and Resilience Plan, Investment PE8 - Project Age-It: "Ageing Well in an Ageing Society". Disclosures. EC and SB received grants from Italian Ministry of Health (IMH); FV is Associate Editor (AE) JAD; BP received compensation from Liquidweb srl; AE Frontiers in Neuroscience; VS received compensation from AveXis, Cytokinetics, Italfarmaco, Liquidweb S.r.l., Novartis Pharma AG, Amylyx Pharmaceuticals, Biogen and Zambon Biotech SA; received supports from IMH, AriSLA, E-Rare JTC; Editorial Board of ALS/FTD, European Neurology, AJND, Frontiers in Neurology, Exploration of Neuroprotective Therapy; MF received compensation from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, IMH, Italian Ministry of University and Research (IMUR), FISM; FA received speaker honoraria from Biogen Idec, Roche, Eli Lilly, GE Healthcare; receives research supports from IMH, IMUR, AriSLA, ERC, EU JPND Research, Foundation Research on AD (France).

Headache 1

OPR-007 | Probability of response to subcutaneous anti-CGRP monoclonal antibodies in migraine: How long should we wait?

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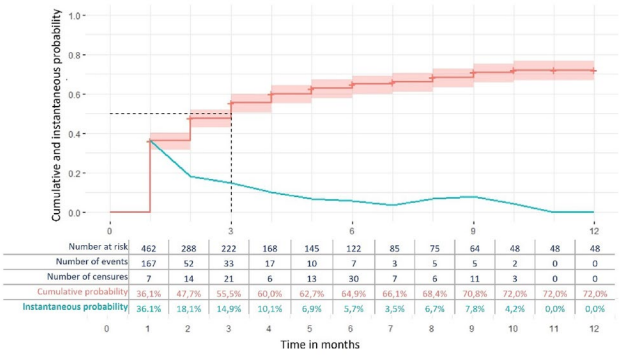
Background and Aims: Guidelines recommend evaluating the response to anti-CGRP monoclonal antibodies (A-CGRP mAbs) at 3–6 months, but studies analyzing month-by-month response probability are lacking.
Methods: Cumulative and instantaneous response probabilities were analyzed in patients treated with subcutaneous A-CGRP mAbs, defining response as a ≥50% reduction in headache frequency. Kaplan-Meier analysis was used to estimate survival function and response probabilities. Cox regression evaluated clinical covariates.
Results: Among 462 patients (76.6% with chronic migraine; 86.8% female; median age 48 years, IQR 41–56), cumulative response probability increased from 36.1% (95% CI: 31.6–40.4) in the first month to 72% (95% CI: 66.7–76.6) at 12 months. Monthly instantaneous response probability decreased from 36.1% (95% CI: 31.6–40.4) in the first month to 14.9% (95% CI: 14.5–15.4) in the third month, remaining below 10% from the fourth month onward. Multivariable analysis showed higher response probability with hemicranial pain (HR 1.31, 95% CI: 1.01–1.70) and photophobia (HR 1.64, 95% CI: 1.07–2.52), but lower in males (HR 0.68, 95% CI: 0.46–0.99), with more prior preventives (HR 0.95, 95% CI: 0.91–0.99), and higher baseline headache frequency (HR 0.97, 95% CI: 0.95–0.99).



Number at risk	462	288	222	168	145	122	85	75	64	48	48	48
Number of events	167	52	33	17	10	7	3	5	5	2	0	0
Number of censures	7	14	21	6	13	30	7	6	11	3	0	0
Cumulative probability	36,1%	47,7%	55,5%	60,0%	62,7%	64,9%	66,1%	68,4%	70,8%	72,0%	72,0%	72,0%
Instantaneous probability	36.1%	18,1%	14,9%	10,1%	6,9%	5,7%	3,5%	6,7%	7,8%	4,2%	0,0%	0,0%
	0	1	2	3	4	5	6	7	8	9	10	11	12

FIGURE 1 Cumulative and instantaneous probability

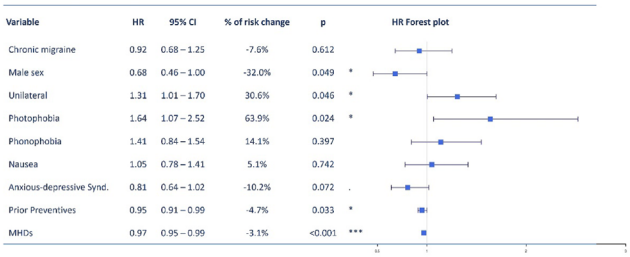


FIGURE 2 Multivariable Cox Regression

Conclusion: The highest response probability occurred in the first trimester and was influenced by factors such as baseline headache burden and photophobia. Although late responses are possible, the low probabilities suggest considering a treatment change unless it represents the last therapeutic option.
Disclosure: Nothing to disclose.

OPR-008 | European multicenter study on the use of anti-CGRP monoclonal antibodies in migraine: The 2-year follow-up

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Background and Aims: To describe the long-term effectiveness of monoclonal antibodies targeting calcitonin gene-related peptide (anti-CGRP mAbs) in a European cohort of migraine patients.
Methods: European multicenter, observational study based on prospective registries of adult patients with high-frequency episodic or chronic (CM) migraine treated with anti-CGRP mAbs. We collected demographic data, efficacy variables (monthly headache days-MHD; monthly migraine days-MMD) up to 24 months (M24). We compared patients reaching M24 (ON-group) with those who discontinued the treatment due to lack of effectiveness at any time (OFF-group).
Results: 1340 patients reached M24 (ON-group: median age 48 years [41,55], 81.7% (1095/1340) females). Median basal frequencies at baseline were: 20 (13, 28) MHD and 15 (11, 21) MMD. At M24, the median reductions were: −10 (−17, −5) in MHD and −9 (−14, −4) MMD. At baseline, 936/1340 (69.9%) had CM; of these 746/936 (79.7%) still fulfilled CM diagnosis at M24, whereas 190/936 (20.3%) converted to EM. 1057 patients discontinued the treatment due to efficacy (OFF-group). Compared to the ON-group, there were no differences in sex or age, but the OFF-group had statistically significant higher proportions of CM (ON: 69.9% vs. OFF: 82.9%), depression (ON: 24.0% vs. OFF: 38.0%), anxiety (ON: 30.7% vs. OFF: 41.0%) and obesity (ON: 7.2% vs. OFF: 19.1%) ($p < 0.001$).
Conclusion: For patients reaching 2 years of treatment, effectiveness is similar to the one reported at short-term. Chronification, psychiatric and metabolic comorbidities hinder treatment response, making early migraine prevention and management of comorbid conditions essential for better care
Disclosure: EC has received honoraria from Novartis, Chiesi, Lundbeck, MedScape, Lilly; his salary has been partially funded by Río Hortega grant Acción Estratégica en Salud 2017–2020 from Instituto de Salud Carlos III (CM20/00217) and Juan Rodés fellowship, Subprograma Estatal de Incorporación de la Acción Estratégica en Salud 2023 (JR23/00065). PPR has received, in the last three years, honoraria as a consultant and speaker for: AbbVie, Biohaven, Chiesi, Eli Lilly, Lundbeck, Medscape, Novartis, Pfizer and Teva. Her research group has received research grants from AbbVie, Novartis and Teva; as well as, Instituto Salud Carlos III, EraNet Neuron, European Regional Development Fund (001-P-001682) under the framework of the FEDER Operative Programme for Catalunya 2014-2020 - RIS3CAT; has received funding for clinical trials from AbbVie, Amgen, Biohaven, Eli Lilly, Novartis, Teva. She is the Honorary Secretary of the International Headache Society.

OPR-009 | Neurosurgical interventions in idiopathic intracranial hypertension: A multicenter study on outcome and referral pattern

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Background and Aims: Neurosurgical interventions are recommended for fulminant or treatment-refractory idiopathic intracranial hypertension (IIH), but evidence on their outcomes, particularly regarding referral patterns and indications, is limited. We evaluated clinical outcomes and referral patterns for neurosurgical interventions in IIH, identifying predictors of beneficial or adverse outcomes.
Methods: A retrospective multicenter study was conducted by the Danish-Austrian IIH Consortium (DASH-IIH) across three centers (Vienna, Odense, Copenhagen). Patients with IIH

meeting revised Friedman criteria who underwent neurosurgical intervention between 2014 and 2024, with at least six months of follow-up, were included. Outcomes assessed at six months post-intervention included visual function, headache frequency (monthly headache days [MHD]), papilledema resolution, and severe adverse events (CTCAE grade ≥3).

Results: Thirty-six female patients were included (mean age 32.5 years, median BMI 37.0, median CSF opening pressure 41 cmH_2O). Ventriculo-peritoneal shunting (VPS) was performed in 27 (75%) patients and optic nerve sheath fenestration (ONSF) in 9 (25%). Acute or imminent visual loss was the primary indication in 83.3%, while 16.7% were referred for refractory headache. Visual function improved in 41.7%, papilledema resolved in 89.7%, and 30.6% experienced a ≥50% reduction in MHD (median reduction 4.5 days). Multivariate analysis showed no significant differences in outcomes or adverse events between VPS and ONSF. Referrals for refractory headache alone did not result in visual improvement (0%) and were significantly less likely to reduce headache frequency (OR 0.11, $p=0.012$).

Conclusion: VPS and ONSF are effective for acute or imminent visual loss in IIH. However, refractory headache alone may be an inappropriate indication for neurosurgical referral.

Disclosure: Gabriel Bsteh: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene/BMS, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting Biogen, Celgene/BMS, Merck, Novartis, Roche, Sanofi-Genzyme and Teva. He has received unrestricted research grants from Celgene/BMS and Novartis.

OPR-010 | Acute headache treatment in idiopathic intracranial hypertension: Treating to the phenotype?

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Background and Aims: Effective acute headache treatment is essential for improving the quality of life in people with idiopathic intracranial hypertension (pwIIH), though current guidance to "treat to the phenotype" lacks robust data.

Methods: This retrospective analysis used standardized headache diaries from the Vienna Idiopathic Intracranial Hypertension (VIIH) database (1-JUL-2021 to 30-JUN-2023). Three classes of acute medications (acetaminophen [APAP], NSAIDs, and triptans) were analyzed, with NSAIDs and ibuprofen as references. Headache attacks were classified per ICHD-3 as migraine (M), tension-type (TTH), or other (O). A 2-level nested logistic regression adjusted for individual covariance and propensity-weighted for age, sex, and headache severity.

Results: We analyzed 35,640 medication-outcome pairs from 23,507 headache attacks (45.3% M, 21.1% TTH, 33.6% O) in 156 patients (89.7% female, mean age 32.9 years). NSAIDs were most commonly used (M: 60.5%, TTH: 69.8%, O: 70.7%), followed by APAP and triptans. Triptans were the most effective across all headache types (OR for M: 4.8 [CI 3.9–6.1], TTH: 2.9 [CI 1.8–4.3], O: 3.1 [CI 2.2–4.3]). APAP was less effective for migraine (OR 0.81 [CI 0.74–0.90]) but similar to NSAIDs in TTH and O. In migraine, eletriptan and zolmitriptan (OR 6.0 and 5.8) were slightly more effective than sumatriptan (OR 5.0).

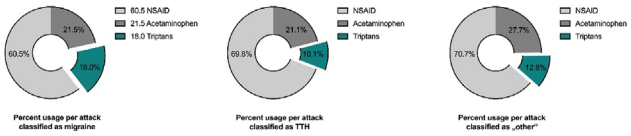

FIGURE 1

Conclusion: Triptans outperform NSAIDs and APAP in treating headaches in pwIIH, particularly for migraine-type attacks. These findings support the preferential use of triptans and challenge the "treating to the phenotype" approach.

Disclosure: GB: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene/BMS, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting Biogen, Celgene/BMS, Novartis, Roche, Sanofi-Genzyme and Teva. He has received unrestricted research grants from Celgene/BMS and Novartis.

OPR-011 | CGRP increase in tear fluid of migraine patients is reversed by anti-CGRP monoclonal antibodies

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Background and Aims: CGRP has emerged as a key player in migraine pathophysiology, but challenges remain in its use as a biomarker. The eye is richly innervated by trigeminal fibers, making CGRP measurement in tear fluid a possible direct assessment of trigeminal activation. This study aimed to compare CGRP in tear fluid of migraine patients compared to healthy controls (HCs).

Methods: Tear fluid was collected from migraine patients and HCs through Schirmer test strips; CGRP concentration was assayed using ELISA. Clinical characteristics of migraine, severity and disability scores were collected. As a proof-of-concept, tear CGRP levels were measured before starting anti-CGRP monoclonal antibodies and after 6 months (T6).

Results: 51 patients with migraine (9 [17.6%] chronic, 16 with aura [31.4%]) and 24 age-matched HCs were included. Tear CGRP concentrations were significantly elevated in migraine patients (7.4±7.6pg/mL) than HCs (3.5±4.4pg/mL) ($p=0.022$). In the migraine group, tear CGRP levels were higher in the ictal phase (10.59±7.7pg/mL) compared to the interictal phase

(5.8±7.3pg/mL) and in patients with aura (10.4 ±9.2pg/mL) versus without (6.1±6.4pg/mL) ($p=0.042$). The ROC curve analysis for CGRP revealed an AUC of 0.71 (95% CI=0.57–0.84). A CGRP value of 0.84 pg/mL had 88% sensitivity in differentiating migraine patients and HCs. Tear CGRP concentration in five patients before starting anti-CGRP mAbs (6.9±2.3pg/mL) and T6 (2.4±3.2pg/mL) showed a significant decrease ($p=0.026$).

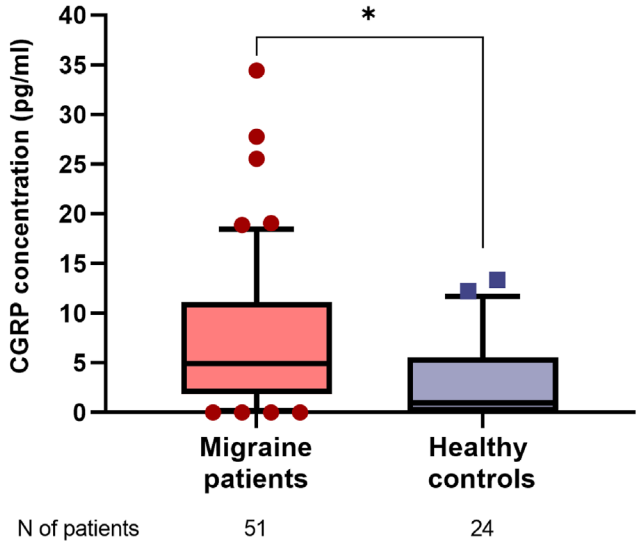

FIGURE 1 CGRP levels in tear fluid of migraine patients compared to healthy controls. Data are reported in box plots as mean and range 10–90 percentile.

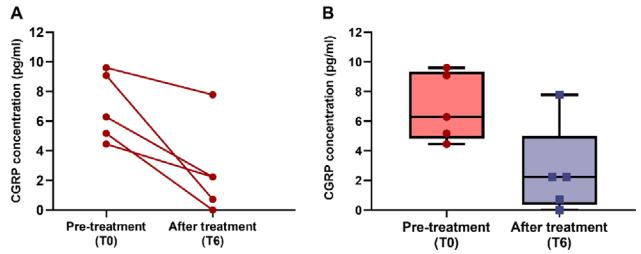

FIGURE 2 CGRP levels in tear fluid in five migraine patients before starting treatment with anti-CGRP monoclonal antibodies (baseline) and after 6 months of treatment. Patients-single data points (A) and box blots (mean with min-max).

Conclusion: Tear fluid CGRP is significantly elevated in migraine patients, particularly in ictal phase and in patients with aura. Measuring CGRP in tears offers a rapid, non-invasive method with potential utility for diagnosis and monitoring treatment response.

Disclosure: Nothing to disclose.

OPR-012 | GLP-1R agonists for the treatment of migraine: A pilot prospective observational study

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Background and Aims: Migraine affects 14.7% of individuals worldwide and remains difficult to treat. Emerging evidence suggests that even slightly elevated intracranial pressure (ICP) can exacerbate migraine by reducing intracranial compliance and increasing trigeminal pathway sensitization. Glucagon-like peptide-1 receptor (GLP-1R) agonists, which lower cerebrospinal fluid (CSF) production, have shown success in idiopathic intracranial hypertension (IIH) by reducing ICP and improving headache frequency. Therefore, this study investigates GLP-1R agonists as a potential promising approach to alleviating migraine.

Methods: In this pilot prospective observational study, 26 obese migraine patients (BMI ≥30) at our tertiary Headache Centre received subcutaneous Liraglutide 1.2 mg daily for 12weeks. Papilledema was excluded to rule out IIH. Mean monthly headache days were tracked via standardized diaries. The primary outcome was the change in headache days after 12weeks; secondary outcomes included BMI reduction, MIDAS score improvement, and adverse events.

Results: Mean monthly headache days decreased from 20.04±6.38 to 8.81±6.01 (mean difference 11.23, $p<0.001$), while MIDAS scores dropped from 62.58 to 27.23 (mean difference 35.35, $p<0.001$). Although BMI declined from 34.01 to 33.65, this was not significant ($p=0.060$). Analysis of covariance indicated no influence of BMI reduction on headache frequency (B=0.190, $p=0.949$). Mild gastrointestinal adverse events, primarily nausea and constipation, occurred in 10 patients (38%) but did not prompt discontinuation.

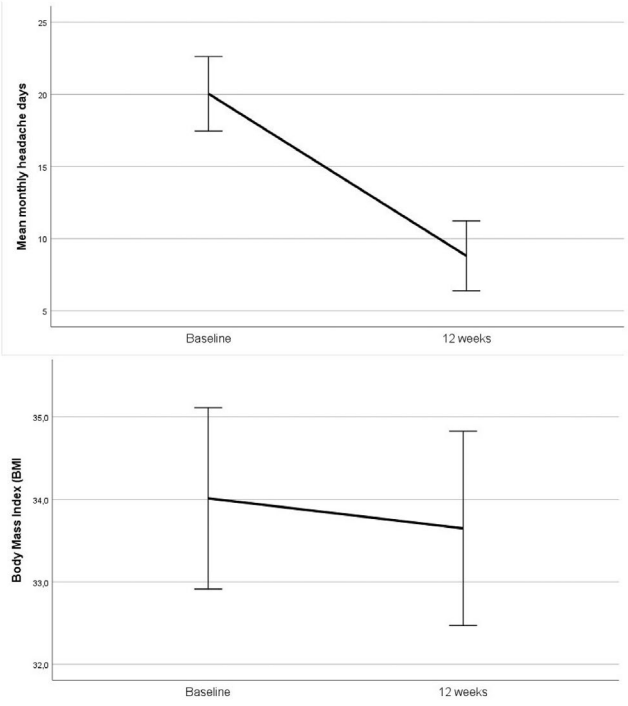

FIGURE 1 Headache and BMI Reduction

Conclusion: GLP-1R agonists appear to effectively reduce migraine burden regardless of weight loss, highlighting a possible pathophysiological role of CSF volume and pressure regulation in migraine. Further, larger studies are warranted to confirm these findings.
Disclosure: Nothing to disclose.

Ageing and Dementia 1

OPR-013 | Abstract withdrawn

OPR-014 | Sentence comprehension deficits in Italian and English nfvPPA: A cross-linguistic perspective

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Background and Aims: There is a growing awareness on the need of cross-linguistic assessment in Primary Progressive Aphasia (PPA). In particular, differences in language domains, such as morphology, might have an impact on the characterization of patients' profile. In this work, we aim to compare the performance of English and Italian non-fluent (nfvPPA) and semantic (svPPA) PPA patients in a sentence comprehension task.
Methods: 76 PPA patients (38 English, 28 Italian; 21 svPPA, 17 nfvPPA), matched for age, sex, Mini-Mental State Examination and Clinical Dementia Rating scale, completed a sentences comprehension task adapted for each language. The task involved 24 oral sentences of different syntactic complexity, and participants had to indicate the matching picture. Composite scores were calculated for High (HSC), Medium (MSC), and Low (LSC) levels of syntactic complexity. Performances were analysed across svPPA and nfvPPA independently from their language, and across languages, using MANCOVA models.
Results: NfvPPA were generally more impaired than svPPA in HSC and MSC scores ($p < 0.045$) independent of language. Cross-linguistically, Italian nfvPPA patients showed lower scores in MSC and LSC compared to English nfvPPA (all $p < 0.010$). No differences were observed between English and Italian svPPA patients ($p = 0.772$).
Conclusion: The sentence comprehension task confirmed syntactic processing deficits in nfvPPA patients in both languages. However, the task was more sensitive in identifying syntactic processing deficits in Italian sample, and specifically in nfvPPA patients. This difference is consistent with the known higher morphological complexity of Italian language. This study suggests the importance of tailored language assessment for efficient diagnostic process.
Disclosure: Funding. European Research Council (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer Disease. Co-funding by the Next Generation EU [DM 1557 11.10.2022]. Disclosures. GS, FF, LL, ZM, DPB, JDL, BLT, VC, SFC, MLG have nothing to disclose; EC receive research supports from the Italian Ministry of Health; MF received compensation for consulting services or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM. FA received speaker honoraria from Biogen Idec, Roche, Eli Lilly, GE Healthcare; receives research supports from IMH, IMUR, AriSLA, ERC, EU JPND Research, Foundation Research on AD (France).

OPR-015 | Advancing in vivo diagnosis of limbic-predominant age-related TDP-43 encephalopathy (LATE): A memory clinic cohort study

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Background and Aims: The amygdalar atrophy scale (AAS) is an MRI-based visual rating system for assessing amygdalar atrophy, categorized into AAS0 (no atrophy), AAS1 (mild-to-moderate atrophy), and AAS2 (severe atrophy). AAS correlates with amygdala volume, complements the medial temporal atrophy (MTA) scale, and is linked to TDP-43 pathology, a hallmark of limbic-predominant age-related TDP-43 encephalopathy (LATE-NC). This study evaluated the utility of AAS in identifying patients with probable LATE-NC during memory clinic workups.
Methods: 1653 subjects who underwent baseline T1-MRI, clinical, and neuropsychological assessments, were included and classified as cognitively unimpaired (CU), mild cognitive impairment (MCI), or dementia. Using AAS and Alzheimer's disease (AD) biomarkers, individuals were grouped as probable

AD neuropathologic changes (ADNC, AAS0 with positive AD biomarkers, $N=146$), LATE-NC (AAS1-2 with negative AD biomarkers, $N=36$), and AD/LATE-NC (AAS1-2 with positive AD biomarkers, $N=107$). Clinical, neuroimaging, and cognitive trajectories over 30 months were assessed.
Results: AAS1-2 was more frequent in MCI and dementia than CU ($p<0.001$) and correlated with age (rho = 0.41, $p<0.001$). LATE-NC exhibited milder cognitive impairment (MMSE: 26.2) than ADNC (24.2) and AD/LATE-NC (22.5) ($p<0.001$). MCI was more prevalent in LATE-NC (67%) than ADNC (58%) or AD/LATE-NC (51%), while dementia was less frequent ($p<0.001$). Reduced volumes and cortical thickness in TDP-43-related brain regions were observed in the LATE-NC and AD/LATE-NC. LATE-NC showed slower cognitive decline ($p=0.017$).
Conclusion: Incorporating AAS into memory clinic workups may serve for differentiating suspected ADNC and LATE-NC cases. Given its reliability and complementary nature to the MTA scale, the AAS offers promise as a diagnostic tool in clinical practice.
Disclosure: Nothing to disclose.

OPR-016 | Blood-derived microRNAs associated with hippocampal structure and atrophy rate: Findings from the Rhineland study

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Background and Aims: MicroRNAs are critical for neuronal function and development. Understanding which microRNAs are involved in brain health and neurodegeneration requires determining their relation to key brain regions. Here, we examined the associations of blood-derived microRNAs with hippocampal structure and atrophy, features related to cognition and dementia, in the general population.
Methods: Using data from 2062 participants of the population-based Rhineland Study, we measured expression of microRNAs and their putative target genes at study baseline in whole blood using RNA sequencing. Hippocampal and total brain volumes were measured using 3T MRI at baseline and follow-up (4.6 to 8.0 years later). We examined microRNA associations with left and right hippocampal volume, hippocampal asymmetry, and total brain volume cross-sectionally using linear regression, and longitudinally using mixed-effects models. Moreover, we identified genomic loci influencing microRNA expression and used them for two-sample Mendelian Randomization analysis.
Results: Cross-sectionally, five microRNAs were associated exclusively with left hippocampal volume. Longitudinally, another six microRNAs were associated with left hippocampal, right hippocampal, and total brain atrophy rates. Nineteen microRNAs were exclusively associated with total brain atrophy rate. Several identified microRNAs regulate target genes involved in brain development, memory, axon guidance, and synapse assembly. Mendelian Randomization suggested that larger hippocampal volume causes lower expression of one microRNA.
Conclusion: We identified microRNA signatures that were - partly side-specifically - related to hippocampal structure and atrophy, suggesting different influences of microRNAs during brain development and aging. Some identified microRNAs have been previously linked to dementia and may be useful as pre-symptomatic blood-based biomarkers of neurodegeneration.
Disclosure: Nothing to disclose.

OPR-017 | Creutzfeldt-Jakob disease in Northern Portugal: Retrospective study of clinical characteristics over 10 years

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Background and Aims: Creutzfeldt-Jakob disease (CJD) is the most common prion disease, most often in its sporadic type. It manifests as a combination of rapidly progressive dementia and other neurological signs such as myoclonus or ataxia. It is invariably fatal and is associated with significant demographic and clinical impact.
Methods: Retrospective multicentre study that included cases diagnosed with probable CJD in 10 centres in northern Portugal since 2011. Statistical analysis of demographic, clinical characteristics and ancillary testing.
Results: We included 61 patients diagnosed with probable sporadic CJD (30 men). Median age was 69 years (44–88). Half the patients were diagnosed 2 (23 days - 24) months after symptom onset. The main presentation was dementia (95.1%), myoclonus (75.4%), extra-pyramidal signs (59%) and ataxia (55.7%). Neuropsychiatric symptoms coexisted in 68.9%, most frequently apathy and depression. EEG showed periodic activity in 63.3% of cases; MRI showed T2/FLAIR hyperintensity and/or cortical restricted diffusion in 85.2% and/or of the basal nuclei in 68.9%. Protein 14-3-3 in CSF was positive in 96.5% of cases. Three patients had mutations in the PRNP gene. Median survival after diagnosis was 3 months (1–43), with 22 patients undergoing autopsy with diagnostic confirmation. Analysis using Mann-Whitney test identified extrapyramidal signs associated with lower survival after diagnosis, with statistical significance ($U=262$; $p=0.019$).
Conclusion: We aimed to illustrate clinical heterogeneity of CJD, impacting timely diagnosis, clinical approach and survival.
Disclosure: Nothing to disclose.

OPR-018 | Tenecteplase in central retinal artery occlusion study

A. Aamodt[1]; S. Ryan[1]; Ø. Jørstad[2]; M. Skjelland[1]; C. Simonsen[3]; P. Ijäs[4]; T. Bek[5]; D. Strbian[4]; Khanevski[6]; R. Lemmens[7]; I. Nakstad[8]; L. Christensen[9]; H. Ellekjær[10]; V. Matijošaitis[11]; T. Truelsen[12]; E. Rødahl[13]; J. Krohn[13]; M. Mazya[14]; K. Kraglund[1]; H. Lisether[15]; K. Devik[16]; V. Malmberg[17]; J. Valaikiene[18]; P. Ylikotila[19]; M. Moe[2]

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Background and Aims: Central retinal artery occlusion (CRAO) is an ophthalmologic emergency that, without prompt reperfusion, bears high risk of permanent blindness. No evidence-based treatment is currently available. Whether prompt reperfusion with thrombolytic agents can improve the outcome in CRAO, as proved in ischemic stroke, remains unanswered. The main aim is to assess the effect of systemic tenecteplase within 4.5 hours of onset of central retinal artery occlusion

Methods: The trial is an ongoing prospective, randomised-controlled, double-dummy, double-blind phase 3 multi-centre trial of TNK 0.25 mg/kg + placebo vs. ASA + placebo (2 arms with 1:1 block randomisation). Patients are recruited after an ophthalmologist has confirmed CRAO and they can be treated within 4.5 hrs. After observation in the stroke unit, patients are re-examined by an ophthalmologist and a neurologist as an outpatient at 30 and 90-day follow-up. The primary outcome is the proportion of patients with ≤0.7 logMAR best-corrected visual acuity (BCVA) corresponding to decimal best-corrected visual acuity ≥0.2 at *p* in the affected eye at 30 days after treatment, representing an improvement in BCVA of at least 0.3 logMAR.

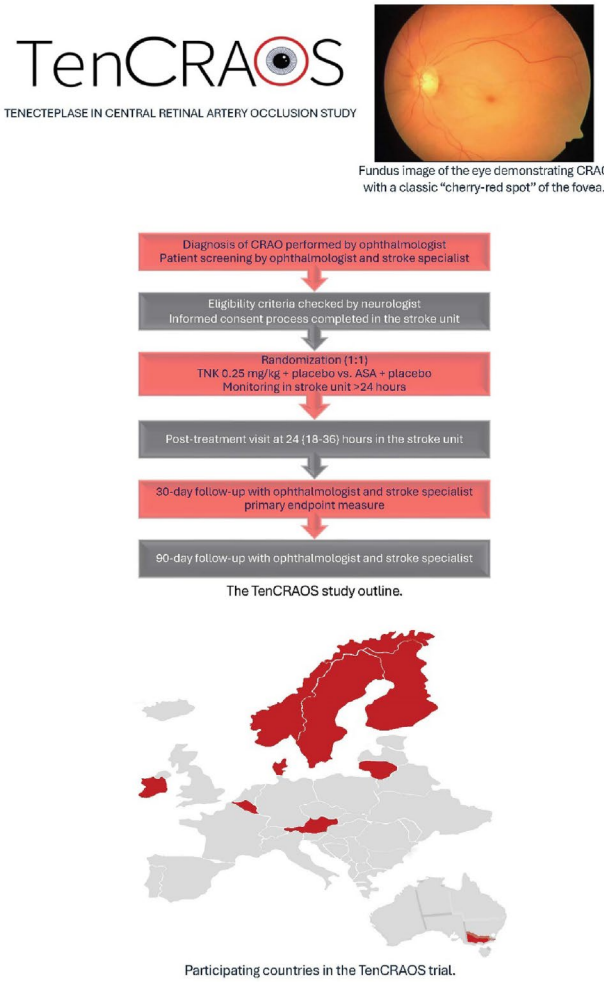

FIGURE 1 Study outline, fundus image of the eye demonstrating CRAO and map with participating countries.

Results: 8 countries are participating with 29 centres activated during the course of the study. Currently there are 7 countries activated for recruitment. We have recruited 76 of 78 patients so far, 32 in Norway, 19 in Denmark, 11 in Finland, 7 in Belgium, 4 in Lithuania and 3 in Sweden. All patients have been included within the strict parameters of the study.

Conclusion: The main results will be presented at the conference.

Disclosure: Boehringer-Ingelheim provided tenecteplase and intravenous placebo free of charge as well as financial support to the sites outside Norway but had no influence on the study conduct, analysis, or interpretation.

OPR-019 | Enhancing moyamoya diagnosis and care: A multi-disciplinary study on Norway's first moyamoya cohort

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Background and Aims: Moyamoya angiopathy (MMA) is a rare and progressive cerebrovascular disorder of uncertain etiology, predominantly affects young women posing a high risk of stroke and disability without optimal care. To address these challenges, we established a dedicated multi-disciplinary moyamoya task force and started a quality improvement project in 2021. The aim of this project was to evaluate the project.
Methods: Strong multidisciplinary collaboration, common moyamoya clinic, standardizing of imaging including H2[15O]-PET, quality registry and international collaboration were key elements in the development of common pathway (Figure 1). Information portal and courses were established with extensive user involvement to strengthen health literacy. Dissemination was performed through podcasts, blog-interviews and lectures. Functional outcomes and patient reported outcome measures were collected. Additionally, yearly interviews of patients, next-of-kin and health care providers were performed.

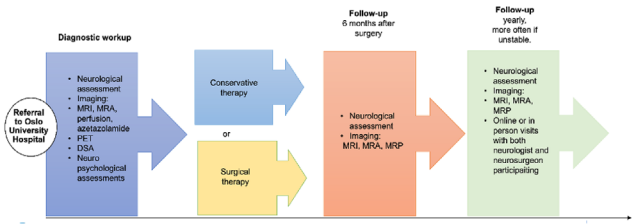

FIGURE 1 Moyamoya pathway

Results: A quality registry encompassing 100 MMA patients (1/2 treated with revascularization surgery) was established. In the present substudy, 56 patients were included: 89.2% moyamoya disease, 10.8% moyamoya syndrome. Mean age 47.2 (SD 11.46) years, 78.9% women, mean mRS 1.7, EQ-5D-5L VAS distribution 61.8 of 100 (SD 21.3), mean total mental fatigue score 18.0 (>10 indicates mental fatigue). The participants reported the project to have considerable impact on several aspects and how to cope with the situation (Figure 2).

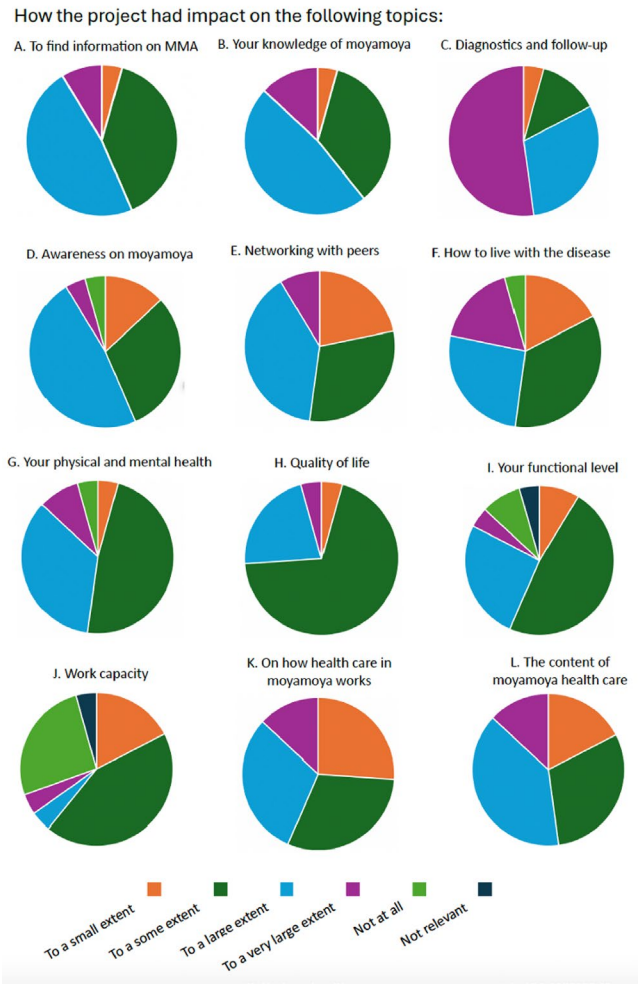

FIGURE 2 Results of the quality improvement project - evaluation from patients, next-of-kin and health-care providers.

Conclusion: The implemented MMA model with strong user involvement was feasible and resulted in improved quality of care.
Disclosure: None

OPR-020 | Abstract withdrawn

OPR-021 | Clinical impact of endovascular treatment implementation in primary stroke centers of catalonia

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Background and Aims: We aim to evaluate whether the implementation of endovascular thrombectomy (EVT) capabilities in areas covered by primary stroke centers (PSC) improves outcomes in patients with ischemic stroke associated with anterior circulation vessel occlusion.

Methods: We analyzed registry data to identify ischemic stroke patients with anterior circulation vessel occlusions in catchment areas of 3 PSC that transitioned to thrombectomy-capable centers (TCCs, 1 full time, 2 during working hours). The study compared the proportion of patients treated with EVT, complete reperfusion(mTICI2C-3), symptomatic intracranial hemorrhage(sICH) and time from first hospital admission to puncture (ATP) before (January 2017–June 2020) and after (July 2020–December 2023) the implementation was fully active (COVID-19 pandemic).

Results: Of the 1,467 patients included, 859 (59%) were evaluated after the implementation. The proportion of patients treated with EVT increased from 406/608(67%) before the implementation to 667/859(77%) after the implementation (OR 1.78; 95% CI 1.369–2.182), with a decrease in the time from first ATP times of 25 minutes (95% CI 3.370–46.443). Among treated patients, no significant differences were observed in rates of complete reperfusion (222[55.4%] vs 363[54.4%]; OR 0.861; 95% CI 0.668–1.110) or sICH (21[5.2%] vs 51[7.6%]; OR 1.518; 95% CI 0.899–2.563).

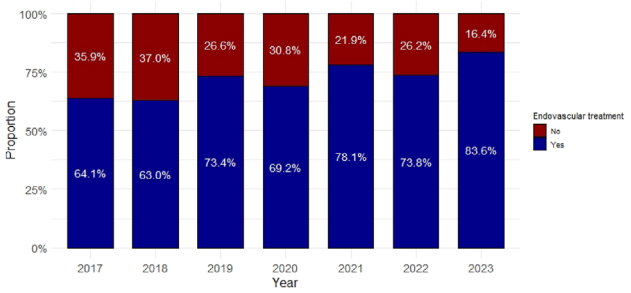

FIGURE 1 Proportion of vessel occlusions treated with thrombectomy

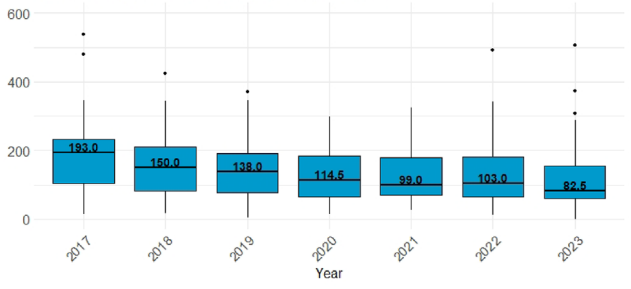

FIGURE 2 Time from first hospital admission to arterial puncture (minutes)

Conclusion: Integration of EVT capabilities into PSCs has significantly enhanced access to EVT in densely populated areas by increasing treatment rates and reducing ATP times. These operational advancements have been achieved without compromising reperfusion outcomes or safety standards. Further expansion of TCCs could improve both access and timeliness of EVT, helping to address geographic disparities and improving quality of stroke care for patients.

Disclosure: Nothing to disclose.

OPR-022 | Timing of anticoagulation following decompressive surgery for cerebral vein and sinus thrombosis: An observational study

M. C. Taveira[1]; S. Aaron[2]; J. M. Ferreira[3]; J. M. Coutinho[4]; P. Canhão[1]; A. Conforto[5]; A. Arauz[6]; M. Carvalho[7]; J. Masjuan[8]; V. K. Sharma[9]; J. Putaala[10]; M. Uyttenboogaart[11]; D. J. Werring[12]; R. Bazan[13]; S. Mohindra[14]; J. Weber[15]; B. A. Coert[16]; P. Kirubakaran[2]; M. Sanchez van Kammen[4]; P. Singh[2]; D. Aguiar de Sousa[1]; J. M. Ferro[1]

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Background and Aims: Anticoagulation is the mainstay therapy for acute cerebral venous thrombosis (CVT). Decompressive surgery is necessary in patients with large parenchymal lesions and impending herniation, requiring a temporary suspension of anticoagulation. This study sought to identify the optimal timing for initiating/resuming anticoagulation following decompressive surgery.

Methods: Data were collected from the Decompressive Surgery for CVT Study 2 (DECOMPRESS2), a multinational cohort study of 118 patients with CVT treated by decompressive surgery. We assessed the frequency of new hemorrhagic and venous thrombotic events in patients who started/resumed anticoagulation <24h and >=24 following surgery. Death and disability were evaluated by the modified Rankin scale (mRS >2) at discharge and at one year follow up.

Results: Of the 90 patients available for analysis, 35 (39%) started/resumed anticoagulation within 24 hours following surgery while 55 (61%) did so later than 24 hours. Overall frequency of patients with new hemorrhagic or venous thrombotic events

was 26.7% (24 patients). Distribution of major hemorrhagic events was 8 (23%) bleedings in the <24-hour group, and 9 (16%) in the >=24h. No CVT recurred. Two venous thrombotic events occurred in <24h (6%) and 5 in the >=24h (9%) group. Timing of anticoagulation was not associated with death or disability at discharge (OR 1.65. 95% CI 0.30 to 9.01, $p=0.56$), or one year follow up (OR 2.19, 95% CI 0.78 to 6.10, $p=0.14$).

Conclusion: The results suggest that timing of anticoagulation therapy following decompressive surgery does not significantly influence the risk of new bleeding or venous thrombotic events or disability.

Disclosure: Nothing to disclose.

Neuropathies

OPR-023 | Chat-GPT-4o in diagnosis and management of real- life polyneuropathy cases: Comparative analysis with neurologists

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Background and Aims: Accurate diagnosis and management of polyneuropathies remain challenging, particularly for non-specialist neurologists. Generative Pre-trained Transformer (GPT) models show potential to enhance diagnostic accuracy despite their general-purpose design. This study evaluated GPT-4o's performance in diagnosing polyneuropathies and guiding confirmatory testing compared to specialist and non-specialist neurologists.

Methods: Data from 100 confirmed polyneuropathy cases were collected from tertiary care centers. Cases were presented to GPT-4o using a zero-shot chain-of-thought prompt to generate a leading diagnosis, two differentials, and a confirmatory test. Diagnoses and tests from 26 neurologists (14 specialists, 12 non-specialists) across 19 centers in 10 countries were collected before and after reviewing GPT-4o's output. Accuracy was compared using paired t-tests, and inter-output reliability was assessed with Cohen's kappa.

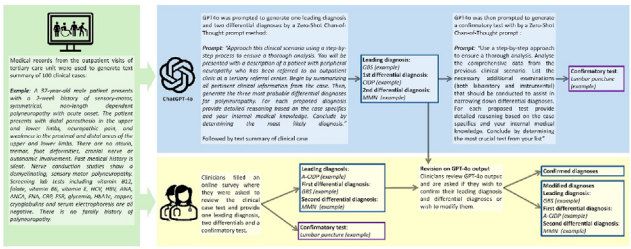

FIGURE 1 Flowchart representation of materials and methods

Results: GPT-4o demonstrated high inter-output consistency (kappa=0.8, $p<0.001$) and outperformed non-specialists in leading diagnosis accuracy (65.5% vs 54.4%, $p=0.007$) but it was inferior to specialists (73.9%, $p=0.024$). Including differential diagnoses, GPT-4o outperformed non-specialists (82.0% vs. 68.5%, $p<0.001$) but remained below specialists (88.1%, $p=0.042$). Non-specialists improved their accuracy after reviewing GPT-4o's suggestions (54.4% to 57.0%, $p=0.007$), whereas specialists showed a non-significant increase (73.9% to 75.0%, $p=0.069$). GPT-4o errors included over-reliance on laboratory findings or past history (38%), overlooking clinical information (16%), vague conclusions (16%), limited internal knowledge (9%), and reasonable but incorrect responses (22%). GPT-4o matched experts in recommending diagnostic tests (68.0% vs 67.3%, $p=0.874$) and surpassed non-specialists (45.3%, $p<0.001$).

Conclusion: GPT-4o shows promise as diagnostic support tool, improving non-specialists' accuracy and guiding confirmatory testing. Its supervised integration could help bridge expertise gaps in neurological care.
Disclosure: Nothing to disclose.

OPR-024 | Plasma lipidomic patterns associated with disease activity in chronic inflammatory demyelinating polyradiculoneuropathy

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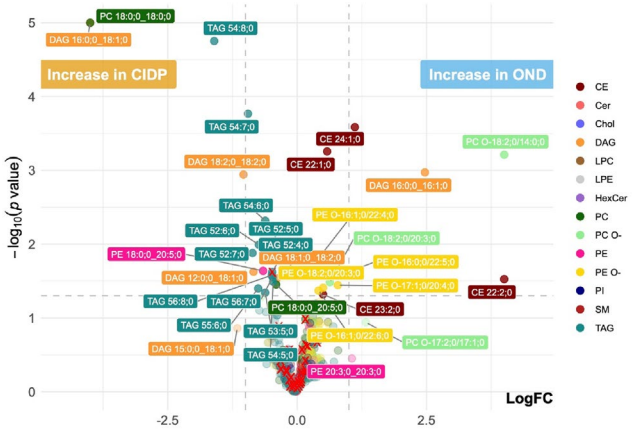
Background and Aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) is an immune-mediated neuropathy that leads to significant disability and substantial healthcare costs. Although the exact pathogenic mechanisms remain unclear, it is known that inflammation results in segmental demyelination, accompanied by the release of myelin lipids into the extracellular space. This study aims to investigate the plasma lipidomic profile of CIDP patients to identify lipid patterns associated with disease activity.
Methods: We employed high-throughput shotgun lipidomics to analyze and compare the plasma lipidome of 30 patients with CIDP (mean age ± SD: 60.7 ± 12.2 years) with that of 30 individuals diagnosed with non-demyelinating neurological disorders (OND; mean age ± SD: 52.8 ± 10.3 years). Lipid classes and subspecies were quantified in absolute [pmol] and relative concentrations [mol%], and their correlation with CIDP disease activity and clinical disability scores (R-ODS, INCAT and MRC) was assessed. To control confounders such as age and weight, strongly correlated lipids were excluded.
Results: The analysis identified 669 molecular lipid species across 15 lipid classes; with a significant elevation in the diacylglycerol (DAG) class in CIDP patients. Furthermore, specific lipid subspecies, including triacylglycerol (TAG), DAG, and ether-linked phosphatidylcholine (PC O), were significantly correlated with disease activity. A distinct lipid subspecies set including phosphatidylcholine (PC), lyso-phosphatidylcholine (LPC), phosphatidylinositol (PI), sphingomyelin (SM), and cholesterol ester (CE) showed strong associations with clinical disability scores.



Volcano-Plot showing the differences in lipid subspecies in participants from the CIDP- vs. OND-cohort. n = 30 vs. 30. Colors represent lipid class classification. The horizontal dashed line indicates a p-value of 0.05 in the Welch's t-test. The vertical dashed line indicates a log2 fold change of 1. Only lipids with an absolute log2 fold change > 1 were annotated. Lipids marked with red × have a high correlation with age and BMI.

FIGURE 1 Differences of lipid subspecies in control vs. CIDP patients

Conclusion: These findings indicate that CIDP is characterized by distinct lipidomic profiles, offering potential lipid biomarkers for disease activity and severity. Such biomarkers could enhance diagnostic precision and inform clinical management.
Disclosure: We declare no conflict of interest.

OPR-025 | Elevated serum concentrations of GFAP in hereditary transthyretin amyloidosis since pre-symptomatic stages

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Background and Aims: Hereditary transthyretin amyloidosis (ATTRv) is a rare disorder caused by pathogenic TTR gene variants. Glial fibrillary acidic protein (GFAP) and neurofilament light chain (NfL) are potential biomarkers for astrocyte activation and neuroaxonal damage, respectively. This study investigates serum GFAP (sGFAP) and NfL (sNfL) levels in ATTRv patients, pre-symptomatic subjects, and healthy controls (HCs) to evaluate their utility as biomarkers of disease progression and CNS involvement.

Methods: Our multicenter cross-sectional study included 111 ATTRv patients (56 symptomatic, 55 pre-symptomatic subjects) and 183 HCs. Serum levels of sGFAP and sNfL were measured using ultrasensitive immunoassays. Statistical comparisons were performed using ANCOVA models (age and sex adjusted), with correlations examined between serum biomarkers and disease severity (Neuropathy Impairment Score, NIS).
Results: sGFAP levels were elevated in symptomatic (median: 238.35 pg/ml) and pre-symptomatic subjects (median: 105.50 pg/ml) vs. HCs (median: 75.5 pg/ml, $p < 0.001$). sNfL was elevated only in symptomatic patients (median: 43.68 pg/ml) compared to pre-symptomatic subjects (median: 9.36 pg/ml) and HCs (median: 7.54 pg/ml, $p < 0.001$). Both biomarkers correlated significantly with NIS, reflecting disease severity. Female HCs had higher sGFAP levels than males (median 88.6 pg/ml vs. 59.8 pg/ml; p 0.011).

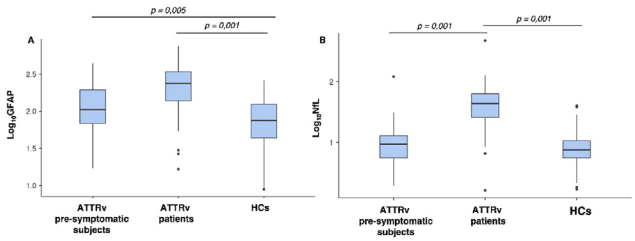

FIGURE 1 Comparison of sGFAP and sNfL levels (expressed as Log10-GFAP and Log10-NfL, respectively) across the three groups. (A) sGFAP levels were significantly higher in both ATTRv patients and pre-symptomatic subjects compared to healthy controls (HCs).

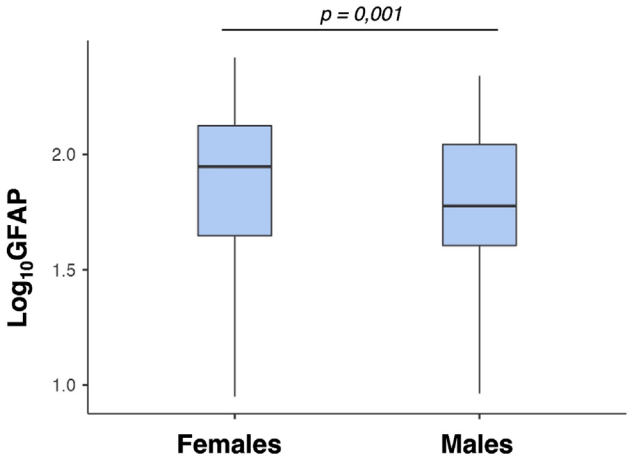

FIGURE 2 Comparison of sGFAP levels (expressed as Log10-GFAP) between females and males in the HCs cohort, demonstrating significantly higher sGFAP values in females compared to males.

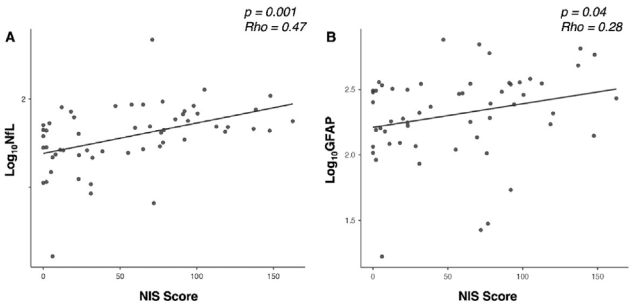

FIGURE 3 Correlation between sNfL and sGFAP levels (expressed as Log10-NfL and Log10-GFAP, respectively) with NIS scores, demonstrating a significant positive relationship between both biomarkers and clinical impairment.

Conclusion: sGFAP and sNfL mark distinct ATTRv stages, with sGFAP indicating early preclinical changes and sNfL correlating with neurological progression. Sex differences in sGFAP levels among HCs suggest that sex should be considered as a covariate in biomarker analyses.
Disclosure: Nothing to disclose.

OPR-026 | Baseline characteristics of patients with transthyretin amyloidosis with polyneuropathy: Results from overTTuRe

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Background and Aims: Transthyretin amyloidosis with polyneuropathy (ATTR-PN) is a rare, debilitating, and ultimately fatal disease, which manifests as progressive peripheral nerve damage. The condition is associated with misdiagnosis and diagnostic delays before patients receive appropriate treatment. The objective of this analysis was to report on baseline characteristics of patients with ATTR-PN from OverTTuRe.
Methods: OverTTuRe is a multi-country, retrospective, observational study generating real-world evidence from adult patients diagnosed with ATTR amyloidosis. The study population included patients recorded in the Swedish Transthyretin Amyloidosis Registry (SveaTTR, 2000–2024) and patients sampled through chart review at 11 Spanish hospitals (2009–2023). Analyses from Germany are ongoing and will be presented. Patients were assigned to ATTR-PN and mixed phenotypes according to baseline clinical presentation and based upon clinician judgement (Spain) and neurological and cardiac symptoms recorded in SveaTTR (Sweden).

Results: In total, 279 patients were included from Sweden and 257 from Spain. Baseline patient characteristics are presented in the table. Peripheral neuropathy was the most common neurological manifestation at diagnosis in both countries. Non-neurological manifestations were defined differently in both data sources but clearly indicated a greater prevalence in patients with mixed phenotype.

TABLE Baseline characteristics of patients with ATTR-PN and ATTR-Mixed at diagnosis in Spain and Sweden. (1 of 2)

	Spain		Sweden	
	ATTR-PN N=107	ATTR-mixed N=150	ATTR-PN N=206	ATTR-mixed N=73
Patient characteristics				
Mean age at diagnosis (SD), in years	54.8 (14.9)	74.1 (11.4)	61.1 (13.8)	71.3 (6.7)
Males, n (%)	57 (53.3%)	108 (72.0%)	151 (73.3)	57 (78.1)
Medical history, n (%)				
Hypertension	27 (26.7)	76 (50.7)	56 (27.2)	21 (28.8)
Ischemic heart disease	n<5	8 (5.4)	21 (10.2)	11 (15.1)
Diabetes	10 (10.1)	40 (26.8)	13 (6.3)	7 (9.6)
Chronic kidney disease	n<5	27 (18.2)	7 (3.4)	5 (6.8)
Carpal tunnel syndrome	38 (38.0)	52 (34.7)	21 (10.2)	24 (32.9)
Disease characteristics				
Genotype, n (%)				
Mutation detected	107 (100.0)	88 (58.7)	185 (89.8)	45 (61.6)
No mutation detected	0 (0.0)	50 (33.3)	n<20	10 (13.7)
Not tested	0 (0.0)	12 (8.0)	n<5	18 (24.7)
Type of mutation, n (%)				
Val30Met	62 (76.5)	49 (61.3)	177 (95.7)	44 (>95.0)
Val122Ile	8 (9.9)	9 (11.3)	0 (0.0)	0 (0.0)
Other	n<5	14 (17.5)	8 (4.3)	n<5
Diagnostic procedures				
Biopsy performed, n (%)	28 (26.2)	43 (28.7)	180 (87.4)	41 (56.2)
Time from 1st manifestation to diagnosis, years				
Mean (SD)	2.5 (5.1)	4.5 (5.9)	2.8 (3.0)	1.9 (2.5)
Median	0.4	1.7	1	1
Laboratory parameters				
Serum TTR levels (mg/dL), mean (SD), n	23.0 (4.6), 17	10.0 (9.4), 4	20.0 (10.0), 21	20.0 (10.0), 7
Creatinine (mg/dL), mean (SD)	0.8 (0.2)	1.2 (0.8)	0.9 (0.24)	1.1 (0.64)
eGFR (mL/min/1.73m^2), mean (SD)	84.7 (12.3)	65.1 (23.6)	68.5 (15.2)	60.0 (15.3)
NT-proBNP (pg/mL), mean (SD)	297 (646)	2932 (3372)	640 (994)	1657 (1534)
Disease staging				
Mean Neuropathy Impairment Score (SD), n	9.6 (13.3), 56	20.2 (17.5), 35	22.2 (17.0), 28	n<5
PND score, n (%)				
0	-	-	6 (2.9)	0 (0.0)
1	52 (77.6)	49 (57.0)	68 (33.0)	17 (23.3)
2	10 (14.9)	24 (27.9)	35 (17.0)	5 (6.8)

TABLE Baseline characteristics of patients with ATTR-PN and ATTR-Mixed at diagnosis in Spain and Sweden. (2 of 2)

3A	n<5	n<10	10 (4.9)	n<5
3B	n<5	n<10	17 (8.3)	n<5
4	0 (0.0)	n<5	5 (2.4)	0 (0.0)
Missing/Not done	0	0	65 (31.6)	47 (64.4)
NYHA class, n (%)				
I	50 (90.9)	35 (31.0)	54 (26.2)	9 (12.3)
II	n<5	65 (57.5)	15 (7.3)	24 (32.9)
III	n<5	13 (11.5)	n<5	8 (11.0)
IV	0 (0.0)	0 (0.0)		0 (0.0)
Missing/Not done	0	0	136 (66.0)	32 (43.8)
Clinical manifestations				
Clinical manifestations at baseline[a], n (%)				
Neurological				
Peripheral neuropathy	88 (83.0)	73 (48.7)	186 (90.3)	57 (78.1)
Autonomic neuropathy	34 (33.7)	30 (20.1)		
Gastrointestinal dysfunction	39 (36.8)	31 (20.7)	36 (17.5)	15 (20.5)
Erectile dysfunction	23 (22.3)	33 (22.0)	21 (10.2)	8 (11.0)
Orthostatic hypotension	14 (13.9)	17 (11.3)	9 (4.4)	17 (23.3)
Pain	27 (26.7)	23 (15.5)	61 (29.6)	78 (28.0)
Non-neurological				
Atrial fibrillation	n<5	56 (37.8)		
Heart failure	n<5	59 (39.9)		
Cardiomyopathy	n<5	93 (62.0)		
Oedema	n<5	26 (17.6)		
Dyspnea	8 (8.3)	74 (50.0)	0 (0.0)	40 (54.8)
Spinal stenosis	7 (7.4)	17 (11.5)	9 (4.4)	12 (16.4)
Bradycardia			0 (0.0)	n<5
Fainting			0 (0.0)	6 (8.2)
Tachycardia			0 (0.0)	18 (24.7)
Fatigue			0 (0.0)	42 (57.5)
Stroke/TIA			0 (0.0)	5 (6.8)
Visual disturbances			0 (0.0)	19 (26.0)

[a]Defined as manifestations at diagnosis (Spain) and symptoms at onset (Sweden)
Note: data have been suppressed where n<5 and masked in corresponding cells, as appropriate

Conclusion: These results provide contemporary real-world insights into the characteristics of patients with ATTR-PN from two different countries, highlighting that a considerable proportion of patients show evidence of a mixed phenotype with cardiac manifestations already present at the time of diagnosis. The next phase of OverTTuRe will aim to longitudinally assess the development of ATTR-related manifestations and disease progression over time.
Disclosure: Nothing to disclose.

OPR-027 | Proteomic profiling of Guillain-Barré Syndrome using aptamers: Identifying and Validating Potential Biomarkers

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Background and Aims: There is a lack of large-scale serum proteomic data in Guillain-Barré syndrome (GBS). Our aim is to examine proteomic differences at disease onset and after one year to identify potential biomarkers and relevant pathways, some of which could be druggable.
Methods: We analysed serum samples from 20 GBS patients across Spanish centres, comparing their proteomic profiles at disease onset and after one year, as well as against 15 healthy controls (HC). A multiplex aptamer-based proteomic platform (Somalogic) was used to quantify 6383 serum proteins. Enrichment analysis identified disease-associated pathways, and candidate proteins were validated with conventional laboratory methods.
Results: Nineteen proteins were differentially expressed between onset and remission, with overexpression of pathways related to B cell activation, cell cycle regulation, and deubiquitination at onset. Compared to HC, 177 proteins were differentially expressed at onset in GBS, particularly in pathways related to muscle sarcomere, antimicrobial response, and lipid metabolism. Serum Amyloid A1 (SAA1), an acute response protein, showed the largest change between onset and remission, confirmed by Meso Scale Discovery: GBS patients had a geometric mean SAA1 concentration of 14.529 ng/mL at onset, decreasing to 4.613 ng/mL at 12 months ($p < 0.001$) and 2.523 ng/mL in HC ($p < 0.001$). None of the differentially expressed sarcomeric proteins tested so far were detected using ELISA.

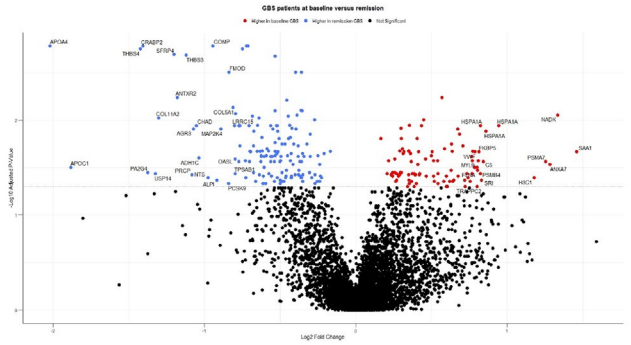

FIGURE 1 Volcano plot showing differentially expressed proteins in the serum of patients with Guillain-Barré Syndrome at baseline comparing with the same patients at one year.

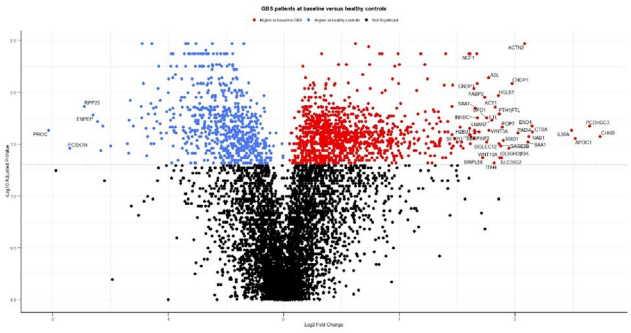

FIGURE 2 Volcano plot showing differentially expressed proteins in the serum of patients with Guillain-Barré Syndrome at baseline comparing with healthy controls.

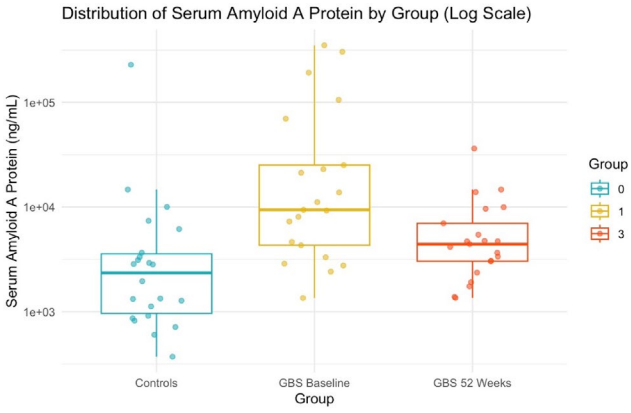

FIGURE 3 Serum amyloid A1 (SAA1) levels in Healthy Controls and Guillain-Barré syndrome patients at onset, and at one year.

Conclusion: This first large-scale plasma proteomic analysis in GBS patients highlights multiple disease-associated proteins and pathways. SAA1 emerges as a potential biomarker in GBS, but further validation is needed to confirm its clinical utility. Further analysis in additional candidate proteins is also ongoing.
Disclosure: Nothing to disclose.

OPR-028 | Exploring PML risk assessment: A comparative study of STRATIFY JCV™ DxSelect™ and IMMUNOWELL™ JCV IgG tests in RRMS

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Background and Aims: In the clinical management of Multiple Sclerosis (MS) patients, the primary concern associated with natalizumab therapy remains the risk of developing Progressive Multifocal Leukoencephalopathy (PML), a rare but potentially fatal opportunistic infection of the central nervous system caused by the J.C. virus (JCV).
Methods: This study compared two tests for assessing the risk of PML in patients with relapsing-remitting MS (RRMS) treated with natalizumab (branded, Tysabri®): the STRATIFY JCV™ DxSelect™ test and the IMMUNOWELL™ JCV IgG test. The main objective was to determine the comparability of these tests in classifying PML risk. Demographic data, clinical characteristics, treatment history, and results from both STRATIFY JCV™ DxSelect™ and IMMUNOWELL™ JCV IgG tests were collected on the same day. Patients were classified into three risk categories (low, intermediate, high) based on each test's threshold values.
Results: The analysis showed 85.5% agreement between the two tests for risk classification. Ten discordant cases were identified, mainly between intermediate and high-risk categories. IMMUNOWELL™ tended to classify more patients in higher risk categories than STRATIFY JCV™ DxSelect™. No significant association was found between discordance and prior use of immunosuppressant drugs and number of administrations>24. The agreement between tests, assessed with the weighted Kappa coefficient, was moderate ($\kappa = 0.6222$).
Conclusion: Our study first described in a real-world setting that the IMMUNOWELL™ JCV test tends to classify more patients in higher risk categories compared to STRATIFY JCV™ DxSelect™. Further longitudinal studies are needed to evaluate the clinical impact of these differences in PML risk assessment.
Disclosure: Nothing to disclose.

OPR-029 | Clinical manifestation progression and long term outcome of anti-KLHL11 encephalitis

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Background and Aims: Anti-Kelch-like protein 11 (KLHL11) encephalitis was discovered in 2019 in middle-aged males with testicular seminoma and rhombencephalitis. This study aimed to comprehensively define phenotype and outcome of KLHL11-encephalitis.

Methods: We tested 1361 patients with features of possible KLHL11-encephalitis (680 serum; 1164 cerebrospinal fluid) referred to our national reference center. The KLHL11 antibodies were screened using in-house HEK293 KLHL11 overexpression cell-based assay and positive samples were further analyzed by immunohistochemistry. Detailed clinical and follow-up information was collected.
Results: Seventeen patients with KLHL11-encephalitis were identified. The median age of patients was 59 (range 28–76) years old, 12 individuals (71%) were male. Common phenotypes were cerebellar ataxia ($n=12$, 71%), brainstem encephalitis ($n=12$, 71%), opsoclonus myoclonus ($n=8$, 47%), limbic encephalitis ($n=3$, 18%) and respiratory or consciousness disorder ($n=4$, 24%). Meningitis was observed in 1 patient. Concurrent antibodies included NMDAR ($n=2$), GFAP ($n=1$) and CASPR2 ($n=1$). MRI was abnormal in 8 cases (47%), showing hyperintensity in rhombencephalon ($n=3$, 18%) or limbic system ($n=4$, 24%). Tumors were identified in 11 (65%) cases, including seminoma ($n=5$, 29%), teratoma ($n=2$, 12%), small cell lung cancer, renal cell carcinoma, urinary tract cancer, unknown primary (all $n=1$). Fifteen patients received first-line immunotherapy (88%), and 6 second-line immunotherapy (35%). Improvement or stabilization was achieved in 10/15 (67%) patients. The median follow-up duration was 20 (1.5–180) months and 6 patients died in this period.

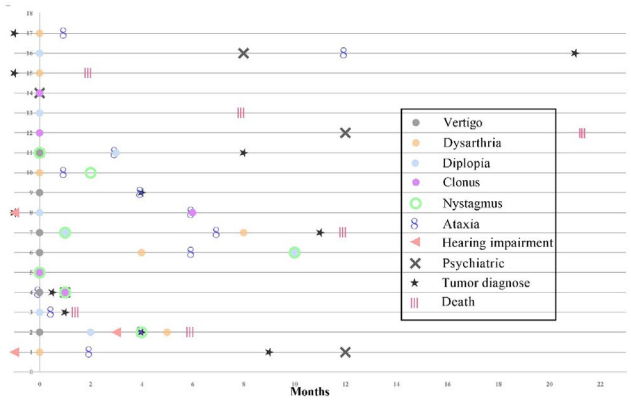

FIGURE 1 Timeline of KLHL11 patient's initial symptoms, tumor diagnose and death.

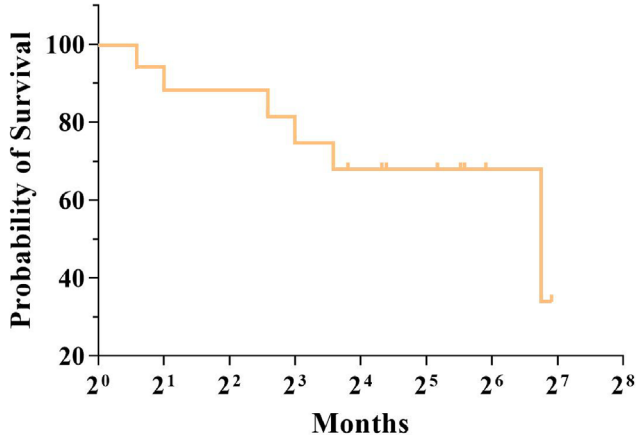

FIGURE 2 Kaplan-Meier curve shows the survival probability of KLHL11 patients

Conclusion: KLHL11-encephalitis mainly related to infratentorial involvement, but can present as limbic encephalitis. Early diagnosis enables early oncological and immunological treatment, improving outcomes.
Disclosure: M.J. is supported in part by the Chinese scholarship council program (Project ID 202308430038) and the First Affiliated Hospital of Nanchang University.

OPR-030 | Age-related dynamics of GFAP blood levels in normal ageing: Implications for biomarker studies in neurological diseases

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Background and Aims: GFAP is an astrocytic biomarker that is upregulated in various neurological conditions, including multiple sclerosis (MS). In MS, higher serum GFAP (sGFAP) are associated with disability worsening and MS-related MRI changes. For correct interpretation of sGFAP, detailed knowledge of its variability with age and its temporal dynamics in neurologically inconspicuous individuals is crucial. This has not been investigated.
Methods: 316 (mean age = 64.5±10.7 years, range = 38–82, 184 female) neurologically inconspicuous individuals participating in a community-dwelling cohort study, with longitudinal data (mean follow-up duration = 5.6±1.0 years) available from 89 participants, were included. Participants underwent comprehensive diagnostic work-up including a detailed neurological examination, 3T-brain-MRI, cognitive, and laboratory evaluation. sGFAP was measured using a single molecule array.
Results: sGFAP significantly increases with age ($r=0.5$, $p<0.001$) (< 50 years (pg/mL, mean±SD) (73.1±25.4, 50–60 years (86.8±35.1), 60–70 years 136.9±48.4), >70 years (154.6±60.7) and tendentially higher sGFAP levels are found in females compared to males ($p=0.05$). The increase of sGFAP with age is accompanied with an increase in the variability of this marker in the older age groups ($p<0.05$). Longitudinal analyses showed a significant difference between males and females ($p=0.02$), with a larger sGFAP increase in females.
Conclusion: sGFAP levels increase with age, which is accompanied by a higher variability of this marker in older individuals. This high variability of sGFAP in neurologically normal individuals needs to be taken into account when interpreting this marker in neurological disorders and requires the establishment

of normative values, e.g. based on percentiles or Z-scores. Analyses of potential relationships between sGFAP, brain-MRI, cognitive measures, and other factors are ongoing.

Disclosure: R.D: received travel funding from Janssen, Novartis and Sanofi D.P: is in the advisory board for "Cognition and MS" for Novartis and received speaking honoraria from Biogen, Novartis, MedAhead and Bristol-Myers Squibb S.H; B.H: received speaking honoraria from Roche and Bristol-Myers Squibb D.L: was Chief Medical Officer of GeNeuro until end of 2023 J.K: has received speaker fees, research support, travel support, and/or served on advisory boards by Swiss MS Society, Swiss National Research Foundation (320030_212534/1), University of Basel, Progressive MS Alliance, Alnylam, Bayer, Biogen, Bristol Myers Squibb, Celgene, Immunic, Merck, Neurogenesis, Novartis, Octave Bioscience, Quanterix, Roche, Sanofi, Stata DX. C.E: has received funding for traveling and speaker honoraria from Biogen Idec, Bayer Schering Pharma, Merck Serono, Novartis, Genzyme and Teva Pharmaceutical Industries Ltd./Sanofi-Aventis, Shire; received research support from Merck Serono, Biogen Idec, and Teva Pharmaceutical Industries Ltd./Sanofi-Aventis; and serves on scientific advisory boards for Bayer Schering Pharma, Biogen Idec, Merck Serono, Novartis, Genzyme, Roche, and Teva Pharmaceutical Industries Ltd./Sanofi- Aventis M.K: received travel funding and speaker honoraria from Bayer, Biogen, Novartis, Merck, Sanofi and Teva and serves on scientific advisory boards for Biogen, Bristol-Myers Squibb, Gilead, Merck, Novartis, and Roche. He received research grants from Biogen, Novartis and Teva Others: no disclosures.

OPR-031 | Conformational antibodies to proteolipid protein-1 in patients with CNS autoimmune demyelinating disorders

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Background and Aims: Antibodies to proteolipid-protein-1 (PLP1-IgG), a major central myelin protein also expressed in the PNS as the isoform DM20, have been previously identified mostly in patients with MS, with unclear clinical implications. However, most studies relied on non-conformational immunoassays and included few patients with non-MS CNS autoimmune demyelinating diseases (ADD).

Methods: After devising a live cell-based assay (CBA) for PLP1-IgG, we tested a retrospective cohort of ADD patients ($n=284$; non-MS=160 ADD; MS=124) and controls ($n=177$) for these antibodies. We validated our findings on a prospective cohort of suspect ADD patients ($n=820$). PLP1-IgG-positive samples were tested for IgG subclasses, DM20-IgG, and on rat brain tissue-based assay (TBA). PLP1-IgG-positive MS and MOGAD patients' clinical features were compared with those of the PLP1-IgG-negative.

Results: PLP1-IgG were found in 0/177 controls and 42/1104 ADD patients mainly diagnosed as other-ADD (19/42) with frequent myelitis/encephalomyelitis (14/19) and co-existing PNS involvement (13/19). PLP1-IgG were also found in MOGAD (11/42), more frequently with PNS involvement ($p=0.01$), and in MS (12/42), more frequently with atypical features ($p<0.001$). PLP1-IgG a) co-localized with their target on CBA-TBA, where their binding was abolished after immunoadsorption and fixation-induced conformational epitope alteration; b) mostly pertained to the IgG1/IgG3 subclass (68.3%) and were able to induce CDC; c) co-reacted with DM20 in all 12 patients with PNS involvement tested.

Conclusion: Conformational PLP1-IgG are mainly found in non-MS ADD, where they allow to identify patients with peculiar phenotypes. DM20 co-reactivity provides a rationale for the PNS involvement. PLP1-IgG might also represent detrimental prognostic markers in MOGAD and MS.

Disclosure: Nothing to disclose.

Sunday, June 22 2025

Child Neurology/Developmental Neurology

OPR-032 | The role of brain biomarkers in the clinical course of status epilepticus in the pediatric population

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Background and Aims: Biomarker study offers a modern approach in the multimodal evaluation of status epilepticus (SE) as

per the cytokines' role in epileptogenesis through neuroinflammation and microglial activation. The research aims to assess the cytokine profile of paediatric patients with SE providing insights into future neurotherapeutic strategies.

Methods: This retrospective case-control study examined 55 paediatric patients with SE of various etiologies and 54 control subjects who were admitted at the Mother and Child Institute from 2019 to 2023. The TGF, Il-6, Il-1 alpha, Il-1 beta and the Il-1Ra/Il-1 F3 ratio were investigated by the ELISA immunoenzymatic method. The data analysis was performed using IBM-SPSS statistical software.

Results: Upon the t-student analysis, the average values of TGF-beta 1 showed statistically significant differences between the SE and control subjects (4409,4 pg/ml vs. 179,9pg/ml, $p < 0.001$) supporting greater degree of neuroinflammation. Similar results supporting this statement were obtained in the evaluation of Il-6 (1431 pg/ml vs 82 pg/ml, $p < 0.001$), Il-1 beta (90.62 pg/ml vs 5.84 pg/ml, $p < 0.001$), Il-1 alpha (367.1 pg/ml vs 7.2 pg/ml, $p < 0.001$) serum concentration. The calculated ratio between Il-1 Ra/ Il-1 F3, used to profile the capacity of neurons to maintain homeostasis, revealed greater disbalance in SE subjects (480 pg/ml vs 86 pg/ml, $p < 0.021$).

Conclusion: The analysis of cytokine levels suggests disruption of immunomodulatory processes with a strong proinflammatory state and compromised protective mechanisms, which could contribute to the pathogenesis of status epilepticus in children. Further research is required to explore the usage of cytokine profiles to guide care in SE.

Disclosure: Nothing to disclose.

OPR-033 | Early predictors of long-term clinical outcomes in pediatric multiple sclerosis: A 12-year longitudinal study

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Background and Aims: This study investigates clinical and MRI predictors of key long-term clinical outcomes in pediatric MS over a median follow-up of 12.3 years.

Methods: Timing of first and subsequent relapses, 6-month confirmed Expanded Disability Status Scale (EDSS) worsening and EDSS worsening at last follow-up were recorded. Conventional, volumetric and diffusion tensor MRI sequences were acquired to assess lesion count, brain and choroid plexus (CP) volumetric measures, normal-appearing (NA) WM fractional anisotropy (FA), mean, axial and radial diffusivities.

Results: At follow-up, 69% (36/52) of patients experienced a clinical relapse, 21% (11/52) had a confirmed disability worsening event and 35% (18/52) had EDSS worsening. Higher number of infratentorial lesions (hazard ratio[HR] = 1.09, 95%-confidence interval[CI] = 1.02;1.18), presence of spinal cord lesions (HR = 2.45, 95%-CI = 1.18;5.10), higher CP volume (HR = 1.58, 95%-CI = 0.93;2.68), and lower thalamic volume (HR = 0.77, 95%-CI = 0.60;0.99) at baseline predicted a shorter time to first relapse, whereas use of high-efficacy treatment (HET) showed protective effect (HR = 0.20, 95%-CI = 0.06;0.68). Higher EDSS (HR = 1.29, 95%-CI = 0.96;1.73), brain WM lesion volume (HR = 1.52, 95%-CI = 0.95;2.44), the presence of spinal cord lesions (HR = 1.04, 95%-CI = 1.01;1.06), and higher CP volume (HR = 1.35, 95%-CI = 1.00;1.83) at baseline increased relapse risk, whereas HET lowered relapse risk (HR = 0.21, 95%-CI = 0.11;0.40). Younger age (HR = 0.82, 95%-CI = 0.68;0.98) and lower NAWM FA (HR = 0.67, 95%-CI = 0.51–0.88) were associated to a shorter time to a confirmed disability worsening event. Lower NAWM FA also predicted greater EDSS worsening ($\beta = -.26$, 95%-CI = −0.50; −0.03) at follow-up.

Conclusion: MRI markers of focal and diffuse inflammatory activity and thalamic atrophy predict long-term disease outcomes in pediatric MS. HETs delayed time to first relapse and reduced overall relapse risk.

Disclosure: MAR consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche, and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva. MM grants and personal fees from Sanofi Genzyme, Merck Serono, Roche, Biogen, Amgen, Novartis. MA, EP, FM nothing. PP speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon, Sanofi. LM consulting and speaking fees from Biogen, Bristol-Myers Squibb, Novartis, Roche, Sanofi-Genzyme, Merck-Serono, Biogen, Alexion. MP grants and personal fees from Roche, Merck Serono, Janssen-Cilag, Sanofi, Biogen, Novartis, Amgen, Alexion, Almirall. ET speaking fees from Biogen Idec, Bristol-Meyers-Squibb. VTC consulting or speaking fees from Biogen Idec, Teva, Novartis, Genzyme, Almirall. MF consulting or speaking fees from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; research support from Biogen Idec, Merck-Serono, Novartis, Roche.

OPR-034 | Mapping upper cervical cord abnormalities in early pediatric multiple sclerosis

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Background and Aims: Spinal cord lesions and atrophy, particularly in the cervical region, are common in adult multiple sclerosis (MS) patients and correlate with clinical disability. In pediatric MS, spinal cord damage remains largely unexplored, with two studies reporting neither significant atrophy nor microstructural abnormalities compared to healthy controls (HC). In this study, we aimed to investigate the relationship between upper cord lesions, cord area, and clinical disability in pediatric MS.
Methods: Thirty-eight pediatric MS patients and 13 age- and sex-matched HC underwent clinical and 3T MRI evaluations. Global and voxel-wise assessment of upper cord lesions and area were performed using brain 3D T1-weighted scans.
Results: Twelve (32%) pediatric MS patients (67% females, median disease duration [interquartile range] = 1.0 [0.4;2.5] year) had 1 or more cervical lesions. No significant differences in upper cord area were observed between HC and MS patients (estimated mean difference [EMD] = 1.7, 95% confidence interval [CI] = −3.4;6.9, $p = 0.508$), or between patients with and without cord lesions (EMD = 3.9, 95% CI = −2.6;10.2, $p = 0.238$). Voxel-wise analysis revealed no cord atrophy in pediatric MS compared to HC. Increased cord area at C2-C3 level was observed in patients with cord lesions compared to those without lesions and HC ($p < 0.001$, uncorrected, conjunction analysis). Voxels indicating increased cord area were located in the posterior columns and tended to co-localize with lesions.
Conclusion: No significant upper cord atrophy was observed in pediatric MS patients. Regional area increase in patients with lesions likely reflects inflammation and edema, highlighting the need for prompt, effective treatment in pediatric MS patients.
Disclosure: MM grants and personal fees from Sanofi Genzyme, Merck Serono, Roche, Biogen, Amgen, Novartis. PV, MR, MG nothing. PP speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon, Sanofi, and grants from Italian Ministry of Health and FISM. LM consulting and speaking fees from Biogen, Bristol-Myers Squibb, Novartis, Roche, Sanofi-Genzyme, Merck-Serono, Biogen, Alexion. MF compensation for consulting or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM. MAR consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche, and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva; grants from the MS Society of Canada, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM.

OPR-035 | Comprehensive analysis of clinical, imaging, and genetic features in pediatric metachromatic leukodystrophy: A 15-year follow up

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Background and Aims: MLD is a rare lysosomal disorder inherited in an AR pattern, which results from the abnormal accumulation of sulfatides in the CNS. Sulfatides, serve as physiological substrates for (ARSA) enzyme, and play a critical role in the structural integrity of myelin. Mutations in the ARSA gene and less frequently in the PSAP gene lead to the accumulation of sulfatides causing progressive myelin damage in the CNS and PNS.
Methods: This cross-sectional observational study was conducted in the Mofid Children's Hospital and enrolled 30 patients with the diagnosis of MLD referred to the Neurometabolic Clinic March 2009-March 2024. The diagnosis was based on clinical, MRI findings, EMG-NCV, ARSA enzyme deficiency and was confirmed through direct ARSA gene sequencing. In cases with indecisive ARSA gene sequencing, PSAP direct gene sequencing was performed.
Results: In this study, 10 patients showed behavioral disorders and ADHD before MLD presentation. 3 patients presented as motor delay and brain MRI findings were in normal limits. (30.0%) passed away, HPSC was conducted in 7 patients. Among these, 4 patients died post-transplantation. Of the 3 surviving patients, symptoms stabilized in 2 cases, while in 1 case, where the transplant was received from a carrier brother, symptoms continued to worsen.
Conclusion: The current study provides significantly important clinical, laboratory, electromyoneurography, and genetic findings of the pediatric MLD population in a Neurometabolic center in Mofid Children's Hospital in Iran. A critical assessment of the disease characteristics enables a clearer understanding of the pathogenesis for possible of curative therapeutic approaches.
Disclosure: Nothing to disclose.

OPR-036 | Echocardiographic evaluation of left ventricular function in children with SMA under nusinersen treatment

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Background and Aims: Spinal muscular atrophy (SMA) is a genetic neuromuscular disease associated with cardiovascular abnormalities. The impact of nusinersen treatment on myocardial function in children with SMA remains unclear. This study aimed to evaluate changes in left ventricular (LV) function in children with SMA before and after nusinersen treatment using echocardiography.
Methods: A prospective observational study was conducted on 35 children with SMA who received six doses of nusinersen within 10 months at a tertiary hospital in China. 35 healthy controls were included for comparison. LV function was assessed using echocardiography at baseline and after 10 months of treatment. LV dyssynchrony and myocardial strain were measured using two-dimensional speckle tracking echocardiography.
Results: The mean age of the SMA children was 6.58 ± 3.11 years. Before treatment, the global longitudinal strain (GLS) in the SMA group was significantly lower than in the control group ($p < 0.001$), and LV systolic synchronization was poorer ($p < 0.001$). Following nusinersen treatment, GLS increased ($p < 0.001$) and synchrony improved ($p = 0.004$) in the SMA group. However, even after 10 months of treatment, GLS in the SMA group remained lower than in the control group ($p = 0.011$), and LV synchronization was still inferior ($p = 0.028$).
Conclusion: Short-term nusinersen treatment improved LV function in children with SMA, as evidenced by changes in LV myocardial strain indicators. Further research is warranted to explore the treatment of myocardial injury in SMA patients.
Disclosure: nothing to disclose.

MS and Related disorders 1

OPR-037 | Ocrelizumab versus Natalizumab in multiple sclerosis: A propensity-score study

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Background and Aims: Ocrelizumab (OCR) and Natalizumab (NTZ) are highly effective treatments widely used in Multiple Sclerosis (MS). We aim to compare long-term clinical effectiveness, safety and treatment persistence between the two drugs.
Methods: We retrospectively analyzed data from relapsing and progressive patients who started treatment between 2010 and 2019 at "La Sapienza" and "Federico II" Universities. Between-group differences in age, sex, previous treatment status, clinical and MRI activity at baseline, phenotype and disease duration were adjusted via propensity-score nearest-neighbor matching, while differences in the length of follow-up were adjusted with pairwise censoring. Cox proportional hazard regression models were used with Evidence of disease activity (EDA-3) and its components (relapses, MRI activity, and confirmed disability progression) as outcomes. Treatment discontinuation and occurrence of adverse events (AEs) were tested using logistic regressions.
Results: We identified 308 patients (140 on OCR, 168 on NTZ) with a mean (SD) follow-up of 75.7 (30.8) months. Patients treated with OCR were older, less active, and less frequently naïve at baseline than NTZ-treated patients. The PS-matching procedure retained 140 (70 pairs) patients with a mean follow-up of 55.9 (14.3) months. No significant differences were found between NTZ and OCR regarding relapses, MRI activity or confirmed disability progression. OCR was associated with a higher risk of AEs, though treatment discontinuation rates were comparable.

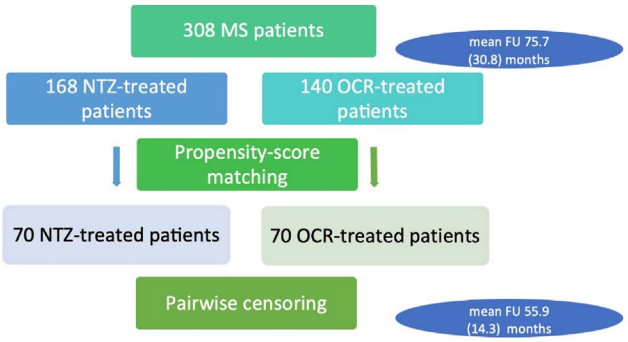

FIGURE 1 Study flow-chart. FU: follow-up, MS: multiple sclerosis, NTZ: natalizumab, OCR: ocrelizumab.

TABLE 1 Demographic and clinical characteristics of the total cohort and of the matched cohort. a. t-test for independent values b. X2 c. Mann–Whitney DMT: disease modifying treatment, EDSS: expanded disability status scale, IQR: interquartile range.

	ORIGINAL COHORT			MATCHED COHORT		
	Natalizumab(168)	Ocrelizumab(140)	p	Natalizumab(70)	Ocrelizumab(70)	p
Age(years), mean(sd)	42(11)	49.9(11)	**<0.001**[a]	44.7(11.1)	45.1(11)	0.813[a]
Female sex, n(%)	121 (72)	85 (60.71)	**0.036**[b]	45 (64.28)	47 (67.14)	0.722[b]
Disease duration (years) mean(sd)	15.7(8.04)	15.9(8.18)	0.806[c]	14.6(8.01)	14.4(7.68)	0.98[c]
Naïve patients, n(%)	57(33.9)	32(22.86)	**0.033**[b]	21 (30)	23 (32.86)	0.716[b]
Active patients at baseline[d], n(%)	147 (87.5)	59 (42.14)	**<0.001**[b]	52 (74.29)	51 (72.86)	0.848[b]
Phenotype at DMT start			**<0.001**[b]			0.829[b]
RRMS	152	57		56	55	
SPMS	13	47		11	13	
PPMS	3	36		3	2	
EDSS at baseline, median (IQR)	3 (0-6.5)	4.5 (0-7.5)	**<0.001**[c]	3(0-6.5)	2.75(0-7.5)	0.924[c]

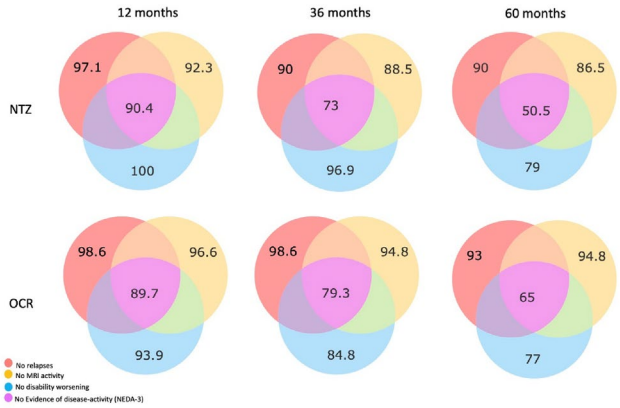

FIGURE 2 Probability of being free from relapses, MRI activity, EDSS progression and to be NEDA-3 at 12, 36 and 60 months.

Conclusion: This study provides evidence of comparable effectiveness and treatment persistence between OCR and NTZ over 5 years, with OCR being associated with a higher incidence of mild/moderate AEs.

Disclosure: Antonio Carotenuto disclosed research grants from ECTRIMS-MAGNIMS and Almirall, Marcello Moccia has received from MUR PNRR Extended Partnership (MNESYS no. PE00000006, and DHEAL-COM no. PNC-E3-2022-23683267), ECTRIMS- MAGNIMS, UK MS Society, and Merck and salary as Editorial Board Member from Neurology (AAN, MN, US) and Multiple Sclerosis Journal (Sage, UK); Vincenzo Brescia Morra research grants from Italian MS Federation and Roche, Carlo Pozzilli from Biogen, Teva, Novartis, and Genzyme, Maria Petracca from Baroni Foundation and the Italian Ministry of University and Research. Antonio Carotenuto, Marcello Moccia, Vincenzo Bresciamorra, Carlo Pozzilli, Serena Ruggieri, Giovanna Borriello, Roberta Lanzillo received honoraria and funding Novartis, Janssen, Roche, Merck, BMS, Biogen, Almirall, Sanofi- Genzyme, Teva, Bayer, Mylan, Viatris, Actelion, HEALTH&LIFE S.r.l., AIM Education S.r.l., FARECOMUNICAZIONE E20. Elena Barbuti, Alessia Castiello, Valeria Pozzilli, Ilaria Tomasso have nothing to disclose.

OPR-038 | Real-world effectiveness and safety of ofatumumab in multiple sclerosis: Data from a 12-months follow-up study

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Background and Aims: Ofatumumab (OFA) is a highly effective therapeutic option for multiple sclerosis (MS), but real-world data on its efficacy and safety remain limited. This study evaluated the efficacy and safety of OFA in a real-world cohort of relapsing MS patients over 12 months. Additionally, frailty, an age-related vulnerability assessed using a frailty index (FI), was examined to better characterize the patient population selected for OFA treatment.

Methods: Clinical and MRI data were retrospectively collected from 12 MS clinics in Central Italy. Outcomes included the annualized relapse rate (ARR), relapse occurrence, radiological activity, and safety profile. Frailty was categorized using FI.

Results: A total of 242 MS patients were included (66% female; mean age 38.9±10.3 years; disease duration 7.7±7.6 years). Of these, 95 were treatment-naïve, and 147 were switchers (60.8% first switch). The Expanded Disability Status Scale (EDSS) remained stable during follow-up ($p > 0.05$). Only four relapses occurred, all within the first six months (mean time to relapse: 3.0±1.8 months). ARR significantly decreased from 0.9 to 0.02 ($p < 0.001$). MRI activity was detected in 10 patients within six months and in 3 of the 77 patients at 12 months. Adverse events included flu-like symptoms (34.3%), injection-site reactions (8.2%), and infections (18.5%). Among 239 patients assessed for frailty, 187 were fit (FI≤0.10), 30 were less fit (0.10 < FI≤0.21), and 22 were frail (FI>0.21).

Conclusion: This real-world study confirms OFA as an effective and safe therapy, primarily prescribed to patients with low disability and mild frailty.

Disclosure: The authors declare no conflicts of interest related to this study.

OPR-039 | Perivascular cuffs suggest local B- and T-cell interaction in association with lesion formation in multiple sclerosis

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Background and Aims: Perivascular aggregation of mononuclear cells is a prevalent pathological observation in multiple sclerosis (MS), known as cuffing. Still, little is known about the characteristics of cuffs and their relationship to lesion initiation and progression. Here, we aimed to study ongoing processes in the perivascular compartment of the MS brain in spatial association with white matter (WM) lesion presence.

Methods: We characterized $n = 255$ donors from the Netherlands Brain Bank for the presence of perivascular cuffing and investigated the association of this trait with clinical and pathological

characteristics. With immunohistochemistry, we quantified proportional abundance of different cell types and functional markers in $n = 457$ cuffs present in different WM lesion-types in a cohort of $n = 18$ MS brain donors.
Results: Donors with detected cuffing (25%) showed a younger age at death, an increased presence of microglia nodules, and a higher brainstem lesion count. Regarding cell type composition, a similar abundance of T cells characterized cuffs in lesions compared to normal-appearing WM (NAWM). However, CD79a+ B-lineage cells had a higher abundance in perivascular cuffs in lesions compared to NAWM. Moreover, we show a positive relationship between the ratio of CD4+ to CD8+ cells and the abundance of CD38+ cells, and these CD38+ cells correlated with the abundance of PCNA+ cells, supporting local activation.
Conclusion: We show that B-cell presence spatially associates with lesion presence in MS. The correlation between T-cell distribution and CD38+ B-cell presence highlights the importance of perivascular T- and B-cell interaction for lesion formation in MS.
Disclosure: JS received research support and/or speaker and/or consulting fee of Biogen, Merck, Novartis, Roche, and Sanofi-Genzyme. IH and HH received research support from Biogen.

OPR-040 | Impact of vascular risk factors on motor performance and sensorimotor network integrity in multiple sclerosis patients

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Background and Aims: Vascular risk factors (VRFs) are associated with more severe disability and neurodegenerative processes in multiple sclerosis (MS). This study explored the impact of VRFs on motor performance, as well as integrity of brain and spinal cord sensorimotor regions in MS patients.
Methods: In this cross-sectional study, 268 MS patients and 180 healthy controls (HC) were grouped by VRF presence (HC-VRF[+]), MS-VRF[+]) or absence (HC-VRF[-], MS-VRF[-]). Disability and motor performance were assessed using the Expanded Disability Status Scale, Timed 25-Foot Walk and Nine-Hole Peg Test. Volumetric and diffusion-weighted MRI data were used to assess brain sensorimotor network and spinal cord structural integrity. Group differences in clinical and MRI measures and interactions between disease status and VRFs were explored. In MS patients, associations between clinical and MRI data were analyzed, focusing on VRF influence.
Results: Seventy-four (41%) HC and 179 (68%) MS patients had VRFs, with smoking being the most prevalent factor. MS-VRF(+) patients were significantly more disabled and showed worse motor performance compared to MS-VRF(-) (pFDR≤0.004). A significant interaction between VRF and disease status on motor performance, deep gray matter volume, anterior cerebellar motor area volume, and medial lemniscus mean diffusivity was found (pFDR≤0.039). In MS patients, the interaction between VRFs and medial lemniscus fractional anisotropy significantly influenced disability ($\beta = 1.931$, $p = 0.042$).
Conclusion: VRFs are associated with worse disability, motor impairment, and structural damage of specific sensorimotor structures of the brain in MS patients, while sparing spinal cord integrity. Preventing strategies targeting modifiable VRFs could mitigate their impact on MS progression.
Disclosure: Matteo Albergoni, Gloria Ritroso, Nicolò Tedone, Elisabetta Pagani, Loredana Storelli, Paola Valsasina have nothing to disclose. PP received speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon and Sanofi. He received research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). MF received compensation for consulting services or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM. MAR received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche, and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva, she receives research support from the MS Society of Canada, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM.

OPR-041 | Assessing structural differences in late-onset compared to adult-onset multiple sclerosis: A multiparametric MRI study

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Background and Aims: Previous studies have identified MRI differences between late-onset multiple sclerosis (LOMS) and adult-onset MS (AOMS), but a comprehensive analysis of global

and regional white matter (WM) and gray matter (GM) metrics is lacking. By using a multiparametric approach, we compared the structural MRI profiles of LOMS and AOMS, focusing on global and regional assessment of WM lesions, GM volume and WM diffusivity abnormalities.

Methods: 3T MRI scans were acquired for 40 LOMS, 195 sex- and disease duration (DD)-matched AOMS and 175 sex- and age-matched healthy controls (HC, divided into HC-AOMS = 125, HC-LOMS = 50). We applied false discovery rate (FDR) for conventional MRI analyses and family-wise error correction (FWE) for voxel-wise analyses, with a $p < 0.05$ considered significant.

Results: Both MS groups showed significant reductions in all volumetric measurements and higher T2 lesion volumes (T2-LV) compared to HC, with LOMS showing greater T2-LV than AOMS (FDR-p ≤ 0.015). Compared to AOMS, LOMS had higher frequency of WM lesions in the anterior thalamic radiation and forceps major/minor (FWE-p ≤ 0.002). Compared to HC, both MS groups showed reduced fractional anisotropy and increased mean, axial, and radial diffusivity in most WM tracts, along with widespread GM volume loss (FWE-p < 0.05). No differences were found between LOMS and AOMS in WM diffusivity metrics, but LOMS showed greater GM volume loss compared to AOMS in the left paracentral lobule, insula, bilateral putamen, and right pre-/post-central gyrus (FWE-p ≤ 0.040).

Conclusion: Compared to DD-matched AOMS, LOMS had a worse structural profile, mostly characterized by more severe GM volume loss and higher WM lesion burden.

Disclosure: Funding: Supported by Fondazione Italiana Sclerosi Multipla (FISM2023/S/1). Competing interests. NT, AM, DM and FE nothing to disclose. PP received speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon and Sanofi. He received research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). MF received compensation for consulting services or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM. MAR received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche, and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva, she receives research support from the MS Society of Canada, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM.

OPR-042 | Time from clinical suspicion to lumbar puncture; A novel approach to assessing compliance with meningitis guidelines

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Background and Aims: Bacterial meningitis is a rapidly evolving and time critical condition, with mortality as high as 30%. The diagnosis is pathological with National Institute for Health and Care Excellence recommending a lumbar puncture (LP) within 1 hour (h) of hospital admission, ideally prior to antibiotics. Despite this, the largest UK study to date reports a median time to LP of 16.5h and that most patients are started on antimicrobial beforehand. In this study, we used the novel approach of assessing time of clinical suspension of meningitis to LP as a means of evaluating clinical efficacy.

Methods: A retrospective analysis was conducted of 101 patients admitted to a single, tertiary NHS hospital with suspected meningitis over 19 months consecutively. Results reported using descriptive statistics, R-Studio.

Results: The median time for first attempt of LP from clinical suspicion was 15.6h, with median time of successful LP of 21.2h. Overall, 5.9% had a LP attempt within 1h and 23.5% had a successful LP within 4h. Of those delayed beyond one hour, 31.2% were related to preventable factors, including staffing.

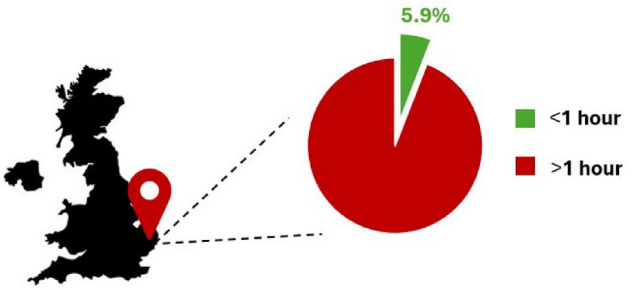

FIGURE 1 Time From Clinical Suspicion of Meningitis to First Lumbar Puncture Attempt. Time in hours, expressed as percentage (%). Less than ().

Conclusion: This study emphasises that even when applying time to LP from clinical suspicion, the average consistently exceeds national guidelines. This, combined with decreased diagnostic accuracy of LP following antibiotics, may lead to continuing unnecessary therapy, longer hospital stays and increased antibiotic resistance risk. Contributing factors included shortage of trained staff, procedural challenges and unnecessary imaging. This study stresses the need for further, prospective, investigations into delays of LP's, which will translate to improved practice.

Disclosure: Nothing to disclose.

OPR-043 | Status epilepticus and stroke-like symptoms: The role of syphilis testing in atypical presentations

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Background and Aims: Neurosyphilis can occur at any stage of syphilis. Its diagnosis in the era of widespread penicillin use is challenging, due to its varied neurological manifestations and low suspicion index. Late-stage neurosyphilis presenting with status epilepticus is rare, especially in our setting.
Methods: We present a case of late-stage neurosyphilis presenting with general paresis, meningovascular involvement, stroke-mimic and status epilepticus.
Results: A 70-year-old male with history of diabetes, bladder cancer, and benign prostatic hyperplasia was referred under a stroke code for sudden left hemispheric dysfunction, including hemiplegia, speech disturbance, and forced oculocephalic deviation. Neuroimaging excluded acute ischemia but revealed chronic ischemic lesions and intracranial stenoses consistent with large-vessel vasculitis (Figure 1). Family history disclosed gait disturbances with parkinsonian features, and behavioral changes over the prior year. The patient later developed forced left oculocephalic deviation and ipsilateral facial myoclonus. EEG confirmed status epilepticus (Figure 2), which resolved with antiseizure therapy, though the patient remained aphasic with delayed responses, only single-step command following, and frontal release signs. Cerebrospinal fluid analysis revealed mild pleocytosis (158 cells/mm^3, 89% lymphocytes) and hyperproteinorrhachia (1.459 g/L), with negative cultures and molecular tests. A diagnosis of late-stage neurosyphilis was made thanks to syphilis screening (RPR: 1/64; VDRL: reactive). A PET/CT scan excluded involvement of other organs. IV penicillin and corticosteroids were initiated, resulting in a favorable recovery to baseline.

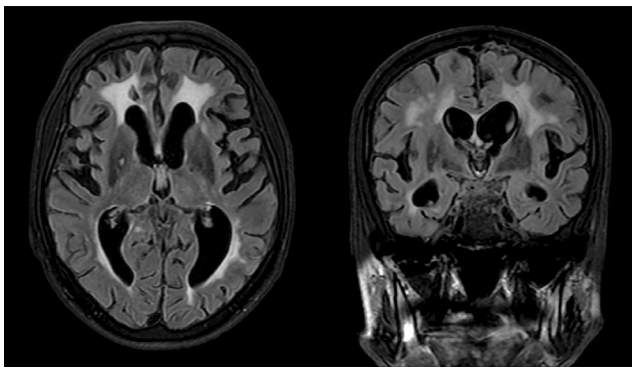

FIGURE 1 Brain MRI severe brain atrophy, mainly hippocampus and temporal lobes. Also hydrocephalus of chronic characteristics, with confluent T2 hyperintensity affecting the periventricular white matter, related to demyelination of probable chronic hypoxic origin

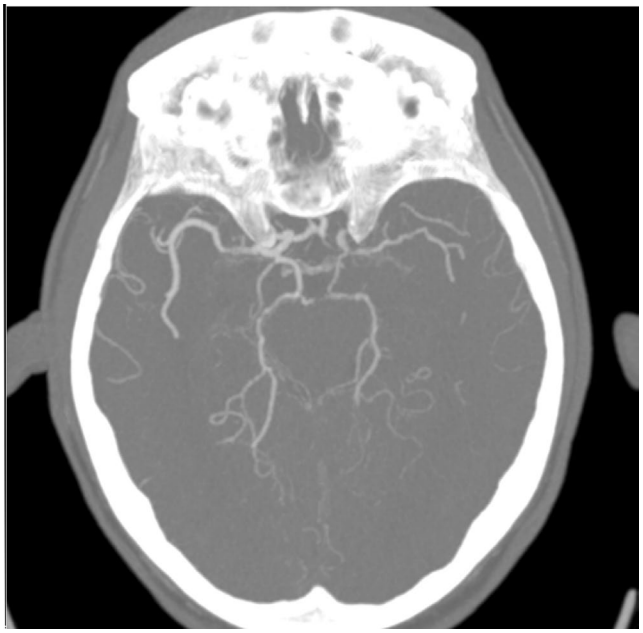

FIGURE 2 CT angiography showed multifocal intracranial arterial narrowing and beading, involving both the anterior and posterior circulation.

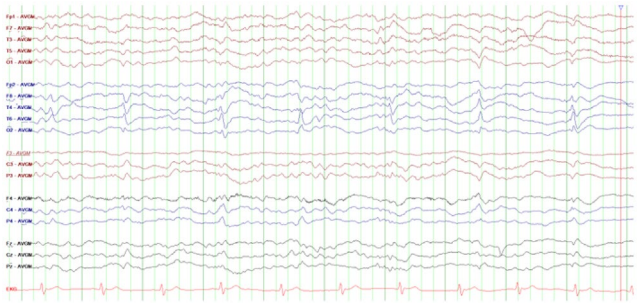

FIGURE 3 Initial EEG with periodic lateralized discharges (LPDs) in the form of sharp waves in the right posterior quadrant (right occipito-temporoparietal region).

Conclusion: Although rare, neurosyphilis should be considered in unexplained status epilepticus or stroke, particularly if preceded by meningitis or encephalitis symptoms and lacking traditional risk factors, to ensure timely diagnosis and effective treatment.
Disclosure: Nothing to disclose.

OPR-044 | Predictors of cerebral complications in pediatric tuberculous meningitis patients: A systematic review and meta-analysis

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Background and Aims: This systematic review and meta-analysis included three studies with four groups analyzing BTK inhibitors for RMS. A comprehensive search of PubMed,

Embase, and Cochrane databases was conducted following PRISMA guidelines. Risk of bias was assessed, and a meta-analysis was performed using Review Manager 4.1.

Methods: This systematic review and meta-analysis included 13 studies focusing on three key categories: molecular, clinical, and imaging factors. A comprehensive search of PubMed, Embase, and Cochrane databases was conducted following PRISMA guidelines. Risk of bias was assessed, and a meta-analysis was performed using Review Manager 4.1.

Results: A total of 2,336 pediatric patients were included. Stage III TBM was a strong predictor of adverse outcomes (OR 3.27; 95% CI 1.56–6.83; I^2 85%; $p=0.002$). Hydrocephalus also increased risk (OR 1.57; CI 95% 1.06–2.33; I^2 35%; $p=0.02$), especially non-communicating hydrocephalus. Glasgow Coma Scale (GCS) scores <7 were seen in 30–50% of patients with complications, correlating with stroke risk. Elevated inflammatory markers like IL-6, TNF-α, and CSF protein >1 g/L were associated with higher complications, while CSF glucose <40 mg/dL was significantly lower in affected patients. Clinical manifestations, such as hemiparesis or hemiplegia, were observed in 45% to 64% of patients with cerebrovascular complications. Lastly, malnutrition was identified as a critical factor influencing prognosis, whereas a shorter illness duration (<1 month) was found to exert a protective effect.

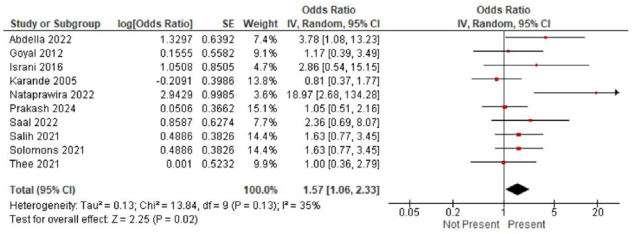

FIGURE 1 Hydrocephalus

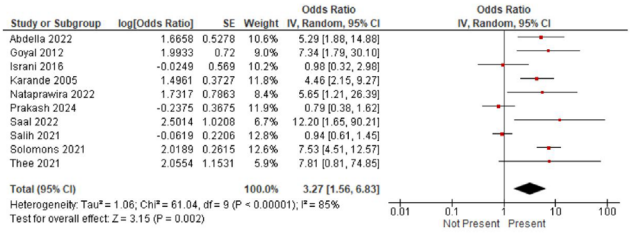

FIGURE 2 TBM Stage III

Conclusion: This review highlights molecular and clinical predictors of cerebrovascular complications in pediatric TBM, emphasizing their role in improving early diagnosis and guiding targeted management to enhance outcomes.

Disclosure: Nothing to disclose.

OPR-045 | Unmasking undiagnosed HIV through cerebral toxoplasmosis: Two case illustrations

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Background and Aims: Cerebral toxoplasmosis is one of the most frequently reported opportunistic central nervous system (CNS) infections in individuals with advanced HIV/AIDS. Despite advances in antiretroviral therapy, missed or delayed HIV diagnoses can result in life-threatening presentations of toxoplasmosis.

Methods: We retrospectively reviewed the clinical, radiological, and laboratory data of two patients who presented to our institution with acute neurological deficits and were subsequently diagnosed with HIV-related cerebral toxoplasmosis. Diagnostic evaluations included computed tomography (CT), magnetic resonance imaging (MRI), comprehensive serological panels, and targeted therapeutic interventions.

Results: A 47-year-old woman with a three-month history of fever, night sweats, and weight loss presented with acute mental status changes, global aphasia, and mild right hemiparesis. Neuroimaging revealed multiple contrast-enhancing lesions, prompting suspicion of metastatic disease or an infectious etiology. Serology confirmed newly diagnosed HIV and markedly elevated Toxoplasma gondii IgG titers. Despite prompt high-dose trimethoprim-sulfamethoxazole and corticosteroid treatment, her condition deteriorated rapidly, culminating in multisystem organ failure and death. A 50-year-old man presented with progressive cognitive impairment and mild tetraparesis. Initially presumed to have hemorrhagic metastases, he was later found to have uncontrolled HIV infection. Strongly positive T. gondii serologies and characteristic ring-enhancing lesions on magnetic resonance imaging established the diagnosis of neurotoxoplasmosis. Targeted antiparasitic therapy led to partial neurological improvement.

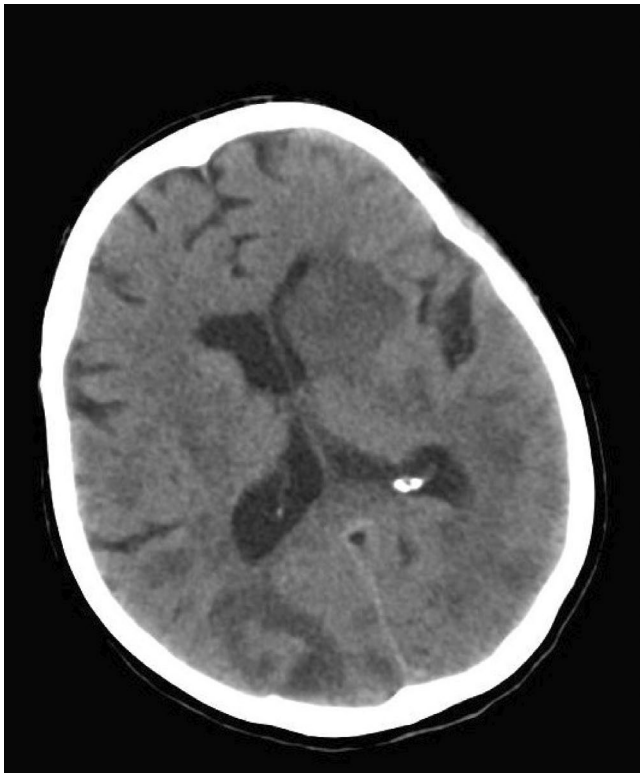

FIGURE 1 CASE 1 Noncontrast enhanced computed tomography demonstrating multiple hypodense lesions, most prominent in the left basal ganglia and right parietal lobe.

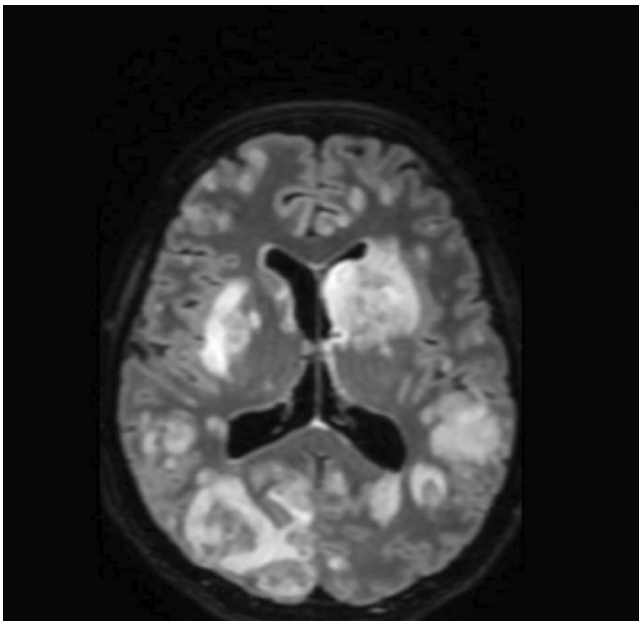

FIGURE 2 CASE 1 Multiple FLAIR-hyperintense lesions, with the concentric target sign seen in the deep parenchymal lesions.

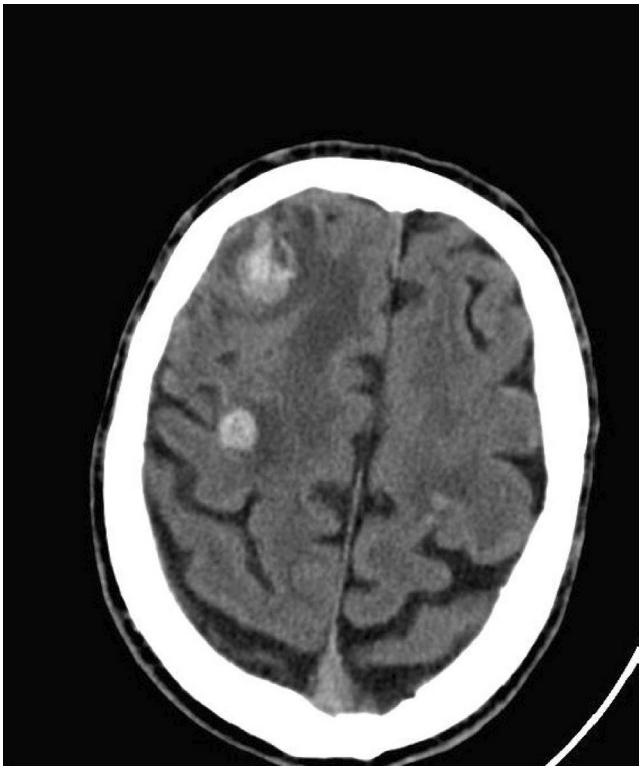

FIGURE 3 CASE 2 Noncontrast enhanced computed tomography revealing several intraparenchymal hyperdense rounded lesions and surrounding vasogenic edema.

Conclusion: These cases illustrate the diagnostic complexity and potentially fulminant course of cerebral toxoplasmosis in the setting of undisclosed or undertreated HIV/AIDS. Early identification of immunosuppression, prompt neuroimaging, and serological testing are paramount to initiate life-saving therapy and mitigate the risk of severe neurological sequelae.
Disclosure: Nothing to disclose.

OPR-046 | The hidden face of tuberculosis: A retrospective study of central nervous system manifestations in Nepal

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Background and Aims: Mycobacterium tuberculosis is the cause of (CNS-TB), a group of neurological syndromes with a comparatively high death and morbidity rate. Meningitis is the most frequent symptom of CNS-TB, followed by tuberculoma, tuberculous brain abscess, and Pott's illness. About 1% of cases of tuberculosis are attributed to CNS-TB. The objective is to know the clinico-demographic profile of patients with central nervous system tuberculosis (CNS TB) along with their hospital outcomes.
Methods: This is a single-centered retrospective study conducted among adult CNS-TB patients in our center over one year.
Results: A total of 61 patients (57.4% males) were diagnosed with CNS TB with a mean age of 42.10 (16.96) years. The majority were TB meningitis (55.7%) followed by tuberculoma 13 (21.3%) with few cases of tubercular abscess and spinal TB. Common presenting symptoms included fever (62.9%), headache (73.3%), weight loss (31.1%), vomiting (49.1%), seizures (26.2%), altered mental status (47.5%), and only a few cases of facial deviation and of visual loss. On examinations, neck stiffness was positive at 26.2%, and focal neurological deficit was found at 32.8%. Bacteriological and radiological imaging were done. The majority were treated with ATT of which three had side effects like ATT-induced hepatitis and ethambutol toxicity and only seven hydrocephalus cases had a shunt surgery done. The majority were discharged (86.9%) while 16.4% of cases were intubated and one case had mortality.
Conclusion: Early diagnosis through various investigations and appropriate management strategy is the cornerstone for the treatment of CNS-TB. More multi-center studies focusing on larger sample sizes are necessary.
Disclosure: Nothing to disclose.

Movement Disorders 1

OPR-047 | The language of gait: Interpreting emotional states through gait features

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Background and Aims: The complex interplay between gait alterations and emotions in Parkinson's disease (PD) requires further investigation. This study aimed at investigating whether the observation of emotional gait conditions can modulate spatio-temporal gait parameters and gait-related functional brain correlates in healthy subjects (HC) and PD patients by evoking those emotions.

Methods: We first administered a questionnaire containing videos of an actress walking with different gait patterns according to specific emotions (e.g. happiness, sadness, fear/anxiety and neutral) in order to select the videos with the mostly recognized emotional gait patterns in a cohort of 110 HC. Then, we administered the selected videos to 19 HC and 21 PD, which were asked to imitate the emotional gait patterns observed in the videos and to report the intensity and valence of the evoked emotions. The spatio-temporal gait parameters were monitored using six inertial sensors. All subjects observed the same videos during a functional MRI (fMRI) task in order to obtain neural correlates of emotional gait observation.

Results: In both HC and PD, happiness promoted an improvement in gait kinematics (e.g., increased stride length, turn velocity, upper limb and trunk movement amplitude) and an enhanced recruitment of the sensorimotor network during the fMRI task in PD. Sadness and anxiety were associated with a worsening of spatiotemporal gait parameters and to an extensive reduction of fMRI activity of sensorimotor areas, mirror neuron system and cerebellum.

Conclusion: This study suggests that positive and negative emotions specifically influence gait kinematics and fMRI activity of the sensorimotor system.

Disclosure: MP, AG ER, SM, LA, EP nothing to disclose. ES, EC, SB received grants from the Italian Ministry of Health. FA is Associate Editor of NeuroImage: Clinical, has received speaker honoraria from Biogen Idec, Italfarmaco, Roche, Zambon and Eli Lilly, and receives or has received research supports from the Italian Ministry of Health, the Italian Ministry of University and Research, AriSLA (Fondazione Italiana di Ricerca per la SLA), the European Research Council, the EU Joint Programme—Neurodegenerative Disease Research (JPND) and Foundation Research on Alzheimer Disease (France). MF is Editor-in-Chief of the Journal of Neurology, Associate Editor of Human Brain Mapping, Neurological Sciences, and Radiology; received compensation for consulting services from Alexion, Almirall, Biogen, Merck, Novartis, Roche, Sanofi; speaking activities from Bayer, Biogen, Cel- gene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neo- pharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research and Fondazione Italiana Sclerosi Multipla.

OPR-048 | Bridging pixel precision and clinical intuition: Quantifying 'movement disorders phenomenology' with 2D pose estimation

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Background and Aims: Identifying phenomenology in movement disorders is a core step in patient management. However, semantic definitions can be ambiguous, and clinical scales are often subjective and incompletely capture movement [1,2]. Human pose estimation offers objective motion capture with the potential to develop a set of tools that can complement existing clinical expertise. We have developed a pipeline for extracting quantifiable metrics from clinical recordings, focusing on hyperkinetic disorders detailed in 'Phenomenology in Movement Disorders' [3].

Methods: Multiple pose estimation applications were compared and MMPose had the highest-performing models for this context [4]. We analysed all videos featuring hyperkinetic movement disorders and after applying clinical and technical inclusion/exclusion criteria 1176 segments were extracted from the 650 source videos resulting in 2h37m of content. 2D pose estimation was implemented and post-processing ensured keypoint reliability.

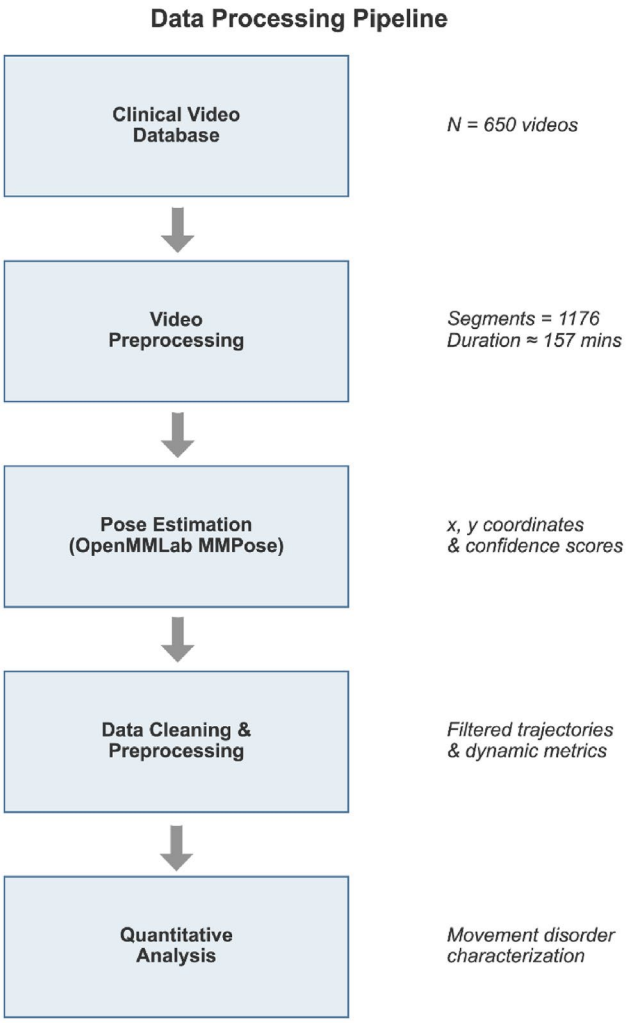

FIGURE 1 Analysis pipeline transforming clinical videos into quantifiable movement metrics. Key steps include video preprocessing, pose estimation with MMPose, trajectory filtering, and disorder-specific analysis.

Results: Our curation yielded structured data across five phenotypes: chorea ($n = 119$), dystonia ($n = 261$), myoclonus ($n = 228$), tics ($n = 211$), and tremor ($n = 357$). Initial analysis demonstrates phenotype-specific signatures: tremor exhibited characteristic frequency peaks, chorea showed shifting generalised dyskinetic patterns, and tics displayed spatial-temporal similarity.

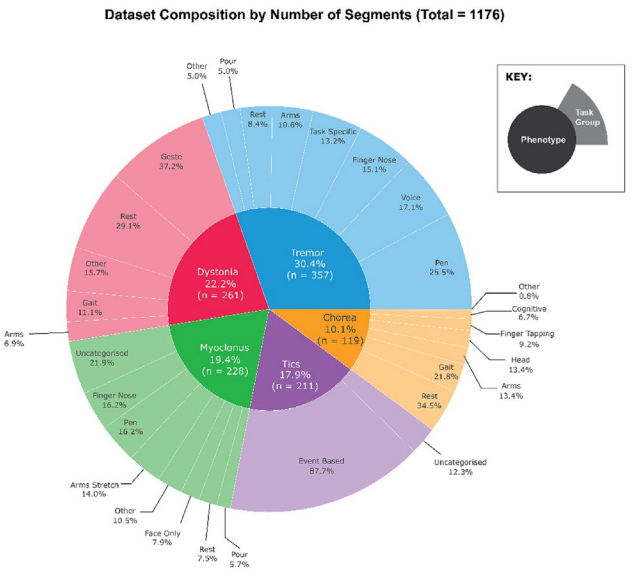

FIGURE 2 Data composition by segment number showing phenomenology categories (inner ring) and breakdown by tasks (outer ring). 'Uncategorised' indicates not fitting directories for other clinical examination tasks or actions. 'Other' groups categories with >5%.

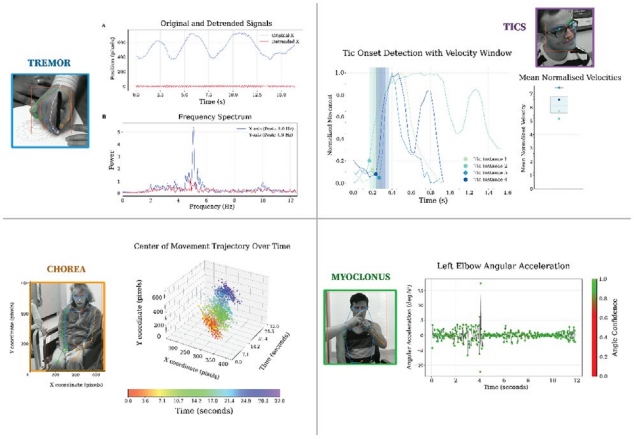

FIGURE 3 Representative analysis of phenotype movement patterns: tremor frequency analysis showing 4–5 Hz peaks, tic onset velocity profiles, chorea center-of-movement trajectory showing dispersed movement progression, and myoclonus angular acceleration spikes.

Conclusion: This proof-of-concept application establishes a framework for automated movement pattern analysis with ongoing work exploring the reliability and specificity of different kinematic features across phenotypes. 2D pose estimation can bridge the gap between subjective clinical assessment and objective movement quantification. Beyond improving diagnostic precision, this methodology offers new possibilities for treatment monitoring and research in movement disorders.

Disclosure: Nothing to disclose.

OPR-049 | Concordance of imaging and clinical based STN-DBS programming improves motor outcomes of directional stimulation in PD

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Background and Aims: Advances in STN-DBS technology, among which directional stimulation, improved Parkinson's disease (PD) treatment efficacy, while increasing the clinical programming complexity. Lead localization software may aid the stimulation contact selection process. We aimed to assess the concordance between imaging-suggested (IGP) and conventional-programming (CP) selected stimulation contacts one year after surgery and its impact on motor outcomes.
Methods: Sixty-four PD patients with bilateral STN-DBS were enrolled. Lead localization was reconstructed with BrainlabTM software. For each electrode, the vertical contact level and, when applicable, the directionality predicted by the lead reconstruction software to be the most effective were established and compared to the stimulation parameters clinically activated one year post-surgery. IGP/CP concordance ratio was calculated for both stimulation level and directional contacts. Post-operative modifications of PD motor symptoms severity were compared among groups of concordant and discordant IGP/CP programming.

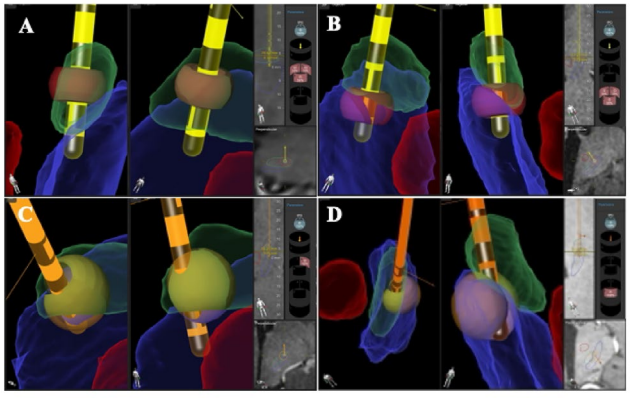

FIGURE 1 Examples of assessments of level contact and directionality CP/IGP concordance from our cohort. A: CP/IGP concordant contact level; B: CP/IGP discordant contact level; C: CP/IGP concordant directionality; D: CP/IGP discordant directionality.

Results: One-year post-surgery, IGP/CP concordance was 80% for active stimulation vertical contact level and 51% for directionality. No significant difference in motor outcomes was found between IGP/CP concordant and discordant patients for contact level activation, whereas patients with concordant IGP/CP active directional stimulation (c-Direction) showed superior motor outcomes at one-year follow-up than those discordant (d-Direction) (UPDRS-III stimulation-induced improvement: c-Direction = −25.66±13.74 vs d-Direction = −12.54±11.86; $p = 0{,}011$).

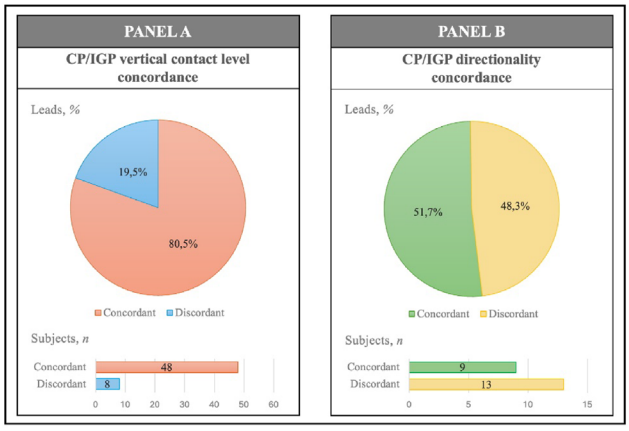

FIGURE 2 CP/IGP concordance analysis for vertical contact level (panel A) and directionality (panel B). In each panel, CP/IGP concordance regarding leads is displayed on top while that regarding subjects is depicted on the bottom.

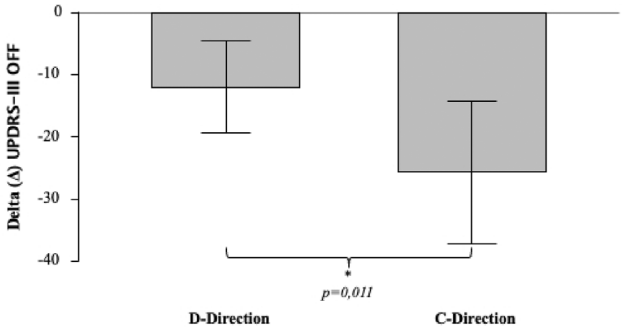

FIGURE 3 Motor outcome comparison per directionality concordance. Stimulation-induced motor improvement is expressed as Delta (Δ) UPDRS-III OFF = (post-operative UPDRS-III ONstim/OFFmed) - (pre-operative UPDRS-III OFFmed).

Conclusion: Visual reconstruction software correctly predicted the most clinically effective stimulation contact levels in most patients. Imaging therefore facilitates classic STN-DBS clinical programming while assuring similar outcomes. Moreover, better motor outcomes were reached by patients with concordant IGP/CP directional parameters, suggesting that visualization can represent an added value in particular for directional stimulation programming.
Disclosure: Nothing to disclose.

OPR-050 | Elucidating the pathophysiology of GBA-PD using functional brain connectome

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Background and Aims: To investigate functional brain network alterations in Parkinson's disease (PD) subjects carrying glucocerebrosidase (GBA) mutation (GBA-positive) and PD non-carriers (GBA-negative) using graph analysis and connectomics.
Methods: Thirteen GBA-positive, 39 GBA-negative PD patients and 60 age- and sex-matched controls underwent clinical evaluation, 3DT1-weighted and resting-state functional MRI (rs-fMRI). Functional connectome for each subject was obtained from rs-fMRI scans as the Pearson's correlation coefficient between time-series in 83 cortical and subcortical brain regions identified by the Desikan Atlas. Graph analysis and connectomics assessed global and local functional topologic network properties (betweenness centrality, nodal degree, nodal strength, mean distance and path length), and regional functional connectivity using Network Based Statistics (NBS). All analyses were adjusted for age, sex, and the UPDRS-III score (within the patients' group only).
Results: Relative to controls, GBA-positive PD patients showed severe global functional network alterations (lower betweenness centrality and nodal degree), while GBA-negative patients showed relatively preserved functional brain architecture. GBA-positive patients demonstrated reduced graph analysis measures in frontal, sensorimotor, parietal and temporal areas relative to controls, and in occipital areas relative to GBA-negative PD patients. Those patients showed only decreased connectivity in the right frontal lobe relative to controls. Considering NBS analysis, functional connectivity breakdown in the parietal lobe, left temporal, and occipital, sensorimotor, and right frontal differentiated GBA-positive PD patients from controls ($p = 0.04$).
Conclusion: Functional graph analysis and connectome measures may be a useful tool for monitoring and predicting PD progression in accordance with the genetic background.
Disclosure: Funding. Ministry of Education, Science, and Technological Development, Republic of Serbia [grant 175090] and Italian Ministry of Health [grant RF-2018-12366746]. Disclosures. SB, ES, EC received grants from the Italian Ministry of Health. TC, ES, RB, IS, AT, FM nothing to disclose. TS received speaker honoraria from Actavis and Alzheimer's Association International Research Grant. ES received speaker honoraria from Actavis. VSK received speaker honoraria from Actavis and Solveo. FA received speaker honoraria from Biogen Idec, Roche, Eli Lilly and GE Healthcare; and grants from Italian Ministry of Health, Italian Ministry of University and Research, AriSLA, European Research Council, EU Joint Programme—Neurodegenerative Disease Research, and Foundation Research on Alzheimer Disease (France). MF received compensation for consulting services or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM.

OPR-051 | Genetic insights into functional neurological and somatoform disorders: Pilot findings from the first GWAS

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Background and Aims: The mechanisms underlying functional neurological disorders (FND) are poorly known, even though FND is common, with significant impact on healthcare. Positive family history and small-scale candidate-gene studies indicated a genetic role in FND. However, large-scale genetic studies, which can provide a necessary first step in the genetics of disorders, have not yet been carried out.
Methods: We performed the first large-scale genome-wide association study (GWAS) meta-analysis in FND and somatoform disorders (SD) using data from Nordic countries (Estonia, Denmark, Finland, Iceland, Norway), the UK and the USA (FND N cases = 4269, N controls = 1852274, SD N cases = 18536,

N controls = 1819203). GWASes were performed separately in each cohort (covariates: age, sex, first 20 PCs and genotyping batch). We used cleansumstat pipeline for harmonization, METAL for meta-analysis and LDSC tool for heritability and correlation assessment.
Results: We found one genome-wide significant locus on chromosome 8 in FND GWAS and two loci, on chromosome 8 and 16, in SD GWAS. LDSC analysis of the GWAS data showed that the estimated observed-scale SNP heritability for FND is 14 % and for SD is 7%. The FND and SD were strongly genetically correlated (rg = 0.942) suggesting a similar genetic basis. Significant LDSC correlations were revealed with all major psychiatric disorders, chronic pain, neuroticism and migraine.
Conclusion: Current results can help us to understand functional disorder pathophysiology, as well as genetic role in FND and SD. We showed shared genetic aetiology for FND and SD with chronic pain, migraine, neuroticism and major psychiatric disorders.
Disclosure: This work was made with support from RCN grant 324252. We want to acknowledge the participants and investigators of the FinnGen, MOBA, UK and Estonia biobank, AllofUs studies, DBDS genetic consortium and deCODE, Iceland.

Muscle and Neuromuscular Junction Disorder 1

OPR-052 | Association between new-onset myasthenia gravis and COVID-19 infection and vaccination. A population-based study

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Background and Aims: The potential link between myasthenia gravis (MG) and COVID-19 infection or vaccination remains unclear. This study aimed to evaluate the relationship between these factors and new-onset MG.
Methods: A case-control study was conducted using two cohorts from Clalit Health Services' database. We applied a machine learning algorithm to reduce diagnostic misclassification. The study examined adults aged 18 or older between January 2020 and December 2022 for COVID-19 infection (Infection Cohort) and between January 2021 and December 2022 for COVID-19 vaccination (Vaccination Cohort). For each new MG case, three matched controls by age and sex were selected. Prior exposure to either infection or vaccination was assessed within 90 and 180 days for cases and controls.
Results: In the infection cohort, 253 new MG cases were identified. A multivariate logistic regression model showed an odds ratio (OR) of 1.44 (95% CI 0.708–2.92) within 90 days post-infection and 1.67 (95% CI 0.98–2.84) within 180 days. In the vaccination cohort, 177 new MG cases were detected, with an OR of 1.76 (95% CI 1.049–2.95) within 90 days post-vaccination and 2.45 (95% CI 1.51–3.95) within 180 days.
Conclusion: The study suggests no increased risk of new-onset MG following COVID-19 infection, but vaccination appears to be associated with a higher risk of developing MG, particularly within 180 days of vaccination.
Disclosure: Nothing to disclose.

OPR-053 | Targeted immunotherapy with ANX005 reduces ventilation requirements in Guillain-Barré syndrome (GBS)

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Background and Aims: Guillain-Barré syndrome (GBS) is a neuromuscular emergency requiring hospitalization and necessitating mechanical ventilation in severe cases. GBS-02, a randomized, double-blind, placebo-controlled Phase 3 trial, assessed the safety and efficacy of ANX005, a C1q inhibitor that inhibits the classical complement pathway, in GBS. This analysis evaluates ANX005's impact on duration of ventilation, a critical disease burden marker.
Methods: Ventilation duration was analyzed using a zero-inflated negative binomial (ZINB) model. Study patients who die or die early while on mechanical ventilation could bias ventilation duration. Therefore, death and treatment exposure at time of ventilation were considered intercurrent events, with those never ventilated assigned a duration of zero days, while those who died on ventilation were imputed with 182 days (trial length). This includes one patient in each active arm who died without ventilation. Subgroups who required ventilation during the study or were ventilated before treatment were assessed with a Kruskal–Wallis test.
Results: The ZINB model showed significant reduction in ventilation duration with ANX005 compared to placebo (28-day median reduction, $p = 0.0356$ for ANX005 30 mg/kg; 34-day median reduction, $p = 0.0011$ for ANX005 75 mg/kg). In ventilated patients without imputation, median duration of ventilation was reduced by 15 days for ANX005 30 mg/kg ($p = 0.0079$) and 20 days for ANX005 75 mg/kg ($p = 0.0080$). Similar reductions were observed when analyses were restricted to patients receiving treatment during ventilation ($p = 0.0034$).
Conclusion: These results demonstrate that ANX005 significantly reduces ventilation duration in GBS, even for patients already ventilated at treatment initiation, highlighting its potential to improve critical outcomes in severe GBS.
Disclosure: The study was sponsored by Annexon Biosciences (Brisbane, CA, USA). HAK: Employee and shareholder of Annexon Biosciences QDM: Consultancy/advisory role with Annexon Biosciences JN: Consultancy/advisory role with Annexon Biosciences GM: Employee and shareholder of Annexon Biosciences PL: Employee and shareholder of Annexon Biosciences RG: Consultancy/advisory role with Annexon Biosciences PC: Employee and shareholder of Annexon Biosciences KAKA: No disclosures ZI: Research funding from Fogarty International Center, National Institute of Neurological Disorders and Stroke of the National Institutes of Health, USA, and Annexon Biosciences KCG: Consultancy/advisory role with Annexon Biosciences, Argenx, Janssen, and Sanofi.

OPR-054 | Real-time MRI and quantitative muscle ultrasound for reliable assessment of dysphagia in myositis and muscular dystrophy

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Background and Aims: Dysphagia frequently debilitates neuromuscular patients. Its reliable identification is important for diagnosis and treatment. We studied real-time MRI and quantitative muscle ultrasound (QMUS) for characterizing dysphagia in two different neuromuscular disorders.

Methods: This prospective cohort study included 18 patients with inclusion body myositis IBM and 13 with oculopharyngeal muscular dystrophy (OPMD) from two Neuromuscular centers (Nijmegen/NL; Göttingen/DE). Swallowing function was assessed by real-time MRI (RT-MRI), FEES (flexible endoscopic evaluations of swallowing) and clinical assessments. T1-mapping and QMUS were used to analyze tissue properties in swallowing muscles. Outcomes were compared between the two muscle diseases. RT-MRI values were compared to 22 matched non-myopathic controls.

Results: RT-MRI revealed significantly prolonged oral transit times in OPMD vs. controls (difference between means = 581.2 ms, 95% CI 225.9–936.4, $p = 0.002$). Pharyngeal transit time was significantly prolonged in IBM vs. controls (difference between means = 1132.8 ms, 95% CI 482.2–1783, $p = 0.001$). A cricopharyngeal bar as a well-established morphological indicator of dysphagia was identified in 80% patients with IBM compared to 53% in OPMD. Fatty degeneration of the tongue in OPMD significantly correlated between MRI-T1 values and ultrasound echogenicity (Spearman's $\rho = -0.52$, $p = 0.005$). ROC revealed excellent discrimination between diseases by combining RT-MRI, T1-mapping and QMUS (AUC = 0.95, 95% CI 0.86–1.00), while FEES and clinical assessments failed to differentiate specific patterns of dysphagia.

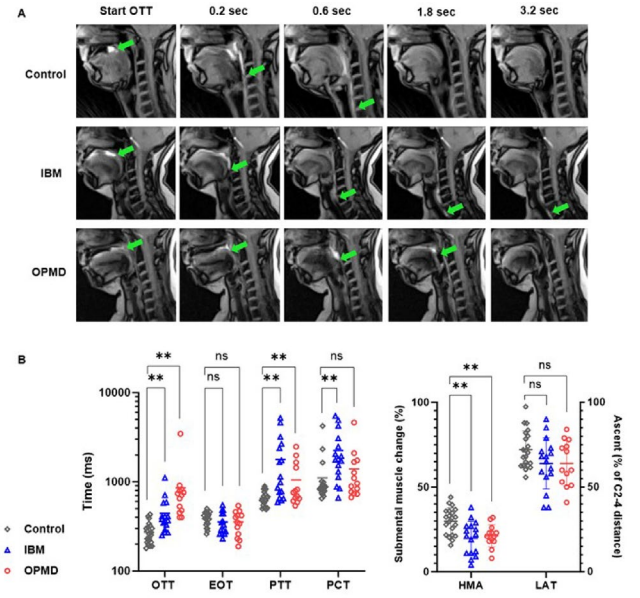

FIGURE 1 Real-time MRI assessment of swallowing in patients with IBM and OPMD versus control subjects.

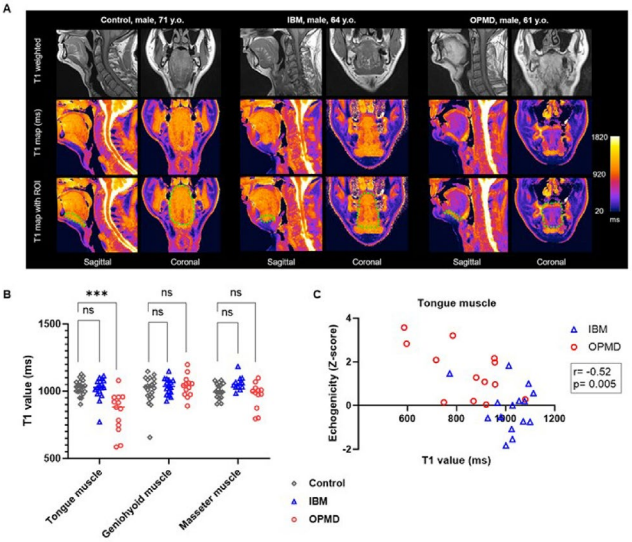

FIGURE 2 T1 mapping of swallowing muscles in patients with IBM and OPMD versus control subject.

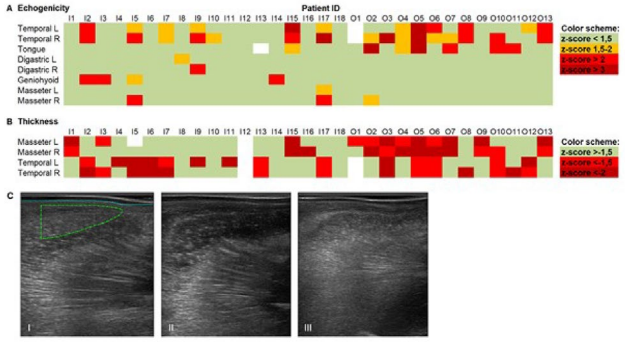

FIGURE 3 Quantitative muscle ultrasound (QMU) of orofacial muscles in IBM and OPMD patients.

Conclusion: This study supports the value of novel MRI and ultrasound techniques for clinical use by identifying the pathophysiology and severity of impaired swallowing. Differentiating the phenotypes of dysphagia can aid in the diagnosis and treatment of affected patients.
Disclosure: Nothing to disclose.

OPR-055 | A multicenter, randomized, double blind, phase 3a study of telitacicept in generalized myasthenia gravis

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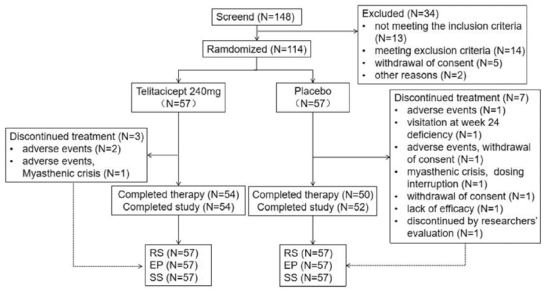
Background and Aims: The recent phase 2 study suggested the safety and good tolerability of telitacicept, a dual BAFF/APRIL inhibitor, in treating gMG. The phase 3a study aimed to further validate these preliminary findings.
Methods: Eligible patients were aged ≥18 years with diagnosis of gMG, a Myasthenia Gravis Foundation of America classification of II–IVa, a Myasthenia Gravis-Activities of Daily Living (MG-ADL) score ≥6, a quantitative myasthenia gravis (QMG) score ≥8, and standard of care treatment. Patients were randomly assigned 1:1 to either receive telitacicept 240mg or matched placebo subcutaneously once a week for 24 weeks. The primary efficacy endpoint was the mean change from baseline to week 24 in MG-ADL score. Secondary efficacy endpoints included mean change in QMG score from baseline to week 24, mean change in MG-ADL score and QMG score from baseline to week 12. Safety and tolerability were assessed.
Results: Between 2023 and 2024, 114 of the 148 patients screened were enrolled in 52 hospitals in mainland China. The mean reduction in MG-ADL score from baseline to week 24 was 6.4 and 1.6 ($p < 0.001$) in the telitacicept 240mg and placebo groups, respectively. In addition, at Week 24, QMG score, Myasthenia Gravis Composite (MGC) scale, Myasthenia Gravis Quality of Life 15-item-revised (MG-QOL15r) questionnaire, MG clinical absolute score were significantly improved in the telitacicept 240mg group than the placebo group ($p < 0.001$). Safety analysis revealed telitacicept did not increase the risk of infection compared with placebo.



	Telitacicept 240 mg (N = 57)	Placebo (N = 57)
Age, yr., mean±SD	49.1±14.7	49.6±15.0
Sex, n (%)		
Male	30 (52.6)	21 (36.8)
Female	27 (47.4)	36 (63.2)
Duration of MG, Mon	83.1±84.5	76.1±87.8
MGFA clinical classification		
Class IIa, n (%)	3 (5.3)	12 (21.1)
Class IIb, n (%)	14 (24.6)	9 (15.8)
Class IIIa, n (%)	25 (43.9)	23 (40.4)
Class IIIb, n (%)	11 (19.3)	12 (21.1)
Class IVa, n (%)	4 (7.0)	1 (1.8)
MG-ADL score[a], mean±SD	10.0±2.6	9.9±2.6
QMG score[b], mean±SD	17.9±3.4	18.8±3.7
MGC scale[c], mean±SD	19.6±5.9	20.6±5.4
MG clinical absolute score[d], mean±SD	22.0±6.8	24.5±8.4
MG-QOL15r score[e], mean±SD	17.9±6.0	18.1±6.4
AChR-Ab		
Negative, n (%)	2 (3.5)	2(3.5)
Positive, n (%)	55 (96.5)	55 (96.5)
MuSK-Ab		
Negative, n (%)	54 (96.4)	55(96.5)
Positive, n (%)	2 (3.6)	2(3.5)

Abbreviations: MGFA = Myasthenia Gravis Foundation of America; MG-ADL=Myasthenia Gravis-Activities of Daily Living; QMG=quantitative myasthenia gravis; MGC=Myasthenia Gravis Composite; MG-QOL15r=Myasthenia Gravis Quality of Life 15-item-revised scale.
[a] Total MG-ADL scores range from 0 (none) to 24 (severe)
[b] Total QMG scores range from 0 (none) to 39 (severe).
[c] Total MGC scores range from 0 (none) to 50 (severe).
[d] Total MG absolute clinical scores range from 0 (normal) to 60 (severe).
[e] Total MG-QOL15 scores range from 0 (none) to 30 (severe).

FIGURE 1 Consort flow diagram. **TABLE 1** Study Population and Baseline Characteristics.

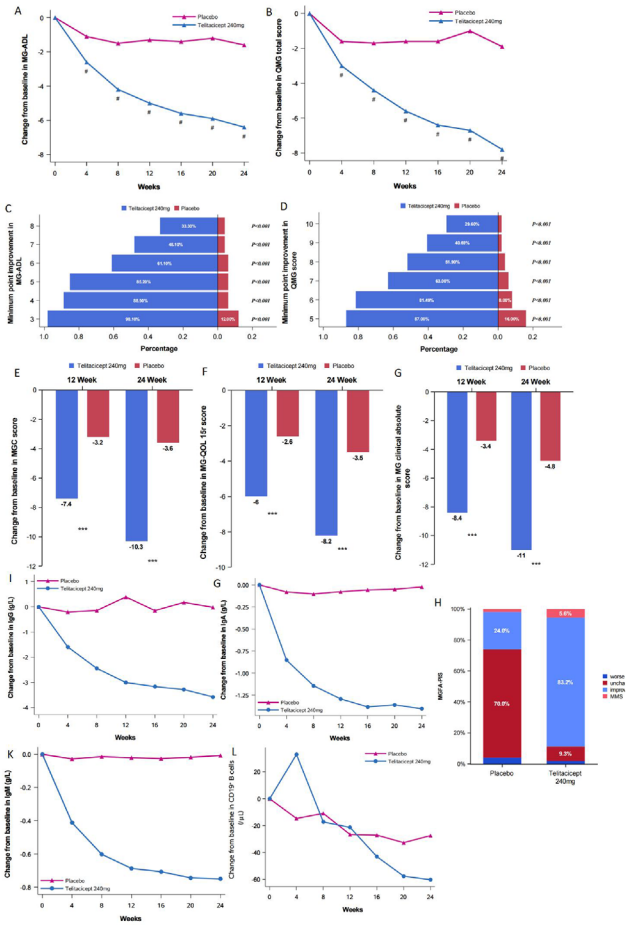


FIGURE 2 Mean change in MG-ADL, QMG, MGC, MG-QOL 15r, MG clinical absolute score from baseline to week 24(A-G). MG-PIS at week 24 (H). Mean percentage change in immunoglobulin levels and CD19+ B-cell counts (I-L).)

TABLE 2 Summary of Adverse Events in All Patients.

	Telitacicept 240 mg (N = 57)	Placebo (N = 57)
AE, n (%)	49(86.0)	49(86.0)
ADR, n (%)	43(75.4)	43(75.4)
SAE, n (%)	4(7.0)	4(7.0)
SADR, n (%)	1(1.8)	1(1.8)
AE leading to dosing interruption, n (%)	7(12.3)	7(12.3)
ADR leading to dosing interruption, n (%)	5(8.8)	5(8.8)
AE leading to discontinuation, n (%)	2(3.5)	2(3.5)
ADR leading to discontinuation, n (%)	1(1.8)	0(0)
Withdrawal owing to AE, n (%)	3(5.3)	3(5.3)
Withdrawal owing to ADR, n (%)	1(1.8)	0(0)
Severe AE, n (%)	3(5.3)	3(5.3)
Severe ADR, n (%)	1 (7.1)	0 (0)
Death owing to AE, n (%)	1(1.8)	0 (0)
Most common TEAEs (≥ 10% in any group), n (%)		
Upper respiratory tract infection	12(21.1)	20(35.1)
Urinary tract infection	9(15.8)	6(10.5)
Blood immunoglobulin M decreased	15(26.3)	0(0)
Blood immunoglobulin G decreased	10(17.5)	3(5.3)
Injection site reactions	8(14.0)	1 (1.8)
Blood immunoglobulin A decreased	7 (12.3)	0 (0)
Immunoglobulin decreased	6 (10.5)	0 (0)

Abbreviations: †AE = adverse event; ‡ADR = adverse drug reaction; §SAE = serious adverse event; ¶SADR = serious adverse drug reaction; ||TEAE = treatment emergent adverse events.

Conclusion: Telitacicept 240mg treatment showed significant clinical benefit and safety in gMG patients in phase 3a study.
Disclosure: Nothing to disclose.

OPR-056 | BCMA/CD19 dual CAR-T cells for refractory myasthenia gravis

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Background and Aims: Myasthenia gravis (MG) is a potentially fatal autoimmune disease, with up to 15% of MG refractory to conventional immunotherapy. This study aims to evaluate the safety and efficacy of low-dose BCMA/CD19 dual chimeric antigen receptor T cells (CAR-T) for patients with refractory MG.
Methods: Three patients with acetylcholine receptor antibody-positive refractory MG received 5x105 BCMA/CD19 dual CAR-T cells per kg without lymphodepletion. Follow-ups were conducted at 1-, 2-, and 3-months post-infusion to assess changes in MG clinical scores (QMG, MG-ADL, MGC and MG-QOL15 scales). Bone marrow and blood samples were collected during follow-ups for flow cytometry and single-cell sequencing to assess CAR-T cell expansion and immune cell profile.
Results: BCMA/CD19 dual CAR-T cells expanded in patients, peaking around day 10 post-infusion, accompanied with rapid B cell depletion and improvement in clinical symptoms. Baseline MG-ADL scores were 8, 7 and 15 in the three patients. At the second month post-infusion, all patients achieved complete symptom remission, with MG-ADL scores reduced to 0, and one patient discontinued all medications. Patients showed a good safety profile, with 2 patients developing transient fever on days 7–8 post-infusion, and no other CAR-T-related complications were identified. The analysis of longitudinal bone marrow and blood samples demonstrated sustained depletion of B cells and plasma cells until the 3-month of follow-up, along with decreasing acetylcholine receptor autoantibody titers.

TABLE The baseline characteristics and treatment details of the 3 MG patients

	Patient 1	Patient 2	Patient 3
Demographics			
Age (years)	29	34	37
Age of onset	26	29	35
Sex (female/male)	male	female	female
Weight (Kg)	68	62	47.5
Clinical characteristics			
Disease duration (months)	36	60	18
MGFA class	IIIb	IIIb	IVb
Thymic status	Normal	Normal	Normal
Previous thymectomy	No	No	No
MG crisis history	No	No	No
MG-ADL score	8	7	15
QMG score	20	16	21
MGC score	19	13	29
MG-QOL15 score	15	17	22
Treatment information			
Daily prednisone dose at enrolment	20mg	10mg	35mg
NSIST at enrolment	Tarolimus	Tarolimus	Tarolimus
Previous NSIST	Tarolimus	Tarolimus	Tarolimus
Previous biologic agents	Batoclimab	Tocilizumab	No

Abbreviations: MG, myasthenia gravis; MGFA, Myasthenia Gravis Foundation of America; MG-ADL, Myasthenia Gravis Activities of Daily Living; QMG, Quantitative Myasthenia Gravis; MGC, Myasthenia Gravis Composite; MG-QOL15, Myasthenia gravis-specific quality of life 15-item scale.NSIST, Non-steroidal immunosuppressive treatments.

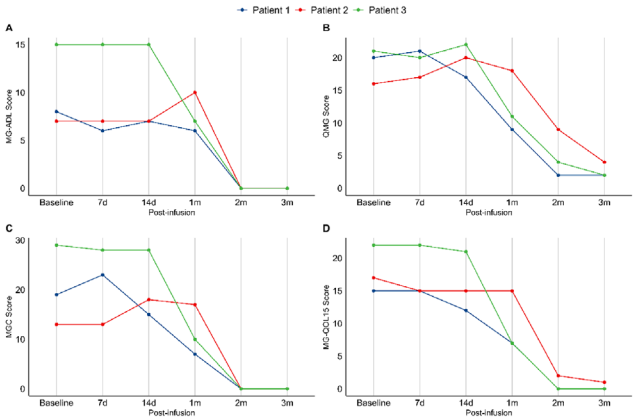

FIGURE 1 Kinetic parameters of Patient MG-1, MG-2 and MG-3, including MG-ADL scale score, QMG score, MGC score and the MGQOL15 questionnaire.

Conclusion: Low-dose BCMA/CD19 dual CAR-T cells are safe and can deplete B cells and plasma cells in patients with refractory MG without lymphodepletion, resulting in rapid clinical improvement.
Disclosure: Nothing to disclose.

OPR-057 | Investigating hypoxic burden in alzheimer's disease: A pilot study

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Background and Aims: Obstructive Sleep Apnea (OSA) is a frequent comorbidity in Alzheimer's Disease (AD), with chronic intermittent hypoxia being one of the hypothesized mechanisms connecting these two conditions. Hypoxic Burden (HB), an indicator of both duration and depth of oxygen desaturations, is a novel OSA severity marker. The primary aim of this pilot study was to explore the correlation between HB and AD biomarkers, clinical, neuropsychological, and neuroimaging measures in AD patients.
Methods: AD stage 3 and stage 4 patients were consecutively enrolled at Center for Neurodegenerative Diseases and Aging Brain, Tricase. All patients underwent 3T brain Magnetic Resonance Imaging (MRI), cerebrospinal fluid (CSF) AD biomarkers analysis, and a comprehensive neuropsychological assessment. Sleep questionnaires and overnight polysomnography were performed in all patients. A MATLAB code was employed for HB calculation, and Brain MRI morphometry was analyzed using the FreeSurfer software.
Results: The cohort consisted of 22 patients (63.6% females, mean age 69.8 ± 7.5). OSA was diagnosed in 40.9% of patients. Mean HB was 46.4 ± 57.4. HB inversely correlated with left hippocampus ($r = -0.621$, $p = 0.014$) and left amygdala ($r = -0.538$, $p = 0.038$) volumes, after controlling for age, sex and disease duration. After controlling for the same factors, HB positively correlated with Dimensional Apathy Scale ($r = 0.74$, $p = 0.014$), Epworth Sleepiness Scale ($r = 0.648$, $p = 0.043$) and Pittsburgh Sleep Quality Index ($r = 0.643$, $p = 0.045$) scores.
Conclusion: Higher HB is associated with left hippocampus and amygdala atrophy, key structures involved in memory consolidation and emotion regulation. These results suggest that chronic hypoxia, measured by a novel OSA metric, may contribute to neurodegeneration in AD.
Disclosure: Nothing to disclose.

OPR-058 | Prevalence of idiopathic REM sleep behavior disorder in the Spanish community

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Background and Aims: To study the prevalence and clinical characteristics of idiopathic REM sleep behavior disorder (IRBD) in a representative Caucasian sample from the elderly community of Barcelona, Spain, attending primary care centers.

Methods: Participants were individuals aged 60 years or older who underwent routine visits in a primary care center (CAP Casanova) between 7th February 2023 and 29th August 2024. They underwent a two-stage study; a validated screening single question for IRBD diagnosis (RBD1Q) followed by, in those who endorsed positive answer, clinical assessment by a neurologist plus video-polysomnography (V-PSG).
Results: Of 332 individuals (62% women, mean age 71.8 ± 7.9 years, range 60–93), 33 (9.9%) endorsed positively the RBD1Q. All 33 were interviewed by a sleep neurologist, and 20 of these 33 accepted a v-PSG. V-PSG ruled out RBD in 16 subjects who had obstructive sleep apnea ($n=10$), periodic limb movement disorder in sleep ($n=4$) and normal sleep ($n=2$). IRBD was diagnosed in four individuals without motor or cognitive complaints, giving an estimated prevalence of 1.20% (95% CI = 0.03–2.37). They were three men and one woman between 64 and 76 years of age, with an interval between estimated RBD onset and V-PSG of 7.5 years (range 0–5–10 years). IRBD patients had constipation ($n=3$), hyposmia ($n=2$), apathy ($n=1$), and depression ($n=1$).
Conclusion: The prevalence of IRBD is 1.2% in the elderly community of Barcelona, similar than in other studies in the Caucasian elderly community.
Disclosure: Nothing to disclose.

OPR-059 | Sleep and longevity: Insights from sleep macroarchitecture and nocturnal heart rate variability

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Background and Aims: Healthy aging is priority in public health. Emerging evidence indicates that sleep-wake disorders are causally linked to adverse health outcomes, suggesting that sleep represents a key preventive target. We aimed to identify sleep phenotypes associated with selected incident comorbidities using real-world data.
Methods: This is an analysis of the Bernese Sleep-Wake Registry ($n \approx 11000$). Using polysomnography, we quantified sleep macroarchitecture according to AASM criteria and nocturnal heart rate variability (21 parameter) as the marker of autonomic functioning. 36 incident comorbidities at polysomnography and during the follow-up were classified into eight major groups. Association between comorbidities and sleep parameters were explored with multiple logistic regression adjusted for age and sex.

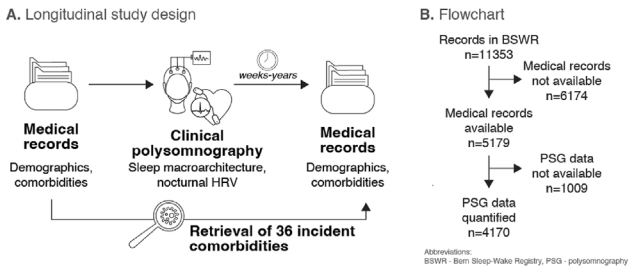

FIGURE 1 Study design and flowchart.

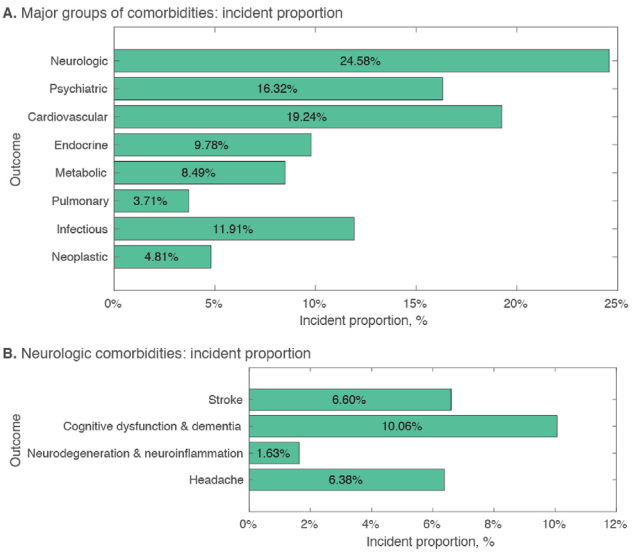

FIGURE 2 Incident proportion of eight major groups of comorbidities that emerging during the follow-up.

Results: 4170 participants were included in the analysis (age: 48±19 years, 63% men, total observation time: 13217 person-years). Sleep macroarchitecture showed limited associations with incident comorbidities, with sleep-disordered breathing being linked to cardiovascular, endocrine, and metabolic diseases. In contrast, HRV was prevalently associated with incident comorbidities. Specifically, neurologic diseases were related to high and complex HRV. In a subanalysis, stroke demonstrated strong associations with HRV. Psychiatric diseases (i.e., depression in 92% cases) were associated with low HRV, accompanied by reduced complexity and parasympathetic dominance. Metabolic diseases were linked to high HRV with a high very low-frequency component.

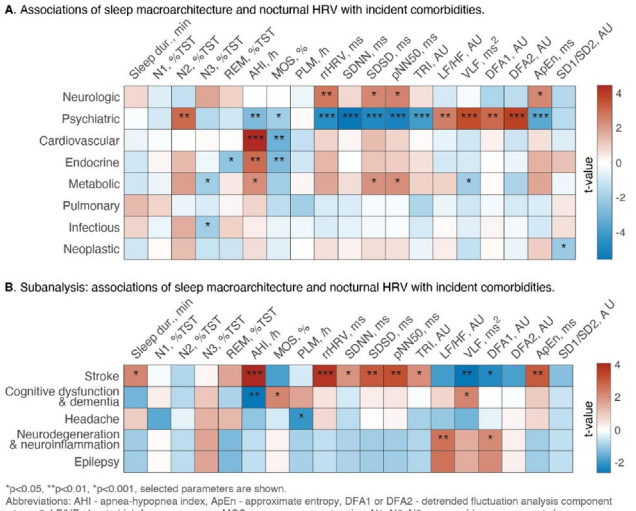

FIGURE 3 Main findings. Heatmap of the t-values of the multiple logistic regression adjusted for age and sex.

Conclusion: These findings highlight sleep profiles linked to unfavorable health outcomes in a longitudinal analysis.

Nocturnal HRV emerges as a relevant marker for neurologic and psychiatric diseases, suggesting its potential in brain health. We will further explore the link between health outcomes and sleep microarchitecture.

Disclosure: Nothing to disclose.

OPR-060 | REM-sleep saw-tooth waves: Cortical topography and associations with cognition

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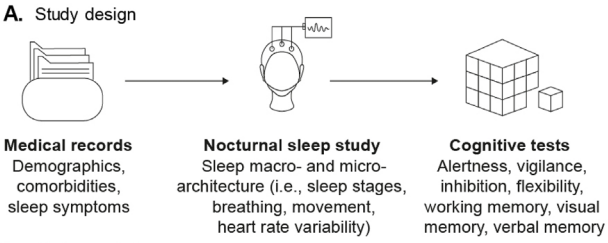
Background and Aims: Saw-tooth waves (STWs) are a hallmark of REM sleep, however, their association with cognition remains poorly understood. This exploratory analysis comprehensively addressed this research gap.

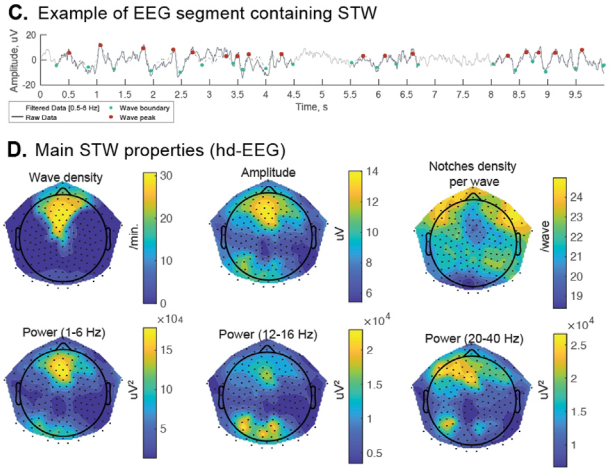
Methods: The "Sleep and cognitive functioning" study included volunteers in good or excellent health condition (Eastern Cooperative Oncology Group grade of 0-1). Demographics, medical history, cognition, and sleep architecture by polysomnography (electroencephalography [EEG] was recorded either with 6 electrodes or 256 electrodes [high-density EEG, hd-EEG]) were assessed at study inclusion (Figure 1AB). STWs were detected using a feature-based data-driven algorithm in MATLAB (Figure 1C). Associations between STW properties as dependent variables and cognition were explored using multivariate linear regression adjusted for age and arousal index.

Results: 60 participants were included (hd-EEG in 52%; Figure 1B). STW were expressed in the fronto-central areas, with 0.5–6 Hz and 20–40 Hz activity dominating in the frontal regions and 12–16 Hz activity - in the posterior regions. EEG analysis based on 6 electrodes showed limited associations between STW and cognition (e.g., low SWT amplitude with vigilance or alertness; Figure 2), whereas high-density EEG analysis identified multiple associations of interest with a distinct topography (e.g., visual memory with high EEG spectral power in lateral regions; Figure 3).



B. Study population

Parameter	Overall	hd-EEG (n=31)	PSG (n=29)	P-value
Age, years	52.7 [32.9, 64.6]	37.1 [30.7, 64.7]	54.9 [49.0, 61.1]	0.141
Sex	33 (55.0)	18 (58.1)	15 (51.7)	0.796
Hypertension	16 (26.7)	7 (22.6)	9 (31.0)	0.563
Dyslipidemia	7 (11.7)	2 (6.5)	5 (17.2)	0.247
Diabetes	2 (3.3)	0 (0.0)	2 (6.9)	0.229
Obesity	9 (15.0)	3 (9.7)	6 (20.7)	0.292
TRT, min	7.25 [6.5, 8.2]	8.1 [7.1, 8.5]	6.7 [6.1, 7.3]	0.001*
TST, min	5.45 [4.4, 6.4]	5.9 [4.5, 7.1]	4.8 [3.9, 5.8]	0.019*
SE, %	76.4 [62.1, 85.3]	78.1 [65.9, 85.4]	74.2 [62.1, 82.4]	0.476
Arousal index, /h	24.3 [16.1, 34.3]	24.7 [17.8, 37.1]	24.4 [14.6, 32.8]	0.595
NREM1, %TST	18.3 [12.0, 26.1]	18.9 [12.2, 28.1]	16.9 [11.8, 25.8]	0.524
NREM2, %TST	39.0 [33.4, 46.7]	381 [32.9, 46.0]	41.7 [33.8, 46.8]	0.354
NREM3, %TST	20.5 [15.3, 28.5]	17.0 [14.2, 26.4]	23.5 [17.3, 30.8]	0.060
REM, %TST	17.3 [12.4, 21.5]	19.6 [13.9, 22.5]	15.5 [11.9, 17.8]	0.050
AHI, /h	5.1 [1.6, 15.9]	2.9 [0.8, 4.6]	14.3 [7.3, 23.5]	0.003*



Abbreviations: AHI – apnea-hypopnea index, hd-EEG – high-density electroencephalography, NREM – non-rapid eye-movement sleep, PSG – polysomnography, REM – rapid eye-movement sleep, SE – sleep efficiency, TRT – total recording time, TST – total sleep time.

FIGURE 1 Study design (A, B) and STW detection (C, D).

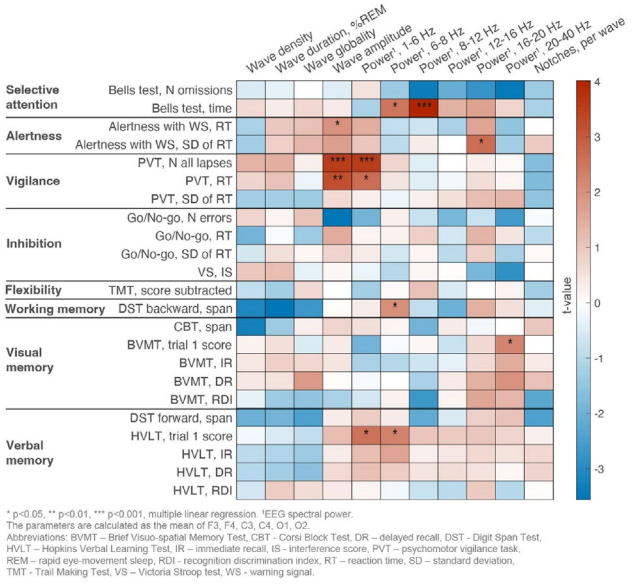


FIGURE 2 Associations between STW and cognition (basic analysis, $n = 60$).

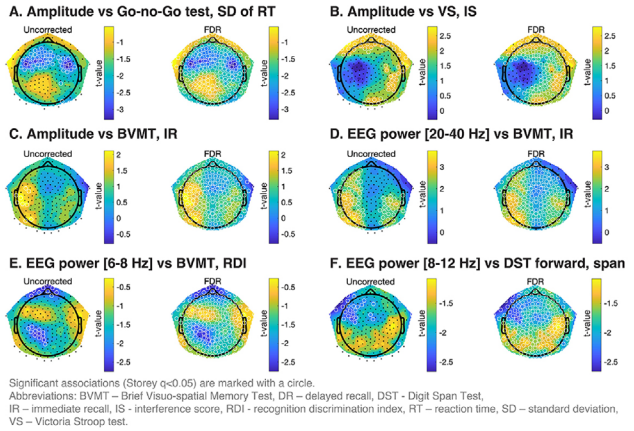


FIGURE 3 Selected associations between STW and cognition (topographic analysis, $n = 30$).

Conclusion: This is the first description of the automatically detected STW in PSG and in hd-EEG. STW activity appears to have distinct associations with cognition, showing a positive link with memory but a negative link with attention and executive functioning.

Disclosure: European Stroke Research Foundation 2021.

OPR-061 | Phenotypic traits of sleep-apnea post-stroke: Insights from the analysis of the pan-European ESADA cohort

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Background and Aims: Obstructive sleep apnea (OSA) is highly prevalent post-stroke and is associated with a worse prognosis. International guidelines recommend OSA screening post-stroke, but epidemiological evidence of their application is lacking. We aimed to describe the prevalence and phenotypic traits of stroke patients in a prospective real-life cohort of patients with suspected OSA.

Methods: Adult patients (age 18–80 years) with suspected OSA were prospectively included in the European Sleep Apnea Database (ESADA, 39 sleep medicine centers). Exclusion criteria are previous diagnosis of OSA, limited life expectancy, and alcohol or drug abuse. Demographic and anthropometric data, Epworth Sleepiness Scale score, and medical history, including stroke, were recorded. OSA diagnosis was based on polysomnography or cardio-respiratory polygraphy.

Results: Among the 33,359 patients prospectively included between 2007 and 2022, 793 (2.4%) patients presented a history of stroke. Stroke patients were significantly older (median [IQR] age = 63.0[55.0;71.0] years vs. 54.0[44.0;62.0], $p < 0.001$), predominantly males (73.5% vs. 70.1%, $p = 0.04$), and presented a significantly higher apnea-hypopnea index (26.7[13.0;47.0] events/h vs. 24.0[9.6;46.3], $p = 0.003$), and higher rate of comorbid insomnia (5.2% vs. 3.4%, $p = 0.005$). Stroke patients presented a higher prevalence of hypertension (68.6% vs. 43.7%), ischemic heart disease (21.7% vs. 7.7%), or diabetes (27.9% vs. 15.2%) (all $p < 0.001$). No difference was observed in body mass index, ESS scores, and prevalence of other sleep comorbidities.

Conclusion: Stroke patients referred to OSA screening present specific phenotypic traits, including greater OSA severity and prevalence of comorbid insomnia. Structured care pathways are required to improve OSA screening post-stroke.
Disclosure: Nothing to disclose.

Neuro-oncology

OPR-062 | Deciphering glioblastoma metabolic signature: Molecular profiling and NADH-FLIM imaging

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Background and Aims: Recent breakthroughs in single-cell analysis reveal distinct metabolic cellular states of glioblastoma (GBM) and allow the detection of GBMs which are dependent on oxidative phosphorylation (OXPHOS). The aims of the study were to explore the prevalence of molecular/metabolic subtypes of GBM and to evaluate the efficacy of Fluorescence Lifetime Imaging (FLIM) microscopy of NADH in discerning the metabolic subtype of FFPE GBM tumor tissue.
Methods: We analyzed 3' mRNA NGS FFPE tumor tissue of IDHwt glioblastomas. We selected OXPHOS and glycolytic/plurimetabolic (GPM) cases for the NADH-FLIM microscopy study on FFPE slides.
Results: RNA Sequencing of 95 newly diagnosed IDHwt GBM patients found 37 OXPHOS (39%), 16 GPM (15%), 4 NEU (4%), 27 not classifiable NC (28%) and 12 PPR cases (14%). Sixteen out of the 37 OXPHOS patients exhibited top-scoring mitochondrial activity and were defined as OXPHOS_high. Longitudinal analysis of 11 pairs of GBM untreated and recurrent tumors found that 3 OXPHOS_high patients maintained the OXPHOS status at recurrence. We assessed FGFR3-TACC3 (F3T3) status in 62 cases and we found that all 4 FGFR3-TACC3+ overexpressed OXPHOS genes. Four OXPHOS patients and 3 GPM cases were selected for the NADH-FLIM study: NADH bound/free curves significantly differed between metabolic subtypes [$p < 0.0001$]. PCA analysis of NADH FLIM features showed different clustering according to the OXPHOS and GPM subtype.
Conclusion: F3T3 fusions are tightly associated with the OXPHOS signature and the OXPHOS status can be maintained at recurrence. OXPHOS and GPM glioblastoma clusters significantly differed in NADH bound/free distribution curves. Supplementary cases are currently under study.
Disclosure: Nothing to disclose.

OPR-063 | Next steps after the INDIGO trial: May we use IDH-inhibitors in oligodendrogliomas grade 3 after surgical resection?

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Background and Aims: Oligodendrogliomas IDH-mutant 1p19q-codeleted grade 3 (OG3) are traditionally associated with worse outcome compared to OG2. Standard treatments include maximal safe resection followed by adjuvant radiochemotherapy, a standard of care established in the pre-molecular era.
Methods: We retrospectively reviewed a dataset of patients with a diagnosis of molecularly defined OG3-OG2 treated from 1996 to 2024 in our institution.
Results: We included 80 patients (OG2: 60%; OG3: 40%). Median age was 40 (OG2) and 49 years (OG3). Gross-total resection prevailed among OG2 (31.3% vs 6.3%, $p = 0.007$). After surgery, 54.2% of OG2 underwent observation, while 45.8% received temozolomide (TMZ); 68.8% of OG3 received upfront TMZ and 31.3% underwent chemoradiation (RT+TMZ). Median follow-up was 118 months with a median progression-free survival (mPFS) of 53.9 in OG2 and 54.9 months in OG3. mPFS did not significantly differ in OG3 patients receiving TMZ upfront vs early RT+TMZ (66.2 vs 41.5 months). Median overall survival (mOS) was similar in OG2 and OG3 (237.6 months vs not reached, $p = 0.326$) and did not significantly differ among OG3 treated with TMZ upfront + RT at recurrence and those with early RT+TMZ after surgery (not reached vs 121.7 months, $p = 0.866$). Multivariable analysis showed histological grading did not significantly affect survival outcomes.
Conclusion: In our series, OG3 showed survival outcomes comparable to OG2 and those treated with TMZ upfront and RT at recurrence, had similar mPFS and mOS of those receiving early chemoradiation. These findings, along with results from the INDIGO trial on IDH inhibitors, suggest potential for IDH inhibitors in OG3 post-surgical treatment.

Disclosure: Nothing to disclose.

OPR-064 | Rapid molecular classification of brain tumors through DNA methylation analysis with nanopore sequencing

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Background and Aims: DNA methylation is a key epigenetic marker in cancer diagnostics, reflecting somatically acquired and cell-of-origin changes. In brain tumors, methylation profiling aligns with histopathological classifications. Conventional diagnostics using hematoxylin-eosin staining, immunohistochemistry (IHC), and molecular profiling via EPIC array or TSO500 panel sequencing take 2–4 weeks, delaying integrated tumor board diagnosis and precision therapy onset. Our study evaluates nanopore sequencing as a real-time diagnostic tool, enabling molecular classification of brain tumors within 24 hours. This accelerates targeted IHC and allows us to obtain integrated diagnosis within approximately five days.

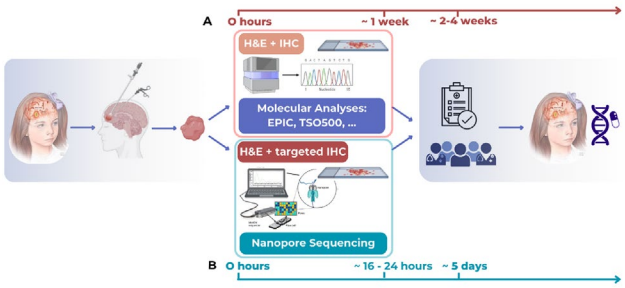

FIGURE 1 A. Routine brain tumors neuropathological analysis, B. Nanopore sequencing workflow at our department. H&E: hematoxylin-eosin staining, IHC: immunohistochemistry, EPIC: Infinium MethylationEPIC array, TSO500: TruSight Oncology 500 panel sequencing.

Methods: We analyzed 18 tumor samples using nanopore sequencing. DNA was extracted, quantified, and sequenced on the MinION device. Data analysis was performed using the NanoDX Pipeline (Euskirchen et al.), which includes base-calling, mapping, quality control, copy number variations estimation, and methylation classification based on the Capper et al. reference cohort.

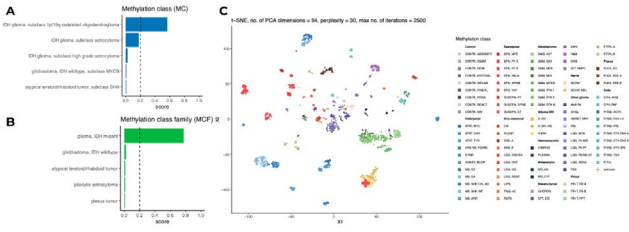

FIGURE 2 A. Tumor Methylation classes and B. Methylation classes family with the highest prediction scores and recommended probability threshold >0.2. C. Dimensionality reduction plot indicating the tumor's location within the reference dataset of the classifier.

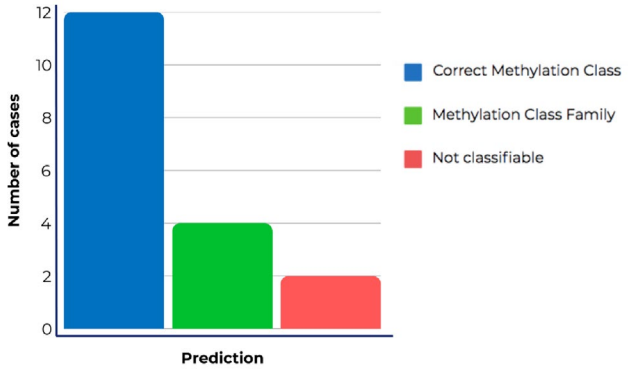

FIGURE 3 Concordance of the nanopore classifier prediction with Infinium MethylationEPIC array-based reference classifier.

Results: The nanopore classifier was concordant with the EPIC-based reference in 12 cases (66.7%). In 4 cases (22.2%), the model predicted a different methylation class within the same methylation class family. In 2 cases (11.1%), no prediction was made due to low confidence.
Conclusion: Nanopore sequencing significantly reduces brain tumors diagnostic turnaround, potentially enabling precision therapy onset within five days. While promising, classifier refinement is needed for rare tumors and samples with low tumor fractions. Our ongoing research aims to determine whether the early achievement of integrated diagnosis leads to better clinical outcomes. Obtained results highlight the potential of real-time sequencing to bridge the gap between traditional histology and precision oncology.
Disclosure: Nothing to disclose.

OPR-065 | Molecularly defined vs histologically defined glioblastoma: An AINO study

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Background and Aims: Molecularly defined glioblastomas (mGBMs) are IDH-wildtype astrocytomas with either EGFR amplification, pTERT mutation, or +7/-10 chromosomal changes, regardless of histological grade. The Italian Association of Neuro-Oncology (AINO) conducted a multicentric study to compare mGBMs with histologically defined glioblastomas (hGBMs).

Methods: This retrospective study compared 70 mGBM patients (with grade 2 histology and no enhancement on MRI) with a cohort of 66 hGBM patients.

Results: Median age of mGBM vs hGBM was similar (59 vs 60 years). Seizures prevailed in mGBMs (46/70, 66% vs 13/66, 20%). MGMT methylation rates were comparable (23/53, 43% vs 30/66, 45%). 23/59 (39%) mGBMs showed EGFR amplification and 55/66 (83%) pTERT mutation. After surgery, mGBMs received radiotherapy (RT) +/- temozolomide (TMZ) in 39 (56%), observation in 15 (21%), upfront TMZ in 13 (19%), while all hGBMs underwent RT/TMZ. Median progression-free survival (mPFS) and overall survival (mOS) were longer in mGBMs (mPFS: 13 vs. 9 months, $p=0.011$; mOS: 27 vs. 22 months, $p=0.036$). MGMT methylation did not affect the mGBM outcome (mPFS: 13 months; mOS: 38 vs. 25 months, $p=0.291$), but significantly influenced hGBM outcome (mPFS: 12 vs. 8 months, $p<0.001$; mOS: 32 vs. 15 months, $p<0.001$). Patients with isolated pTERT mutation showed better trends in mOS with RT/TMZ (45 vs. 17 months, $p=0.06$).

Conclusion: In our study, GBMs had a higher incidence of seizures and significantly longer mPFS and mOS; also, MGMTp methylation did not affect their outcome. A trend for better mOS was seen in mGBM patients with isolated pTERT mutation after RT/TMZ.

Disclosure: Nothing to disclose.

OPR-066 | The Triglyceride-Glucose Index as predictor of cognitive decline in alzheimer's spectrum disorders

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Background and Aims: Metabolic disorders influence Alzheimer's disease (AD) pathogenesis, but their impact on progression remains unclear. This study assessed insulin resistance as a progression marker.

Methods: Single-center retrospective study (2014–2024) analyzed non-diabetic neurodegenerative patients with a CSF based diagnosis of AD or other neurodegenerative conditions (NDD). Patients underwent baseline clinical, biochemical and follow-up clinical assessment (≥6 months). TyG index stratified patients into tertiles (low, medium, high). Baseline clinical features and CSF biomarkers were compared using chi-squared tests or non-parametric ANCOVA. Cox regression models were implemented considering cognitive decline and disease progression as outcome (MMSE loss >2.5 points/year), adjusted for age, sex, MMSE at baseline, disease duration, AD therapy, and BMI.

Results: Final sample of 315 patients entered the study: 210 AD (mean age 71.51, Male % 79) and 115 NDD (mean age 69.19, % male 60). Only in AD high TyG was linked to worse BBB markers and interacted with the APOE ε4ε4, with no effect in NDD. AD patients with high TyG exhibited more cardiovascular risk factors, comparable baseline characteristics (sex, education, APOE genotype, and CSF biomarkers). During follow-up, in the MCI-AD subgroup ($n=161$; 77% male), high TyG was significantly associated with faster cognitive decline over three years (HR=4.08, 95% CI [1.06–15.73]). A similar, though non-significant, trend was observed for MCI-to-dementia conversion ($p=0.086$). No significant TyG-APOE interaction was found for progression. TyG showed no impact on clinical progression in NDD group.

Conclusion: Insulin resistance predicts cognitive decline in early phases of AD, aiding risk stratification and guiding early interventions.

Disclosure: Nothing to disclose.

OPR-067 | Mortality after hip fracture surgery in patients with dementia: Large Swedish study of over 111 000 patients

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Background and Aims: This study aimed to investigate whether dementia is associated with increased mortality following hip fractures and how different dementia subtypes affect mortality outcomes.
Methods: Utilizing data from the Swedish Hip Fracture Register (SHR), Swedish Registry for Cognitive/Dementia Disorders (SveDem), National Patient Register (NPR), and National Prescribed Drug Register (PDR), we conducted a retrospective analysis of 111,353 patients who underwent hip fracture surgery between 2010 and 2018. Multivariable Cox regression analyses were used to evaluate mortality risk factors.
Results: Of the study sample, 22% had dementia. Dementia patients exhibited higher mortality rates at 30 days with 13% vs. 6%, ($p < .001$), 4 months with 27% vs. 12%, ($p < .001$). and at 1 year with 39% vs. 20%, post-fracture ($p < .001$). Higher ASA grades, poor baseline walking ability, and long-term care residency were also associated with increased mortality. Parkinson´s disease dementia was associated with a higher mortality compared to other dementias during the first 4 months post operatively.
Conclusion: The study found that patients with dementia had significantly higher mortality rates at 30 days, 4 months, and 1-year post-hip fracture compared to those without a diagnosis of dementia. Subtypes such as Parkinson's disease dementia and dementia with Lewy bodies posed particularly high risks, highlighting the need for tailored postoperative care in these patients.
Disclosure: None

OPR-068 | Distinct resting-state EEG biomarkers predict amyloid status and conversion to Alzheimer's dementia in a memory center

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Background and Aims: This study examined the diagnostic and prognostic potential of resting-state EEG (RS-EEG) biomarkers in Alzheimer's disease (AD) by differentiating patients based on cerebrospinal fluid (CSF) amyloid status and predicting the conversion of mild cognitive impairment (MCI) to AD dementia.
Methods: A total of 295 cognitively impaired patients were grouped by CSF β-amyloid 42/40 ratio into A+ ($n = 184$) and A- ($n = 111$). Among them, 106 had MCI, further classified as MCI A+ ($n = 61$) and MCI A- ($n = 45$). A subset of 39 MCI A+ patients was tracked for two years, with 23 converting to AD dementia. RS-EEG data were analyzed through current source densities (CSD) and linear lagged connectivity (LLC) within the Default Mode Network (DMN) and Salience Network (SN) using sLORETA. Support vector machine (SVM) analysis was applied to classify patients based on selected EEG features.
Results: In both the DMN and the SN, A+ patients showed a global slowing of cortical electrical activity; MCI A+ patients showed higher theta density and connectivity. MCI converters demonstrated reduced alpha density (DMN only) and lower alpha connectivity in both networks. An SVM model using the top five features achieved 60% accuracy in predicting MCI A+ conversion.
Conclusion: RS-EEG biomarkers, notably theta CSD connectivity, are promising early AD indicators, with AI-driven analysis further enhancing their potential. Alpha connectivity shows prognostic value for MCI-to-AD conversion. Larger studies with higher-density EEGs are needed to validate these findings.
Disclosure: Funding. Next Generation EU/National Recovery and Resilience Plan, Investment PE8-Project Age-It.

OPR-069 | The two cut-offs approach for plasma p-tau217 to detect Alzheimer's Disease in preclinical and prodromal stages

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Background and Aims: Plasma p-tau217 is becoming a notable biomarker for its accuracy in detecting Alzheimer's Disease (AD) pathology even in preclinical stages. Our study aimed to try out the applicability of plasma p-tau217 in the identification of patients with Subjective Cognitive Decline (SCD) and Mild Cognitive Impairment (MCI) carrying AD pathology in a real-world setting.
Methods: We included 187 patients (50 SCD, 87 MCI and 50 AD-demented) undergoing neurological and neuropsychological examination, CSF and blood collection to dose plasma p-tau217 with Lumipulse G600II assay. Patients were classified according to the Revised Criteria of Alzheimer's Association Workgroup as Core1+ or Core1-.
Results: MCI Core1+ had higher plasma p-tau217 levels than MCI Core 1- ($p<0.001$); just like SCD Core1+ compared to SCD Core1- ($p=0.023$). Plasma p-tau217 was highly accurate for discriminating between Core1+ and Core1- patients (AUC=0.92) with an optimal cut-off value of 0.274 pg/ml, revealing a good accuracy (86.29% [95%CI 81.20-91.39]), PPV (88.18% [95%CI 83.40-92.96]) and NPV (83.09% [95%CI 77.52-88.63]). When applying a two cut-offs approach (0.245 pg/ml and 0.516 pg/ml), plasma p-tau217 showed higher accuracy (91.11% [95%CI 86.31-95.91]), a PPV of 96.25% [95%CI 93.05.99.45] and a NPV of 83.63% [95%CI 77.40-89.88%]).

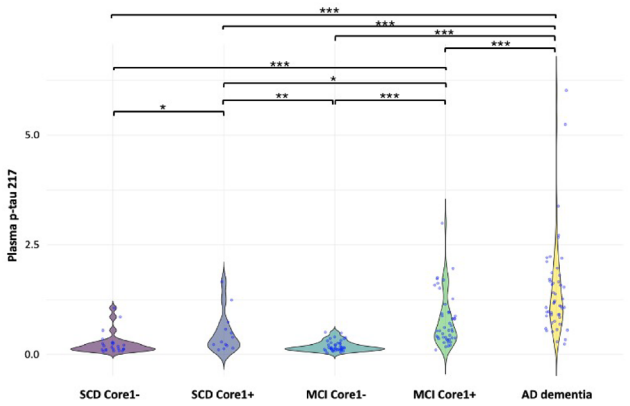
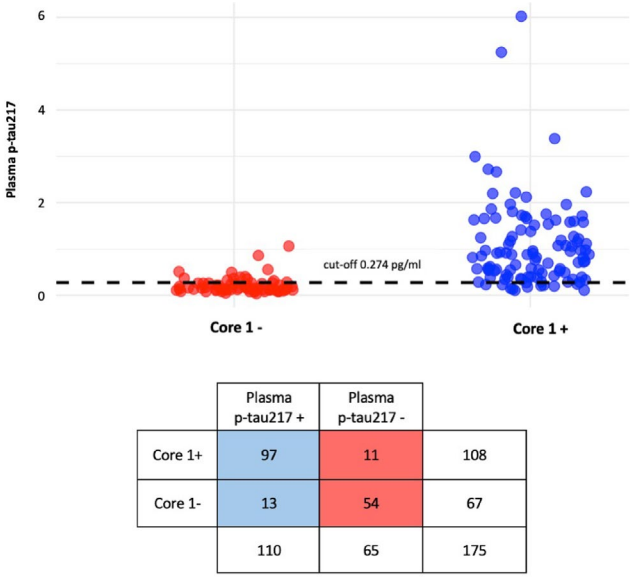


FIGURE 1



	Plasma p-tau217 +	Plasma p-tau217 -	
Core 1+	97	11	108
Core 1-	13	54	67
	110	65	175

FIGURE 2

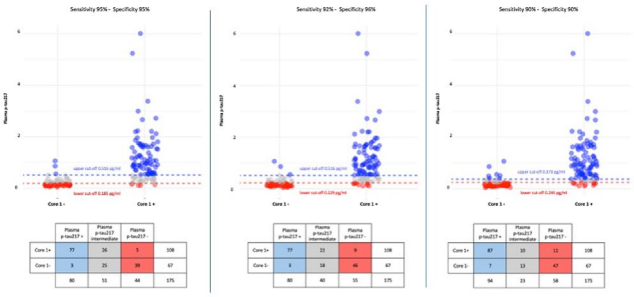


FIGURE 3

Conclusion: Plasma p-tau 217 represents a meaningful biomarker to differentiate carriers of AD pathology from non-carriers, also in the prodromal and preclinical stages of the disease, considering a real-world population. The two cut-offs approach provides for stronger accuracy, PPV and NPV than single cut-off, making more reliable the clinical application of plasma p-tau217 for the early detection of AD in real-world settings.
Disclosure: Nothing to disclose.

OPR-070 | Progression of multimodal MRI biomarkers in Frontotemporal Dementia

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Background and Aims: We investigated longitudinal changes in brain white matter microstructure and gray matter volumetry in non-fluent (nfPPA) and semantic (svPPA) variants of primary progressive aphasia (PPA), behavioral variant frontotemporal dementia (bvFTD), and bvFTD with motor neuron disease (bvFTD-MND) using diffusion tensor imaging (DTI) and atlas-based volumetry (ABV).
Methods: MRI datasets from 29 nfPPA, 27 svPPA, 65 bvFTD, 18 bvFTD-MND patients and 39 controls, were analyzed. White matter fractional anisotropy (FA) was assessed in Tracts of Interest (TOIs) using Tract-Wise Fractional Anisotropy Statistics (TFAS) and without a priori assumptions via Whole Brain-based Spatial Statistics (WBSS). Gray matter volumetric differences in Regions of Interest (ROIs) were also calculated. Longitudinal scans from 10 nfPPA, 6 svPPA, and 19 bvFTD patients over 12 months were analyzed to assess progression. FA maps were correlated with FTLD-CDR scores.
Results: At baseline, white matter degeneration was revealed in frontal, temporal, and callosal regions in nfPPA and in the inferior longitudinal fasciculus (ILF) in svPPA. bvFTD and bvFTD-MND showed widespread FA reductions in the frontotemporal lobes and anterior corpus callosum, with additional corticospinal involvement in bvFTD-MND. Longitudinally, nfPPA showed frontal and callosal progression, bvFTD exhibited progression along frontal, callosal, and posterior temporal tracts, while svPPA showed localized left ILF progression. Correlations with FTLD-CDR scores were observed in left frontal (nfPPA), posterior temporal (svPPA, bvFTD), callosal (bvFTD) white matter as well as in the basal ganglia (bvFTD).

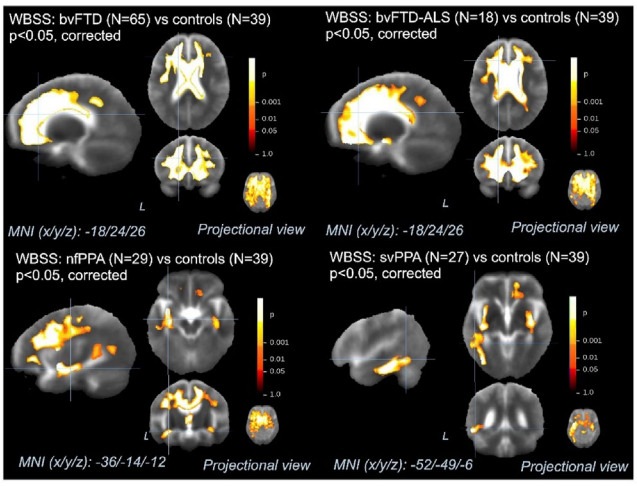

FIGURE 1 Cross-sectional Fractional Anisotropy Changes in bvFTD, bvFTD-MND, nfPPA and svPPA compared to controls.

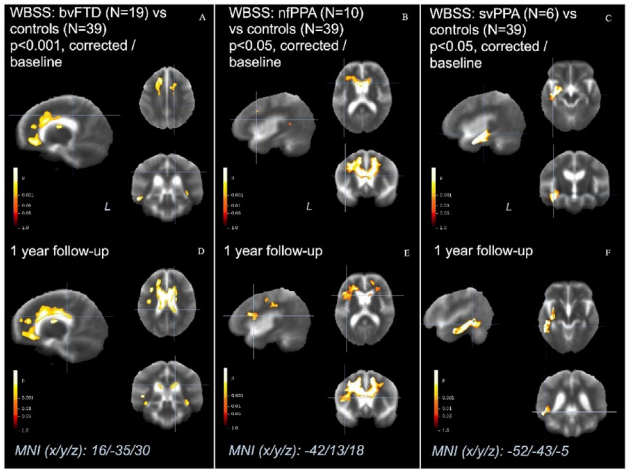

FIGURE 2 Longitudinal Fractional Anisotropy Changes in bvFTD, nfPPA and svPPA compared to controls.

Conclusion: Distinct degeneration patterns emerged across syndromes, supporting early differential diagnosis and allowing tracking of disease progression.
Disclosure: This study was conducted as part of the first author's EAN Clinical Fellowship 2024.

OPR-071 | Preventing dementia in Italy: Estimations of modifiable risk factors and public health implications

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Background and Aims: Dementia represents a growing global public health challenge, with over 50 million cases worldwide in 2020. Preventing dementia by targeting modifiable risk factors is crucial, particularly in ageing populations like Italy. This study aimed to update Population Attributable Fractions (PAFs) and introduce Potential Impact Fractions (PIFs) for dementia risk factors, providing national and regional estimates to inform public health interventions.
Methods: Using 2017-2019 data from two national surveillance systems, PASSI and PASSI d'Argento, we estimated PAFs for 11 modifiable risk factors identified by the 2020 Lancet Commission. PIFs were calculated to simulate dementia case reductions under partial risk factor reductions. Regional PAFs were compared with health policies outlined in Italian Regional Prevention Plans. Statistical analyses incorporated communality adjustments to account for interdependent risk factors.
Results: The combined national PAF was 39.6% (95% CI: 20.8-55.9), with midlife hypertension (6.5%) and physical inactivity (5.8%) as leading contributors (Fig. 1). Cardiovascular factors explained over 50% of preventable cases. Regional PAFs ranged

from 31.7% to 47.5%, showing a north-south gradient (Fig. 2). A 10% reduction in risk factors could prevent 54,495 dementia cases nationally, with regional PIFs ranging from 3.7% to 6.0%. Significant disparities were found in regional health policy alignments with identified risk factors, particularly for air pollution (Fig. 3).

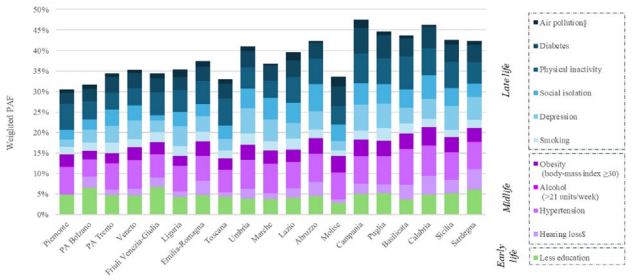

FIGURE 1 Regional estimates of weighted Population Attributable Fractions of dementia cases. Years 2017-2019.

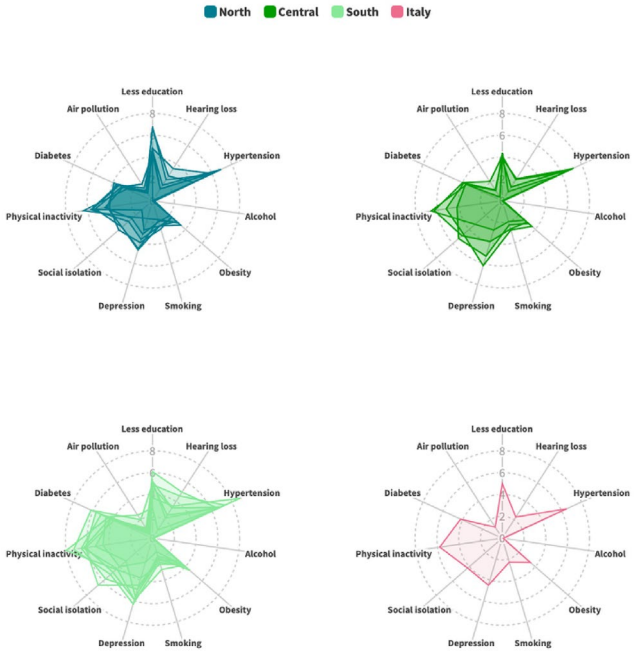

FIGURE 2 Regional estimates of weighted Population Attributable Fractions of dementia cases by macroarea. Years 2017-2019.

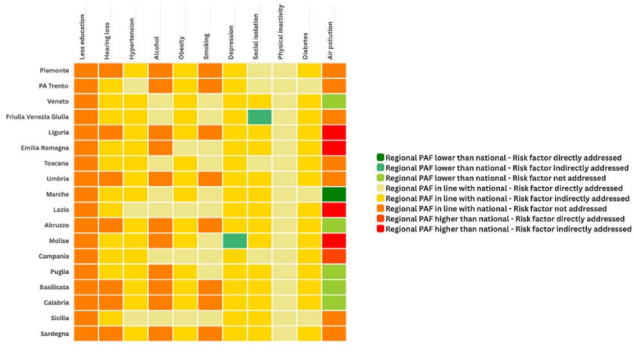

FIGURE 3 Coherence between regional PAFs for dementia and population-level interventions by risk factor.

Conclusion: This study underscores the potential to reduce dementia incidence in Italy through targeted interventions, particularly addressing cardiovascular risk factors. Regional variations in PAFs and policy alignment highlight the need for tailored, evidence-based strategies.

Disclosure: This research was supported by the Italian Ministry of Health.

Headache and Pain

OPR-072 | Calcitonin gene-related peptide induces headache exacerbations in people with idiopathic intracranial hypertension

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Background and Aims: Calcitonin gene-related peptide (CGRP), known for its role in migraine pathogenesis, may also underlie headache generation in idiopathic intracranial hypertension (IIH), which commonly presents with migraine-like features.

Methods: A randomized, double-blind, placebo-controlled, two-way crossover trial was conducted. Seventeen adults with IIH and no prior migraine were randomly assigned to receive a 20-min continuous intravenous infusion of CGRP (1.5 μg/min) or placebo (isotonic saline) on two separate experimental days. Primary outcome was the difference in incidence of typical IIH headache exacerbations with migraine features between CGRP and placebo during a 12-h observational period post-infusion. Secondary outcomes were the differences in area under the curve (AUC) for headache intensity, intracranial pressure (ICP) and cerebrovascular haemodynamics.

Results: Twelve (71%) participants developed migraine-like headaches after CGRP infusion, compared with three (18%) after placebo ($p=0.0077$). The AUC for headache intensity was higher following CGRP infusion ($p=0.0157$). Although the AUC of mean ICP remained unchanged, ICP amplitude increased significantly after CGRP ($p=0.0052$). Cerebrovascular haemodynamics were significantly altered after CGRP (increased: heart rate ($p<0.0001$), tissue oxygenation index ($p=0.0413$), oxygenated haemoglobin ($p<0.0001$) and decreased: mean arterial pressure ($p=0.0099$), middle cerebral artery blood velocity ($p=0.0455$)).

Conclusion: These findings suggest that CGRP is a potent inducer of migraine-like headaches in IIH and may represent a promising therapeutic target.

Disclosure: A.Y. reports receiving speaker fees from Teva, UK. A.Y. is funded by an Association of British Neurologists

and Guarantors of the Brain fellowship. S.P.M. has received honoraria for speaker events from Heidelberg engineering; Chugai-Roche Ltd and Teva. Honoraria for advisory boards for Invex Therapeutics, Gensight and ocular therapeutix. Consultancy fees Neurodiem and Invex Therapeutics. Research funding from the UK Space Agency. M.A. has received personal fees from AbbVie, Amgen, Astra Zeneca, Eli Lilly, GlaxoSmithKline, Lundbeck, Novartis, Pfizer, and Teva Pharmaceuticals outside of the submitted work; has received research support from Lundbeck Foundation, Novartis, and Novo Nordisk Foundation; and has served as associate editor of Cephalalgia, associate editor of The Journal of Headache and Pain, and associate editor of Brain. A.J.S. is funded by a Sir Jules Thorn Award for Biomedical Science. A.J.S. reports personal fees from Invex therapeutics in her role as Director with stock holdings, during the conduct of the study; other from Allergan, Novartis, Cheisi and Amgen. All other authors declare no competing interests. All declared interests are outside the area of this submitted work.

OPR-073 | Insula deep brain stimulation for refractory neuropathic pain treatment: A randomized, sham-controlled cross-over trial

P. Cunha[1]; L. Dongyang[1]; J. Lapa[2]; G. Kubota[1]; J. Rosi Junior[1]; A. Fernandes[1]; R. Thibes[3]; D. Pinheiro[4]; R. Iglesio[1]; K. Duarte[1]; J. Sato[3]; V. Silva[1]; L. Lucato[1]; E. Figueiredo[6]; C. Carlotti Junior[6]; L. Yeng[1]; M. Teixeira[1]; D. Ciampi de Andrade[7]
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Background and Aims: Neuropathic pain (NeP) affects a considerable portion of the population and is often refractory to pharmacological interventions, which makes important to find alternative treatments. This study investigated the safety and efficacy of deep brain stimulation (DBS) targeting the posterior-superior insula in patients with chronic NeP who had previous response to repetitive transcranial magnetic stimulation of the same region.
Methods: A phase II randomized, double-blind, sham-controlled, cross-over trial was performed with ten participants. DBS electrodes were stereotactically implanted in posterior-superior insula. The study had three phases: double-blind (three months), single-blind (three months), and open-label (six months). Pain intensity was measured using a verbal numeric rating scale. The primary outcome was defined as achieving a >=30% reduction in average pain intensity. Secondary outcomes included assessments of pain interference, quality of life, and neuropsychiatric issues.
Results: Active DBS resulted in an 82.3% likelihood of achieving the primary outcome, with long-term responders reporting a mean pain reduction of 81.3%. Significant improvements in pain-related interference with sleep and mood were found, with probabilities exceeding 95% during follow-up. Quality-of-life scores, specially the related to physical health, also improved significantly. No major adverse events occurred, and the intervention was well tolerated.

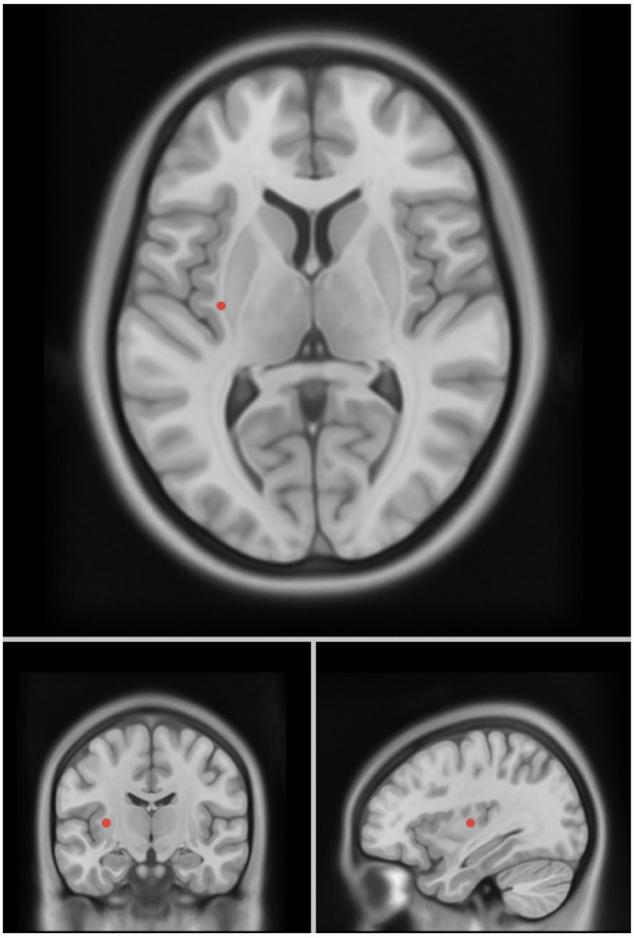

FIGURE 1 "Hot spot" for PSI-DBS

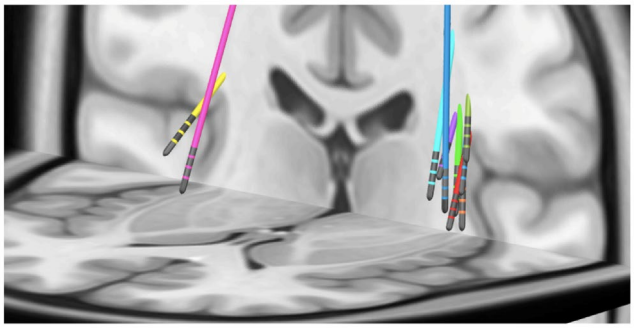

FIGURE 2 Electrodes reconstruction scenario

Conclusion: These findings suggest that posterior-superior insula DBS is a feasible and promising treatment for chronic refractory neuropathic pain, with a favorable safety profile. Larger phase III trials are recommended to confirm efficacy and assess broader applicability.
Disclosure: Nothing to disclose.

OPR-074 | Occipital nerve stimulation for chronic cluster headache: A double-blind, randomized, placebo-controlled study

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Background and Aims: Chronic cluster headache (CCH) is a debilitatingly painful disorder that can be very difficult to treat sufficiently. Occipital nerve stimulation (ONS) has shown promising results in attack prevention in patients with CCH, but evidence from controlled trials is scarce. Conventional (tonic) ONS elicits paresthesias, hampering blinded comparison to placebo. Using paresthesia-free burst ONS, we conducted a randomized, placebo-controlled trial.
Methods: The study is an investigator-initiated, double-blind, randomized, placebo-controlled clinical trial involving patients with CCH. It comprised a four-week baseline, a 12-week trial with transcutaneous electrical nerve stimulation, ONS implantation, a 12-week randomized, double-blind burst ONS treatment period, and a 12-week open-label tonic ONS treatment period. The primary outcome was the proportion of participants reporting a ≥30% reduction in attack frequency in the randomized and open-label trial phases.
Results: Thirty-eight patients underwent ONS implantation and were randomly assigned to burst ONS ($n=19$) or placebo ($n=19$). After the randomized trial phase, the proportion of ≥30% responders was 18.81% (95%CI 0.28%-37.87%) in the burst ONS group and 50.02% (26.87%-73.09%) in the placebo group. The likelihood of reaching the primary endpoint was 31.20% (1.29%-61.23%, $p=0.042$) higher in the placebo group. After the open-label phase, 42.09% (19.91%-64.34%) in the burst ONS group and 51.11% (27.32%-74.88%) in the placebo group had ≥30% frequency reduction.
Conclusion: ONS reduced attack frequency but was not superior to placebo. The results indicate that a part of the preventive effect of ONS may be attributed to a placebo response and call for attention to sufficient placebo control when planning further studies.
Disclosure: The study was funded by a grant from the Novo Nordisk Foundation (NNF19OC0058805). JCHS has received a restricted research grant (for the institution) from the Novo Nordisk Foundation. KM has received teaching fees from Medtronic and consulting fees from Salvia BioElectronics. KM and JCHS are co-owners and co-founders of the neuromodulation database company Neurizon. RJ received restricted research grants (for the institution) from Lundbeck Pharma and the Novo Nordisk Foundation. RJ has received personal fees for educational and teaching activities from Pfizer, Teva, Novartis, Abbvie, Lundbeck Pharma, and Eli-Lilly, and a fee (for the institution) for serving on the Lundbeck Pharma Advisory Board. RJ is the chair of the Master of Headache Disorders, Director of the Danish Headache Center, and unpaid activities as Director in Lifting the Burden. ASP has received a restricted research grant (for the institution), conference attendance from Lundbeck Pharma, and personal fees from Pfizer for teaching activities. ISFA has nothing to declare.

OPR-075 | PACAP-38 is increased in cluster headache; A new treatment target? A prospective, case-control study

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Background and Aims: Pituitary adenylate cyclase-activating peptide-38 (PACAP-38) is an essential neuropeptide in central nociception but estimates of its activity in cluster headache is sparse. We aimed to investigate whether plasma-levels of PACAP-38 differ between disease states (i.e., bout, remission, chronic) and compared to headache-free controls. Additionally, we assessed a possible correlation between plasma-levels of PACAP-38 and calcitonin gene related peptide (CGRP).
Methods: Emanating from the Danish cluster headache biobank, plasma samples collected from 312 participants were analyzed for plasma-levels of PACAP-38 and CGRP in a prospective, observational, case-control-study. Headache-free controls and participants with chronic cluster headache were sampled once, while participants with episodic cluster headache were sampled twice (in- and out of bout). Plasma-levels were measured with validated immunoassays.
Results: Plasma derived from 205 patients with cluster headache according to ICHD-3-criteria and 101 sex- and age-matched headache-free controls. PACAP-38 plasma-levels were significantly higher in all three disease states of cluster headache as to headache-free controls with collectively a mean PACAP-level 34.3% (95%CI: 20.1-48.6%, $p<0.0001$) higher than controls. We did not demonstrate a correlation between plasma-levels of PACAP-38 and CGRP (Spearman's $r=0.08$, $p=0.10$).
Conclusion: This large-scale study demonstrated increased PACAP-38 levels in all disease states of CH compared to headache-free controls, strengthening the hope of a possible effect of PACAP-38-targeting treatment in future trials.
Disclosure: The study was funded partly by an investigator-initiated grant from Lundbeck Pharma. Lundbeck Pharma paid for the analyses of the samples. Payments were made directly to the laboratorium, Celerion, Switzerland. Lundbeck Pharma did not influence the design, conduct, or interpretation of this study.

OPR-076 | Inflammatory biomarkers are affected in cluster headache

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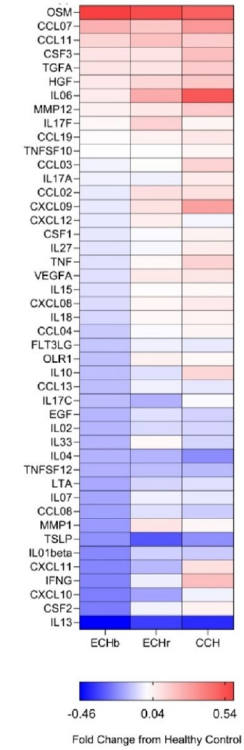
Background and Aims: The role of the inflammatory system in cluster headache (CH) has long been a topic of debate. Only few methodologically solid studies exist, and their findings are diverging. We therefore aimed to explore its role by measuring 45 different cytokines in a large cohort of CH patients and controls.
Methods: People with episodic CH (ECH) and chronic CH (CCH) from the Danish Cluster Headache Biobank were included and compared with headache-free controls, matched for age and sex. Serum was analyzed by the validated Olink Target 48 Cytokine kit.
Results: In total, 99 CCH patients, 110 ECH patients both in bout and in remission, and 100 controls partici-pated. For all patient groups, oncostatin m, a pro-inflammatory cytokine, was elevated compared with controls (2.87 pg/ml ($p < 0.0001$), 3.06 pg/ml ($p < 0.0001$), 2.99 pg/ml ($p < 0.001$) and 1.91 pg/ml for CCH, ECH bout, ECH remission and HC, respectively). Additionally, the cytokine profile of CCH and ECH in bout exhibited distinct alterations from controls with overall elevated cytokine levels for CCH and overall reduced cytokine levels for ECH (Figure 1).



ECHb: Episodic cluster headache in bout. ECHr: Episodic cluster headache in remission. CCH: chronic cluster headache

FIGURE 1 Heat-map showing the median fold change of cytokines between different stages of cluster headache and matched headache-free controls.

Conclusion: In this large study of inflammatory biomarkers, we confirm the involvement of the inflammatory system in CH. With its receptors' presence in the trigeminal ganglion, we identified oncostatin m as a potential new target of interest. The distinct alterations between CCH and ECH were unexpected and may have clinical implications in relation to treatment and prognosis.
Disclosure: Lundbeck Pharma financed the analyses of the samples, but had no influence on sample handling, data analyses nor interpretation of results and abstract writing. NL has received a personal research grant from the Capital region of Denmark.

OPR-077 | Exploration of prolonged remission and the natural course of cluster headache: An interview-based cohort study

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Background and Aims: This study aims to gain insight into the intriguing yet sparsely documented phenomenon of cluster headache (CH) remission.
Methods: In this cross-sectional cohort study all persons with CH were invited to complete a screening survey. Participants in prolonged remission were invited for an interview. Prolonged remission was defined as (i) no current CH prophylactic treatment and (ii) an attack free period of ≥ 5 years and/or twice the mean between-episode time.
Results: Of the invited persons, 43.2% (778/1801) responded, 625 were included in survey analysis and 125 met prolonged remission-criteria during interview. Median age at CH onset was 29 years (IQR: 20-42) and at remission onset 55 years (48-63). CH lasted 23 (15-33) years before remission. In 62% (N = 78), remission occurred abruptly. Of those with gradual remission (38%, N = 47), attack frequency (65%) and intensity (59%) decreased and between-episode intervals increased (52%) prior to remission. A higher probability of prolonged remission was observed in participants with ECH (hazard ratio (HR) = 6.60), who had quit smoking (HR = 2.53), had a higher attack intensity (HR = 1.28) and a higher age of CH onset (HR = 1.05).

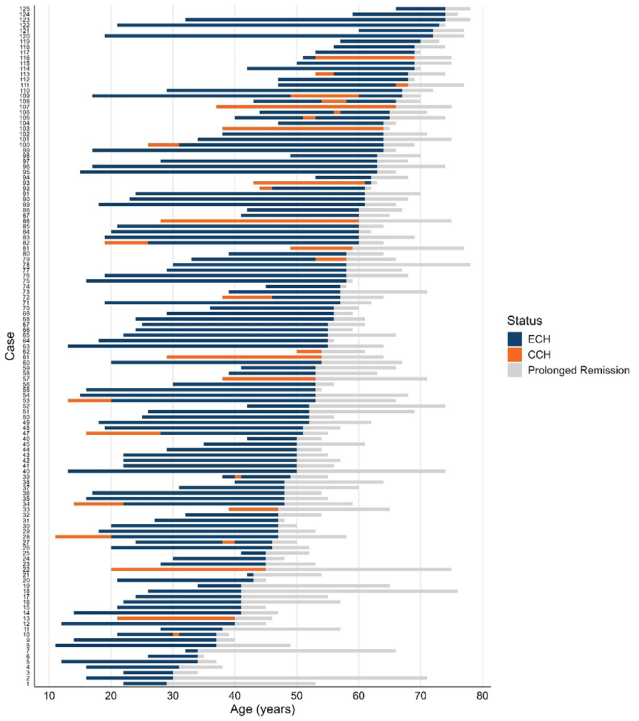

FIGURE 1 Disease course of interviewed participants with prolonged remission.

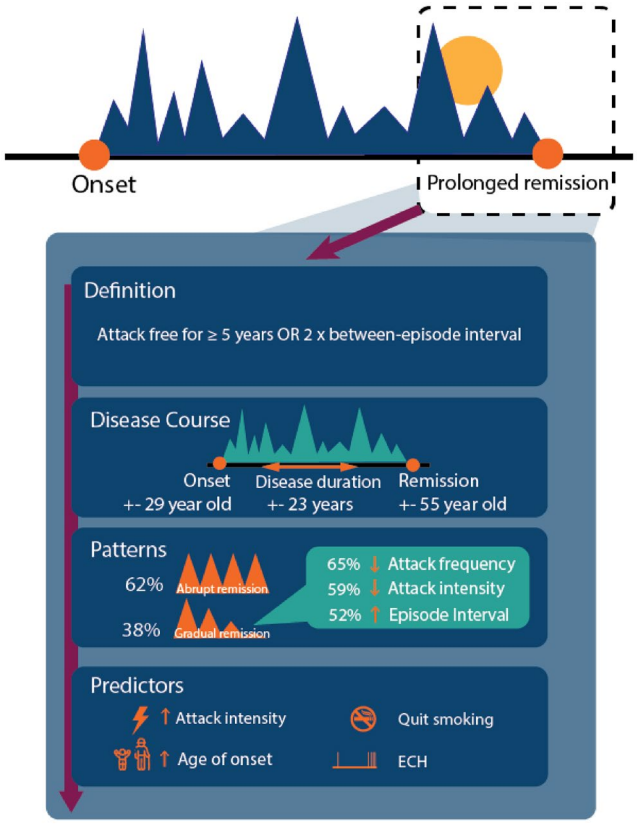

FIGURE 2 Infographic on Prolonged remission in Cluster headache.

TABLE 1 Baseline characteristics for participants.

	Total (N=625)	Interviewed Prolonged remission (N=125)
Interviewed	144 (23%)	125 (100%)
Prolonged Remission	145 (23%)	125 (100%)
Attack-free, years	0.5 (0.2-3.1)	6 (4-11)
Active CH	379 (61%)	0 (0%)
Prophylactic use	257 (41%)	0 (0%)
Male	424 (68%)	98 (78%)
Age at inclusion	58 (48-67)	64 (55-70)
Age of CH onset	29 (20-42)	27 (19-39)
Age at menarche	13 (12-14)	14 (12-14)
Age at menopause	49 (45-51)	51 (49-55)
Disease duration	21 (13-31)	23 (15-33)
Episodic CH[b]	372 (60%)	113 (90%)
Subtype switch	167 (27%)	21 (17%)
Attack frequency	3 (1-4)	3 (1-5)
Attack intensity	9 (8-10)	9 (9-10)
Autonomic symptoms	583 (94%)	111 (90%)
Restlessness	562 (90%)	113 (90%)
Episode duration, *weeks*	8 (5-13)	8 (5-12)
Between-episode interval, *months*	9 (5-12)	9 (4-12)
Comorbid headache	178 (29%)	31 (25%)
Smoker	165 (27%)	17 (14%)
Positive Familiy history	67 (11%)	17 (14%)
Right-sided attacks	256 (41%)	47 (38%)
Bilateral attacks	12 (1.9%)	3 (2.4%)

Descriptives are depicted as median (IQR) or number (percentage). Legend: CH: Cluster Headache, NRS: Numeric rating scale.

Conclusion: This cohort provides a rare insight in prolonged CH remission and showed (i) an average age of CH onset around 30 years, (ii) with 25 years of active CH before (iii) start of remission when patients reach their mid-50s. Disease duration until prolonged remission was shorter in episodic patients who had a high attack intensity, were older at the onset of CH, and had quit smoking.

Disclosure: The authors report no competing interests. RF reports consultancy and lecture fees from Novartis, Lundbeck, AbbVie, Lilly and TEVA, and independent support from the Dutch Brain Foundation, Leiden University Fund and Innovation Fund Dutch Healthcare Providers; these disclosures are not relevant for the topic of this abstract.; WM, PW, WN, PvT, AZ and RB report no relevant conflict of interest.

MS and Related Disorders 2

OPR-078 | Soluble factors may contribute to broad rim lesion-formation in multiple sclerosis

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Background and Aims: Disability progression in multiple sclerosis (MS) is resistant to current therapies. We recently identified mixed active/inactive white matter lesions with a broad rim of HLA-positive myeloid cells (broad rim lesions; BRLs) as

an imageable biomarker of a severe MS course, which could disclose modifiable mechanisms.

Methods: We performed a comprehensive histological analysis of lesion rim thickness of BRLs ($n = 94$) and classical mixed active/inactive lesions (CL, $n = 285$) across MS cases ($n = 52$) within the Netherlands Brain Bank and explored correlations with pathological and clinical traits and lymphocyte-presence.

Results: BRLs displayed broader HLA-positive rims compared to classical mixed lesions (average 1,646 μm vs. 342 μm), with rim thickness across multiple lesions being identified as donor trait (hence referred to as BRL donors). Donors with largest rim sizes reached at earlier age disability milestones as reflected by the age-related MS severity score ($R = 0.46$, $p < 0.001$). Presence of BRLs associated with a higher rate of leuko-cortical but not subpial cortical lesions. Mixed lesions adjacent to ventricles and/or containing perivascular lymphocyte aggregations displayed broader rims, suggesting contributions of soluble factors. Distributions of perivascular CD79α-positive B cells and CD3-positive T cells are being investigated.

Conclusion: We consolidate BRLs as a pathological trait of donors with a more severe course of MS. B- and T-cell populations and soluble factors from perivascular and subarachnoid compartments may contribute to their formation in MS distinctly from subpial lesion accumulation. Additional stainings for lymphocyte subsets and assessment of soluble factors in cerebrospinal fluid may reveal underlying mechanisms.

Disclosure: JS received research support and/or speaker fee and/or consulting fee of Biogen, Merck, Novartis, Roche, and Sanofi-Genzyme. IH and HH received research support from Biogen.

OPR-079 | Temporal dynamics of serum neurofilament light chain in MS: A retrospective study in a clinical routine setting

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Background and Aims: Serum neurofilament light chain(sNfL), a biomarker for neuroaxonal injury, is associated with MS disease activity. Elevated sNfL levels were linked to evidence of disease activity (EDA), compared to clinically/radiologically stable patients. However, the temporal dynamics of sNfL related to relapses and its routine clinical implications remain poorly understood. This study aims to evaluate the temporal changes in sNfL related to MS relapsing activity and their utility in clinical assessments.

Methods: Retrospective longitudinal data from 162MS patients (mean age = 32.5±7.8 years, median [IQR] disease duration 2.1[1-7.1], 64.2% female) were analyzed, with a median of 7[IQR 6–9] serum samples per patient collected over a median follow-up time of 10.4[IQR 7.8-13.8] years. sNfL levels were quantified using Simoa HD-X analyzer, results were adjusted for age and BMI using Z-scores. Radiological activity was assessed through Gadolinium-enhanced lesions using 3T-MRI scans. EDA was defined as occurrence of clinical relapses, confirmed disability worsening (using EDSS scores) or radiological activity, within six months of sampling.

Results: sNfL Z-scores were significantly elevated in patients with future EDA within one year of sampling, but only in samples taken during remission ($p < 0.001$). Additionally, sNfL levels didn't predict EDA beyond this one-year window. The temporal analysis around clinical relapses showed increased sNfL Z-scores at relapse onset ($p < 0.001$), with persisting levels up to 9 months post-relapse.

Conclusion: These findings highlight the importance of monitoring sNfL as a dynamic biomarker for disease activity. Accurate knowledge of sNfL temporal dynamics is essential for correct interpretation in clinical practice and identifying patients at risk of disease activity. This approach could enhance clinical decision-making and improve routine MS-care.

Disclosure: C.T: travel funds, speaker honoraria from Merk R.D: travel funds from Janssen, Novartis, Sanofi A.D: was in sponsored meetings, received speaker honoraria or travel funds from Sanofi-Aventis, Novartis, Janssen D.P: part of the advisory board "Cognition and MS" for Novartis; received speaker honoraria from Biogen, Novartis, MedAhead, Bristol-Myers Squibb D.L: Chief Medical Officer of GeNeuro until end of 2023 J.K: received speaker fees, research support, travel support, and/or was on advisory boards by Swiss MS Society, Swiss National Research Foundation (320030_212534/1),University of Basel, Progressive MS Alliance, Alnylam, Bayer, Biogen, Bristol Myers Squibb, Celgene, Immunic, Merck, Neurogenesis, Novartis, Octave Bioscience, Quanterix, Roche, Sanofi, Stata DX C.E: travel funds and speaker honoraria from Biogen Idec, Bayer Schering Pharma, Merck Serono, Novartis, Genzyme, Teva Pharmaceutical Industries Ltd./Sanofi-Aventis, Shire; received research support from Merck Serono, Biogen Idec, Teva Pharmaceutical Industries Ltd./Sanofi-Aventis; is on scientific advisory boards for Bayer Schering Pharma, Biogen Idec, Merck Serono, Novartis, Genzyme, Roche, Teva Pharmaceutical Industries Ltd./Sanofi-Aventis M.K: travel funding and speaker honoraria from Bayer, Biogen, Novartis, Merck, Sanofi, Teva; is on scientific advisory boards for Biogen, Bristol-Myers Squibb, Gilead, Merck, Novartis, Alexion, Amgen, Roche; received research grants from Biogen, Novartis and Teva Other: no disclosures.

OPR-080 | Effect of rituximab on non-active secondary progressive multiple sclerosis – A retrospective multicenter analysis

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Background and Aims: Non-active secondary progressive multiple sclerosis (naSPMS) is characterized by a steady increase in disability without relapses or MRI activity. Currently, there is no approved immunotherapy available for, and a paucity of studies specifically addressing naSPMS. Rituximab (RTX) has occasionally been used off-label for the treatment of naSPMS. The aim of this study was to investigate the efficacy and safety of RTX on disease progression in patients with naSPMS.
Methods: We conducted a retrospective multicenter study to identify patients with naSPMS lasting for at least six months, treated between February 2008 and October 2024. Baseline characteristics, disability progression before and during RTX treatment, magnetic resonance imaging (MRI) activity and safety aspects were analyzed.
Results: 46 patients with naSPMS and a mean age of 49.46 years (9.80, standard deviation, SD) at treatment start were included. Patients were predominantly male (59%), time since naSPMS onset to treatment was 4.72 (mean, 5.11, SD) years. EDSS at RTX treatment start was 5.45 (mean, 1.26, SD; median 6 (IQR 4-6.5)). 12 months after treatment start, EDSS remained stable ($n = 39$), after 18 months EDSS had increased to 6 (IQR 4.38-6.5, $p = 0.046$; $n = 34$), and to 6 (median, IQR 4,5-6,5, $p = 0,029$; $n = 24$) after 36 months, compared to baseline. After treatment start, three patients had relapses and six MRI activity. Data on walking ability, MRI, B-cells, and safety will be presented at the meeting.
Conclusion: We observed a mild, however, significant increase in disability despite RTX treatment in naSPMS. Treatment was generally well tolerated and safe.
Disclosure: NE, AM, EO, MN, FTN: none KG: travel grants from Nexstim, UCB, Viatris. JH: grant for OCT research from the Friedrich-Baur-Stiftung, Horizon, Sanofi and Merck, personal fees and nonfinancial support from Alexion, Amgen, Bayer, Biogen, BMS, Merck, Novartis and Roche, all outside the submitted work. TK: speaker honoraria and/or personal fees from Novartis Pharma, Roche Pharma, Alexion/Astra Zeneca, Horizon Therapeutics/Amgen, Merck, Chugai Pharma and Biogen. Compensation for serving as a member of a steering committee from Roche (institutional). Her institution has received compensation for clinical trials from Novartis Pharma, Roche Pharma and Sanofi Genzyme, all outside the present work. VR: speaker honoraria and compensation for serving in advisory boards for Alexion, Biogen, Novartis, Pfizer, Roche, Sanofi-Aventis, and Teva. ABe: consulting and/or speaker fees from Alexion, Argenx, Biogen, Horizon/Amgen, Merck, Neuraxpharm, Novartis, Roche and Sandoz/Hexal, and his institution has received compensation for clinical trials from Alexion, Biogen, Merck, Novartis, Roche, and Sanofi Genzyme; all outside the present work. ABa: personal compensation from Merck, Biogen, Novartis, TEVA, Roche, Sanofi/Genzyme, Celgene/Bristol Myers Squibb, Janssen, Sandoz/HEXAL, Alexion, Horizon, Argenx, research support by Novartis, and grants for congress travel and participation from Biogen, TEVA, Novartis, Sanofi/Genzyme, Merck Serono, Celgene, Janssen and Roche. None related to the present work.

OPR-081 | sNfL and GFAP levels are associated with retinal layer thinning in multiple sclerosis

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Background and Aims: Serum neurofilament light chain (sNfL) and glial fibrillary acidic protein (GFAP) are emerging biomarkers of axonal damage and astrocytic activation, both likely paramount in MS associated neurodegeneration. However, their value in predicting retinal layer thinning remains underexplored.
Methods: This prospective observational study included patients with relapsing MS newly initiated on a disease-modifying therapy (DMT). OCT scans were conducted 3–6 months after DMT initiation (rebaseline) and at 12-month intervals measuring peripapillary retinal nerve fiber layer (pRNFL) and ganglion cell-inner plexiform layer (GCIPL) thickness. Serum sNfL and GFAP levels were measured using single-molecule array (Simoa) technology, with z-scores adjusted for age, BMI and – for GFAP – sex.
Results: A total of 116 patients (mean age 34.5 years (SD 8.6)), 73.3% female, median disease duration 2.8 years (IQR 0.3–7.1), median EDSS 1.5 (range 0–5.5)) were included. Both pRNFL ($b = -0.34$; 95% CI −0.67, −0.02; $p = 0.04$) and GCIPL thicknesses ($b = -0.39$; 95% CI −0.65, −0.12; $p = 0.004$) were associated with GFAP – but not sNfL – z-scores at baseline. GFAP z-scores at M6 showed the strongest association with aLpRNFL ($b = -0.24$; 95% CI −0.27, −0.21, $p < 0.001$) and aLGCIPL ($b = -0.15$; 95% CI −0.18, −0.12, $p < 0.001$). Moreover, patients with low sNfL but high GFAP levels at M6 showed the most pronounced inner retinal layer thinning (aLpRNFL: −0.8%/year (1.1), aLGCIPL: −0.8%/year (0.9); both $p < 0.001$).
Conclusion: High GFAP levels – more than sNfL levels – are associated with inner retinal layer thinning in RMS, underscoring their value as biomarkers of disease progression.
Disclosure: All authors declare no conflict of interest relevant to this study.

OPR-082 | Multimodal analysis of brain networks contributes to characterize clinical profiles in multiple sclerosis

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Background and Aims: Multiple sclerosis (MS) presents variable clinical manifestations among individuals. Here, we performed a multimodal analysis of grey matter (GM) structural and functional networks in a multi-center cohort (12 European sites), to evaluate the contribution of structural/functional MRI GM damage in depicting MS clinical features.
Methods: 3D T1-weighted, resting state (RS) functional MRI and clinical evaluations were obtained from 1754 MS patients (66 clinically isolated syndromes [CIS], 1342 relapsing-remitting [RR] and 346 progressive [P] MS) and 597 healthy controls (HC). Parallel independent component analysis (P-ICA) on GM volume and degree centrality maps produced structural/functional network components and corresponding Z-scores.
Results: P-ICA identified six structural GM networks with significant atrophy in MS patients vs HC (p range <0.001-0.02). CIS patients showed atrophy in the default-mode network (DMN) ($p<0.001$), RRMS had additional atrophy in occipital, deep GM, and fronto-parietal networks (all $p<0.001$), while PMS exhibited further atrophy in DMN and occipital networks (both $p=0.002$). P-ICA also identified three sensorimotor networks showing increased functional connectivity (FC) in MS patients vs HC ($p=$ range $0.007/<0.001$), while the DMN, fronto-parietal and salience networks showed decreased FC (all $p<0.001$). CIS patients presented limited FC abnormalities, while more pronounced decrease FC in PMS vs RRMS was found in the DMN ($p=0.002$) and fronto-parietal ($p=0.01$) networks. In MS, most of networks showed decreased structural-functional association (interaction p range $=0.04$ to <0.001), correlating with higher disability and T2 lesion volume.
Conclusion: Multimodal analysis of structural/functional brain networks helped to unravel complex changes of human brain organization associated with MS disease.
Disclosure: Nothing to disclose.

Epilepsy

OPR-083 | The Epilepsy Deaths Register: Friend, family and care-giver reports of SUDEP in adults and older adolescents

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Background and Aims: Sudden unexpected death in epilepsy (SUDEP) is the most common cause of epilepsy related death. Understanding SUDEP characteristics through third-party accounts is vital, yet these valuable narratives remain underutilised. This study is the first comprehensive analysis of adult SUDEP characteristics from accounts in the epilepsy deaths register
Methods: We collected the characteristics of the deceased and narratives surrounding death via the SUDEP action UK epilepsy deaths register (EDR) third-party reports. We included those aged ≥15 years with a post-mortem, death-certificate or narrative in keeping with SUDEP. Duplicate submissions, non-SUDEP causes, and cases without certified causes of death were excluded. We collected the demographics, details of follow-up, events leading to death, and attitudes towards condition and treatment in life.
Results: From 1,056 EDR registrations (2013-2024), 409 met SUDEP criteria. Cases were predominantly male (59.4%), aged 19-49 years (76.3%), and living with family/friends (71.6%). Of determinable cases, 85.9% occurred at night and 80.8% during sleep, with 63.2% found prone. While 90.6% were prescribed antiepileptics and 82.3% had specialist follow-up, SUDEP was not recorded as cause of death in 24.9% despite consistent narratives. Notably, 51.5% of reporters were unaware epilepsy could be fatal.
Conclusion: SUDEP is an underreported cause of death in patients with epilepsy. Third-party reports are an effective tool to sample SUDEP deaths. The heterogeneity of SUDEP cases and the high proportion of respondents unaware of fatal epilepsy

outcomes support universal SUDEP risk counselling and emphasise the value of third-party reporting in deepening SUDEP understanding.

Disclosure: RHT has received honoraria from Angelini, Bial, Eisai, GW Pharma, Paladin, NeuraxPharm, Sanofi, Takeda, UCB Pharma, UNEEG, Zogenix, and unrestricted research funding from Angelini/Arvelle and UCB Pharma, independent of this project - Jacob Brolly has received honoraria from UCB phrarmapharma - Donald P Craig has received a consultancy fee from Eisai - Karen Osland was project lead for the epilepsy deaths register for the UK charity SUDEP action until April 2020. - Ben Donovan is the project lead for the epilepsy deaths register for the UK charity SUDEP Action - Jane Hanna OBE was previously chief executive of the UK charity SUDEP action - Elaine Hughes, participated in multi-centre commercial trials of fenfluramine in treatment of epilepsy in Dravet syndrome and is a member of the GW Pharmaceuticals supported LGS Advisory Board. - Mike P Kerr is Vice Chair of SUDEP Action, the charity that supports the Epilepsy Deaths Register.

OPR-084 | P2Y12 receptor dysregulation in MTLE-HS: Insights from human brain tissue and an in vitro model

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Background and Aims: Chronic microglial activation is a hallmark of mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS). The ADP-sensitive P2Y12 receptor plays a key role in initiating microglial activation. Given the link between prolonged microglial activation and increased synaptic activity, we aimed to study the role of P2Y12R in MTLE-HS by (i) analyzing P2Y12R mRNA expression in human brain tissue and (ii) developing an in vitro model of microglia-like cells derived from peripheral blood monocytes (MMG).

Methods: Hippocampal and temporal neocortex samples were obtained from 19 MTLE-HS patients (8M, 43.5 ±10.0 years) and 10 cadaveric controls (8M, 67.0 ±10.0 years). MMG cells were differentiated from the blood monocytes of 15 MTLE-HS patients and 5 healthy donors. P2Y12R mRNA expression was quantified using Real-Time PCR.

Results: P2Y12R mRNA levels were significantly higher in the hippocampus (1.78-fold, $p = 0.004$) and temporal neocortex (2.89-fold, $p < 0.001$) of MTLE-HS patients compared to controls, with no correlation to age. Homeostatic MMG cells presented a ramified morphology and expressed P2Y12R, Upon LPS stimulation, MMG cells became amoeboid and showed marked P2Y12R downregulation.

Conclusion: P2Y12R expression changes dynamically during epilepsy progression. It initially facilitates microglial activation but is later downregulated to promote migration. Its upregulation in the temporal neocortex suggests a role in MTLE-HS progression. Further research is needed to clarify the interplay between P2Y12R and other purinergic receptors in MTLE-HS. Moreover, our work confirms MMG cells as a valuable in vitro model for studying microglial function in epilepsy and neuroinflammatory conditions.

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OPR-085 | Exploring apolipoprotein ε4 in progressive myoclonic epilepsy type 1

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Background and Aims: Progressive myoclonic epilepsy type 1 (EPM1) is a neurodegenerative disease caused by biallelic alterations in the cystatin B (CSTB) gene. Despite a progressive course, phenotype severity varies among patients, even within families. We studied the possible role of APOE ε4 in modifying phenotypic diversity in EPM1.

Methods: As part of our large EPM1 study, APOE genotypes were determined for 65 genetically verified EPM1 patients homozygous for the CSTB expansion mutation. The Unified Myoclonus Rating Scale (UMRS), Quality of Life in Epilepsy Inventory-31 questionnaire (QOLIE-31), clinical data, and quantitative neuroimaging data were compared between APOE ε4 carriers and non-carriers to assess potential correlations with EPM1 severity.

Results: The cohort included 20 ε4 carriers (16 ε3/ε4 and 4 ε4/ε4) and 45 non-carriers (36 ε3/ε3, 8 ε2/ε3, and 1 ε2/ε2). No significant differences were found in UMRS or disease duration. Carriers had better QOLIE-31 scores in emotional well-being ($p = 0.047$), energy/fatigue ($p = 0.048$), and medical effects ($p = 0.024$). In volumetric analysis, carriers exhibited larger bilateral hippocampus and amygdala volumes but reduced cortical thickness in the left lingual gyrus, right lateral occipital gyrus, and right posterior cingulate ($p < 0.05$). Carriers exhibited widespread white matter degeneration in diffusion tensor

imaging, characterized by reduced fractional anisotropy and increased mean diffusivity.
Conclusion: Despite greater white matter degeneration, APOE ε4 carriers exhibited preserved deep brain volumes and better self-reported well-being. This study highlights the complex interplay between genetic factors and neurodegenerative processes. Our future research aims to provide more natural history data of EPM1 and correlate long-term phenotypic data with additional geno-phenotypic analyses.
Disclosure: Nothing to disclose.

OPR-086 | Morphological and functional evaluation of epileptogenesis in tuberous sclerosis using brain organoids

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Background and Aims: Tuberous sclerosis complex (TSC) is a neurodevelopmental disorder caused by mutations in TSC1 or TSC2, associated with widespread network dysfunction and drug-resistant epilepsy. The mechanisms underlying epileptogenesis remain elusive due to the lack of human-specific biomodels. This study integrates morphological and functional evaluations using patient-derived brain organoids to uncover key processes in TSC-related epileptogenesis.
Methods: Human induced pluripotent stem cells (hiPSCs) from TSC patients and isogenic controls were differentiated into brain organoids. Morphological features were examined using immunohistochemistry and electron microscopy to assess cellular organization, dendritic morphology, and ultrastructural features. Functional network dynamics were evaluated using extracellular silicon probe recordings. Organoid findings were correlated with intraoperative electrocorticography (ioECoG) data and post resection samples from TSC patients.
Results: Histological analyses revealed altered interneuron distribution, including expansion of caudal ganglionic eminence (CGE)-derived populations in TSC organoids. Structural abnormalities, such as MAP2-positive dendritic swellings and mitochondrial disruptions, highlighted excitotoxic damage. Ultrastructural analyses showed pathological synaptic densities and microtubule disarray (Figure 1). Functionally, TSC organoids exhibited hyperexcitability, with increased frequency of pathological high-frequency oscillations (HFOs) and dysregulated network synchronization. These abnormalities were consistent with epileptogenic signatures observed in ioECoG recordings from TSC patients (Figures 2 and 3).

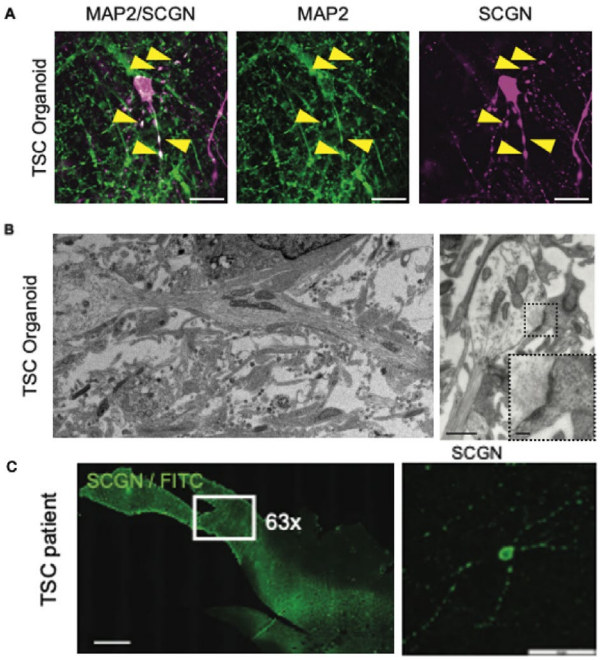

FIGURE 1 A: SCGN+ interneurons in TSC organoids show dendritic beading (SCGN+/MAP2+). B: EM reveals enlarged postsynaptic beads with damaged microtubules and mitochondria. C: TSC resected samples confirm pathological SCGN+ dendritic beading.

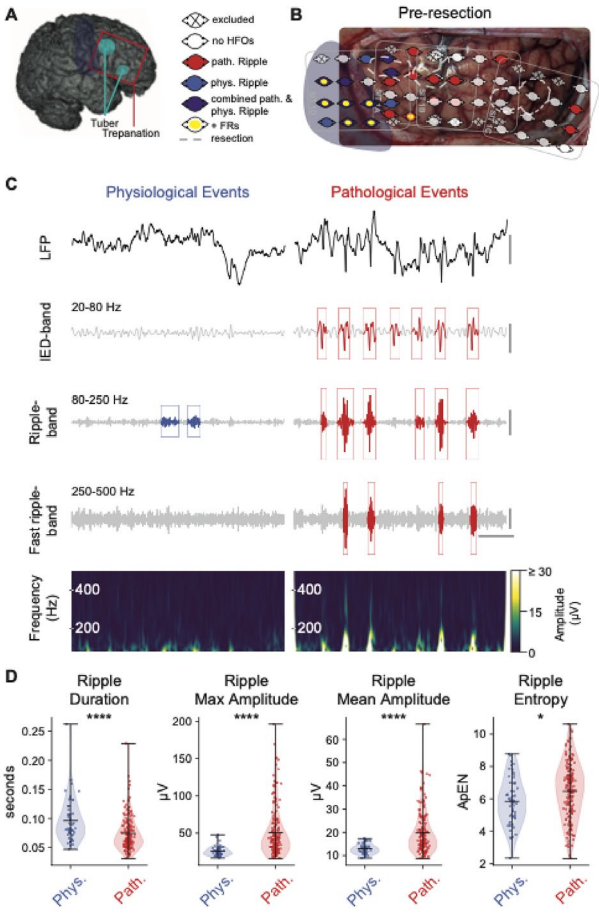

FIGURE 2 A and B: Example of ioECoG recording. C: Characterization of physiological (blue) vs pathological (red) HFOs, which show IED-ripple alignment. D: Ripple metrics reveal significant differences.

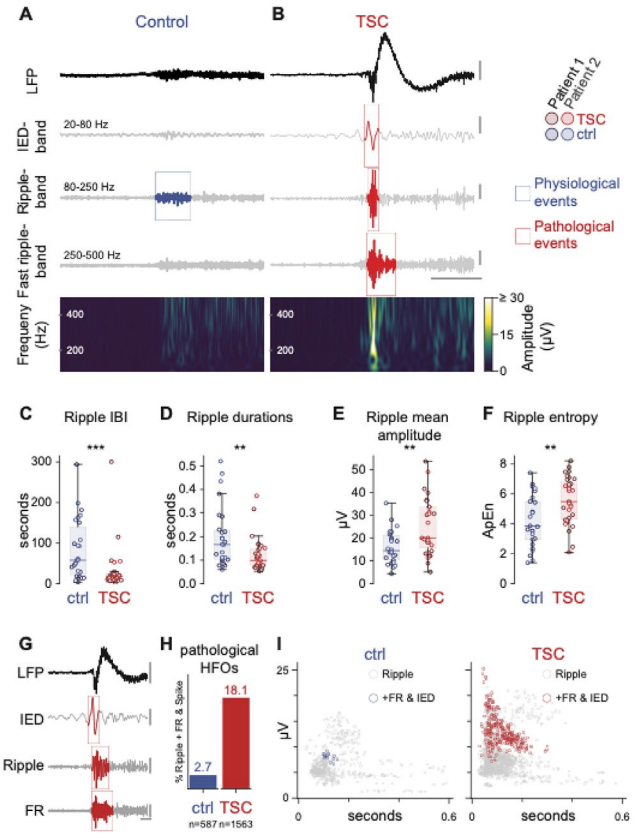

FIGURE 3 A-B: LFP and band-filtered signals show spikes, ripples, and fast ripples (control: blue; TSC: red). C-F: TSC organoids show altered ripple inter-burst interval, duration, amplitude, and entropy. G-I: Epileptogenic properties of TSC organoid.

Conclusion: This study demonstrates that brain organoids can faithfully model morphological and functional changes underlying epileptogenesis in TSC. By integrating structural and electrophysiological evaluations, this approach identifies critical roles for CGE-derived interneurons, dendritic alterations, and pathological network synchronization. These findings provide a platform for advancing mechanistic understanding and exploring therapeutic strategies for TSC and epilepsy.
Disclosure: Nothing to disclose.

OPR-087 | Exploring high-frequency oscillations (HFOs) in human organotypic brain slice cultures: An ex-vivo approach

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Background and Aims: High-frequency oscillations (HFOs) have been studied for over 25 years and emerged as a valuable biomarker in the presurgical assessment of epilepsy patients. The underlying pathophysiologic mechanisms remain incompletely understood. Currently, HFOs in humans are predominantly investigated in-vivo during stereo-EEG (sEEG), limiting coverage and experimental interventions. Human organotypic brain slice cultures (HOBSCs) enable long-term investigations of brain physiology, including the recording of neuronal activity and network properties using multi-electrode arrays (MEA). Here, we present preliminary data demonstrating HFO detection in HBOSCs, offering an ex-vivo model to investigate HFO pathophysiology.
Methods: We obtain brain tissue from epilepsy or tumor surgery to prepare brain slices. Human cerebrospinal fluid (hCSF) is used for slice culturing, granting viability for up to three weeks. We use 256-channel MEAs, covering 3.2x3.2mm2, to record whole-slice electrophysiology, enabling the measurement of local field potentials, action potentials, and propagation dynamics. Computational post-processing includes frequency filtering and semi-automated HFO detection. Slices are exposed to varying temperatures and excitatory or inhibitory agents to assess their impact on HFOs.
Results: We demonstrate a consistent detection of HFOs in HOBSCs from hippocampal resections of temporal lobe epilepsy patients. HFOs spatially correspond to anatomical regions of increased spiking. HFO frequency positively correlates with temperature. Treatment with norepinephrine and GABAA-antagonists increases HFO frequency, while AMPA-antagonists reduce HFO occurrence.

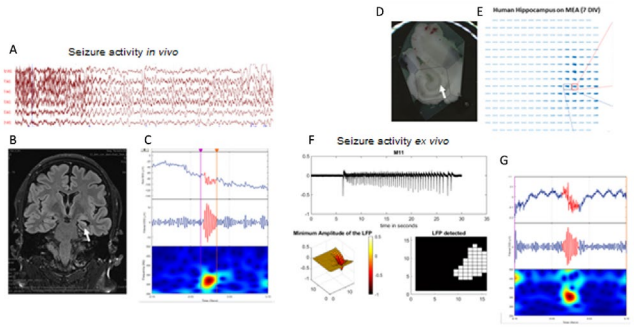

FIGURE 1 A: Surface EEG of patient. B: MRI with hippocampal sclerosis. C: Filtered sEEG show hippocampal HFO. D: Resected hippocampus with superimposed position of MEA grid. E: MEA recording with spontaneous seizure activity. F: Extracted seizure activity.

Conclusion: We introduce a novel approach to study HFOs in human brain tissue, providing a platform for experimental interventions. This opens new perspectives to investigate the pathophysiologic basis of HFOs and their role across different brain lesions.
Disclosure: None.

OPR-088 | The Cerebellar Cognitive Affective Syndrome Scale in early Multiple Sclerosis: A diffusion and functional-MRI study

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Background and Aims: Damage to cerebellar posterior lobes can result in Cerebellar Cognitive Affective Syndrome (CCAS). The validity of the CCAS Scale (CCAS-S), a reliable tool to diagnose CCAS, remains unexplored in MS. In this study, we aimed to determine the ability of CCAS-S to detect CCAS in MS at clinical onset. Using conventional, diffusion (dMRI), and resting state-functional MRI (rs-fMRI), we also assessed the clinical and MRI characteristics of MS patients with CCAS (CCAS+). Lastly, we identified the MRI predictor most strongly associated with CCAS in MS.
Methods: Seventy early MS patients underwent CCAS-S and standard cognitive assessments. Twenty healthy controls and 56 patients also underwent MRI to obtain lesion and volumetric parameters, dMRI metrics, and cerebellum-brain functional connectivity (FC). Regressions were used to study associations between MRI metrics and CCAS-S scores.
Results: CCAS-S identified 9 (13%) MS patients with CCAS and normal scores on standard cognitive assessments. CCAS+ patients showed lower fractional anisotropy in cerebellar normal-appearing white matter ($p=0.020$), and increased cerebro-cerebellar connectivity on rs-fMRI ($p<0.05$). Finally, we found that the cortical lesion volume was the strongest predictor for low CCAS-S performance in MS ($R^2=0.446$, $\beta=-0.009$, $p=0.004$).

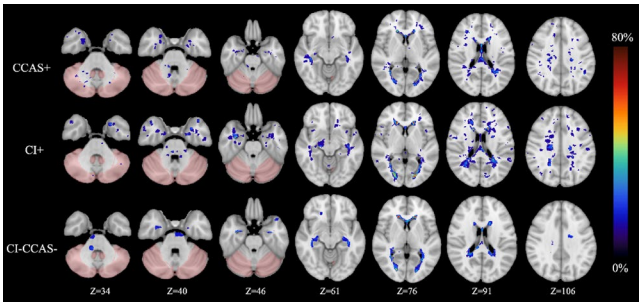

FIGURE 1 Probabilistic lesion map over a selection of axial slices, showing the lesion load percentage in MS patients with CCAS+ ($n=9$), MS patients with impaired standard cognitive test (CI+, $n=10$), and cognitively normal MS patients (CI- CCAS-, $n=37$).

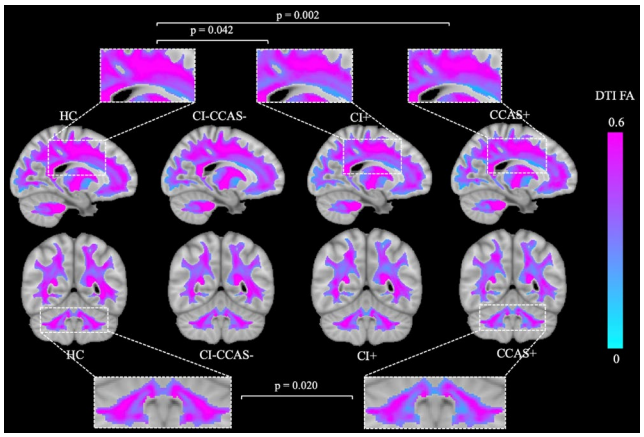

FIGURE 2 DTI maps showing the mean NAWM FA for each group. Both CI+ and CCAS+ patients exhibited significantly lower FA in the brain NAWM compared to HC. Only CCAS+ patients demonstrated lower FA in the cerebellar NAWM compared to HC.

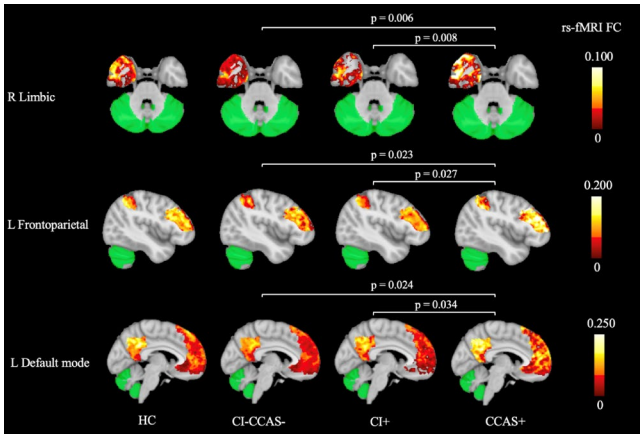

FIGURE 3 Seed-based rs-fMRI connectivity analysis showing differences in functional connectivity across groups. CCAS+ patients showed increased cerebellum connectivity in the right limbic, left frontoparietal, and left DMN compared to CI- CCAS- and CI+ patients.

Conclusion: CCAS-S is a valid tool to complement standard cognitive assessments, enhancing sensitivity in detecting cognitive impairment in MS at clinical onset. CCAS+ patients are characterized by severe microstructural cerebellar damage and increased brain-cerebellar connectivity. Possibly due to a diffuse cortical pathology shared between the brain and cerebellum, the presence of brain cortical lesions is a strong predictor of CCAS in MS.
Disclosure: Nothing to disclose.

OPR-089 | Deep sulcal inflammation drives local cortical atrophy: A self-sustained loop of neurodegeneration in multiple sclerosis

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Background and Aims: Within the cortex of individuals with MS, meningeal inflammation and activated innate immune cells are frequently observed, but their regional distribution

along sulci and relationship with CSF dynamics and cortical atrophy remain unclear. This study examined sulcal inflammation, CSF stagnation, and cortical atrophy over two years in two independent MS cohorts.

Methods: Participants (36 and 40 MS patients, plus healthy controls) underwent baseline [18F]-DPA-714 PET to assess innate immune cell inflammation and annual MRI for 24 months. The validation cohort also underwent low b-value diffusion tensor imaging to estimate CSF stagnation. Comparing [18F]-DPA-714 DVR maps between MS and controls, we identified inflamed cortical sulci and analyzed immune cell distribution, CSF dynamics, and sulcal enlargement over time.

Results: In MS patients, 11.7% of sulci were inflamed, with deeper sulcal regions showing greater immune activation ($p=0.007$). Increased sulcal inflammation predicted local atrophy over two years ($p<0.0001$), with each one-point DVR increase raising atrophy likelihood by 30% (OR = 3.49, $p<0.0001$). The validation cohort confirmed these findings and further linked sulcal inflammation to increased CSF stagnation ($\beta=0.10$; $p<0.0001$).

Conclusion: Cortical inflammation predominantly affects deep sulci, driving atrophy in MS. CSF stagnation may exacerbate this by prolonging exposure to pro-inflammatory components, perpetuating the cycle of chronic inflammation and neurodegeneration.

Disclosure: Nothing to disclose.

OPR-090 | Dysarthria assessment in Multiple Sclerosis patients

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Background and Aims: Multiple Sclerosis (MS) is a disabling disorder affecting young adults. Speech impairment patterns in MS are poorly characterized. Dysarthria Analyzer (DA) is a software allowing a detailed speech analysis.

Methods: All patients underwent clinical assessments (EDSS and BICAMS) and speech evaluation using the DA. Each patient performed 4 tasks: phonation A, phonation I, reading, monologue and syllable repetition. DA automatically extracted 28 speech features, adjusted for age, gender and education toward internal controls (z-scores). A principal component analysis (PCA) was conducted, retaining components with eigenvalues>1. Correlations were assessed through forward stepwise analysis, including age, sex, EDSS, Symbol Digit Modalities Test (SDMT), California Verbal Learning Test (CVLT), Brief Visuospatial Memory Test Revised (BVMTR) and smoking status as covariates.

Results: We enrolled 72 patients [50 females; mean age 48.1±10.9 years; median disease duration of 14(0–34) years and a median EDSS of 3(1.5–6.5)]. PCA identified an 8-component model: Monopitch, Nasal Voice, Slow Sequential Motion Rates, Monoloudness, Prolonged Pauses, Tremor Voice, Speech Timing, Respiration Quality. Higher Monoloudness scores were associated with lower SDMT scores (corr.coeff = -0.04, $p=0.001$). Prolonged Pauses and Shorter Speech Timing correlated with higher EDSS (corr.coeff = 0.25, $p=0.03$ and corr.coeff = -0.3, $p=0.001$).

Conclusion: Detailed speech analysis can reflect various aspects of MS disability. Possibly, cognition is crucial in speech modulation for conveying meaning in social interactions, while motor disability is more closely linked to muscle control involved in phonation and speech articulation in MS patients.

Disclosure: A.E. has received honoraria from Novartis. M.M. has received research grants from ECTRIMS-MAGNIMS, the UK MS Society, and Merck, and honoraria from Biogen, BMS Celgene, Ipsen, Janssen, Merck, Novartis, Roche, and Sanofi-Genzyme. M.P. has received research grants from the Italian MS Foundation and Baroni Foundation, honoraria from Health & Life and Biogen, and sponsorship for travel/meeting expenses from Novartis, Roche, and Merck. R.L. has received honoraria from Biogen, Merck, Novartis, Roche, and Teva. V.B.M. has received research grants from the Italian MS Society and Roche, and honoraria from Bayer, Biogen, Merck, Mylan, Novartis, Roche, Sanofi-Genzyme, and Teva. A.C. has received research grants from Almirall, research grants from ECTRIMS-MAGNIMS, and honoraria from Almirall, Biogen, Roche, Sanofi-Genzyme, Merck, Ipsen, and Novartis. None of the other authors has any conflict of interest to disclose.

OPR-091 | Failure to suppress effector B cells is associated with resistance to ocrelizumab treatment in multiple sclerosis

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Background and Aims: The aim of this study was to explore the utility of peripheral blood cell subsets in prediction of treatment response to ocrelizumab, a CD20-targeting monoclonal antibody, in relapsing remitting multiple sclerosis (RRMS).

Methods: Thirty-one patients with RRMS resistant to first-line immunomodulating agents were enrolled and followed-up for 12 months under ocrelizumab treatment. Disease activity was monitored by 6-monthly assessments of EDSS and cranial-spinal magnetic resonance imaging. No evidence of disease activity (NEDA-3) status was determined, and peripheral blood mononuclear cells were immunophenotyped by flow cytometry.

Results: NEDA-3 status was achieved by 19 patients, who exhibited elevated baseline populations of regulatory CD49d+ T- and B-1a-cells and reduced post-treatment (month 6 or 12) populations of switched memory B-cells. Flow cytometry analysis of the intracytoplasmic cytokine production revealed increased ratios of CD19+IL-10+, CD19+IL-35+ and CD19+TGFβ+ cell subsets, which negatively correlated with EDSS and/or attack

numbers. Despite a moderate elevation of serum BAFF levels at month-6, ocrelizumab treatment significantly reduced BAFF-mediated CD19+ and CD19+CXCR5+ B cell chemotaxis.
Conclusion: Response to ocrelizumab is linked to regulatory and effector B-cell subset ratios. Specific B-cell subsets may serve as markers of treatment efficacy for ocrelizumab.
Disclosure: Nothing to disclose.

OPR-092 | Real-world efficacy and safety of off-label rituximab in a cohort of middle eastern multiple sclerosis patients

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Background and Aims: This study investigates the efficacy and safety of rituximab in Middle Eastern multiple sclerosis (MS) patients in a clinical practice setting.
Methods: This was a multicenter, observational, retrospective study including MS patients treated with off-label rituximab from 7 Middle Eastern countries by analyzing data from the MENACTRIMS registry. The primary efficacy outcome was the annualized relapse rate (ARR). Data on disability progression and magnetic resonance imaging (MRI) activity were collected from medical charts.
Results: A total of 774 MS patients were included in the study: 482 relapsing-remitting MS (RRMS) and 292 progressive-relapsing MS (PRMS). Treatment consisted of 500 mg or 1000 mg rituximab IV every 6–12 months. The cohort was predominantly female (72.1%), with a mean (SD) age of 39.6 (9.1) years and mean (SD) disease duration of 11.9 (6.3) years from symptom onset. The ARR decreased significantly from 1.65 at baseline to 0.18 during treatment in RRMS and from 2.03 to 0.02 in PRMS ($p<0.001$). The median Expanded Disability Status Scale (EDSS) remained unchanged in RRMS, while it significantly increased by 1.0 in PRMS ($p<0.001$). No MRI lesions were reported in 89.1% of RRMS compared to 8.1% of PRMS. NEDA-3 was achieved in 47.3 % of RRMS. A total of 491 adverse events (AEs) were observed, primarily mild infusion-related reactions (92.4%). Only four patients experienced serious AEs requiring hospitalization.

TABLE 1 Baseline clinical and demographic data of MS patients.

Characteristics	RRMS (n=482)	PRMS (n=292)	Total (n=774)
Age, y, mean (SD)	38.6 (9.3)	41.2 (8.4)	39.6 (9.1)
• Age at symptoms onset, y, mean (SD)	27.2 (7.9)	28.3 (8.5)	27.6 (8.2)
Sex, n (%)			
• Female	342 (71.0)	216 (74.0)	558 (72.1)
Disease duration, y, mean (SD)			
• Since Symptoms onset	11.4 (6.5)	12.9 (5.8)	11.9 (6.3)
• Since Diagnosis	9.8 (5.8)	11.5 (5.3)	10.4 (5.7)
Baseline EDSS score, median (IQR)	3.0 (1.5-4.0)	6.0 (6.0-6.0)	4.0 (3.0-6.0)
Number of relapses 1 year prior RTX, mean (SD)	1.65 (0.87)	2.03 (0.61)	1.80 (0.81)
Relapses prior RTX, n (%)			
• 0	43 (8.9)	2 (0.7)	45 (5.8)
• 1	170 (35.3)	45 (15.4)	215 (27.7)
• 2	186 (38.6)	187 (64.0)	373 (48.2)
• 3	81 (16.8)	58 (19.9)	139 (18.0)
• 4	2 (0.4)	-	2 (0.3)
Proportion of patients with prior DMT use n (%)			
• Treatment naive	92 (19.1)	7 (2.4)	99 (12.8)
• 1 previous DMT	270 (56.0)	223 (76.4)	493 (63.7)
• 2 previous DMTs	91 (18.9)	62 (21.2)	153 (19.8)
• 3 Previous DMTs	22 (4.6)	-	22 (2.8)
• 4 Previous DMTs	6 (1.2)	-	6 (0.8)
• 5 previous DMTs	1 (0.2)	-	1 (0.1)
Last DMT prior to RTX, n (%)	n= 390	n=285	n= 675
• IFN/GA	175 (44.9)	196 (68.8)	371 (55.0)
• Fingolimod	117 (30.0)	25 (8.8)	142 (21.0)
• Natalizumab	72 (18.4)	64 (22.4)	136 (20.2)
• Azathioprine / Mycophenolic acid	11 (2.8)	-	11 (1.61)
• DMF	7 (1.8)	-	7 (1.0)
• Plasmapheresis	3 (0.8)	-	3 (0.44)
• Alemtuzumab	2 (0.5)	-	2 (0.30)
• Teriflunomide	2 (0.5)	-	2 (0.30)
• Ocrelizumab	1 (0.3)	-	1 (0.15)
Reason for switching to RTX, n (%)	n= 390	n=285	n=675
• Inefficacy	249 (63.8)	185 (65.0)	434 (64.3)
• Positive JCV	74 (19.0)	50 (17.5)	124 (18.4)
• Approval restrictions	35 (9.0)	49 (17.2)	84 (12.44)
• Adverse events	17 (4.4)	-	17 (2.5)
• Personal preference	10 (2.6)	1 (0.3)	11 (1.62)
• Pregnancy planning	3 (0.7)	-	3 (0.44)
• Non-compliance	2 (0.5)	-	2 (0.3)
Maintenance Dose of RTX (mg), n (%)	n= 482	n= 292	n=774
• 500	13 (2.7)	1 (0.3)	14 (1.8)
• 1000	469 (97.3)	291 (99.7)	760 (98.2)
Dose frequency (months), n (%)			
• 6	476 (98.8)	292 (100.0)	768 (99.2)
• >6 and <12	4 (0.8)	-	4 (0.5)
• 12	2 (0.4)	-	2 (0.3)

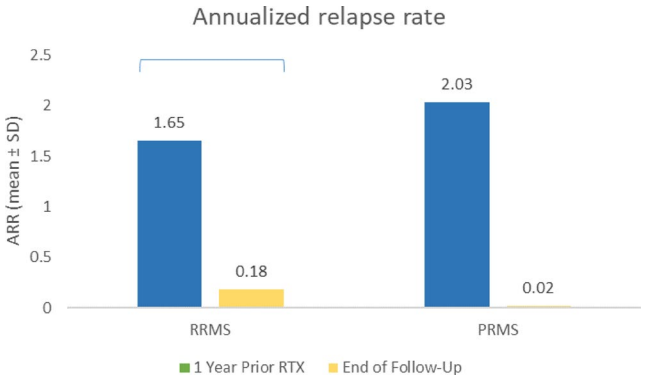

FIGURE 1 Annualized relapse rate pre- and post-rituximab.

TABLE 2 Safety profile of rituximab.

n (%)	RRMS	PRMS	Total
Any adverse event	218 (44.4)	273 (55.6)	491
Adverse events requiring hospitalization	3 (75.0)	1 (25.0)	4
Adverse event leading to discontinuation of drug	1 (100.0)	-	1
Adverse Events – Description			
• Infusion reactions	184 (84.4)	270 (98.8)	454 (92.4)
• Infections	23 (10.5)	1 (0.4)	24 (5.0)
• Depression	4 (1.8)	-	4 (0.8)
• Dermatological disorder	3 (1.3)	-	3 (0.6)
• Elevated liver enzymes	1 (0.5)	1 (0.4)	2 (0.4)
• Blood dyscrasia	1 (0.5)	-	1 (0.2)
• Thrombosis	-	1 (0.4)	1 (0.2)
• Malignancy	1 (0.5)	-	1 (0.2)
• Humoral Immunodeficiency	1 (0.5)	-	1 (0.2)
Infusion reactions, severity	n= 184	n=270	n=454
• Mild	183 (99.5)	270 (100.0)	453 (99.8)
• Moderate	1 (0.5)	-	1 (0.2)
• Severe	-	-	-
Infusion reactions, at which dose			
• 1st Dose	181 (98.4)	268 (99.2)	449 (98.9)
• 2nd Dose	3 (1.6)	1 (0.4)	4 (0.9)
• 3rd Dose		1 (0.4)	1 (0.2)

Conclusion: Off-label rituximab demonstrated significant real-world efficacy by reducing relapses in RRMS and PRMS patients, stabilizing disability and MRI findings in RRMS, and maintaining a well-tolerated safety profile.
Disclosure: Nothing to disclose.

OPR-093 | Retinal microglia: A marker of inflammation or neurodegeneration in patients with multiple sclerosis?

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Background and Aims: Retinal hyperreflective foci (HRF) are biomarkers of microglial activation in multiple sclerosis (MS). Studies show increased HRF in MS patients compared to controls, correlating with pro-inflammatory cytokines in cerebrospinal fluid (CSF), radiological activity, and cortical lesions. HRF levels appear unaffected by treatments like Natalizumab, suggesting microglial activation is independent of adaptive immunity. HRF have also been identified in the outer retina of relapsing-remitting MS (RRMS) patients. This study aimed to: (1) investigate the correlation between HRF and brain volumes as neurodegeneration markers, (2) explore relationships between HRF and CSF biomarkers of neuroinflammation (YKL-40), neurodegeneration (NfLs), and intrathecal inflammation (IgG index), and (3) assess HRF presence in the outer retina of RRMS patients and controls.
Methods: Sixty-six RRMS patients and 33 controls underwent neurological exams, lumbar puncture, optical coherence tomography (OCT), and MRI. OCT measured retinal thickness and volumes, with HRF independently counted by two observers. Brain MRI quantified gray (GM) and white matter (WM) volumes and inflammatory lesions. CSF levels of NfLs and YKL-40 were analyzed via ELISA. Generalized estimating equation models adjusted for age, sex, and optic neuritis history were used.

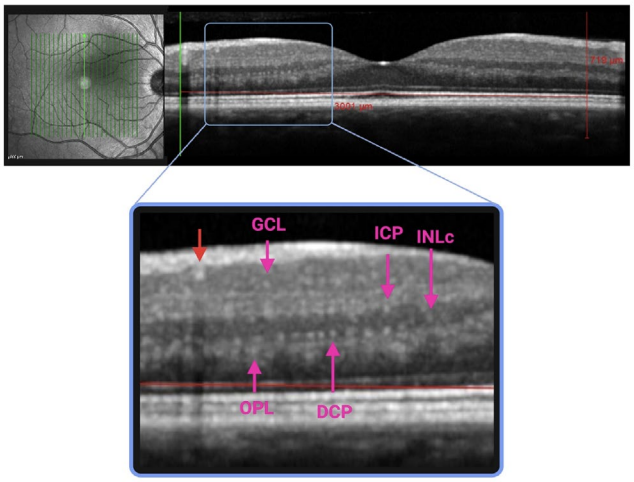

FIGURE 1 Linear scan centered on the macula and passing through the fovea. The magenta arrows indicate retinal HRF in the ganglion cell layer (GCL), near the intermediate capillary plexus (ICP), near the deep capillary plexus (DCP), and in the central portion of t.

Results: RRMS patients had significantly higher HRF across all retinal layers ($p<0.001$). GCPL HRF correlated positively with WM ($\beta=0.0022$; $p<0.001$), GM ($\beta=0.0017$; $p<0.001$), and YKL-40 ($\beta=0.11$; $p=0.018$), but not NfLs. OPL-ONL HRF correlated negatively with the IgG index ($\beta=-0.23$; $p=0.017$).

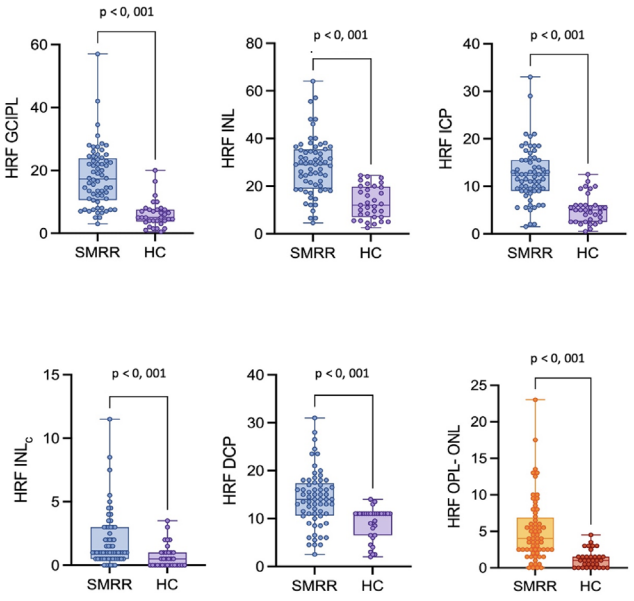

FIGURE 2 Hyper-reflective foci (HRF) in the various retinal layers in patients with RRMS and healthy controls (HC). The HRF count is significantly higher in RRMS patients compared to healthy controls across all retinal layers considered. Blue and purple indicate H.

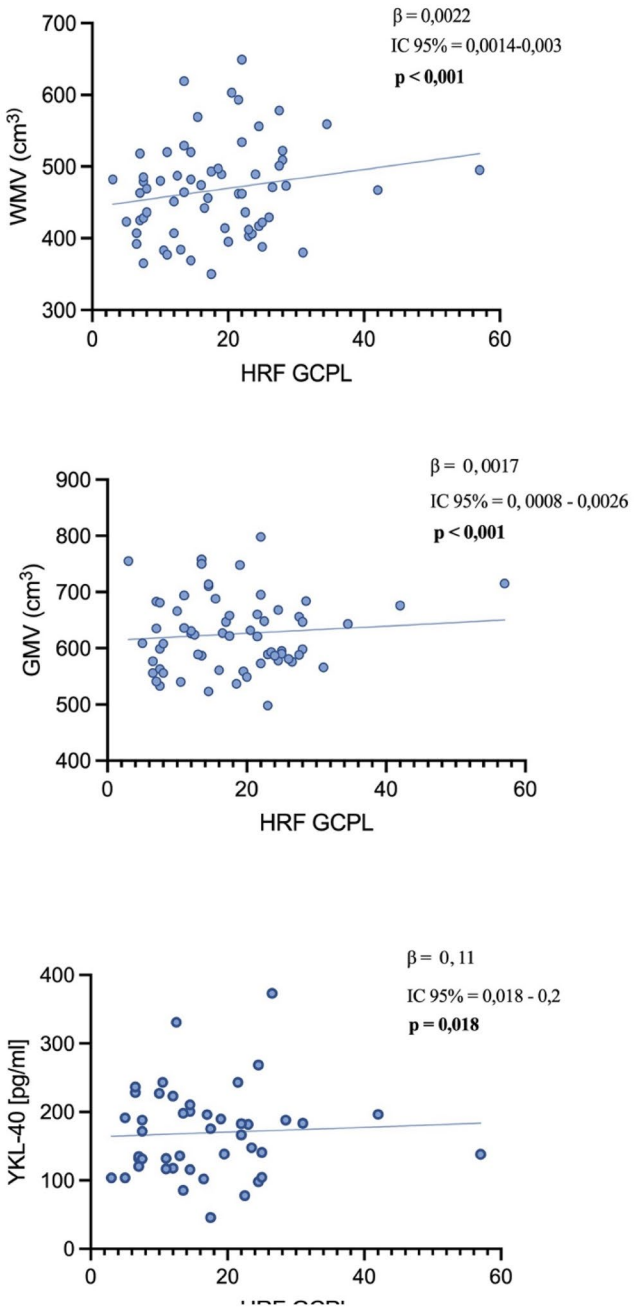

FIGURE 3 Association of GCPL HRF with white matter (WM) and gray matter (GM) volumes, and the amount of chitinase (YKL-40) in cerebrospinal fluid in pg/ml in patients with RRMS.

Conclusion: HRF, particularly in GCPL, may indicate neuroinflammation rather than neurodegeneration in RRMS.

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Movement Disorders 2

OPR-094 | Significant weight loss in Parkinson´s disease. A 5-year follow-up study

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Background and Aims: Significant weight loss (SWL) is considered a common complication of Parkinson's disease (PD). Our aim was (1) to compare the frequency of SWL in PD patients vs. controls, (2) to identify predictors of SWL in PD, and (3) to analyze the relationship between SWL and quality of life (QoL) and autonomy for activities of daily-living (ADL).

Methods: In this prospective 5-year follow-up population-based observational study, PD patients and controls from the COPPADIS cohort (Santos-García et al. 2016) with repetitive weight examinations over 5 years were included. A decrease > 10% in weight at 5 years (V5) compared to baseline (V0) was defined as SWL (Kristiansen et al. 2024). Regression models were applied to identify predictors of SWL.

Table 1. Factors associated with the presence of SWL at 5-year follow-up in PD patients from the COPPADIS cohort.

Variables at baseline (V0)	Adjusted R-squared	OR	CI 95%	p
	0.18			
Δ UPDRS-IV		1.182	1.069 – 1.306	**0.001**
Δ BDI-II		1.055	1.013 – 1.099	**0.009**
Age at baseline		1.053	1.010 – 1.097	**0.014**
Δ PD-CRS		0.984	0.967 – 1.001	0.069

Dependent variable: Significant weight loss at V5 (5-year follow-up visit). Δ = value at V5 (5-year follow-up visit) – value at V0 (baseline visit). Covariates were included in the multivariate analyzes using sequential logistic regression methods. Age and disease duration at baseline, and sex were included as covariates. Hosmer and Lemeshow test = 0.399.

Variables with significant values were adjusted to the value of the same variable at baseline (UPDRS-IV at V0, BDI-II at V0, and PD-CRS at V0). After this adjustment, only Δ PD-CRS showed a trend of significance ($p<0.05$ for Δ UPDRS-IV and Δ BDI-II).

BDI-II, Beck Depression Inventory-II; PD-CRS, Parkinson´s Disease Cognitive Rating Scale; UPDRS, Unified Parkinson's Disease Rating Scale.

Results: Mean weight decreased in PD patients (N = 407; 61.9 ± 8.9 years old, 57% males) from 75.5 ± 13.2 at V0 to 73.8 ± 13.5 at V5 ($p<0.0001$) but not in controls (N = 110; 61.9 ± 7.4 years old, 52.7% males; from 75.9 ± 13.8 at V0 to 76.3 ± 15.1 at V5 [$p=0.878$]). The frequency of SWL was twice as high in PD patients than in controls (18.2% [74/407] vs 9.1% [10/110]; $p=0.013$). SWL at V5 was associated with a worse QoL and autonomy for ADL ($p<0.0001$; Figure 1). To be older ($p=0.014$) and an impairment from V0 to V5 in motor complications (UPDRS-IV) ($p=0.001$) and mood (BDI-II) ($p=0.009$) were associated with SWL (Table 1).

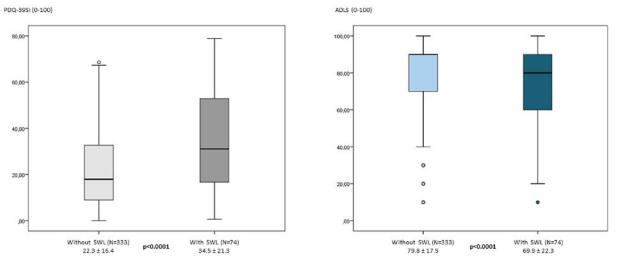

Figure 1. QoL (PDQ-39SI) and autonomy for ADL (ADLS) in PD patients at 5-year follow-up according to the presence or not of having significant weight loss (SWL). Data are presented as box plots, with the box representing the median and the two middle quartiles (25-75%). Mild outliers (O) are data points that are more extreme than Q1 - 1.5. PDQ-39SI, 39-item Parkinson's disease Questionnaire Summary Index; ADLS, Schwab and England Activities of Daily Living Scale.

Conclusion: SWL is frequent in PD and is associated to a worse QoL and decreased autonomy for ADL.
Disclosure: The authors report no conflict of interest.

OPR-095 | Multidomain cognitive tele-rehabilitation for Parkinson's disease with mild-to-moderate cognitive decline

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Background and Aims: Cognitive decline is a non-motor symptom of Parkinson's disease (PD) that significantly impairs quality of life. Cognitive stimulation (CS) has demonstrated efficacy in enhancing cognitive function in PD-related cognitive impairment. However, logistical challenges, like mobility limitations, frequently restrict access to regular in-person CS programs. Telerehabilitation offers a promising, home-based alternative that uses technology to deliver personalized interventions. This study aims to evaluate the efficacy of remote CS in individuals with mild-to-moderate PD-related cognitive impairment.
Methods: Forty-five PD patients were randomized into a tele-rehabilitation group (TRG, $n=25$) or a control group (CG, $n=20$). The TRG underwent daily remote CS sessions, while the CG performed traditional paper-and-pencil-based cognitive exercises. Clinical and neuropsychological assessments were conducted at baseline, immediately post-intervention, and six months post-intervention.
Results: In the TRG, participants significantly improved in executive, attentional, and visuospatial abilities, demonstrating the effectiveness of tele-rehabilitation in addressing key cognitive deficits in PD. The CG showed similar benefits associated with a significant reduction in depressive symptoms, highlighting the added benefits of social interactions in traditional approaches. The cognitive decline observed at the six-month follow-up suggests the need for sustained engagement and long-term interventions to preserve these benefits over time.
Conclusion: Telerehabilitation effectively enhances cognitive domains such as attention, executive function, and visuospatial skills, presenting a feasible and accessible solution for individuals with PD and mild-to-moderate cognitive decline. Future approaches may benefit from hybrid models that combine telerehabilitation's accessibility with the psychosocial benefits of in-person interventions to maximize cognitive and emotional outcomes for PD patients.
Disclosure: This work was supported by the Ministry of Health, project title: "Development and implementation of common strategy for the management of community- dwelling older subjects with multimorbidity and polypharmacy: integration with a multicomponent intervention platform by using domotic, robotic and telecare systems. MULTIPLAT_AGE"; project code: NET-2016-02361805.

OPR-096 | LRRK2-related PD: Hints at increased cancer risk

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Background and Aims: Pathogenic variants in the LRRK2 gene are the most common monogenic cause of Parkinson's Disease (PD). Previous in-vitro and mouse model studies suggested that pathological variants in LRRK2 gene may contribute to tumorigenesis. The aim of this study is to examine whether

PD patients carrying pathogenic variants in LRRK2 gene (mutLRRK2-PD) have a higher prevalence of malignancies compared to PD non mutated in LRRK2 gene (wtLRRK2-PD).
Methods: We included only PD patients genetically tested for PD-associated genes from the Foundation IRCCS Ca' Granda Ospedale Maggiore Policlinico of Milan and from the AUSL-IRCCS of Reggio Emilia. We retrospectively collected data on personal history of malignancies in mutLRRK2-PD and wtLRRK2-PD patients to compare tumor prevalence between these groups.
Results: 519 PD patients were included: 477 wtLRRK2-PD (male: 300) and 42 mutLRRK2-PD (male: 21). mutLRRK2-PD patients had a significantly greater prevalence of oncological disease compared to wtLRRK2-PD (33% vs. 19%, $p=0.03$). All mutLRRK2-PD patients with cancers carried the G2019S variant, except for five. The most prevalent malignancy in the mutLRRK2-PD cohort was cutaneous melanomas.
Conclusion: This study suggests that mutLRRK2-PD patients may be more susceptible to specific malignancies compared to PD patients without LRRK2 mutations. If confirmed, the management of these patients could be enhanced by providing not only follow-up care for PD, but also early malignancy screening.
Disclosure: The authors have no conflicts of interest to declare that are relevant to the content of this abstract.

OPR-097 | Spatiotemporal Deep Neural Networks for differentiation of iRBD, Parkinson's Disease, and controls using rs-fMRI

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Background and Aims: This study aimed to develop and evaluate a spatiotemporal deep-neural-network (stDNN) leveraging resting-state fMRI (rs-fMRI) data to identify brain biomarkers associated with idiopathic REM sleep behavior disorder (iRBD) and Parkinson's disease (PD) and to differentiate these conditions from controls.
Methods: Data were collected from three cohorts: the IRCCS San Raffaele Scientific Institute (HSR), the Parkinson's Progression Markers Initiative (PPMI), and the Movement Disorders Unit at the University of Campania (MDU). The final sample included 771 subjects, comprising 423 patients with PD, 144 with iRBD, and 204 controls. stDNN model was applied to mean time series extracted for each subject from rs-fMRI data. By integrating spatio-temporal features, the network classified subjects based on distinct neural patterns. Model generalizability was assessed using a train-fold-validation split combined with k-fold cross-validation. Explainable artificial intelligence (XAI) methods were applied.
Results: stDNN achieved balanced accuracy rates of 74.9% in distinguishing controls from PD and up to 82.4% in moderate-to-severe PD cases. It also demonstrated over 80% accuracy in differentiating controls from iRBD. However, performance declined when differentiating iRBD from PD, likely due to overlapping functional characteristics. XAI analysis highlighted the involvement of the temporal pole, calcarine sulcus and precuneus in distinguishing controls from PD. Considering iRBD, the supplementary motor area (SMA), left superior temporal pole, and left middle temporal areas were identified as key regions.
Conclusion: This study demonstrates the potential of stDNN to differentiate between iRBD, PD, and controls using fMRI data.
Disclosure: Funding. Italian Ministry of Health [grant RF-2018-12366746]. Disclosures. SB, ES, SM, RB grant support from Italian Ministry of Health. AGa, LZ, MM, AGr, AC, DMR, TA, MS, FM nothing to disclose. LFS received speaker honoraria from Biprojet, Idorsia, Italfarmaco, and Takeda, and receives or has received research support from the Italian Ministry of Health and the Italian Ministry of University and Research. MF received compensation for consulting services or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM. FA received speaker honoraria from Biogen Idec, Roche, Eli Lilly and GE Healthcare; and grants from Italian Ministry of Health, Italian Ministry of University and Research, AriSLA, European Research Council, EU Joint Programme—Neurodegenerative Disease Research, and Foundation Research on Alzheimer Disease (France).

OPR-098 | Inventory of non-ataxia signs in the European friedreich's ataxia consortium for translational studies study

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Background and Aims: Friedreich ataxia is a rare neurodegenerative multisystem disorder. While ataxia is a hallmark, non-ataxia symptoms and signs, including muscle weakness, spasticity and dysphagia are equally disabling. The Inventory of Non-Ataxia Signs (INAS) is a 16-item symptom list that can be transformed to a count. We sought to validate the INAS in this patient population.

Methods: Participants were drawn from the European Friedreich's Ataxia Consortium for Translational Studies (EFACTS). The INAS-count (presence/absence, 0–16 scale) and newly-derived INAS-sum (severity-weighted, 0–84 scale) were evaluated using linear mixed models and standardised response means (SRMs).

Results: 1129 participants (mean age 32.3) were assessed for up to 12 years. At baseline, the mean INAS-count was 4.3 (±2.1), and INAS-sum was 15.1 (±9.9). Both showed strong correlations with existing outcome measures (SARA and ADL). Longitudinally, the INAS-count increased by 0.15 points/year (95% 0.13, 0.16; $p<0.001$) and INAS-sum by 0.70 points/year (95% CIs 0.67, 0.76; $p<0.001$). The INAS-sum demonstrated greater responsiveness, with SRMs of 0.26, 0.38, 0.53 and 0.80 at 1, 2, 3, and 5 years, respectively, compared to 0.21, 0.34, 0.46 and 0.63 for the INAS-count. In non-ambulatory patients, responsiveness of the INAS-sum was comparable at 3 years (SRM 0.47) and higher at 5 years (SRM 0.82).

TABLE 1 Main demographic and clinical characteristics of participants at baseline.

Characteristic	Overall N = 1,129[1]	Non-ambulatory N = 487[1]	Ambulatory N = 642[1]
Age in years	30 (21, 42)	33 (25, 44)	26 (19, 41)
Adult	962 (85%)	469 (96%)	493 (77%)
Sex (female)	571 (51%)	249 (51%)	322 (50%)
Age at symptom onset	13 (8, 19)	11 (8, 15)	15 (10, 24)
GAA repeats shorter allele	600 (367, 767)	700 (567, 834)	500 (250, 683)
SARA total score	19 (10, 29)	30 (26, 33)	11 (9, 15)
Cardiac hypertrophy	391 (41%)	205 (49%)	186 (34%)
Disease duration	15 (9, 23)	22 (16, 30)	10 (6, 14)
INAS count	4 (3, 6)	6 (5, 7)	3 (2, 5)
INAS sum score	12 (8, 20)	22 (17, 28)	9 (6, 11)
Spasticity	217 (24%)	91 (31%)	126 (20%)
Muscle weakness	587 (54%)	427 (91%)	160 (26%)
Muscle atrophy	470 (43%)	346 (73%)	124 (20%)
Dystonia	50 (4.5%)	36 (7.6%)	14 (2.2%)
Impaired vibration sensation	924 (87%)	436 (96%)	488 (80%)
Urinary dysfunction	406 (37%)	263 (55%)	143 (23%)
Dysphagia	628 (57%)	390 (82%)	238 (38%)
Areflexia	970 (88%)	462 (97%)	508 (81%)
Hyperreflexia	78 (7.1%)	15 (3.2%)	63 (10%)
Extensor plantar reflex	699 (64%)	358 (76%)	341 (55%)
Oculomotor dysfunction	300 (29%)	201 (46%)	99 (17%)
Cognitive impairment	62 (5.6%)	45 (9.5%)	17 (2.7%)
Muscle cramps	476 (43%)	266 (56%)	210 (34%)

[1]Median (Q1, Q3); n (%)

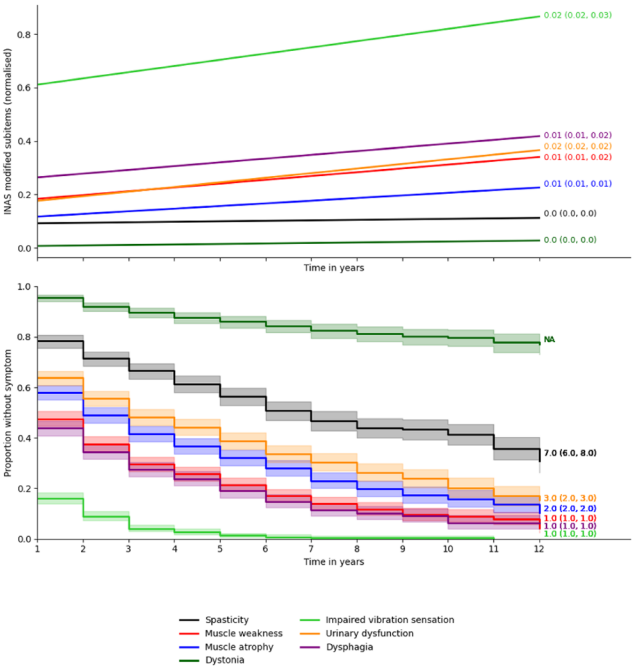

FIGURE 1 Longitudinal evolution of INAS subitems over time.

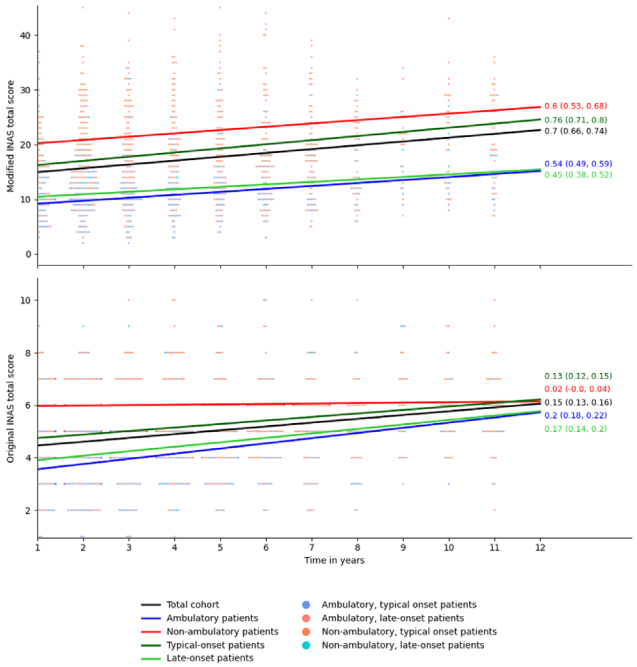

FIGURE 2 Longitudinal evolution of the INAS summed and the INAS count total score.

Conclusion: The INAS-sum showed good responsiveness in the medium-term but not in the short-term follow-up. It may supplement existing outcome measures, contributing to a more holistic assessment of this multisystem disease, especially in non-ambulatory patients, where ataxia-focussed measures may be constrained by ceiling effects.

Disclosure: SL received speaker honoraria from Biogen unrelated to this study. MGE received research support from the German Ministry of Education and Research (BMBF) within the European Joint Program for Rare Diseases (EJP-RD) 2021 Transnational Call for Rare Disease Research Projects (funding number 01GM2110), from the National Ataxia Foundation (NAF), Ataxia UK, and Biogen Germany, and received consulting fees from Healthcare Manufaktur, Germany, and Biogen Germany - all unrelated to this study. W. Nachbauer has received speaker and advisory honoraria from Biogen and Reata Pharmaceuticals. S. Boesch reports consultancies from VICO Therapeutics, Reata pharmaceuticals and Biogen, Honoria from Ipsen, Merz, Abbvie and Reata and advisory boards for Biogen and Reata. L. Schöls received consultancies from VICO Therapeutics, Vigil Neuroscience and Novartis unrelated to this work. The remaining authors report no disclosures relevant to the abstract.

OPR-099 | Decoding the immune-brain axis: Advancing neurovascular models for neuroinflammation and T cell trafficking research

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Background and Aims: The immune system and the brain are deeply interconnected, shaping both normal function and disease. This complex crosstalk is key to neuroinflammatory disorders like Multiple Sclerosis (MS), yet studying immune interactions at the neurovascular interface remains a challenge due to the scarcity of infiltrating cells.
Methods: To bridge this gap, we developed a microfluidic Neurovascular-Unit (NVU) model integrating primary human or animal cells, enabling real-time investigation of immune cell transmigration.
Results: When exposed to TNFα, NVU prototypes exhibited reduced TEER, increased permeability, and higher immune infiltration—hallmarks of a neuroinflammatory response. To push the boundaries further, we engineered a personalized human blood-brain barrier (BBB) model using primary endothelial cells and autologous immune cells from MS patients, allowing patient-specific insights into immune interactions. In vivo, we leveraged EGFP+ T cell adoptive transfer to track immune cells infiltrating the brain. Transmigrating leukocytes were precisely quantified via real-time PCR, detecting EGFP+ cells in tissue. For precise immune profiling, we developed an isolation protocol followed by multi-color flow cytometry, enabling absolute immune cell counting and characterization of subsets crossing brain borders compared to periphery.
Conclusion: By integrating these approaches, we provide insight into the immune-brain axis, paving the way for breakthroughs in neuroimmunology and novel therapeutic strategies for brain disorders.
Disclosure: Nothing to disclose.

OPR-100 | Safety-driven ocrelizumab discontinuation vs. continuation: Comparative insights from MSBase

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Background and Aims: Safety concerns leading to treatment discontinuation pose significant challenges in Multiple Sclerosis (MS) management.
Methods: A multi-center, longitudinal cohort study was conducted using data from the MSBase registry. Patients aged >18 years, diagnosed with relapsing-remitting MS (RRMS) who

had been treated with OCR, for a minimum of one year who recorded one safety event during treatment. Patients were categorized into two groups: those who discontinued Ocrelizumab (OCR) due to safety concerns (Switchers) and those who continued treatment despite adverse events (Continuers). The outcomes of the study were to compare the two groups in terms of total count of relapses, time to first relapse, confirmed-disability-worsening (CDW) at 24&48 weeks, and Progression Independent of Relapse Activity (PIRA). Propensity-score-matching with inverse-probability-weighting (PS-IPTW) was used to balance baseline characteristics between groups.

Results: From an initial cohort of 10,774 patients, 310 Switchers and 1,315 Continuers were identified. After propensity score matching, 66 pairs were analyzed. The mean time on OCR for Switchers was 2.7 ±1.2 years, whilst for the Continuers was 4.4±1.2 years. Infections (43.9%) and cancers (9.1%) were the main safety events leading to discontinuation. Among matched pairs, Switchers had a higher trend in relapse count than Continuers (PS-IPTW RR 2.62, 95%CI 0.96–7.15, $p = 0.060$). Time to first-relapse showed no differences. CDW at 24 weeks trended higher for Switchers (HR 2.08, 95% CI 0.96–4.51, $p = 0.064$), with no differences at 48 weeks. PIRA-risk also trended in Switchers (HR 2.45, 95% CI 0.95–6.29, $p = 0.063$).

Conclusion: Switching from OCR due to safety concerns may increase relapse risk, mitigated by transitioning to high-efficacy DMTs.

Disclosure: Tim Spelman received compensation from servicing on steering committees and advisory boards from Biogen Marzena Fabis-Pedrini received travel compensation from Merck Allan G Kermode Served on Scientific Advisory Boards for Bayer, BioCSL, Biogen-Idec, Clene Nanomedicine, Esai, Innate Immunotherapeutics, Lgpharma, Merck, Mitsubishi Tanabe Pharma, NeuroScientific Biopharmaceuticals, Novartis, Progenis, Roche, Sanofi-Aventis, Sanofi-Genzyme, Teva, and View Health William M Carroll "Recipient of travel assistance and honoraria for participation in industry sponsored meetings from and provided advice to, Bayer Schering Pharma, Biogen-Idec, Novartis, Roche, Genzyme, Sanofi-Aventis, CSL, Teva, Merck and Cellgene" Anneke van der Walt served on advisory boards and receives unrestricted research grants from Novartis, Biogen, Merck and Roche She has received speaker's honoraria and travel support from Novartis, Roche, and Merck. She receives grant support from the National Health and Medical Research Council of Australia and MS Research Australia. Helmut Butzkueven received institutional (Monash University) funding from Biogen, Roche, Merck, Alexion and Novartis; has carried out contracted research for Novartis, Merck, Roche and Biogen; has taken part in speakers' bureaus for Biogen, Novartis, Roche and Merck; has received personal compensation from Oxford Health Policy Forum for the Brain Health Steering Committee.

OPR-101 | Contribution of germline mutations to risk of neuromyelitis optica spectrum disorder

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Background and Aims: Neuromyelitis optica spectrum disorder (NMOSD) is a rare autoimmune disease characterized by optic neuritis and transverse myelitis. Due to its low prevalence, the genetic backgrounds of NMOSD have not been elucidated in detail. We performed a large-scale genome-wide association study (GWAS) in Japanese to find risk variants of NMOSD.

Methods: We conducted a genome-wide association study (GWAS) meta-analysis of NMOSD in Japanese (240 patients and 50,578 controls). We applied human leukocyte antigen (HLA) imputation to fine-map the risk HLA variants. To elucidate the cell-type-specific expression profile of the putative target gene, we performed single-cell RNA sequencing (scRNA-seq) in peripheral blood cells from 25 NMOSD patients and 101 controls.

Results: Our GWAS meta-analysis identified NMOSD risks in the HLA region and CCR6 (rs12193698; $p = 1.8 \times 10^{-8}$, odds ratio [OR] = 1.73), a novel associated gene. HLA fine-mapping showed the strongest association at HLA-DRβ1 amino acid position 11 with NMOSD. In the scRNA-seq analysis, the risk variant at CCR6 showed disease-specific expression quantitative trait loci effects in CD4 memory T cells, especially in T helper 17 (Th17) cells.

Conclusion: This is an initial report of the GWAS-driven NMOSD risk outside the MHC region. We could interpret the GWAS result more efficiently by using the cell-type-specific eQTL analysis and demonstrate the genetic regulation underlying the pathogenic role of Th17 cells in NMOSD.

Disclosure: Nothing to disclose.

OPR-102 | Tumor-specific CSF B cell response in melanoma patients with leptomeningeal spread

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Background and Aims: Meningeosis carcinomatosa is a diffuse dissemination of tumor cells into the cerebrospinal fluid (CSF) and occurs in approximately 5% of patients with malignant melanoma. Previous studies on CSF immune cell subsets have found an elevated CSF B-cell fraction in a subset of these patients. The aim of this study is to evaluate whether these CSF B cells resemble a tumor-specific immune response.
Methods: Single cell analysis of CSF cells was performed in melanoma patients with leptomeningeal spread including whole transcriptome, B cell receptor (BCR) and T cell receptor (TCR) sequencing. After BCR repertoire analysis, recombinant antibodies were generated and tested for antigen specificity using antigen microarrays, flow-cytometry, ELISA, as well as bioinformatic analyses.
Results: We were able to generate representative BCR repertoires in 8 of 9 patients and produced 36 recombinant antibodies. We first tested these antibodies for binding to a melanoma tumor cell line. 8 antibodies were further selected and potential antigen targets were narrowed down by systematic microarrays. Among other potential antigens, specific binding of three antibodies to the individual proteins AKR1A1, KIFC3 and DDX53, a known cancer testis antigen, was detected. Further antibody testing and detailed transcriptome analysis are ongoing.
Conclusion: This study provides strong evidence for a targeted intrathecal B cell response against melanoma cells by clonally expanded CSF B cells. Antibody binding against the targets AKR1A1, KIFC3, and DDX53 indicate that the CSF B cell-derived antibodies may indeed be tumor-specific. These antibodies and their corresponding tumor antigens may be exploited for future tumor treatments.

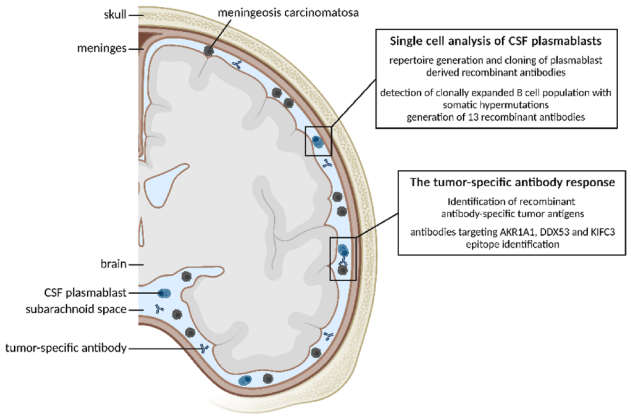

FIGURE 1 Graphical abstract

Disclosure: S.S. has nothing to disclose. N.V. has nothing to disclose. M.K. has served on advisory boards and received speaker fees / travel grants from Merck, Sanofi-Genzyme, Novartis, Biogen, Janssen, Alexion, Celgene / Bristol-Myers Squibb and.

OPR-103 | Differential effect of eculizumab and efgartigimod on subscores of the MG-ADL and QMG in generalized myasthenia gravis

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Background and Aims: Eculizumab (ECU) and Efgartigimod (EFGA) are both approved for the treatment of generalized Myasthenia Gravis (gMG).
Methods: We included 38 patients (22 ECU and 16 EFGA), and retrospectively collected data on the MG activities of daily living (MG-ADL) and quantitative MG scale (QMG). We limited the observation of the MG-ADL to weekly scores for the first 8 weeks of treatment, and of the QMG at baseline and after 5, 12, 24, 36, and 48 weeks. We analyzed the difference between treatments at the subscore level of both scales.
Results: We found a higher response to ECU at the MG-ADL at week 7 (−6.3 vs 3.8; $p=0.038$), and at the QMG at week 24 (−6.0 vs −0.9; $p=0.032$), 36 (−7.7 vs −1.7; $p=0.020$), and 48 (−8.5 vs −2.6; $p=0.018$). We found no differences for the ocular and limb subscores of both the MG-ADL and QMG. Response for the bulbar subscores at the MG-ADL ($p=0.037$) and QMG ($p=0.037$), was higher with ECU treated patients. For the MG-ADL, this occurred at week 6 (−3 to 4 vs −1.2, $p=0.009$), and 7 (−3.1 vs −1.2, $p=0.020$), and for the QMG at week 12 (−2.1 vs −.8, $p=0.025$) and 36 (−3.0 vs −1.1, $p=0.018$). Mean QMG score for the forced vital capacity (FVC) decreased more with ECU throughout the entire observation period ($p=0.036$).
Conclusion: Our study shows a deeper effect of Eculizumab on bulbar scores compared to Efgartigimod. This could be considered when treating patients with high bulbar scores and ventilatory insufficiency.
Disclosure: Francesco Saccà received public speaking honoraria from Alexion, argenx, Biogen, Genpharm, Medpharma Madison Neopharm Israel, Pharma, Sanofi, Zai Lab; he also received compensation for Advisory boards or consultation fees from Alexion, Amgen, argenx, AstraZeneca, Alexis, Biogen, Dianthus, Johnson&Johnson, Lexeo, Novartis, Reata, Roche, Sandoz, Sanofi, Takeda, UCB, Zai Lab; he is PI in clinical trials for Alexion, argenx, Dianthus, Immunovant, Lediant, Novartis, Prilenia, Remgen, Sanofi.

OPR-104 | Patterns and predictors of therapeutic response to efgartigimod in AChR(+) generalized myasthenia gravis subtypes

L. Jin[1]; Z. Zou[2]; Q. Wang[3]; W. Zeng[4]; Q. Jiang[5]; J. Chen[6]; J. Shi[7]; Y. Yu[8]; D. Hong[8]; Q. Zeng[9]; S. Tan[9]; Y. Yue[10]; Z. Zhang[11]; Y. Zhang[11]; X. Guo[12]; L. Du[13]; Z. Zhao[14]; S. Huang[14]; Y. Chen[15]; Z. Wu[16]; C. Yan[1]; J. Xi[1]; J. Song[1]; S. Luo[1]; C. Zhao[1]
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Background and Aims: Efgartigimod is an approved biologic for generalised myasthenia gravis (gMG), which is an autoimmune disease and can potentially be life-threatening. However, the therapeutic response to efgartigimod among the acetylcholine receptor gMG (AChR-gMG) subtypes remains inconclusive.
Methods: This prospective, observational study included AChR-gMG patients treated with efgartigimod at 15 centres in China with a follow-up for at least 20 weeks. The primary outcome was the proportion of MSE responders, denoted by a MG-ADL score of 0 or 1 within 4 weeks and maintained for ≥4 weeks. AChR-MG subtypes were classified into EOMG, LOMG, and TAMG. The predictive factors for MSE responders were identified by univariate and multivariate logistic regression analysis.

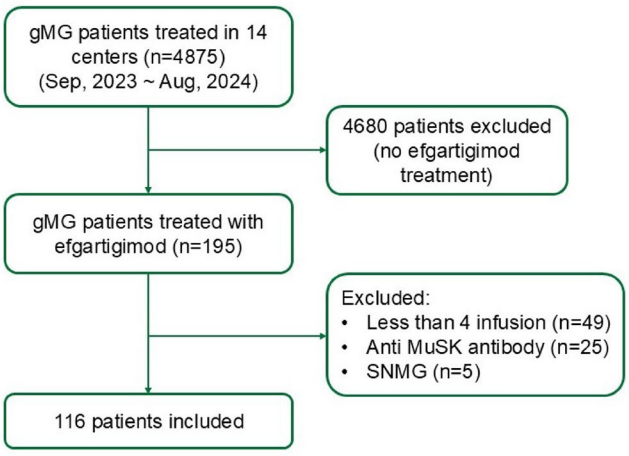

FIGURE 1 Study flowchart.

Results: 116 patients were included with a median follow-up duration of 238 days (172.5–306.3). There were 50 (43.1%) patients with EOMG, 28 (24.1%) with LOMG, and 38 (32.8%) with TAMG. After efgartigimod initiation, 35 (30.2%) patients were MSE responders, and the proportion of MSE responders was highest in the LOMG group (42.9%). Response patterns to efgartigimod among the AChR-MG subtypes differed as measured by the proportion of improved patients and MSE. LOMG presented sustained symptom control, while EOMG and TAMG showed more fluctuations. Eight TAMG patients (21.1%) switched to another biologic ($p = 0.005$). Baseline MG-ADL was an independent predictor for therapeutic response to efgartigimod ($p < 0.001$).

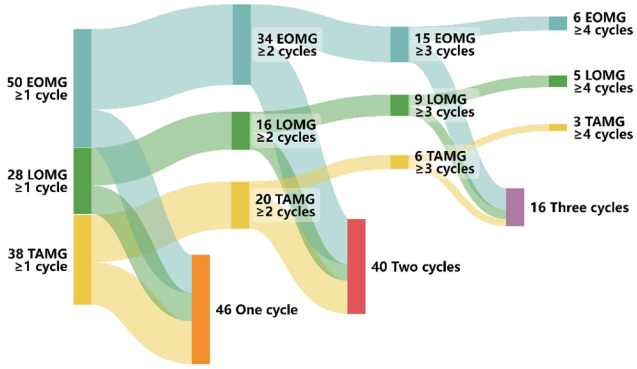

FIGURE 2 Treatment cycles in different gMG subtypes. EOMG: early-onset MG; LOMG: late-onset MG; TAMG: thymoma-associated MG.

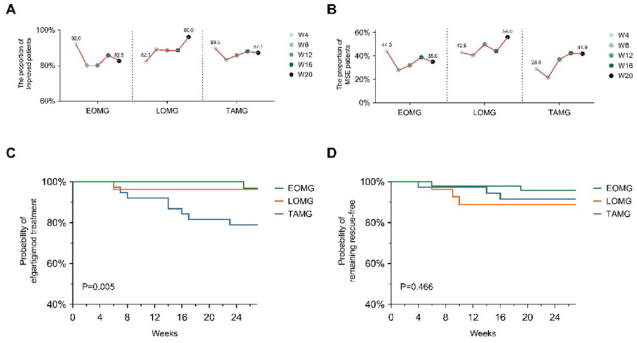

FIGURE 3 The patterns of therapeutic response among AChR-MG subtypes. The trajectories of improvement status and MSE varied among the three subtypes (A-B). Time to treatment switch analysis presented significant differences ($p = 0.005$) (C).

Conclusion: Our findings revealed patterns of treatment responses among AChR-gMG subtypes, with LOMG patients potentially presenting a more sustained response. These findings likely provide preliminary data for precision therapy in MG in the era of biologics.

Disclosure: This study is supported by financial grants from the National Key research and development plan (2022YFC3501305, 2022YFC3501303), the National Natural Science Foundation of China (82071410, 82471426), and Shanghai Hospital Development Center Program (SHDC2023CRD007).

L. Töpert[1]; R. Zeng[1]; O. Al-Bourini[2]; L. Lettermann[3]; U. Olgemöller[4]; S. Hofer[1]; M. Boentert[5]; T. Friede[6]; M. Nietert[7]; D. Voit[8]; J. Frahm[8]; M. Uecker[9]; A. Seif Amir Hosseini[2]; J. Schmidt[10]

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Background and Aims: Respiratory dysfunction significantly impacts morbidity and mortality in patients with neuromuscular diseases. In late-onset Pompe disease (LOPD), early stages of respiratory muscle weakness can remain unnoticed due to compensatory breathing capacity. This study aims to evaluate real-time MRI (RT-MRI) for the characterization of breathing patterns in LOPD patients compared to standard diagnostic modalities.

Methods: Eleven LOPD patients and matched healthy controls underwent RT-MRI with a temporal resolution of 20 frames per second. Breathing patterns during natural breathing and dynamic respiratory maneuvers were analyzed manually and through U-Net-based segmentation (Figure 1). RT-MRI findings were compared with pulmonary function tests and diaphragm ultrasound. Fast T1 mapping was conducted for non-invasive assessment of tissue composition of the diaphragmatic crurae. This enabled the comparison of morphological and functional diaphragm characteristics.

Results: RT-MRI precisely quantified reduced diaphragmatic motion in LOPD patients and uniquely revealed compensatory thoracic movement during breathing maneuvers (Figures 1 and 2). In 7 out of 11 patients, the sniff maneuver unmasked paradoxical diaphragmatic movement. U-Net-based segmentation facilitated an in-depth analysis of respiratory mechanics, including diaphragmatic/thoracic synchronicity and velocity during sniff maneuvers. T1 mapping demonstrated fatty infiltration in the diaphragm, which correlated significantly with ultrasound findings of the diaphragm, and with functional respiratory parameters from RT-MRI and pulmonary function tests.

Conclusion: RT-MRI provides a detailed and quantitative assessment of respiratory muscle function in LOPD. T1 mapping offers a non-invasive approach to evaluate diaphragmatic morphology and its functional implications. These imaging techniques hold promise for enhancing early detection and monitoring of respiratory involvement in neuromuscular diseases.

Disclosure: Jens Frahm, Martin Uecker and Dirk Voit are co-inventors and patent holders of the software describing the real-time MRI technique used here. The remaining authors declare no conflict of interest. RZ and JS are members of the European Reference network for rare Neuromuscular disorders (ERN EURO-NMD). This work incorporates the results of the

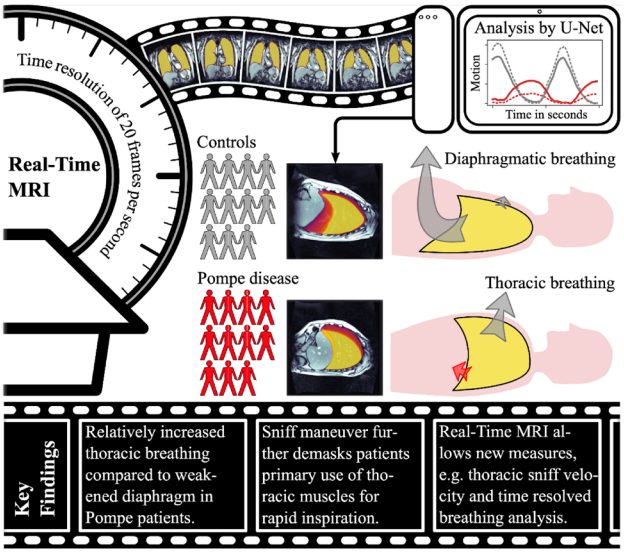

FIGURE 1 Graphical Abstract of the study with exemplary heath maps of the lungs during sniff maneuver.

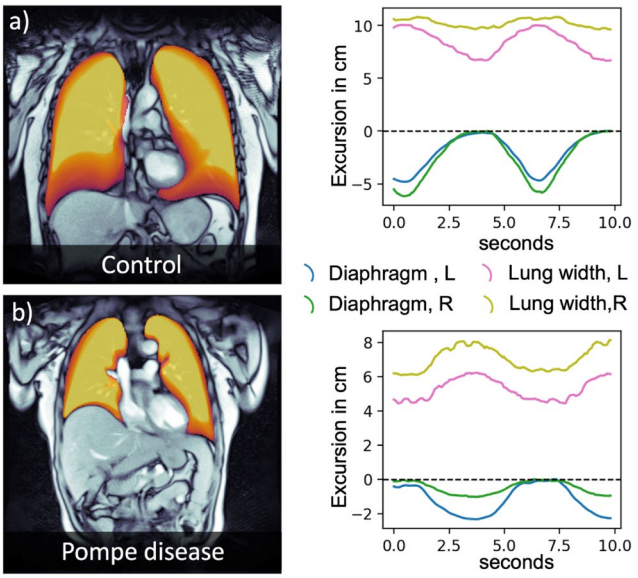

FIGURE 2 RT-MRI assessment of diaphragmatic and chest wall motion in patients with late-onset Pompe disease and controls. Exemplary heath maps (left) and time series (right) show the dynamics of the diaphragmatic motion and chest wall motion (lung width).

dissertation submitted by LT at the Faculty of Medicine of the University of Goettingen. Funding by German patient support group (DGM) (application number Sc21/2) and German Research Foundation (DFG) within the Clinician Scientist Program "Cell Dynamics in Disease and Therapy" at the University Medical Center Goettingen (project number 413501650).

OPR-106 | Motor Unit Number Index (MUNIX) as a biomarker of disease progression in myasthenia gravis

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Background and Aims: Myasthenia gravis (MG) is an autoimmune disorder causing impaired neuromuscular transmission. Currently, no neurophysiological biomarker of disease progression is available. This pilot study evaluates the role of the motor unit number index (MUNIX) as biomarker of motor unit function and disease monitoring in MG, by comparing MUNIX values between MG patients and healthy controls (HCs), alongside their correlations with clinical and electrophysiological measures.

Methods: Compound motor action potential (CMAP), MUNIX, and motor unit size index (MUSIX) were assessed in the abductor pollicis brevis (APB) and orbicularis oculi (OO) muscles in the symptomatic or non-dominant side. Clinical severity was evaluated using MGCS, MG-ADL, and MGFA classification. Statistical analyses included ANOVA, Spearman correlations, and multivariate analysis ($p<0.05$).

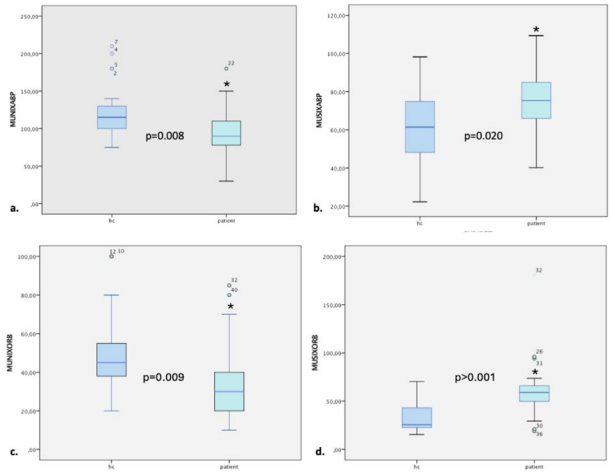
Results: 42 MG patients (63.1 ± 12.7 years) and 21 age-matched HCs (59.7 ± 8.7 years) were enrolled. MUNIX values were lower in MG patients than HCs for APB ($p=0.022$) and OO ($p=0.028$), while MUSIX was higher (APB: $p=0.047$; OO: $p=0.002$). Age negatively correlated with CMAP APB ($p=0.010$) and MUNIX APB ($p=0.033$) but positively with MUSIX ($p=0.045$ for APB, $p=0.020$ for OO). Disease duration negatively correlated with CMAP, MUNIX, and MUSIX, while MuSK serotype showed lower CMAP ORB values ($p=0.001$). CMAP ORB ($p=0.001$) and MUSIX ORB ($p=0.002$) predicted disease duration.

TABLE 1 Electrophysiological comparison between MG and HCs.

	MG	HCs	p.
CMAP			
APB	7.9 ± 3	7.7 ± 2.7	0.07
OO	1.5 ± 0.6	1.8 ± 0.6	**0.05**
MUNIX			
ABP	97.5 ± 37.7	125.2 ± 37	**0.008**
OO	35.2 ± 20	50.7 ± 23.6	**0.009**
MUSIX			
APB	73.5 ± 19	61 ± 20	**0.020**
OO	62 ± 33	33.5 ± 15.8	**<0.001**

p.<0.05

Abbreviations: MG, Myasthenia gravis; HCs, Healthy controls; CMAP, Compound muscle action potential; ABP, Abductor pollicis brevis; OO, Orbicularis Oculi; MUNIX, Motor Unit Number Index; MUSIX, Motor Unit Size Index.



a. MUNIX from ABP. **b.** MUSIX from ABP. **c.** MUNIX from OO. **d.** MUSIX from OO. Abbreviations: MUNIX, Motor Unit Number Index; MUSIX, Motor Unit Size Index; ABP, Abductor Pollicis Brevis; OO, Orbicularis Oculi.

FIGURE 1 Comparison of MUNIX and MUSIX values between MG patients and HCs.

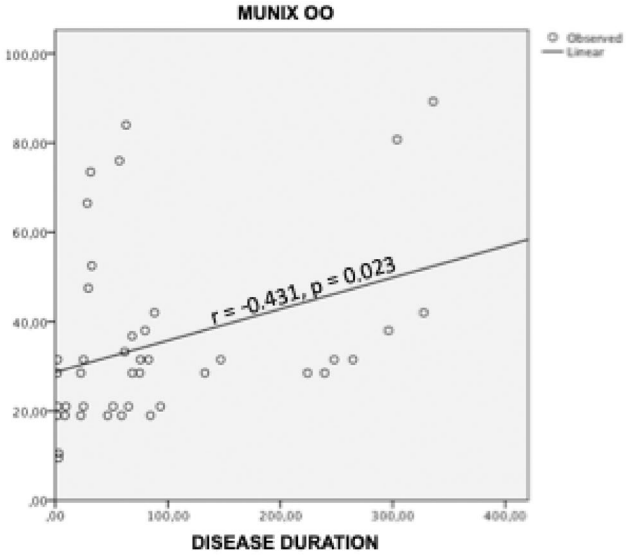


FIGURE 2 Univariate analysis showing significant negative correlation between MUNIX (OO) and disease duration.

Conclusion: MG patients showed reduced CMAP and MUNIX, indicating motor unit loss and impaired neuromuscular transmission, while higher MUSIX suggests compensatory remodeling. Correlations with disease duration and clinical severity underscore MUNIX's potential in disease monitoring. Further research with larger cohorts and longitudinal designs are warranted.

Disclosure: Nothing to disclose.

OPR-107 | The supporting role of visual evoked potentials for the diagnosis of optic neuritis

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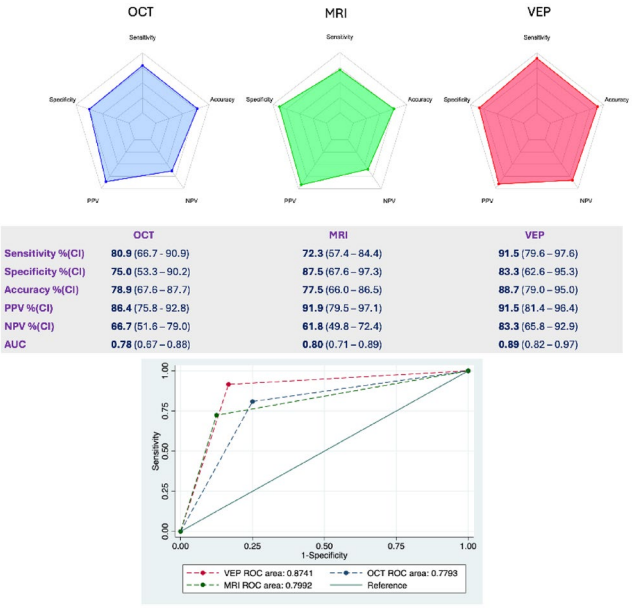
Background and Aims: Visual evoked potentials (VEPs) are commonly employed in the assessment of optic neuritis (ON). The International Consortium on Optic Neuritis (ICON) diagnostic criteria only included MRI and optical coherence tomography (OCT) as supportive paraclinical tests, as VEPs were considered non-specific. We aimed to assess the diagnostic performance of VEPs in a large consecutive cohort of patients with suspected ON.

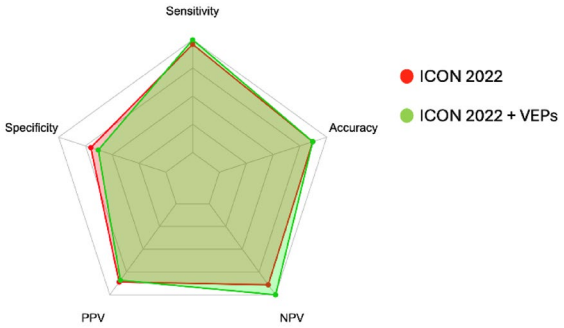
Methods: We screened 207 consecutive patients with suspected ON and eventually included 71 with available clinical, MRI, OCT and VEPs data within 30 days of clinical onset. ON diagnosis was established according to the judgment of two expert neuro-ophthalmologists after exclusion of other causes. We calculated diagnostic performance measures for each test and for the ICON criteria with and without VEPs as an additional paraclinical test.

Results: VEPs were the most sensitive paraclinical test (91.5%) with good specificity (83.3%). Positive and negative predictive value (PPV, 91.5%; NPV, 83.3%) were also high. MRI showed the highest specificity and PPV (87.5% and 91.9%). VEPs also had the highest overall diagnostic accuracy (88.7%) and area under curve in the ROC analysis (0.89) followed by OCT (78.9%, 0.78) and MRI (77.5%, 0.80). The addition of VEPs improved ICON criteria sensitivity (95.7% to 100.0%, identifying two additional patients) and NPV (89.5% to 100.0%), maintaining the same diagnostic accuracy (87.3%), although lowering their specificity (70.8% to 62.5%).



	OCT	MRI	VEP
Sensitivity %(CI)	**80.9** (66.7 - 90.9)	**72.3** (57.4 – 84.4)	**91.5** (79.6 – 97.6)
Specificity %(CI)	**75.0** (53.3 – 90.2)	**87.5** (67.6 – 97.3)	**83.3** (62.6 – 95.3)
Accuracy %(CI)	**78.9** (67.6 – 87.7)	**77.5** (66.0 – 86.5)	**88.7** (79.0 – 95.0)
PPV %(CI)	**86.4** (75.8 - 92.8)	**91.9** (79.5 – 97.1)	**91.5** (81.4 – 96.4)
NPV %(CI)	**66.7** (51.6 – 79.0)	**61.8** (49.8 – 72.4)	**83.3** (65.8 – 92.9)
AUC	**0.78** (0.67 – 0.88)	**0.80** (0.71 – 0.89)	**0.89** (0.82 – 0.97)

FIGURE 1 Diagnostic measures and receiver operating curves for OCT, MRI and VEPs.



	ICON 2022	ICON 2022 + VEPs
Sensitivity %(CI)	**95.7** (85.5 – 99.5)	**100.0** (92.5 - 100)
Specificity %(CI)	**70.8** (48.9 – 87.4)	**62.5** (40.6 – 81.2)
Accuracy %(CI)	**87.3** (77.3 – 94.0)	**87.3** (77.3 – 94.0)
PPV %(CI)	**86.5** (77.5 . 92.3)	**83.9** (75.7 – 89.8)
NPV %(CI)	**89.5** (68.1 – 97.1)	**100.0** (78.2 – 100.0)

FIGURE 2 Diagnostic performance of the ICON criteria with and without VEPs as a further paraclinic test.

Conclusion: VEPs can identify additional cases of ON that would remain undiagnosed with the current criteria and could be helpful in selected cases with high pre-test probability.

Disclosure: Nothing to disclose.

OPR-108 | Eye movements mirror vertigo symptoms in vestibular migraine

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Background and Aims: Interpreting vertiginous symptoms is challenging and crucial for understanding pathophysiological mechanisms. We aimed to correlate video-oculographic findings with vertigo symptoms in vestibular migraine (VM).
Methods: Ten healthy participants (HP) and 10 participants with VM, diagnosed per Bárány Society and ICHD-3 criteria, underwent neuro-otological assessment and 3D video-oculography in primary gaze with and without visual fixation, for 20 seconds each. Subjective reports during ocular motor assessment were recorded. Nitroglycerin (0.5 μg/kg) was administered to one patient and one healthy participant as part of the NITROVest study (IRAS 312478).
Results: VM participants described several spinning, oscillating and sliding sensations across axes and planes, pulsions and unsteadiness. All participants had stable gaze with, and ocular drifts without, fixation. In VM, horizontal (cases 1,4–9) or vertical drifts and nystagmus (1–3, 5–6, 8–10) aligned with the reported vestibular sensations. Nitroglycerin induced spinning symptoms in the yaw axis in a VM (case 1), corresponding to a moderate-amplitude fast-phase left-beating nystagmus, and no symptoms in the HP (case 11). A VM participant had migraine on the assessment day with a 2-second backwards spinning sensation coinciding with moderate-amplitude fast-phase upbeat nystagmus, which she identified as typical of her "roller-coaster" symptom (case 9).
Conclusion: The minor findings observed, even if not frankly abnormal, show a remarkable oculo-perceptual congruence. Motion illusions in VM may result from altered central modulatory mechanisms amplifying eye movements, leading to the perception of self-motion. Thorough characterization of subjective motion symptoms and their correlation with objective ocular-motor findings could be key for understanding VM.
Disclosure: None of the authors have relevant disclosures for this abstract.

OPR-109 | Head circumduction – A simple technique to examine peripheral and central function of the torsional VOR

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Background and Aims: We introduce a novel clinical paradigm to induce the torsional vestibulo-ocular reflex (VOR) using head circumduction - a circular motion of the head combining neck extension, rotation and flexion. We (i) evaluated the reliability of this manoeuvre in generating torsional nystagmus, (ii) explored the impact of post-rotational head tilt on induced responses (iii) assessed this paradigm as a clinical test of vestibular function.
Methods: Fourteen healthy participants were tested using an eye-tracker to record eye movements induced by the circumduction, performed at a frequency of 0.75 Hz. Participants were recorded on stopping in either a head-up or head-down condition. Exploratively, we also tested two patients with bilateral vestibular failure (BVF).
Results: All healthy participants showed robust post-rotational torsional nystagmus. This was significantly shorter during head-up (duration = 10.7±2.4 s) compared to head-down (duration = 15.7±3.7 s; $p = 0.0001$). Vertical nystagmus was also observed in most healthy participants, which was either disconjugate or overtly skewed. The two patients with BVF did not show any post-rotational nystagmus.
Conclusion: The shortening of torsional nystagmus duration and time constant in the head-up position supports (i) a role for the velocity storage mechanism in the torsional VOR (which was previously disputed) and (ii) the existence of otolith dumping effects in the torsional VOR. The vertical ocular findings during the stopping response confirm that skewed eye movements can be generated by vertical semicircular canal activity. These findings show that head circumduction is a simple method for assessing the torsional VOR – further supported by the lack of post-rotational response in BVF patients.

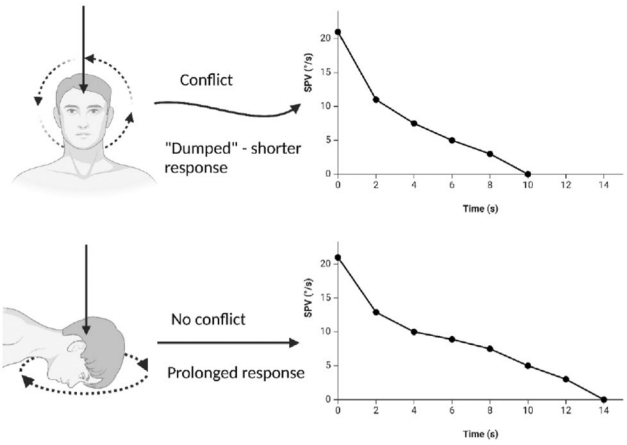

FIGURE 1 Stopping response with vertical canal stimulation after circumduction: upright head position causes a conflict between dynamic canal signals (rolling) and static otolith signal, shortening nystagmus. Forward head tilt aligns signals, reducing the conflict.

Disclosure: Nothing to disclose.

OPR-110 | Vestibular Migraine: Course of symptoms during a four-year follow-up

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Background and Aims: Data about the prognosis of vestibular migraine (VM) is scarce.
Methods: VM patients on follow-up for at least four years were included in this multicenter study to evaluate the course of symptoms. A structured questionnaire was used inquiring demographic features, age of onset of migraine headaches and vertigo attacks, headache and vertigo attack frequency, severity, associated features and the presence of interictal dizziness and positional vertigo. Menopause, history of motion sickness, family history of migraine was recorded. Answers of the first visit were compared with the answers of the last visit. In addition, variables considered were evaluated regarding their effect on symptom course.
Results: 203 patients were studied. Median vertigo and headache attack frequency and severity had significantly dropped during follow-up ($p < 0.01$ for all comparisons). Complete resolution was reported by only 5.4%. Dizziness in between the attacks was present in 67% and positional vertigo was reported by 20.2%. Univariate analysis showed that aural symptoms ($p = 0.013$) and menopause ($p = 0.016$) were risk factors for ongoing frequent vertigo attacks. History of motion sickness ($p = 0.019$) and a family history of migraine ($p = 0.004$) were associated with the risk of frequent migraine headaches. Presence of allodynia ($p = 0.002$) was associated with severe headache attacks when an early age of onset of vertigo attacks ($p = 0.005$) was a risk factor for continuing high frequency vertigo attacks.
Conclusion: In conclusion, though the frequency and severity of the headache and vertigo attacks decrease, complete resolution is reported by a minority
Disclosure: Nothing to disclose.

Sleep-wake Disorders 2

OPR-111 | Nightmares accelerate biological aging and predict premature mortality in humans

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Background and Aims: Nightmares are associated with an increased risk of developing neurodegenerative diseases. Whether nightmares increase the risk of other age-related health outcomes is unknown. This study investigated whether nightmares increase the risk of premature mortality and accelerated biological aging in the general population.
Methods: Data from 4,196 participants (ages 26–74) from four population-based cohort studies (Midlife in the United States [MIDUS]; MIDUS Refresher; Wisconsin Sleep Cohort; The Osteoporotic Fractures in Men Study) were used in this longitudinal analysis. Nightmare frequency was self-reported at baseline. Premature all-cause mortality (age < 75 years) was defined using study records. Cox regression was used to examine the prospective association between nightmare frequency and premature mortality. Participants' biological aging rates were measured at baseline using a composite of three epigenetic clocks (DunedinPACE, GrimAge, PhenoAge). Mediation analysis was performed to determine whether accelerated biological ageing mediates the nightmare-mortality association.
Results: During 18-years of follow-up, 227 premature deaths occurred. A higher frequency of nightmares was linearly associated with a greater risk of premature death ($p < 0{\cdot}001$). Compared with adults who had no nightmares at baseline, those who reported having weekly nightmares had a 3-fold risk of premature mortality (adjusted hazard ratio = 2·73; $p < 0.001$). Furthermore, individuals with a higher frequency of nightmares exhibited faster rates of biological aging ($p < 0.001$). Accelerated biological ageing mediated 39% of the nightmare-mortality association.
Conclusion: Adults with frequent nightmares experience faster biological aging and die at younger ages. Future studies are needed to determine whether treating nightmares could slow biological ageing and reduce mortality risk in the general population.
Disclosure: Nothing to disclose.

OPR-112 | Actigraphy for wake-sleep rhythm characterization in patients with post-traumatic confusional state

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Background and Aims: Post-traumatic confusional state (PTCS) is a syndrome that often occurs after a severe traumatic brain injury (TBI). PTCS is characterized by cognitive impairments, disorientation, attention fluctuations, sleep-wake disturbances, agitation and psychotic-like symptoms, and represents a critical phase of recovery, with its duration closely linked to long-term functional outcomes. Sleep-wake rhythm disturbances may exacerbate the cognitive and functional impairments seen in these patients. This study evaluates actigraphy-based metrics for sleep-wake rhythm profiling in PTCS and their potential to predict recovery trajectories.
Methods: We included 28 patients with severe TBI undergoing rehabilitation. Seven-day actigraphy was used to measure sleep efficiency (SE), wake efficiency (WE), and the expected wake-sleep rhythm (EWSR). Clinical assessments, including the Confusion Assessment Protocol (CAP), Barthel Index, and agitation scores, were performed at T0 (admission) and T1 (discharge).
Results: Actigraphy metrics were significantly altered compared to healthy reference values in the whole TBI-cohort. SE, WE and EWSR were more impaired in confused patients than in controls. Moderate-severe agitation was associated with greater SE and EWSR impairment. Using SE = 85% as cut-off, the CAP sleep item failed to identify 15 out of 22 patients with impaired SE, resulting in a 71% false-negative rate, underscoring its limitations in identifying objective sleep disturbances. Univariate analyses identified WE and EWSR as significant predictors of PTCS persistence and duration, respectively. Finally, a significant correlation was observed between WE and Barthel Index improvement at T1.
Conclusion: Actigraphy can provide objective, clinically relevant metrics to assess sleep-wake rhythm disturbances in PTCS, offering predictive insights for rehabilitation outcomes.

Disclosure: This work is supported by the Italian Ministry of Health—(Ricerca Corrente 2025–2027).

OPR-113 | Impacts of physical exercise and keto diet on idiopathic hypersomnia, narcolepsy type 2: A randomized, controlled trial

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Background and Aims: Behavioural treatment recommendations for narcolepsy type 2 (NT2) and idiopathic hypersomnia (IH) are mainly based upon expert opinion. The aim of this study is to investigate the effects of regular physical activity and ketogenic diet in NT2 and IH.
Methods: In our 10-week trial adult patients with NT2 and IH were randomized into two intervention groups: ketogenic diet, and regular physical exercise following a training plan, and a control group. Study parameters included demographic and clinical data, ketone levels, power-walking tests, and questionnaires on daytime sleepiness (ESS), sleep quality (PSQI), fatigue (FSMC), well-being, recovery and life quality (SF-12, WHO-5).
Results: In total 45 patients with IH ($n=19$) and NT2 ($n=26$) were randomized, 34 completed the study. In the IH-Keto group ($n=7$), daytime sleepiness improved significantly, with a reduction of 30% after 10 weeks of intervention (ESS1: 16 vs. ESS2: 9). Fatigue and quality of life also showed significantly improvements only in this group. In NT2, significant improvements were observed in the Keto group for sleep quality, physical health, and quality of life, while only a positive trend in daytime sleepiness, fatigue and sleep quality was noted in the exercise group. Additionally, an average weight loss of 5 kg was observed in both Keto groups.
Conclusion: The ketogenic diet showed a strong treatment effect in IH and can be considered an effective non-drug therapy. Both ketogenic diet and regular physical exercise also indicate improvements for individual parameters.
Disclosure: The authors declare no conflict of interest.

OPR-114 | Measuring REM-sleep without atonia (RWA) on v-PSG: Does the scoring method make a difference? (preliminary data)

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Background and Aims: Within the multicentric BRAVA Project, REM-Sleep without atonia (RWA) was measured using an adapted protocol following the SINBAR criteria. We compared RWA measurements using the BRAVA protocol with the AASM criteria for scoring RWA to analyse differences in RWA indices.
Methods: We analysed v-PSG data from a subgroup of 14 subjects from the centre in Kassel: 3 Parkinson Disease (PD) without RBD, 4 PD with RBD, 4 iRBD and 3 controls. RWA was measured using AASM criteria for the entire REM Sleep and the BRAVA protocol-REM-sleep periods were scored and a simplified version of the SINBAR criteria quantifying RWA in 3-s mini-epochs as "any" chin activity and/or phasic FDS activity (without specifications of the side) was applied.
Results: The study group consisted of 5 (36%) men and 9 women (64%), with a mean age of 63,43± 15,96 years. RWA indices did not significantly differ between the two methods (37,95 ± 30,53% with BRAVA protocol vs 38,11 ± 30,36% with AASM, $p=0.99$). When using the BRAVA protocol 6 (43%) subjects presented RWA above the cutoff of 31,9%, compared to 8 (57%) subjects above the AASM cutoff of 27,2% ($p=0.43$). With the BRAVA protocol fewer 3s-mini-epochs (669,71± 547,14) were analysed compared to the AASM criteria (990,93 ± 541,67).
Conclusion: When measuring RWA using the BRAVA protocol a number of the REM 3s-mini-epochs was excluded. Nonetheless the two methods resulted in a similar amount of total RWA. Further data with more subjects in different diagnosis groups is currently analysed.
Disclosure: This project was supported in part by the Austrian Science Fund [grant DOI: 10.55776/I5894] and by Bundesministerium für Bildung und Forschung, Projektträger: Deutsches Zentrum für Luft- und Raumfahrt e.V. (01KU2206), under the frame of ERA PerMed.

OPR-115 | Exploring the neural correlates of insomnia: A meta-analysis of functional and structural alterations

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Background and Aims: Insomnia is one of the most common sleep disorders, and a large number of neuroimaging studies have indicated abnormalities in the brain's function and structure in individuals with insomnia. However, the heterogeneity of these findings has hindered the understanding of the underlying mechanisms of insomnia. Increasingly, there is a growing recognition that localizing the disease to brain networks is more informative than focusing on individual anatomical regions.
Methods: We included 53 previously published studies with a total of 66 comparisons. Using a novel functional connectivity network mapping method, we combined the resting-state functional connectivity database from 1,000 healthy volunteers to map the affected coordinates from these studies onto three brain networks.

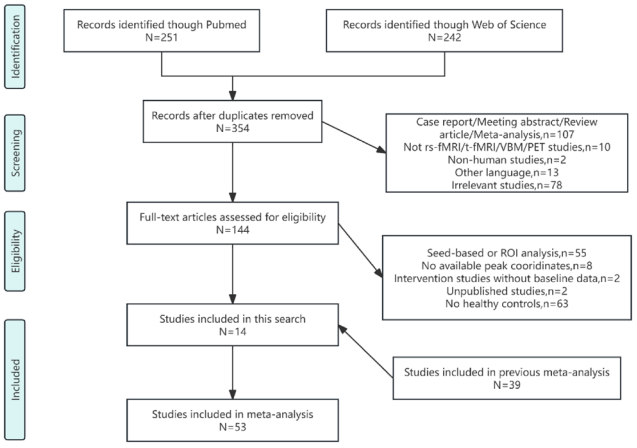

FIGURE 1 Study selection strategy flowchart.

Results: The resting-state, task-state, and gray matter volume networks in insomnia are interrelated yet distinct. Specifically, all three networks are significantly associated with the cingulo-opercular network. Additionally, the resting-state network is closely linked to the default mode network and the salience network. The task-state network is primarily associated with the ventral attention network, while the gray matter volume network is mainly connected to the ventral/dorsal attention networks and the somatomotor network.

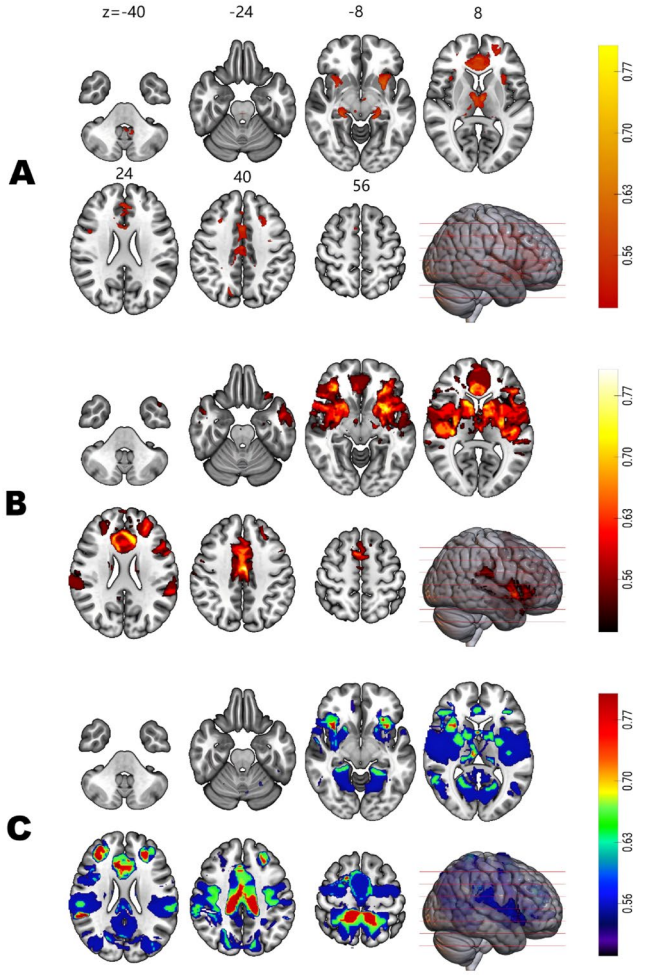

FIGURE 2 Network localization of insomnia in resting-state (A), task-state (B), and gray matter volume (C), with the network threshold set between 50% and 80% as shown in the figure.

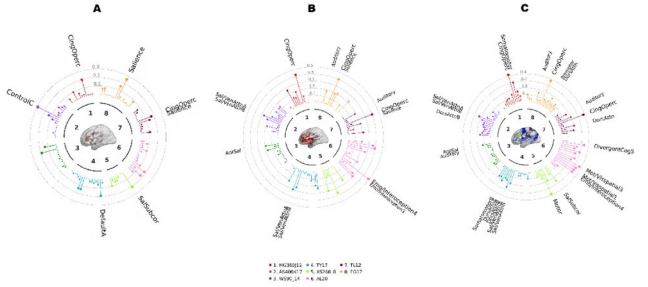

FIGURE 3 Overlap analysis of insomnia networks in resting-state (A), task-state (B), and gray matter volume (C) with classical brain network atlases. Named networks are significantly associated with abnormal insomnia networks.

Conclusion: Our meta-analysis integrates previous inconsistent findings from the perspective of network localization, which not only helps to elucidate the unique neurobiological mechanisms of insomnia but also provides insights for further research and clinical interventions in insomnia.
Disclosure: Nothing to disclose.

ABSTRACT

ePresentation

Saturday, June 21, 2025

Ageing and dementia 1

EPR-001 | Blood pTau217 distinguishes amyloid-positive from amyloid-negative subjects across the Alzheimer's disease continuum

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Background and aims: Alzheimer's disease (AD) is the leading cause of dementia worldwide, and cost-effective tools to detect amyloid pathology, particularly in its early stages, are urgently needed. Blood-based Tau phosphorylated at threonine 217 (pTau217) seems promising, but its reliability as a proxy for cerebrospinal fluid (CSF) status and ability to identify patients within the AD spectrum remain unclear.
Methods: We performed a systematic review and meta-analysis on the potential of blood pTau217 to differentiate amyloid-positive (A+) and amyloid-negative (A-) subjects. We included original studies reporting quantitative data on pTau217 concentrations in both blood and CSF in the AD continuum. The single-group meta-analysis computed the pooled pTau217 levels in blood and in CSF, separately in the A+ and A- groups, while the head-to-head meta-analysis compared the mean pTau217 concentrations in the A+ versus A- subjects, both in blood and CSF, stratifying by assessment method in both cases.
Results: Ten studies (819 A+; 1,055 A−) were included. The mean pTau217 levels resulted higher in CSF than in blood and, crucially, in A+ individuals than in A− ones, regardless of the laboratory method employed, including Meso Scale Discovery (MSD), Single Molecule Array for Protein Detection (Simoa), and immunoprecipitation with mass spectrometry. Most importantly, all these laboratory techniques reliably distinguished A+ from A− subjects, whether applied to CSF or blood samples.
Conclusion: Blood-based pTau217 is a reliable marker of amyloid pathology and might be a non-invasive, scalable biomarker for early AD detection, reducing the reliance on more invasive, expansive, and less accessible methods.
Disclosure: Nothing to disclose.

EPR-002 | Exome sequencing identifies a rare damaging variant in GRIN2C in familial late-onset Alzheimer's disease

E. Rubino[1]; M. Italia[2]; E. Giorgio[3]; S. Boschi[1]; P. Dimartino[3]; T. Pippucci[4]; F. Roveta[1]; C. Cambria[5]; G. Elia[1]; A. Marcinnò[1]; S. Gallone[1]; E. Rogaeva[6]; F. Antonucci[5]; A. Brusco[1]; F. Gardoni[2]; I. Rainero[1]
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Background and aims: Alzheimer's disease (AD) is a progressive neurodegenerative disorder influenced by both genetic and environmental factors. While early-onset AD has well-established genetic determinants, the genetic basis of late-onset AD remains unclear. This study examined a large Italian family with late-onset autosomal dominant AD, identifying a novel rare missense variant in GRIN2C gene.
Methods: Affected family members were screened for genetic variants in APP, PSEN1, and PSEN2, as well as 77 genes

associated with neurodegenerative diseases using the NeuroX array assay. Exome sequencing was performed on three patients and two healthy relatives. Bioinformatics analyses were conducted. Functional studies were performed in primary neuronal cultures assessing the impact of the identified variant through immunocytochemistry and electrophysiology.

Results: No pathogenic variants were found in APP, PSEN1, PSEN2 or in genes screened using the NeuroX array. Exome sequencing revealed the c.3215C>T p.(A1072V) variant in GRIN2C gene (NM 000835.6), encoding the glutamate ionotropic N-Methyl-D-aspartate receptor (NMDA) type subunit 2C (GluN2C). This variant segregated with AD in six affected members and was absent in nine healthy relatives. Primary rat hippocampal neurons overexpressing the variant showed increased NMDAR-induced currents, indicating altered glutamatergic transmission. Surface expression assays revealed a higher surface/total ratio of mutant GluN2C, correlating with increased NMDAR current. Immunocytochemistry showed a reduced colocalization of mutant GluN2C with 14-3-3 proteins, suggesting impaired NMDAR trafficking.

Conclusion: This study identifies a rare missense variant in GRIN2C associated with late-onset autosomal dominant AD. Our findings underscore the importance of GRIN2C-containing NMDA receptors in glutamatergic signaling and their potential role in AD pathogenesis.

Disclosure: Nothing to disclose.

EPR-003 | Preliminary RCT insights from a 12-week app-based multidomain intervention in patients with cognitive decline

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Background and aims: With an aging population and limited pharmacological treatments, non-pharmacological interventions for cognitive decline are increasingly important. The MEMODIO app was developed as a multidomain digital health intervention for individuals with mild cognitive impairment (MCI) or mild dementia. This interim analysis presents initial results from an ongoing RCT (data collected until October 2024).

FIGURE 1 Screenshot Health App

Methods: The study includes 140 patients with MCI (MoCA 21-25) or mild dementia (MoCA 14-20), randomized to an intervention group (IG) using MEMODIO alongside standard care or a standard of care group (SoC). MEMODIO provides a 12-week program incorporating cognitive training, physical exercises, psychoeducation on brain-healthy diets, and risk factor management. Assessments occurred at baseline and post-intervention using MoCA, A-IADL-Q-SV, DEMQOL, and PAQ 50+.

Results: Among 69 analyzed patients (mean age: 74.39 years, 32 female), 42 had MCI and 27 had dementia. Preliminary results show a statistically significant MoCA improvement in MCI patients in the IG (-1.162 ± 3.08 SoC vs. 1.375 ± 2.286 IG, $p = 0.000$). Quality of life, physical activity, and daily functioning did not significantly change at interim evaluation.

TABLE 1 Results.

Outcome MCI and Dementia (n=69)	Mean of differences t0 to t1 control group (SD)	Mean of differences t0 to t1 intervention group (SD)	p-Value
Cognitive fuction (MoCA)	-1.162(3.08)	1.375 (2.86)	0.000
QoL (DEMQOL) (n=42)	-2.116 (7.76)	-0.130 (8.16)	0.302
Daily abilities (A-IADL-Q-SV)	0.156 (0.78)	-0.094 (0.35)	0.096
Activity level (PAQ 50+)	0.249 (50.3)	2.351 (80.1)	0.902

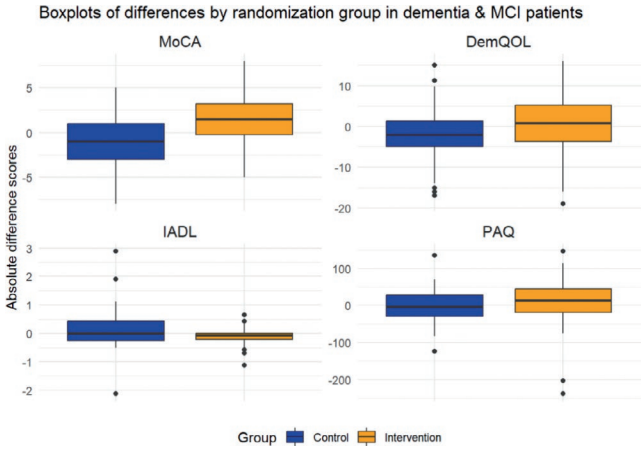

FIGURE 2 Boxplots Results

Conclusion: MEMODIO significantly improved cognitive function in MCI patients, outperforming standard care alone. Ongoing analyses will assess its impact on quality of life, daily activities, and long-term therapeutic potential.
Disclosure: G. Nelles: PI of MEMODIO@APP_CARE, F. Bicu: Shareholder of memodio GmbH, A. Quante: None Declared, T. Steinmann: Employee of memodio GmbH, D. Stein: Shareholder of memodio GmbH, V. Weil: Employee of memodio GmbH, A. Bicu: None Declared, C. Polidori: None Declared

EPR-004 | Cholinergic dysfunction as a biomarker of the Alzheimer's continuum: Insights into early-stage cognitive decline

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Background and aims: Subjective cognitive decline (SCD), characterized by self-reported cognitive dysfunction despite normal performance on standardized tests, is a heterogeneous condition associated with an increased risk of developing mild cognitive impairment (MCI) and Alzheimer's disease (AD). This study aimed to characterize intracortical inhibition and facilitation across the AD continuum using non-invasive transcranial magnetic stimulation (TMS), with a focus on identifying neurophysiological dysfunction as an early biomarker.
Methods: Fifty-eight participants were enrolled, including 20 healthy controls (HC), 10 SCD, 13 MCI, and 15 AD patients, confirmed by cerebrospinal fluid (CSF) analysis. All underwent an extensive neuropsychological assessment and TMS paired-pulse protocols to assess short interval intracortical inhibition (SICI), intracortical facilitation (ICF), and short latency afferent inhibition (SAI), reflecting GABAergic, glutamatergic, and cholinergic circuits, respectively.
Results: TMS revealed significant cholinergic-mediated intracortical inhibition deficits across patient groups. Furthermore, SCD patients showed significantly higher SAI values than HC ($p < 0.05$), but comparable to MCI ($p = 0.408$), suggesting early cortical inhibitory dysfunction. Notably, 50% of SCD participants exhibited SAI alterations despite normal AD CSF markers, indicating that SAI modifications may reflect broader brain health alterations beyond AD-related changes. Partial correlation adjusted for age and sex revealed a positive relationship between MoCA scores and SAI values.
Conclusion: These findings highlight that cholinergic dysfunction in SCD may serve as an early biomarker of cognitive impairment, providing insights into its pathophysiology and identifying at-risk individuals. Further investigations are needed to explore cholinergic-targeted interventions to prevent or slow the progression of cognitive decline.
Disclosure: Nothing to disclose.

EPR-005 | Proteomic changes in prion disease associated with prion-specific, V2 strain-related secondary tauopathy

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Background and aims: Sporadic Creutzfeldt-Jakob disease (sCJD) is a rare neurodegenerative disorder related to prion protein misfolding. Interestingly, a secondary prion-specific tauopathy can occur in sCJD, especially in the subtypes related to the V2 strain (i.e., VV2 and MV2K). By employing a high-throughput proteomics technology (proximity extension assay) on cerebrospinal fluid (CSF) samples from a broad sCJD cohort, we aimed to characterize in vivo the molecular events associated with secondary tauopathy.
Methods: We assayed 797 proteins in the CSF samples of 67 patients with a definite or probable clinical diagnosis of V2-sCJD (34 VV2 and 33 MV2K). Increased CSF p-tau181 levels defined the presence of secondary tauopathy (T+ vs. T- status). Linear models adjusting for age, sex, and sCJD subtype, were used to identify the differentially expressed proteins (DEPs) between T+

and T- sCJD cases. Enrichment analyses were performed with the Gene Ontology database.

Results: 36/67 (53.7%) patients were classified as T+. We found 294 DEPs between T+ and T- sCJD cases. All proteins but two (NBL1 and APLP1) were positively associated with T+ status (Figure 1). Enrichment analyses on upregulated proteins highlighted various biological processes related to synaptic organization and neuronal morphogenesis (Figure 2). The top DEPs are involved in protein folding regulation (FKBP4), cell signaling (NTRK2, NTRK3, TNFRSF11A), ribose metabolism (RBKS), and membrane transportation (SCARB2).

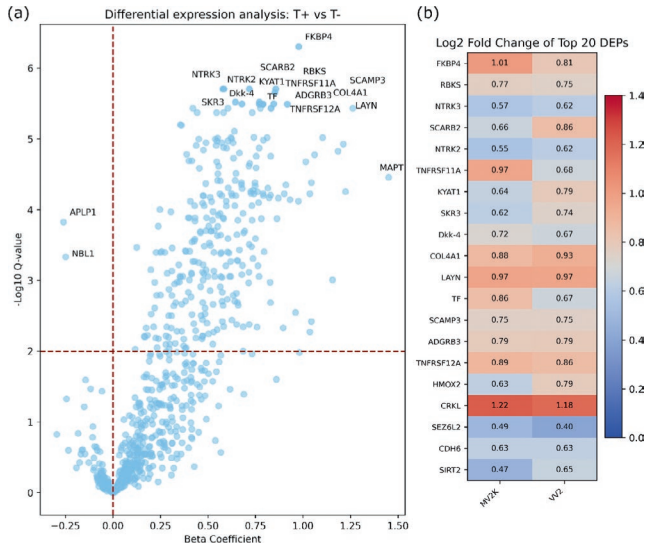

FIGURE 1 Volcano plot showing the DEPs between T+ and T- sCJD patients. The top dysregulated proteins are marked with protein names (a). Heatmap showing the Log2-Fold change distribution of the top DEPs in VV2 and MV2K (b). DEPs, differentially expressed proteins.

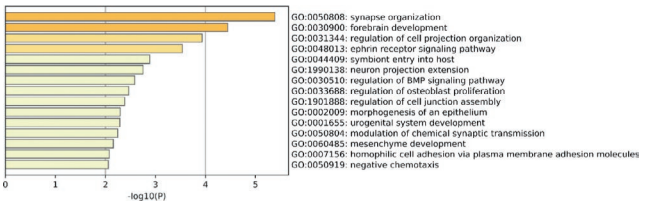

FIGURE 2 Bar graphs showing the biological pathways enriched among proteins upregulated in T+ sCJD. Functional enrichment was performed using Metascape selecting GO Biological Processes as ontology source and setting 797 assayed proteins as enrichment background.

Conclusion: We unveil a distinct protein signature associated with sCJD secondary tauopathy in vivo, shedding new light on the complex molecular events related to tau misfolding in prion disease.

Disclosure: P.P. is supported by the Ministero della Salute (Ricerca Corrente), and the #NextGenerationEU (NGEU) funded by the Ministry of University and Research (MUR), National Recovery and Resilience Plan (NRRP), project MNESYS (PE0000006).

EPR-006 | Sex differences in the efficacy of anti-amyloid monoclonal antibodies

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Background and aims: As first disease-modifying drugs approved for the treatment Alzheimer's disease (AD), anti-amyloid monoclonal antibodies (MABs) represent a milestone in patient care. Sex was noted to modify biomarker deposition, progression and risk, however, sex differences in MABs efficacy have not been sufficiently explored. In this meta-analysis, we aimed to analyze all available sex-disaggregated data for MABs efficacy in the treatment of AD.

Methods: We searched clinicaltrials.gov, Alzforum Therapeutics and PubMed databases to identify publications of phase III MABs clinical trials. We further supplemented our search with reference search and conference presentations. We selected those publications which presented any form of sex-disaggregated data on efficacy. We then extracted sex-disaggregated efficacy data for all available endpoints. We subsequently conducted a random effects meta-regression using mean treatment effects for each endpoint.

Results: We identified 13 publications presenting first full results of a phase III MABs clinical trial, of which 5 (results of aducanumab, donanemab, gantenerumab, lecanemab, and solanezumab clinical trials) presented sex-disaggregated results. The meta-analysis revealed statistically significant sex differences for mean treatment effects of all analyzed endpoints, with greater efficacy in males and limited efficacy in females (ADAS-Cog $p = 0.042$, ADCS-ADL $p = 0.002$, CDR SoB $p = 0.008$).

Conclusion: Our results stress the importance of considering patient sex in anti-amyloid efficacy analyses. Further analyses of detailed sex-disaggregated efficacy and safety results are needed to make personalized risk/benefit assessments.

Disclosure: JNM was supported by project nr. LX22NPO5107 (MEYS): Financed by EU – Next Generation EU.

EPR-007 | CSF biomarkers profiling in cerebral amyloid angiopathy: Relationship with phenotype and hemorrhagic risk

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Background and aims: Cerebral amyloid angiopathy (CAA) is diagnosed in vivo according to Boston Criteria, but it remains unclear whether CSF profile can reliably provide phenotypic and prognostic insight. In this study, we explored the potential of core CSF biomarkers in identifying CAA phenotypes and providing support to hemorrhagic risk stratification.
Methods: We enrolled probable CAA patients (Boston Criteria 2.0) and, as control group, age-matched AD patients without radiological signs of CAA, gathering clinical, neuroimaging and follow up data, together with core CSF biomarkers (Aβ42, Aβ40, pTau181, total-Tau). We grouped CAA patients based on the AT(N) classification (A+CAA vs. A-CAA and A+T+CAA vs. A+T-CAA), to explore clinical and radiological differences. Unsupervised clustering, a data-driven method, was applied to identify biological CAA subgroups on CSF biomarkers levels.
Results: CAA ($n=71$, 71.77 ± 8.45 years) exhibited lower levels of Aβ40 ($p<0.001$), Aβ42 ($p=0.013$), total-Tau ($p=0.040$), and pTau181 ($p<0.001$) compared to AD ($n=32$, 72.97 ± 4.85 years), with similar Aβ42/40 ratio ($p=0.303$). A+CAA showed higher cortical superficial siderosis prevalence than A-CAA (67% vs. 25%; $p=0.016$). A+T-CAA subjects showed higher hemorrhagic risk over time than A+T+CAA (29 vs. 7 events per 100 patient-year, $p=0.010$; survival analysis, log-rank test: $p=0.013$; hazard ratio: 6.30; 95%CI: 1.18–33.72; $p=0.031$). Unsupervised clustering identified two CSF-based CAA subgroups, defined as "pure CAA" and "CAA-AD". The pure CAA group showed greater hemorrhagic risk during follow-up compared to CAA-AD (22 events per 100 patient-years vs. zero events; $p=0.017$; survival analysis, log-rank test: $p=0.011$).
Conclusion: CSF-based profiling effectively identified CAA with different natural history, providing a promising tool for hemorrhagic risk stratification.
Disclosure: MP reports fees from Novartis, Lilly, Eisai, Biogen and research support from Novartis and Nutricia. FM received speaker honoraria from Roche Diagnostics S.p.A and Eli Lilly S.p.A.

EPR-008 | Adiponectin as a potential therapeutic target for cerebrovascular dysfunction in Alzheimer's disease

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Background and aims: Cerebrovascular dysfunction are increasingly recognized as a critical aspect of Alzheimer's disease (AD) pathophysiology. Adiponectin (APN), an adipocyte-secreted hormone, exhibits neuroprotective properties against amyloid beta (Abeta) toxicity. However, its influence on cerebrovascular dysfunction in AD remains largely unexplored.
Methods: APN-deficient AD (5xFAD;APN-/-) mice were generated by crossbreeding 5xFAD and APN knockout (APN-/-) mice. Cerebrovascular integrity was assessed through cerebral blood flow (CBF), neurovascular coupling (NVC), cerebral amyloid angiopathy (CAA), and blood-brain barrier (BBB) permeability. Additionally, 5xFAD mice received intravenous APN to evaluate its effects on CBF and NVC. Primary mouse brain endothelial cells were treated with Human Abeta40 oligomers, with or without APN, to assess the impact of APN on tight junction proteins (TJPs) expression and endothelial barrier integrity.
Results: 5xFAD; APN-/- mice showed more severe NVC impairment as early as 6 months, and significantly lower resting CBF at 9 months than 5xFAD mice. Earlier and severer BBB leakage was observed in 5xFAD;APN-/- mice, alongside increased TJPs reduction. Additionally, more Abeta deposition was observed within the cerebral vessels of 5xFAD; APN-/- mice at 6 months, indicating aggravated CAA pathology. Intravenous APN administration mitigated CBF reduction and NVC impairment in 5xFAD mice. In vitro results showed that Abeta40 reduced TJPs expression and compromised endothelial barrier integrity, which was significantly improved by APN pretreatment.
Conclusion: These findings suggest that APN is beneficial for maintaining cerebrovascular integrity, highlighting its potential as a therapeutic target for cerebrovascular dysfunction associated with AD.
Disclosure: This work was supported by funding for research in AD and dementia from Chan Kin Shing Charitable Trust and private donation of W C S Fung.

EPR-009 | Comparing diagnostic accuracy between plasma and cerebrospinal fluid biomarkers in Alzheimer's disease

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Background and aims: Recently developed plasma biomarkers for Alzheimer's disease (AD) show promise for improving the screening process in clinical settings, facilitating earlier access to emerging treatments. This study aimed to assess the concentrations of plasma AD biomarkers in relation to cerebrospinal fluid (CSF) biomarkers, evaluating their correlation and diagnostic accuracy for AD diagnosis.
Methods: We included 52 participants (18 with suspected AD, 11 with mild cognitive impairment, and 28 healthy controls) from the Memory Clinic at the University of Trieste. Participants underwent lumbar puncture for CSF analysis, and plasma AD biomarkers (Aβ42, Aβ40, p-Tau181) were tested using the LUMIPULSE immunoassay. CSF biomarkers included Aβ42, Aβ40, Aβ42/Aβ40 ratio, t-Tau, and p-Tau181.

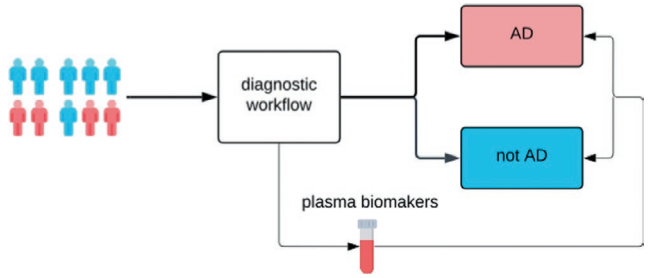

FIGURE 1 Study design

Results: Plasma p-Tau181 concentrations were significantly higher in amyloid-positive (A+) individuals ($p < 0.001$) and increased in the A+/T+ group ($p < 0.001$), but not in A+/T-. Plasma p-Tau181 showed a strong correlation with its CSF counterpart and with the CSF Aβ42/40 ratio. No significant correlation was found between plasma and CSF Aβ42/Aβ40 ratios. Receiver operating characteristic (ROC) analyses indicated plasma p-Tau181's high diagnostic accuracy, with an AUC of 0.82 for differentiating A+ versus A- and 0.83 for A+/T+ versus other CSF A/T statuses.

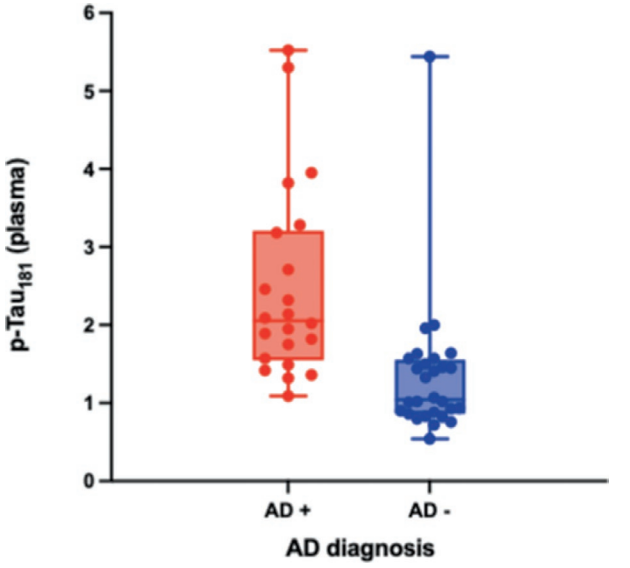

FIGURE 2 Plasma biomarkers concentrations according to AD diagnosis.

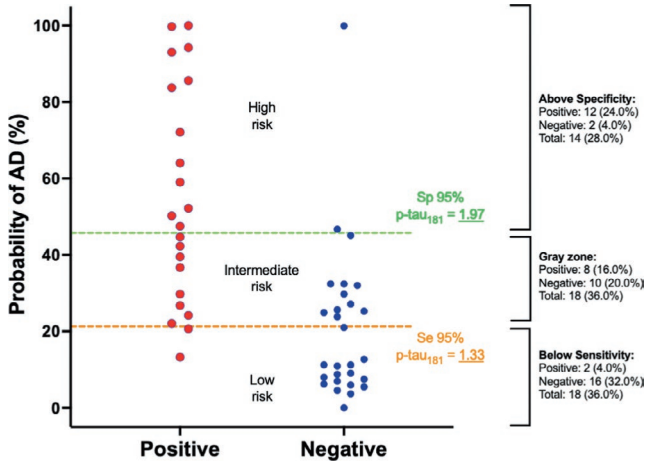

FIGURE 3 Plasma p-Tau181 based risk stratification for AD positivity.

Conclusion: Plasma p-Tau181 is a reliable biomarker with strong correlation to CSF biomarkers and high diagnostic accuracy, supporting its use in AD screening and diagnosis.
Disclosure: Nothing to disclose.

Autonomic nervous system diseases

EPR-010 | MeDeMSA Care protocol: personalized best medical care with integrated telemedicine and mobile palliative support in MSA

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Background and aims: Multiple system atrophy (MSA) represents a major management challenge due to its variable clinical presentation. At the wheelchair-bound stage, barriers often hinder specialized care, leaving patients and caregivers to face complications and fear alone.
Methods: This 18-month, monocentric, randomized, open-label study evaluates the impact of a personalized, multidisciplinary treatment plan, integrating mobile palliative care and telemedicine, on the quality of life (QoL) of MSA individuals, compared to a historical European MSA cohort. Forty-six participants will undergo baseline clinical, psychological, and neurorehabilitation assessments, along with an online interview to identify individual healthcare preferences. These assessments will guide individualized therapeutic plans, including palliative care, self-directed physio-, speech, and occupational exercises. Follow-up visits at 6, 12, and 18 months will reassess needs and adapt plans to address disease progression and changing preferences, ensuring continuous personalization. Repeated interviews at 12 months, phone-calls and satisfaction surveys at Months 1, 7, 13, and 18 will monitor compliance, identify barriers, and gather feedback. Additionally, 23 participants will receive monthly and on-demand telemedicine visits. Informal caregivers will join an 18-month observational study assessing their QoL and burden through repeated evaluations, offering insights into evolving challenges.
Results: MeDeMSA Care startedin April 2023 and will last 60 months. To date, 20 MSA individuals (10 randomized to telemedicine) and 17 informal caregivers were actively recruited.
Conclusion: We hypothesize that multidisciplinary, patient-centered care with integrated telemedicine and mobile palliative support warrants continuity of care and improves the QoL of MSA individuals throughout the disease course. Its acceptance, safety, and cost-effectiveness will also be assessed.
Disclosure: Funded by the FWF-Austrian Science Fund (FG 2700-B).

EPR-011 | Multi-level spinal cord neuromodulation effectively treats postural orthostatic tachycardia syndrome (POTS)

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Background and aims: Postural orthostatic tachycardia syndrome (POTS) is a complex disorder that causes invalidating symptoms (e.g., tachycardia, presyncope, fatigue, dyspnea) after assuming an upright position. In severe cases, patients may become functionally disabled and develop other serious dysautonomia symptoms such as gastrointestinal. It mostly affects young women of childbearing age and prevalence has been reported to spike after COVID. Currently, there is no approved treatment, and management relies on lifestyle and diet changes, heart medications, and other supportive measures that, unfortunately, do not control the symptoms very often.
Methods: We are treating patients with severe POTS with a multi-level Spinal Cord Stimulation (SCS) approach: 4-port system and thoracic and cervical electrodes. Standard assessments for POTS are performed pre- and post-SCS (1, 3, 6, 12 months): pain (VAS), quality-of-life (SF-36), autonomic dysfunction (BASQ), and heart rate response to tilt (ΔHR).
Results: To date, 2 subjects (2 female, 28yo) have been implanted with success. Several other patients will be implanted in the coming months. The first patient (3y evolution) cardinal symptoms included POT (ΔHR = 70bpm), frequent fainting, and dysautonomia with severe sensory deficits, gastrointestinal and urogenital issues. After SCS, response to tilt normalized (ΔHR = 21bpm, 1 month; ΔHR = 12bpm, 12 months), thus no longer meeting criteria for POTS. Dysautonomia symptoms and Quality-of-life also largely improved. The second patient (12y evolution with 7y in wheelchair) had also severe POT (ΔHR = 45bpm) and multi-system dysautonomia. After SCS, similarly, response to tilt decreased (ΔHR = 30bpm, 1 month) and dysautonomia and Quality-of-life largely improved.

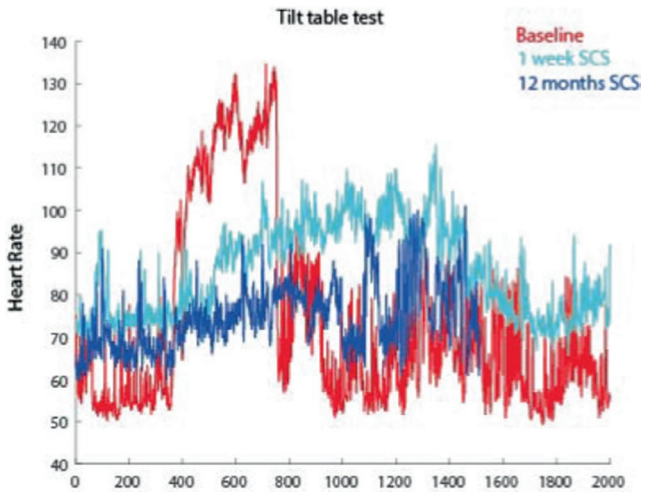

FIGURE 1 Long-term heart rate response to tilt (before and after SCS) of our first patient.

Conclusion: Neuromodulation via the spinal cord holds big promise to effectively treat POTS and associated dysautonomia.
Disclosure: Nothing to disclose.

EPR-012 | Central autonomic network connectivity: Abnormalities in multiple sclerosis and aerobic training effects

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Background and aims: Autonomic dysfunction is common in multiple sclerosis (MS); however, functional abnormalities of the central autonomic network (CAN) are still not investigated in this disease. Here, we explored resting state (RS) functional connectivity (FC) of the CAN in MS and its potential modification after aerobic training (AT).
Methods: A total of 75 MS patients (38 relapsing-remitting [RR] and 37 progressive [P]) underwent 3T RS functional MRI at baseline and after 2 (RRMS) or 3 months (PMS) of AT. Sixty-seven matched healthy controls (HC) served as baseline RS FC reference. Seed-based RS FC analysis used core CAN modulatory regions: left/right ventromedial pre-frontal cortex (vmPFC), mid-cingulate cortex (MCC), amygdala, hypothalamus, anterior and posterior insula.
Results: Compared to HC and PPMS patients (conjunction analysis, $p < 0.001$), RRMS patients were characterized by increased RS FC of the left hypothalamus with the cerebellum. In PMS, compared to RRMS and HC (conjunction analysis, $p < 0.001$), we found increased RS FC of the bilateral insula and amygdala with ipsilateral deep gray matter nuclei, of the vmPFC with posterior cingulate cortex and angular gyrus, and of the MCC with the cerebellum. PMS also showed decreased RS FC of the bilateral insula with cerebellum, and of the MCC with insula. After AT, decreased hypothalamic network RS FC in RRMS was observed, while no changes were detected in PMS.
Conclusion: CAN dysregulation is present in MS, with distinct RS FC abnormalities characterizing RRMS and PMS patients. AT may be insufficient to modulate CAN RS FC in progressive patients.
Disclosure: Funding. Grants from Italian Ministry of Health (GR-2019-12369599) and MS Society of Canada (EGID3185). Disclosures. GG, PV, TM, FR have nothing to disclose. PP received speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon, and Sanofi. He received research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). MF received compensation for consulting services or speaking activities

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EPR-013 | Cardiovascular autonomic failure in isolated REM sleep behavior disorder and Parkinson Disease: A prospective evaluation

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Background and aims: Isolated REM sleep behavior disorder (iRBD) is prodromal to synucleinopathies, including Parkinson's disease (PD). PD with RBD in the early phase (PD+RBD) is associated with more severe symptoms, including cardiovascular autonomic failure (cAF). Whether cAF is more related to RBD or to PD has to be confirmed.
Methods: One hundred early (<3 years) PD (20 with RBD), and 40 iRBD were prospectively evaluated with cardiovascular reflex tests (CRTs) at baseline and after 1.85 ± 0.60 years. Mixed-effects sex- and age-adjusted regression models assessed baseline and longitudinal differences.
Results: At baseline iRBD (mean age 66.57 ± 5.99 years, 17.5% female) exhibited more severe cAF than PD (62.53 ± 8.23 years, 35.0% females), with more frequent neurogenic orthostatic hypotension (nOH – 15.0%vs. 4.0%, $p=0.022$) and abnormal blood pressure responses to CRTs (pathological Valsalva Maneuver – VM overshoot in 47.4% vs. 18.0%, $p=0.001$). The prevalence and severity of cAF was similar between iRBD and PD+RBD (nOH – 20%, $p=0.563$; pathological VM overshoot – 50.0%, $p=0.708$). Longitudinal data demonstrated progressive deterioration of baroreflex function, with increased prevalence of nOH in iRBD and PD+RBD (incident nOH in 4 and 3 patients respectively; yearly odds ratios - OR = 5.47 $p=0.003$ and 2.30 $p=0.046$), not significant in PD-RBD and PD as a whole (OR = 1.80 and 0.99, $p=0.165$ and 0.983). Prevalence of pathological VM overshoot increased only in PD+RBD (OR = 7.83, $p=0.041$).

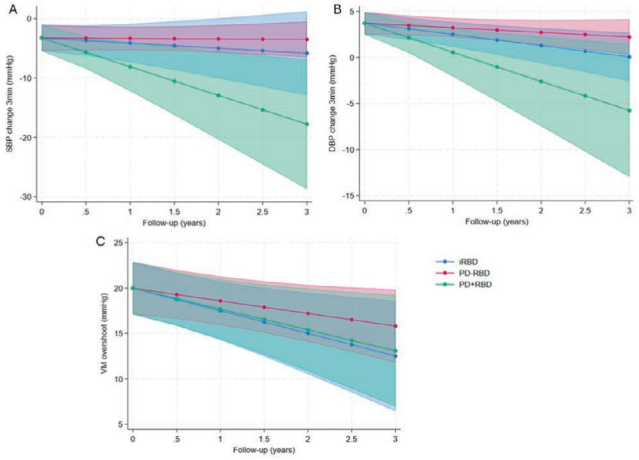

FIGURE 1 Longitudinal model of systolic (A) and diastolic (B) blood pressure change at third minute during tilt test and VM overshoot (C) changes over the years in iRBD, PD patients with (PD+RBD) and without RBD (PD-RBD).

Conclusion: The neurodegeneration underlying cAF is more closely associated with RBD than with PD phenotype. Autonomic dysfunction worsens over time predominantly in the presence of RBD, regardless of phenoconversion status, highlighting RBD as a key driver of autonomic failure.
Disclosure: Nothing to disclose.

EPR-014 | Types of pain in multiple system atrophy

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Background and aims: Pain affects 87% of individuals with multiple system atrophy (MSA), but which pain types mostly contribute to pain burden remains unclear. Here we estimated the prevalence of different pain types in MSA.
Methods: We analyzed the prevalence of different pain types classified by the King's Parkinson's Disease Pain Questionnaire (KPPQ), and of further putative MSA-specific causes (i.e., coat-hanger pain, pain related to catheterization, bladder infections and spasms, pressure sores, bruises, cold hands and feet) in MSA subjects, who answered a web-based survey in 2023. MSA individuals were matched for gender, age (± 3 years), and disease-duration (± 2 years) with PD subjects and HCs from the King's college who had completed the KPPQ.
Results: Among 264 MSA individuals who accessed our survey, 194 were retained after data cleaning, of which 157 with completed KPPQ. Nocturnal (73%), musculoskeletal (63%), fluctuation-related pain (62%) and, among MSA-related types, coat-hanger pain (59%), pain related to cold-hands/feet (48%),

and to bruises (44%) occurred most frequently. In the matched subgroup ($n=96$), all pain types were more frequent in MSA compared to HCs, except musculoskeletal pain, which was as frequent in MSA as in HCs (63% vs. 66%, $p=0.722$) but more common in PD than in MSA (78% vs. 63%, $p=0.023$). Orofacial pain was more frequent in MSA compared to PD (32% vs. 12%, $p<0.001$).

Conclusion: Both disease-related (e.g., orthostatic hypotension-related coat-hanger pain) and unrelated (e.g., musculoskeletal) pain types contribute to pain burden in MSA. Tailored tools may help identify disease-specific pain types that may benefit from optimized symptomatic management of core motor and non-motor features.

Disclosure: Nothing to disclose related to the content of this study.

EPR-015 | Sudomotor innervation in al amyloidosis

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Background and aims: Autonomic nervous system (ANS) is often involved in AL amyloidosis patients. Sudomotor innervation (SI) has recently been established as a reliable index of ANS evaluation. The aim of this study was to assess the SI in AL amyloidosis patients.

Methods: This study included forty-eight recently diagnosed consecutive patients (21men) mean age 59.33 (range 46-70 years), and 31 age and gender matched controls (12 men) mean age 56,64 (range46-79 years). Skin biopsy at the distal leg performed in all subjects and stained with PGP 9.5 panaxonal marker. We used a standardized grid of circles superimposed upon the 20x image immunofluorescent specimen to create a simple pattern of circles over the sweat gland. The percentage of nerve fibers crossed circles was used to quantify the SI.

Results: Average SI was significantly lower for the patients: 21.49 ± 12.74 versus 30 ± 8.95, $p=0.002$ (t-test). Patients with intraepidermal nerve fiber density (IENFD) reduction under the lower for their age limits, showed significantly reduced SG density: 18.09 ± 10.98 versus 28.29 ± 13.6, $p=0.007$ (t-test). In contrary autonomic symptoms were not associated with reduced SI 25.86 ± 16.8 versus 19.89 ± 10.81, $p=0.22$ (t-test).

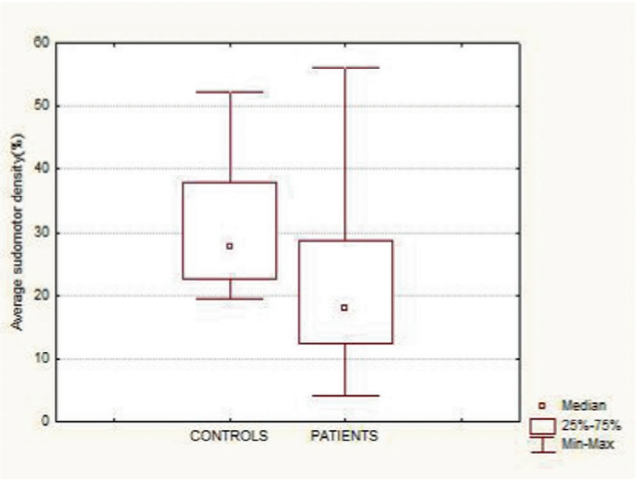

FIGURE 1 Comparison of sudomotor nerve average density in skin biopsy for control and AL amyloidosis patients.

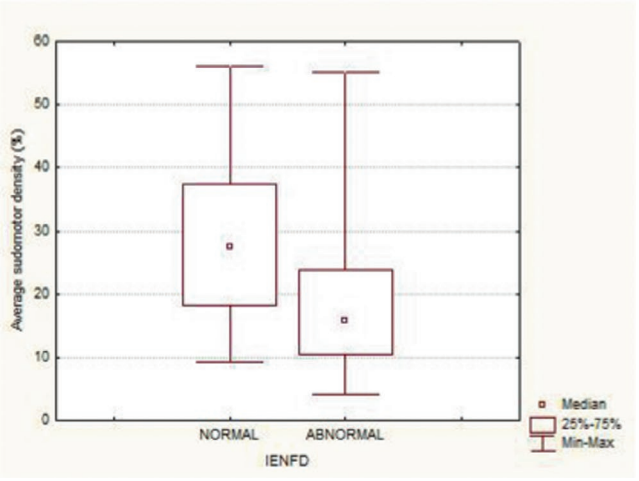

FIGURE 2 Comparison of sudomotor nerve average density for AL amyloidosis patients with normal and abnormal IENFD in skin biopsy

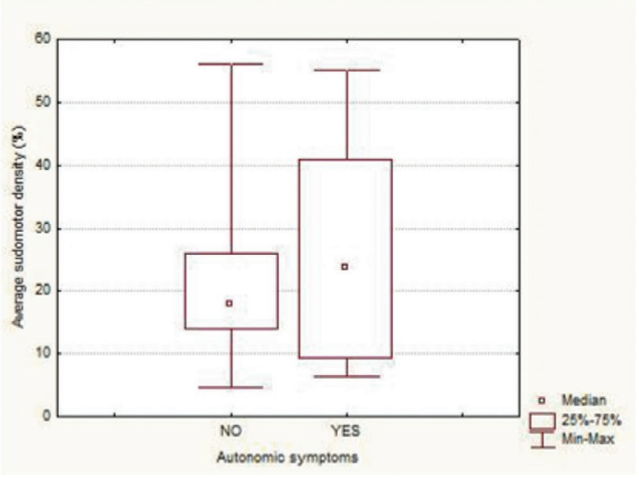

FIGURE 3 Comparison of sudomotor nerve average density in skin biopsy for AL amyloidosis patients with and without autonomic symptoms

Conclusion: SI is significantly reduced in AL amyloidosis patients, specifically those with reduced IENFD, indicating ANS involvement mostly associated with small fiber neuropathy. SI could help with early recognition of small nerve fiber involvement in AL amyloidosis patients and potentially serve as a biomarker for their prognosis.
Disclosure: Nothing to disclose.

EPR-016 | Autonomic cardiovascular reflexes tests in sarcoidosis patients

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Background and aims: Methods The peripheral nervous system is often involved in sarcoidosis, including the autonomic nervous system (ANS). ANS symptoms are mainly associated with small nerve fiber neuropathy (SFN). Most studies investigated heart rate variability (HRV) in patients with sarcoidosis but not the autonomic cardiovascular reflexes tests. The aim of this study was to evaluate the ANS function in patients with sarcoidosis, using the objective Ewing.
Methods: Autonomic cardiovascular reflexes tests (active standing, deep breathing, hand grip and Valsalva maneuver) were performed in 49 patients (24 men) with sarcoidosis mean age 46.52 years (range 29-73). Patients presented mainly with lungs and less cardiac involvement, but without obvious ANS symptoms except in 2 of them.
Results: The reduction of blood pressure below the normal limits during active standing was the most often abnormal finding in 40/49 patients (81.63%). The other tests were mostly normal, but in total 2 or more results were abnormal for 35/49 patients (71.42%), indicating definite ANS dysfunction according to Ewing criteria.

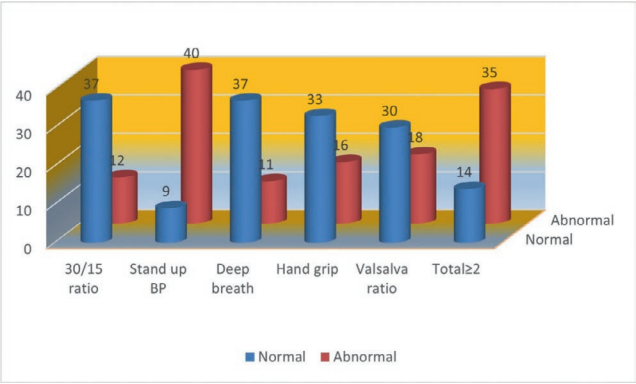

FIGURE 1 The numbers of sarcoidosis patients with normal and abnormal Ewing tests results.

Conclusion: Our results reveal that most sarcoidosis patients present autonomic dysfunction more often than the reports for autonomic symptoms in patients with diagnosis of SFN. The active standing blood pressure reduction has been revealed as the most sensitive Ewing test result for the evaluation of ANS involvement in sarcoidosis. This might serve as a useful biomarker for monitoring as well as for prognosis of the patients with systemic sarcoidosis.
Disclosure: Nothing to disclose.

EPR-017 | Multiple system atrophy associated with postganglionic cardiovascular denervation: A distinct subtype?

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"C. Besta" Neurological Institute, Department of Clinical Neurosciences, Parkinson and Movement Disorders Unit, Milan, Italy.

Background and aims: Cardiovascular autonomic dysfunction in Multiple System Atrophy (MSA) is mostly related to preganglionic degeneration. However, reduced tracer uptake on iodine-123-metaiodobenzylguanidine(123I-MIBG) cardiac scintigraphy, reflecting postganglionic compromise, has been reported in up to one third of MSA patients. Whether these patients have a different phenotype is unclear. The aim of this study was to outline clinical/investigational features and autonomic profile of patients affected by MSA and postganglionic sympathetic denervation.
Methods: A retrospective study on patients affected by MSA, who underwent cardiac 123I-MIBG scintigraphy, was performed. Clinical features, scale scores, MRI markers, plasma catecholamine values, and cardiovascular autonomic tests findings were compared among patients with and without cardiac postganglionic denervation.
Results: Fifty-three patients were included, 42(79.2%) with normal(N) and 11(20.8%) with reduced(R) cardiac sympathetic innervation. 43 patients had parkinsonian and 10 had cerebellar phenotypes. R was associated with hyposmia (patient-reported). Heart rate variability analysis showed that patients with R had reduced LF/HF (low frequencies/high frequencies) ratios while standing on tilt-test. A sub-analysis on patients with MSA-P diagnosis confirmed the association between R and hyposmia; patients with MSA-P and N had more severe and earlier incidence of dysphagia. Other variables examined were comparable among groups.
Conclusion: Postganglionic cardiovascular denervation in patients affected by MSA was associated with self-reported hyposmia, atypical for MSA. Preganglionic degeneration was associated with earlier dysphagia, congruent with "pure" MSA. Patients with R had reduced LF/HF while standing on tilt-test, reflecting sympathetic dysfunction. MSA associated with postganglionic sympathetic denervation may therefore constitute a distinct subtype, but the underlying mechanism remains unclear and needs further investigation.
Disclosure: The authors declare no disclosure.

EPR-018 | Autonomic challenges reveal recovery of cardiovascular autonomic dysfunction three and six months after stroke

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Background and aims: Stroke may cause cardiovascular autonomic dysfunction (CAD). We previously showed that CAD at rest may recover within days. It is unclear whether autonomic challenge-maneuvers uncover post-stroke CAD after several months. Therefore, we assessed cardiovascular autonomic modulation in stroke patients during autonomic challenges within one week, three and six months after stroke-onset.
Methods: In 65 patients with ischemic stroke [26 women, mean age 64.2 ± 8.6 years, median NIHSS 1], we recorded RR-intervals (RRI), systolic, diastolic blood-pressure (BPsys, BPdia), and respiration during metronomic-deep-breathing (MDB), Valsalva-maneuver, and standing-up within one week, three and six months after stroke-onset. We calculated E/I-ratios, Valsalva-ratios, and 30/15-ratios. Values lower than the age-dependent reference values of our laboratory were considered abnormal.
Results: Within one week, three and six months after stroke-onset, E/I-ratios were abnormal in 9/65, 3/65, and 3/65 patients respectively; Valsalva-ratios were abnormal in 4/65, 0/65, and 0/65 patients respectively, 30/15-ratios were abnormal in 2/65, 1/65, and 1/65 patients respectively. Three months after stroke, E/I-ratios, Valsalva-ratios, and 30/15-ratios were significantly higher than the respective values assessed within the first week after stroke. Six months after stroke, Valsalva-ratios and 30/15-ratios also were higher than the respective values of the first week assessment.
Conclusion: The autonomic challenge-maneuvers unveiled CAD only in rather few patients, probably due to the low stroke-severity. MDB was most sensitive and demonstrated post-stroke CAD in 13.8% of patients during the first week, in 6.2 % three and six months after stroke. Valsalva-ratios and 30/15-ratios upon standing-up were less sensitive but also showed CAD-recovery after three and six months.
Disclosure: Nothing to disclose.

Cerebrovascular diseases 1

EPR-019 | Symptomatic intracerebral hemorrhage and CSF biomarkers in cerebral amyoid angiopathy

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[1]Cerebrovascular Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy; [2]Dipartimento di Matematica, Politecnico di Milano, Milan, Italy; [3]Neuropathology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy; [4]Neuroradiology Unit, Fondazione IRCCS Istituto Neurologico Carlo Besta, Milan, Italy; [5]Department of Biomedical and Clinical Sciences, University of Milan, Italy

Background and aims: Cerebral amyloid angiopathy (CAA) typically presents as lobar intracerebral hemorrhage (ICH) or cognitive impairment. The Boston criteria 2.0 are highly accurate in the setting of hemorrhagic phenotypes but yield a much lower diagnostic value in non-hemorrhagic CAA cases. Cerebrospinal fluid (CSF) biomarkers may provide valuable supportive evidence.
Methods: We collected prospective clinical, radiological data along with molecular CSF biomarkers (amyloid-beta-40, amyloid-beta-42, t- Tau, p-Tau, amyloid-beta-42/amyloid-beta-40 and p-Tau/amyloid-beta-42 ratio) from a cohort of CAA patients recruited in our cerebrovascular outpatient clinic. Patients were divided into two groups (CAA-ICH+ and CAA-ICH-, respectively), based on whether they had a symptomatic lobar ICH before the lumbar puncture.
Results: Fifty-four patients were included: 35 CAA-ICH+ and 19 CAA-ICH- (male 62.86% vs. 47.37%, $p = 0.42$, mean age 63.37 vs. 67.79, $p = 0.13$, respectively). Mean age at lumbar puncture was not significantly different (63.80 vs. 67.89, $p = 0.17$, ICH+ vs. ICH-). The number of patients with cognitive impairment was similar in ICH+ and ICH- groups (57.14% vs. 47.37% $p = 0.68$, respectively). Levels of CSF amyloid-beta-42, t-Tau, p-Tau and the ratios of amyloid-beta-42/amyloid-beta-40 and p-Tau/amyloid-beta-42 were comparable in the two groups. However, the mean value of CSF amyloid-beta-40 in CAA-ICH+ was significantly lower than in CAA-ICH- (4701.45 vs. 6651, $p = 0.0016$).
Conclusion: Overall patients with CAA are characterized by low levels of CSF Abeta-40 and Abeta-42. Interestingly, patients who suffered a symptomatic lobar hemorrhage showed lower CSF Abeta-40 levels compared to non-hemorrhagic cases. CSF biomarkers levels could support the diagnosis of non-hemorrhagic CAA cases and stratify the hemorrhagic risk.
Disclosure: Nothing to disclose.

EPR-020 | Monogenic stroke in the young-age stroke in Skåne study

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Background and aims: Our previous studies indicated that 47% of patients with a stroke before age 56 have a positive family history of stroke. Monogenic conditions may play an important role for these groups of patients.
Methods: Since January 2021, our database includes patients under 56 years of age at their first stroke episode. We recruit patients from Skåne Region who were in contact with our hospital. We collect information on their vascular risk factors (hypertension, diabetes mellitus, hypercholesterolemia, heart disease, history of smoking), clinical stroke characteristics and comorbidities. Medical records for both living and deceased family members are reviewed whenever available. Affected and unaffected family members from selected probands are also included. All persons included in the study are examined by one neurologist (the first author). Blood samples are collected from all participants. Whole genome sequencing (WGS) is performed and analyzed using our updated Stroke Gene Panels.
Results: Until December 2024, 187 probands were included in the study, 39% over 49 years and 61 % were men. The etiology

remained "undetermined embolic" for 40% of them, while 5% had non-genetic causes related to secondary anti-phospholipidic syndrome, exposure to toxic substances, paramalignant syndrome, malignancy or cerebral vasculitis. WGS data of 114 probands with heredity for stroke or for similar vascular diseases with the proband or without classical vascular risk factors is analyzed.

Conclusion: We show clinical and genetic data of a larger group of patients with early stroke, systematically included under 4 years interval. Results from 50 patients were previously published, PMID:39498567.

Disclosure: Nothing to disclose.

EPR-021 | Single-cell RNA-seq analysis reveals ferroptosis of venous endothelial cells in cerebral amyloid angiopathy

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Background and aims: CAA is an age-related cerebral small vessel disease (CSVD) defined by β-amyloid (Aβ) deposition in cortical and leptomeningeal vessels. The integrity of both the structure and function of the neurovascular unit is critical for the efficient clearance of excess Aβ accumulated in the brain. Characteristics of cerebrovascular cells in CAA remain poorly understood at single-cell resolution due to their sparsity and dispersion.

Methods: Purified microvessels from the cerebral cortex of three groups of 11-month-old male APP23 transgenic mice and age- and sex-matched wild-type C57BL6J mice were collected for single-cell RNA sequencing (scRNA-seq) analysis. Our findings were verified using western blotting and immunofluorescence.

Results: A total of ~26,000 cerebrovascular cells across 8 subtypes were captured, categorized into three meta clusters, including endothelial cells (arteries, veins and capillaries), mural cells (smooth muscle cells and pericytes), and immune cells (microglia, monocytes and B/NK cells). Endothelial cells (ECs) were particularly decreased in the APP23-Tg group. Functional enrichment analysis indicated the exclusively activated ferroptosis in venous ECs, especially in the APP23-Tg group. Western blotting and immunofluorescence further validated our findings. Intercellular communication network indicated the intense crosstalk between venous ECs and microglia. Mechanically, elevated Il1b from microglia binds to the Il1r1 of venous ECs in the APP23-Tg group to stimulate the downstream NF-κB signaling pathway, leading to ferroptosis of venous ECs.

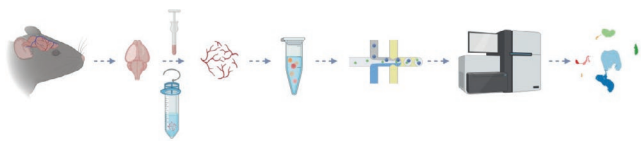

FIGURE 1 Single cell RNA-Seq reveals ferroptosis of venous endothelial cells

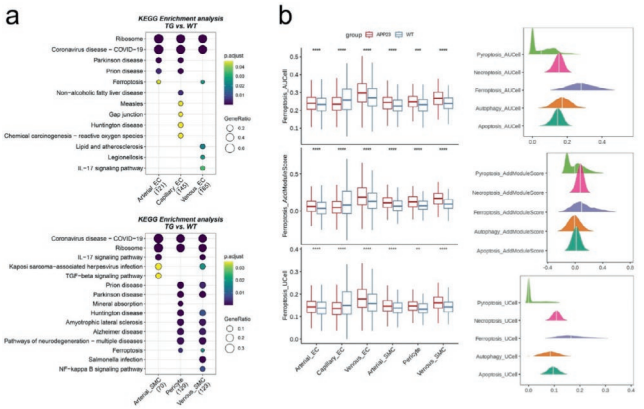

FIGURE 2 Results

Conclusion: Our study discovered the occurrence of ferroptosis in cerebral venous ECs in a CAA animal model, and targeting this process may offer a promising therapeutic strategy.

Disclosure: Nothing to disclose.

EPR-022 | Pentraxin 3 and stroke: A systematic review and meta-analysis

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[1]Faculty of Medicine, University of Indonesia, Jakarta, Indonesia; [2]Department of Neurology, dr Cipto Mangunkusumo National Hospital, Jakarta, Indonesia

Background and aims: Pentraxin 3 (PTX3), a key component of the long pentraxin family, has emerged as a novel biomarker in inflammatory and vascular diseases. Unlike C-reactive protein (CRP), PTX3 is produced locally at sites of inflammation, making it a more specific indicator of vascular injury and immune response. Recent studies suggest PTX3 plays a critical role in cerebrovascular pathology, particularly in stroke. Elevated PTX3 levels have been associated with worse stroke severity and poor functional outcomes. As a potential predictor of stroke prognosis, PTX3 could provide valuable insights for risk stratification and targeted therapeutic interventions.

Methods: A systematic review was conducted using five databases (Pubmed, Proquest, Scopus, Cochrane, and Clinical Key–MEDLINE) and individual searches on 20th January 2025. Keywords include ("Stroke" OR "Cerebrovascular Accident" OR "Cerebrovascular Disorders") AND ("Pentraxin-3" OR "PTX3").

Results: After removing duplicates, we obtained 613 articles from databases and individual searches. After undergoing abstract and full-text screening, this study discussed 9 articles with various results of pentraxin–3. From the combined 7,030 samples, we found a significant mean difference between the PTX–3 level of stroke patients and non-stroke patients (1,48; 95% CI 1,38–1,58) with an overall effect Z-score 21.01 (p-value < 0.0001). Pentraxin–3 was also found having a significant effect on mortality rate based on various studies (z score 6.01; 95% CI 5.96–6,06; p-value < 0.001).

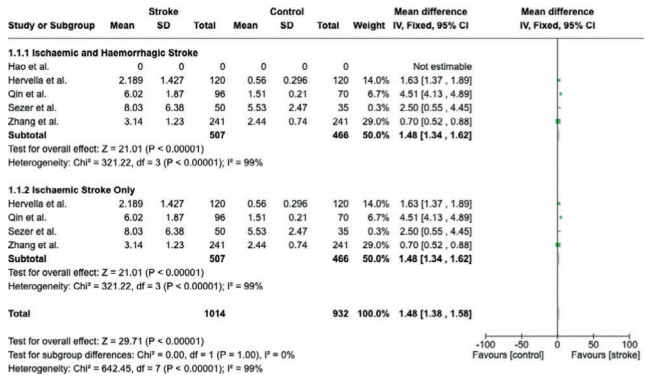

FIGURE 1 Meta-analysis of mean differences between PTX–3 of stroke and non-stroke patients

Fixed and Random Effects

	Q	df	p
Omnibus test of Model Coefficients	54970.505	1	< .001
Test of Residual Heterogeneity	75.614	2	< .001

Note. *p*–values are approximate.
Note. The model was estimated using Fixed Effects method.

Coefficients

					95% Confidence Interval	
	Estimate	Standard Error	z	p	Lower	Upper
intercept	6.011	0.026	234.458	< .001	5.961	6.061

Note. Wald test.

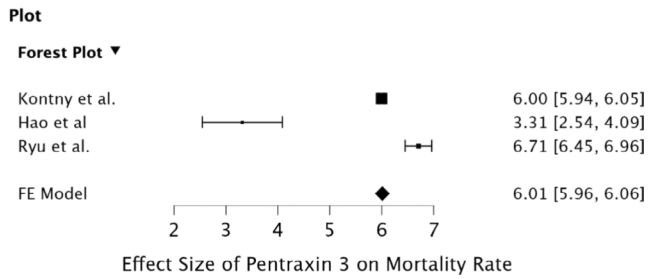

FIGURE 2 Meta–analysis of PTX–3 effect on mortality rate based on various studies

Conclusion: This is the first systematic review and meta-analysis of pentraxin–3 effect on stroke. Our findings suggest that PTX–3 serves as a novel and reliable predictor for stroke outcome.

Disclosure: Nothing to disclose.

EPR-023 | Cortical excitability continuum in ALS: The MEP/CMAP ratio as a prognostic and phenotypic stratification marker

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a heterogeneous neurodegenerative disease characterized by progressive motor neuron degeneration. Cortical excitability, ranging from hyperexcitability to hypoexcitability, is increasingly recognized as a driver of disease progression and a potential prognostic marker. The motor-evoked potential (MEP)/compound muscle action potential (CMAP) ratio offers a clinically accessible measure to assess upper and lower motor neuron function. This study aimed to evaluate the clinical utility of the MEP/CMAP ratio in stratifying ALS patients by phenotype, disease stage, and survival.

Methods: This multicenter, retrospective study analyzed 743 ALS patients from 16 Italian tertiary referral centers. The MEP/CMAP ratio, recorded from upper limb muscles, was categorized into hyperexcitable, normal, and hypoexcitable states. Patients were classified into classical ALS, bulbar, flail arm/leg, lower motor neuron, pyramidal, and primary lateral sclerosis phenotypes. Disease staging followed the King's clinical system, and survival was analyzed using Kaplan–Meier and Cox proportional hazards models.

Results: The MEP/CMAP ratio significantly differed across ALS phenotypes ($p<0.0001$), with hyperexcitability predominant in LMN, flail, classical, and bulbar ALS, while hypoexcitability was more common in pyramidal and PLS phenotypes. Hypoexcitability increased with advancing disease stages ($p<0.0001$). Hyperexcitable patients had shorter survival ($p=0.003$), with a significant difference even within the first year ($p=0.006$). Cox regression confirmed MEP/CMAP ratio as an independent survival predictor (HR = 1.82, 95% CI: 1.2–2.74, $p=0.006$).

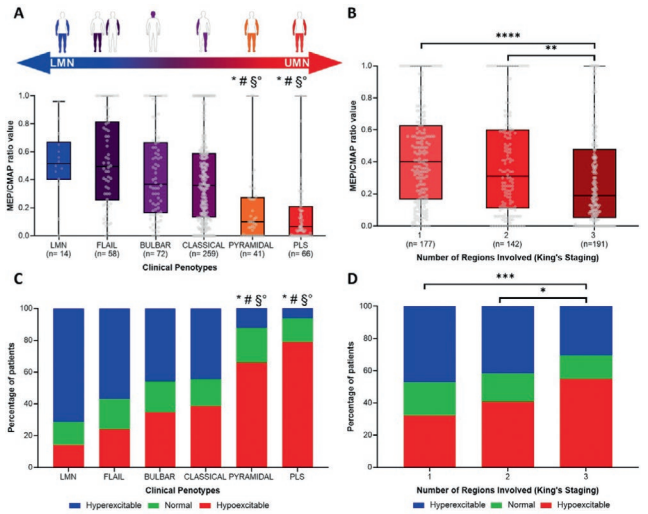

FIGURE 1 Cortical excitability spectrum across region spreading and phenotypes in ALS

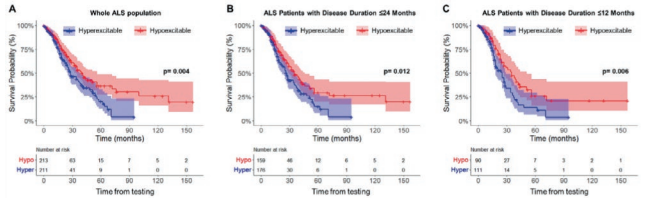

FIGURE 2 Kaplan–meier survival analysis of ALS patients stratified by cortical excitability

Conclusion: The MEP/CMAP ratio is a valuable biomarker for stratifying ALS patients, supporting its integration into routine clinical practice to enhance personalized disease management.
Disclosure: Nothing to disclose.

EPR-024 | Occludin as potential predictor of outcome in acute ischemic stroke: Preliminary results from the NIMBLE study

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Background and aims: Identifying biomarkers that could predict functional outcomes is crucial in acute ischemic stroke (IS) management. The NIMBLE Study aimed to integrate clinical and preclinical stroke research to identify such biomarkers, both serological and neuroradiological, and their interactions. In this preliminary analysis, we evaluated the association between serological biomarkers and the three-month functional outcome of acute IS patients.
Methods: Monocentric prospective observational study set in Careggi University Hospital enrolling consecutive patients with acute (≤12 hours) anterior circulation IS. Serological biomarkers (pro-and anti-inflammatory cytokines and chemokines, metalloproteases and their inhibitors, endothelial dysfunction markers, and tight junction proteins) were obtained at basal and 24 hours. Three-month mRS >2 was considered an unfavorable outcome.
Results: We enrolled 213 patients, median age was 80 years, 46% women, median baseline NIHSS was 10. Recanalization treatment was administered to 150 patients. Higher presenting basal NIHSS, higher pre-stroke mRS, atrial fibrillation and higher baseline occludin levels independently predicted 3-months poor outcome (p-value, OR [95% CI]: $p=0.028$, 3.28 [1.13 – 9.48]; $p<0.001$, 1.14 [1.08-1.20]; $p<0.001$, 3.23 [2.01-5.19]; $p=0.004$, 5.65 [1.74-18.35], respectively).
Conclusion: Our preliminary results show that higher baseline levels of occludin appear to predict clinical outcomes after IS, along with other well-known clinical prognostic factors. Rapid measurement of occludin could help integrate this biomarker into decision-making algorithms for recanalization therapies and therapeutic management. Ongoing analyses are evaluating the association between occludin and neuroradiological markers of IS complications, such as hemorrhagic transformation and cerebral edema.
Disclosure: Nothing to disclose.

EPR-025 | Surgical outcome of cerebral amyloid angiopathy-related cerebral hemorrhage—A multicenter comparative study

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Background and aims: Neurosurgeons are reluctant to perform surgery for lobar intracerebral hemorrhages (ICH) associated to cerebral amyloid angiopathy (CAA) due to a suspected high risk of postoperative rebleeding. Diagnosis of CAA is increasing with an aging population and external Edinburgh criteria validation on computed tomography (CT) scan. We assessed the postoperative risk of CAA-ICH compared to non-related CAA-ICH.
Methods: We included patients admitted between 2008 and 2022 for spontaneous lobar ICH who underwent surgery at three university hospitals. A single-blinded neuroradiologist analyzed the Edinburgh criteria on the initial CT scan before surgery and assessed rebleeding on a repeat CT scan performed within 48 hours after surgery. Patients were classified into the "CAA group" according to the Edinburgh or Boston criteria, and into the "non-CAA group" if they had another cause of ICH.

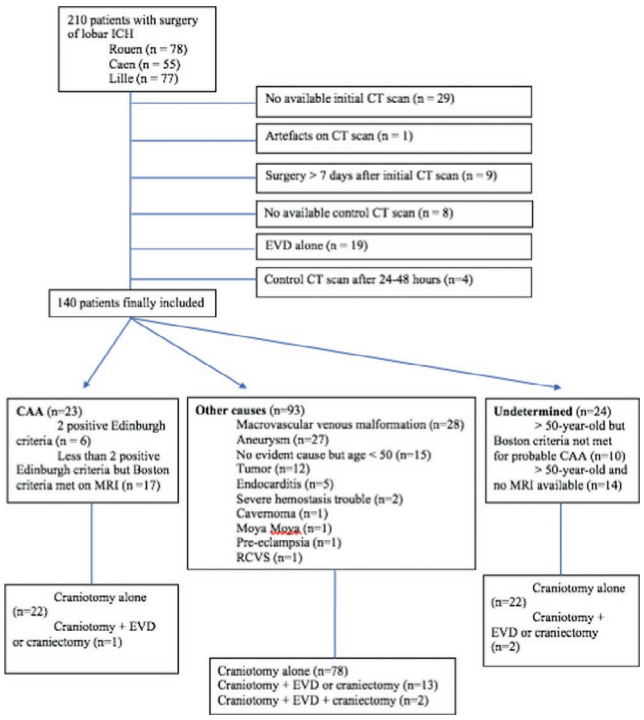

FIGURE 1 Flowchart

Results: A total of 140 patients were included, with 23 in the CAA group, 93 in the non-CAA group, and 24 in the undetermined group. The postoperative rebleeding rate at 24-48 hours did not differ significantly between groups (13% in the CAA group vs. 15% in the non-CAA group, $p > 0.99$). The overall rate of rebleeding associated with clinical deterioration did not differ between groups (9% in the CAA group vs. 6% in the non-CAA group, $p = 0.66$).

TABLE 1 Demographics and pre-operative information in the three groups.

	Total (n=140)	CAA (n=23)	Non CAA (n=93)	Undetermined (n=24)	p
Medical history					
Age at ICH (years), mean ± SD	52,9 ± 14,6	60,4 ± 8,20	48,4 ± 15,3	63,2 ± 6,0	>0.99
Men, No.	78 (56%)	16 (70%)	50 (54%)	12 (50%)	0.17
Chronic hypertension, No.	60 (43%)	15 (65%)	29 (31%)	16 (67%)	<0.003
Tobacco use, No.	38 (27%)	10 (43%)	20 (22%)	8 (33%)	<0.032
Alcohol consumption, No.	21 (15%)	6 (26%)	10 (11%)	10 (11%)	0.09
Vascular history, No.	25 (16%)	8 (22%)	8 (8%)	9 (31%)	<0.004
Active cancer or hematologic disease	11 (7%)	1 (4%)	9 (8%)	1 (3%)	0.23
BMI > 30, No.	24 (17%)	6 (26%)	14 (15%)	4 (17%)	0.23
Previous well-known cognitive impairment, No.	0	0	0	0	
Previous ICH, No.	0	0	0	0	
Antiplatelet use, No.	17 (12%)	7 (30%)	6 (6%)	4 (17%)	<0.004
Anticoagulant use, No.	20 (14%)	4 (17%)	9 (10%)	7 (29%)	0.29
Combined antiplatelet and anticoagulant use, No.	5 (4%)	2 (9%)	2 (2%)	1 (4%)	0.18
Initial features					
Hemostasis disorder, No.	14 (10%)	2 (9%)	10 (11%)	2 (8%)	>0.99
GCS before sedation, No.	34 (24%)	0	29 (31%)	5 (21%)	<0.001
3-6	67 (48%)	14 (61%)	39 (42%)	14 (58%)	
7-12	26 (19%)	9 (39%)	14 (15%)	3 (13%)	
13-14	13 (9%)	0	11 (12%)	2 (8%)	
15					
Initial radiological characteristics					
Edinburgh criteria	67 (48%)	10 (43%)	46 (49%)	11 (46%)	0.65
Subarachnoid hemorrhage, No.	11 (8%)	7 (30%)	3 (3%)	1 (4%)	<0.001
Finger-like projections, No.	9 (6%)	7 (30%)	2 (2%)	0	<0.001
Both, No.					
Initial hematoma volume (mm3), mean ± SD	51,1 ± 18,6	57,6 ± 20,8	49,0 ± 18,9	52,6 ± 21,8	0.11
Initial main axis (mm), mean ± SD	68,1 ± 17,3	70,7 ± 15,7	66,7 ± 18,3	71,0 ± 14,8	0.29
Topography of ICH	55 (39%)	10 (43%)	37 (40%)	8 (33%)	0.83
Frontal, No.	40 (29%)	6 (26%)	29 (31%)	5 (21%)	
Temporal, No.	33 (24%)	6 (26%)	17 (18%)	10 (42%)	
Parietal, No.	8 (6%)	1 (4%)	6 (6%)	1 (4%)	
Occipital, No.	3 (2%)	0	3 (3%)	0	
Insular, No.	1 (1%)	0	1 (1%)	0	
Corpus callosum, No.					

TABLE 2 Postoperative outcome in the three groups

	Total (140)	CAA (n=23)	Non CAA (n=93)	Undetermined (n=24)	p
Median duration of sedation, days (IQR)	5,5 (1 ; 14)	5 (1 ; 10)	6 (1 ;12,5)	2 (2 ; 20,5)	0.62
GCS at sedation removal, No.	6/121 (5%)	0	4/80 (5%)	2/20 (10%)	0.43
3-6	13/121 (11%)	4/21 (19%)	8/80 (10%)	1/20 (5%)	
7-12	31/121 (26%)	6/21 (29%)	18/80 (23%)	7/20 (35%)	
13-14	71/121 (59%)	11/21 (52%)	50/80 (53%)	10/20 (50%)	
15					
Time in intensive care, (days), mean ± SD	22,7± 19,0	28,8± 29,4	20,2± 16,5	22,6 ± 16,3	0.27
Post operative main axis after evacuation (mm), mean ± SD	30,1 ± 18,4	29,1 ± 18,0	31,2 ± 18,2	28,8 ± 21,2	0.66
Rebleeding at 24-48h, No.	21 (15%)	3 (13%)	14 (15%)	4 (17%)	>0.99
Delayed rebleeding 48h-7 days, No.	3 (2%)	1 (4%)	2 (2%)	0	0.49
Symptomatical rebleeding within 7 days, No.	9 (38%)	2 (50%)	6 (38%)	1 (25%)	0.66
Operating site rebleeding within 7 days, No.	17 (71%)	2 (50%)	12 (75%)	3 (13%)	0.73
New surgery (EVD or craniectomy) after rebleeding, No.	4 (3%)	0	4 (4%)	0	0.58
New surgery (EVD or craniectomy) after high	8 (6%)	0	7 (8%)	1 (4%)	0.34

Conclusion: We did not find a significant difference in the postoperative rebleeding rate after ICH associated with CAA compared to other causes.

Disclosure: Nothing to disclose.

EPR-026 | Changes in management of intracerebral hemorrhage over 7 years in a population-based stroke registry

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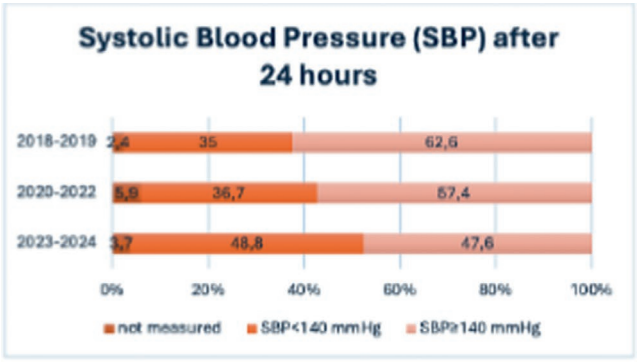
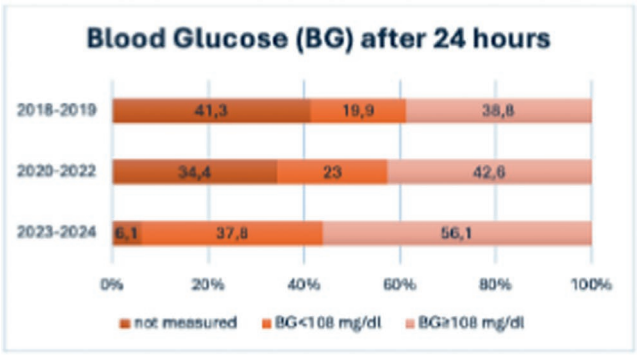
Background and aims: Comprehensive care bundles including rapid blood pressure management, anticoagulation reversal, neurosurgical consultation, control of blood glucose and body temperature, can improve short- and medium-term outcomes in patients with intracerebral hemorrhage (ICH). This study assessed how the acute management of ICH practices evolved in a real-world setting over seven years characterized by global changes in ICH care.

Methods: This study analyzed key clinical parameters of ICH management—blood pressure, blood glucose, body temperature—from a population-based stroke registry (2018-2024) which were classified into three periods: 2018-2019, 2020-2022, and 2023-2024, reflecting the evolution of the "bundle of care" approach to ICH.

Results: We included 545 patients with ICH (55.4% male, median age 75.4 years, interquartile range 69-85). After 24 hours from ICH, the proportion of patients with blood pressure control (systolic blood pressure < 140 mg/dl) improved from 35.0% in the 2018-2019 period, to 36.7% in the 2020-2022 period, and to 48.8% in the 2023-2024 period ($p = 0.069$); the proportion of patients with blood glucose control (< 108 mg/dl) after 24 hours from ICH increased from 19.9%, to 23%, to 37.8% ($p < 0.001$); the proportion of patients with normal body temperature (< 37.0*C) increased from 53.9%, to 61.3%, to 80.5% ($p < 0.001$). Those changes had an impact on 30-day survival after ICH which changed from 65.5% in the 2018-2019, to 64% in the 2020-2022, to 78% in the 2023-2024 period ($p = 0.045$).





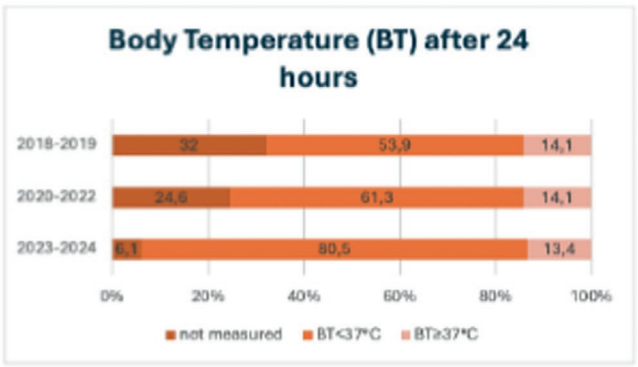


FIGURE 1 Parameters of intracerebral hemorrhage management at 24 hours from symptom onset during the three study periods (2018-2019, 2020-2022, 2023-2024)

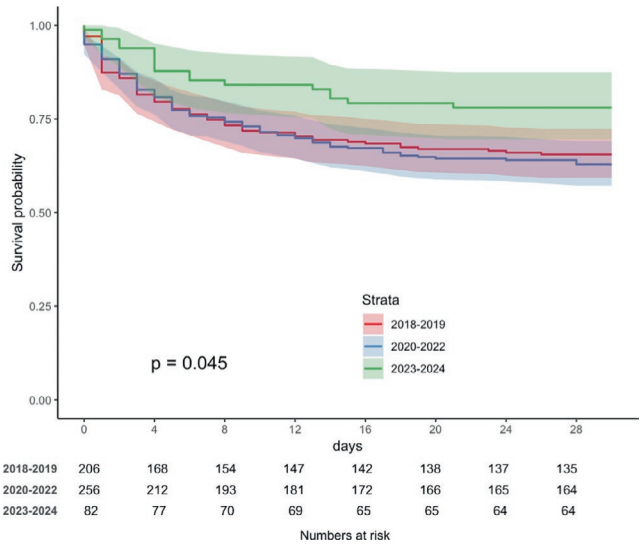


FIGURE 2 Thirty-day case fatality rates during the three study periods (2018-2019, 2020-2022, 2023-2024)

Conclusion: This real-world study demonstrates improvements over time in parameters of acute ICH management with consequent improvements in early prognosis.
Disclosure: Nothing to disclose.

EPR-027 | Clinical and neuroimaging implications of anterior temporal pole white matter hyperintensity in CADASIL

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Background and aims: White matter hyperintensity (WMH) in anterior temporal pole is the hallmark feature of cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL). This study investigates clinical and radiographic differences in CADASIL patients with and without anterior temporal pole WMH.
Methods: This retrospective cross-sectional study included 518 genetically confirmed CADASIL patients from Taipei Veterans General Hospital. Clinical characteristics, cerebral microbleeds (CMBs), lacunes, and WMH volumes were analyzed. WMH burden was assessed using WMH/intracranial volume (WMH/ICV) ratios. Statistical analyses included chi-squared and Student's t-tests.
Results: Among the 518 patients, epidermal growth factor-like repeats (EGFr) 1–6 mutations were more frequently associated with anterior temporal pole WMH than EGFr 7–34 ($p = 2.6\times10\text{^}10$). Patients with anterior temporal pole WMH had significant higher prevalence of stroke, cognitive decline, and headaches ($p < 0.05$). Additionally, patients with anterior temporal pole WMH were more likely to have worse disability (modified Rankin Scale >=3, $p = 0.02$), more lacunes ($p = 5.1x10\text{^} -8$), higher Fazekas scores at periventricular regions and deep white matter ($p = 1.4x10\text{^} -21$ and $7.9x10\text{^} -20$), and greater WMH/ICV ratios ($p = 1.7x10\text{^} -23$). The same analyses were conducted in 429 patients with p.R544C, the most common mutation in Taiwan. It revealed consistent trends and significant differences between patients with or without anterior temporal pole WMH.

TABLE 1 Clinical and neuroimaging features of CADASIL patients.

N (%) or Mean ± SD (range)	All cases (N=518)		P value	p. R544C (+) cases (N=429)		P value
	Anterior temporal WMH (+) N=253	Anterior temporal WMH ( ) N=265		Anterior temporal WMH (+) N=182	Anterior temporal WMH ( ) N=247	
Clinical history						
Onset age	58.4±11.0	59.2±9.8	P=0.414	60.6±9.5	59.8±9.5	P=0.471
Stroke events	0.9±1.1	0.6±0.9	P=0.001**	0.9±1.0	0.6±0.9	P=0.001**
Subjective cognitive decline	126 (50.6)	103 (39.5)	P=0.011**	96 (53.0)	94 (38.7)	P=0.003**
Headache	45 (17.9)	76 (29.1)	P=0.003**	31 (17.0)	73 (30.0)	P=0.002**
Psychiatric features	58 (23.2)	43 (16.5)	P=0.059	43 (23.8)	35 (14.5)	P=0.015**
Seizure[a]	5 (3.1)	11 (5.9)	P=0.217	3 (2.5)	10 (5.7)	P=0.251
Dependent mRS[a]	39 (26.3)	24 (15.8)	P=0.035**	25 (28.7)	23 (16.2)	P=0.024**
Fazekas scale of WMH						
Deep	2.8±0.5	2.1±1.1	$P=7.93x10^{-26}$**	2.8±0.5	2.1±1.1	$P=1.22x10^{-17}$**
Periventricular	2.7±0.5	1.9±1.1	$P=1.40x10^{-23}$**	2.7±0.5	2.0±1.1	$P=1.46x10^{-19}$**
Brain MRI features						
WMH volume (ml)	71.0±35.8	37.2±35.2	$P=1.02x10^{-27}$**	68.9±34.8	37.6±35.6	$P=4.67x10^{-17}$**
WMH/ICV ratio (%)	5.2±2.7	2.7±2.5	$P=1.72x10^{-22}$**	5.0±2.6	2.7±2.6	$P=3.41x10^{-17}$**
CMBs count[a]	35.6±58.7	26.1±57.6	P=0.112	36.3±57.4	25.4±57.1	P=0.095
Lacune number	9.8±11.1	5.0±7.6	$P=5.10x10^{-8}$**	9.1±8.8	4.9±7.6	$P=7.86x10^{-7}$**

Abbreviations: WMH, white matter hyperintensity; mRS, modified Rankin Scale; ICV, intracranial volume; CMBs: cerebral microbleeds.
[a]Information of seizure were available in 350, 266 and 386 patients for seizure, dependent modified Rankin sale (mRS 3-5), and cerebral microbleeds (CMBs), respectively in total population. Information of seizure were available in 297, 229 and 319 patients for seizure, dependent modified Rankin sale (mRS 3-5), and cerebral microbleeds (CMBs), respectively in p.R544C mutation population.
*Chi-square test or Fisher exact test for categorical variables and Student's t- test for continuous variables.
**P value<0.05

Conclusion: Anterior temporal pole WMH is significantly associated with higher burden of MRI markers of small vessel disease and worse clinical outcomes in CADASIL patients. Further studies are needed to assess its long-term impact.
Disclosure: None.

Pain

EPR-028 | The role of dopamine in peripheral mechanisms of migraine: insight from DAT-HET rat model

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Background and aims: Dopamine is considered to play role in the pain transmission in the central nervous system. However, the role of dopamine in regulation of trigeminal-vascular system, a source of migraine-related pain signals, has not been investigated. The aim of study was to evaluate the nociceptive activity of meningeal afferents and the effects of classic algogen serotonin in DAT-HET rats with decreased expression of dopamine transporter (heterozygous rats from DAT-KO).
Methods: Electrophysiological recordings of action potentials (APs) from V1 branch of trigeminal nerve after serotonin (20 μM) application were conducted using isolated half-skull rat preparation with intact dura mater (male rats, P 40-45, wild type (WT) and DAT-HET groups).
Results: In WT group, serotonin increases AP frequency from 275 ± 53 to 486 ± 114 APs ($p = 0.004$, $n = 12$), (Fig. 1A) after 5 minutes and to 711 ± 153 APs after 20 minutes of application ($p = 0.002$, $n = 12$). Peak AP value of serotonin effect was 762 ± 156 APs ($n = 12$, $p = 0.002$), (Fig. 1B). In DAT-HET group, the baseline AP frequency was higher compared to control group and serotonin increased AP frequency from 624 ± 130 to 750 ± 149 APs ($n = 6$) after 5 minutes and to 1228 ± 575 APs after 20 minutes ($n = 6$). The peak value of AP during serotonin application was 1765 ± 527 APs per 5 minutes ($n = 6$, $p = 0.036$).

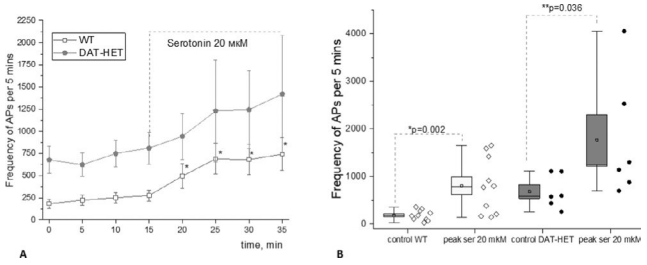

FIGURE 1 Effects of serotonin on AP frequency in trigeminal afferents of WT and DAT-HET rats: A – Dynamics of AP frequency before and during serotonin application; B – Peak frequency of APs after serotonin application compared to baseline control ($p < 0.05$).

Conclusion: Thus, DAT-HET rats demonstrated higher rate of AP generation, which proposes higher excitability of nociceptive afferents. Serotonin demonstrated pro-nociceptive effects in both control and DAT-HET groups.
Disclosure: This study was supported by Russian Science Foundation #23-15-00328.

EPR-029 | Capsaicin 8% completely blocks activation of polymodal nociceptors by heat, but only marginally by slow depolarization

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Background and aims: This study aimed to evaluate (i) the effect of topical capsaicin on mechanical activation of polymodal nociceptors; (ii) sensitization of C-nociceptors outside the capsaicin-denervated skin area; (iii) the differential temporal recovery of capsaicin-induced sensory impairments.
Methods: Two 8% capsaicin patches were applied to the volar forearm skin of 15 healthy human volunteers and renewed for 4 consecutive days. Subjects were assessed weekly over 84 days for pain NRS (0-10) and axon reflex flare (Moor LDI) after electrical, thermal and mechanical impact stimulation, within and just outside the capsaicin treated skin sites. Single electrical sinusoidal (0.5 sec, 1 Hz) and continuous 4 Hz sinusoidal stimuli (2.5 and 60 sec) were used to activate polymodal and silent C-nociceptors.
Results: Capsaicin abolished heat pain and axon reflex flare responses, partially blocked pain by slow depolarizing stimuli, but had only negligible effects on mechanical impact pain. Sinusoidal pain and in particular flare responses showed a slow temporal recovery during 84 days. Acute secondary punctate hyperalgesia was reported during the initial application phase of capsaicin but lasting hypersensitivity around the application sites was not found.
Conclusion: We did not evidence for increased axonal transport into non-treated branches of nociceptors that could sensitize the skin surrounding the capsaicin application site. However, our results suggest that there are differential back-up mechanisms for transduction of heat, slow depolarizing electrical stimuli and mechanical impact stimuli in polymodal nociceptors. The specificity of evoked pain tests to assess nociceptor excitability may provide clinically major implications.
Disclosure: Nothing to disclose.

EPR-030 | Gabapentinoids use and abuse in the neuropathic pain unit setting

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Background and aims: The gabapentinoids (GBPs) pregabalin and gabapentin are increasingly prescribed for various clinical conditions. However, concerns about their potential for misuse

and abuse have emerged in recent years. Given their approved and off-label uses, it is essential to identify patients at risk for such issues.

Methods: In this ongoing observational study, we assess the efficacy and safety of GBPs in a Neuropathic Pain Unit. Patients referred to the Department of Human Neuroscience at Sapienza University of Rome are being recruited and evaluated using a structured questionnaire addressing the main aspects of the GBPs treatment: anamnestic information, comorbidities, the pain condition related to the GBP prescription, S-DN4, treatment information, adverse event, efficacy, and use disorder.

Results: As of now, 119 patients have been enrolled (median age 61, IQR 52-72; 41 males, 77 females). Most patients were diagnosed with peripheral neuropathy (50%), fibromyalgia (19%), or radiculopathy (16%). Of these, 93 were prescribed pregabalin and 26 gabapentin. Seventy-eight patients (57%) reported adverse events, mainly somnolence (47%), confusion (29%), and dizziness (22%), though 89% did not discontinue treatment due to these effects. Patients' pain relief ratings were: much improved (35.6%), minimally improved (26.3%), or unchanged (22.9%). Notably, 9.2% of patients showed signs of GBPs use disorder, and 13.4% reported taking the medication differently than prescribed.

Conclusion: Although patient recruitment is ongoing and final data will be presented at the congress, these early findings suggest that the risk of misuse and developing use disorder should be considered when prescribing GBPs in a neuropathic pain setting

Disclosure: Nothing to disclose.

EPR-031 | Spinal cord stimulation for painful diabetic neuropathy: A systematic review and meta-analysis

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Background and aims: Painful diabetic neuropathy (PDN) is a debilitating diabetes complication that severely impacts quality of life. Conventional treatments often provide inadequate relief. Spinal cord stimulation (SCS) has emerged as a promising option, but its efficacy and safety require further evaluation.

Methods: We conducted a systematic review and meta-analysis of randomized controlled trials (RCTs) and prospective observational studies on SCS for PDN. A comprehensive database search identified 19 studies: 3 RCTs with follow-up studies (312 patients) and 13 observational studies (245 patients). Outcomes included pain reduction, quality-of-life improvements, and adverse events.

Results: Meta-analysis of RCTs revealed a significant reduction in pain with SCS compared to conventional medical management (CMM) ($p < 0.00001$; MD: -5.29, 95% CI: -5.84 to -4.73). At 6 months, 72.5% of SCS-treated patients achieved ≥50% pain relief, compared to only 4.7% in the CMM group ($p < 0.00001$; RR: 14.86, 95% CI: 6.98–31.63). SCS also led to a significant 14.13% improvement in EQ-5D utility scores ($p < 0.00001$) and enhanced patient-reported outcomes. Both RCTs and observational studies showed a 50.99% reduction in pain from baseline at 6 months ($p < 0.00001$; MD: 50.99, 95% CI: 47.55–54.44), with 72.4% of SCS-treated patients achieving ≥50% pain relief at 6 months and 57.7% maintaining this response at 12 months.

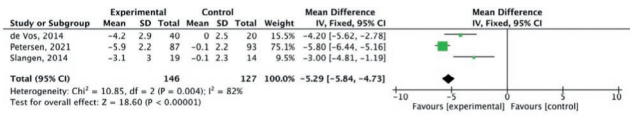

Figure 1. Pain reduction of VAS scores at 6 months follow-up of RCTs.

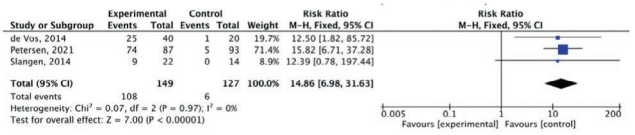

Figure 2. Patients with >50% pain reduction at VAS scale of RCTs.

FIGURE 1 Pain reduction.

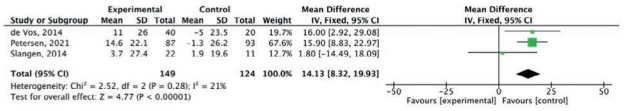

Figure 3. Improvement of EQ-5D utility scores at 6 months follow-up of RCTs.

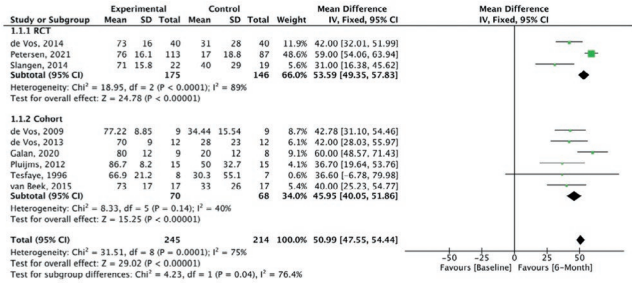

Figure 4. VAS scores at 6 months compared to the baseline of Cohort and RCTs.

FIGURE 2 Pain reduction and quality of life improvement.

Conclusion: SCS offers significant pain relief and quality-of-life improvements in PDN. While observational studies suggest durable benefits, large-scale RCTs with extended follow-up are needed to establish SCS as a standard treatment.

Disclosure: Nothing to disclose.

EPR-032 | The periaqueductal gray density, glymphatic dysfunction, emotional and sleep disorders in patients with chronic pain

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Background and aims: Chronic pain (CP) is a complex process that is influenced by sleep and emotional disorders, and vice versa. Sleep disturbances and CP negatively affect brain homeostasis by reducing glymphatic clearance. Additionally, CP reorganizes the brain structures involved in emotional state and pain modulation. The periaqueductal gray (PAG) plays an important role in anxiety, depression and sleep disorders, as well as brain waste clearance due to its high aquaporin-4 expression.

Methods: 28 patients with CP (CPgroup) and 20 age-match controls were examined by using various questionnaires, polysomnography and neuroimaging studies (table 1).

TABLE 1 Research methods.

Examined patients (CP group)	Patients with chronic primary and secondary musculoskeletal pain
Four-Dimensional Symptom Questionnaire (4DSQ)	Assessment of distress, depression, anxiety and somatization,
Spiegel Sleep Questionnaire (SSQ)	Consisting of 28 items, the SQS evaluates six domains of sleep quality: daytime symptoms, restoration after sleep, problems initiating and maintaining sleep, difficulty waking, and sleep satisfaction.
Visual Analogue Scale (VAS)	Measuring pain intensity
Polysomnography with quantitative EEG spectral power analysis	Measuring patterns of brain activity during NREM and REM sleep.
MRI voxel-based morphometry (VBM)	Assessment of structural changes in various brain structures In addition to standardized MRI morphometry, manual segmentation of the periaqueductal gray matter (PAG) was performed with assessment of its signal intensity.
Diffusion Tensor Image Analysis ALong the Perivascular Space (DTI-ALPS) method with analysis of the ALPS index	Assessment of the glymphatic system (GS)

Results: CPgroup had a higher score on the 4DSQtotal as well as on distress, depression, anxiety and somatization subscales compared to controls (table 2). Both objective and subjective indicators of sleep disturbance were worse in the CPgroup. Slow-wave activity significantly declined especially over frontal regions during NREM with an increase in α-band power over the parietal regions during REM sleep in CPgroup (figure 2). Neuroimaging revealed an increase in PAG density and a decrease in the ALPS index in CPpatients compared to controls. PAG density had positive correlation with 4DSQ and VAS and negative correlation with the ALPS index and sleep disturbance indicators (figure 3).

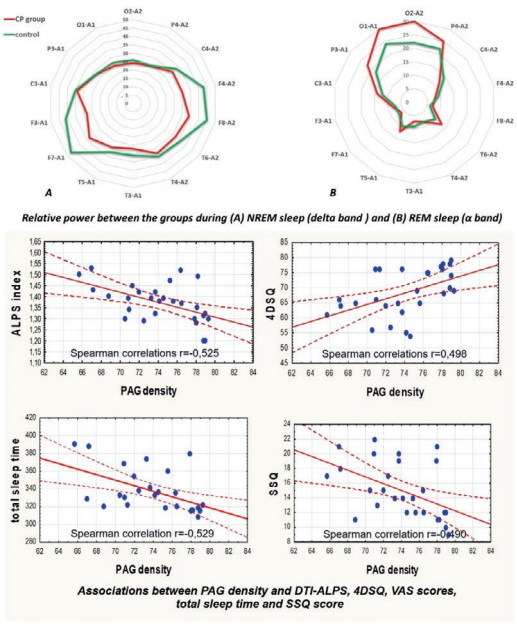

FIGURE 1 Graphical representation of the obtained results

TABLE 2 Comparative assessment of examined patients with chronic pain and controls.

Parameters	CP Group n = 28	Control Group n = 20
	Median (IQR)	
Age, years	49 (44 – 56)	50 (44 – 54)
Men / Women	13/15	9/11
Disease duration (months)	21 (9 – 28)	-
Visual Analogue Scale	4 (4 – 6)	-
4DSQ total	65 (56 – 76)	36 (27 – 46) *
Distress	22 (20 – 25)	13 (10 – 16) *
Depression	6 (2 – 8)	2 (2 – 5) *
Anxiety	12 (7 – 15)	7 (5 – 9) *
Somatization	25 (17 – 28)	13 (10 – 16) *
Spiegel Sleep Questionnaire	14 (10 – 20)	20 (17 – 24) *
	Polysomnography	
Total sleep time (min)	333 (316 - 378)	376 (341–422)*
Sleep onset latency (min)	33 (15 - 58)	15,3 (12,7–18,4)*
Duration of sleep stages (percentage of total sleep time)		
N1 %	12,1 (8,0 – 13,4)	8,8 (7,1–10,5)
N2 %	53,7 (47,4 – 58,8)	52,5 (45,9–57,3)
N3 %	13,2 (11,7 – 18,5)	18,3 (15,0–22,7)*
REM%	21,7 (18,1 – 25,9)	19,5 (17,8–25,2)
MRI morphometry PAG density	73,3 (67,3 – 78,8)	62,5 (58,9 - 74,6) *
DTI-ALPS index (left)	1,39 (1,32 – 1,48)	1,57 (1,41 – 1,68)*
DTI-ALPS index (right)	1,43 (1,31 – 1,52)	1,62 (1,43 – 1,67)*

* - **p ≤ 0,05** - Significant differences between the CP Group and Control (Mann-Whitney test)
DTI-ALPS - Diffusion tensor image analysis along the perivascular space

Conclusion: The relationship between PAG density and emotional changes, pain severity and sleep parameters, as well as glymphatic clearance, indicates that PAG participates in pain chronicity. Therefore, targeting PAG can be considered one of the promising methods for CP treating.
Disclosure: The authors declare that they have no conflict of interest.

EPR-034 | Distinguishing small fiber neuropathy and fibromyalgia-related small fiber pathology: Insights from SKIN BIOPSY Analysis

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Background and aims: Small fiber neuropathy and fibromyalgia syndrome frequently share overlapping clinical features, including reduced intraepidermal nerve fiber density, as assessed by skin biopsy. Clinical observations suggest that the reduction in intraepidermal nerve fiber density is generally more severe in small fiber neuropathy than in fibromyalgia, which is commonly classified as a small fiber pathology. This study aimed

to compare the severity of intraepidermal nerve fiber density reduction in patients with small fiber neuropathy and those with fibromyalgia-related small fiber pathology, and to evaluate whether the difference could aid in distinguishing between the two conditions.

Methods: We retrospectively analyzed data from 132 patients diagnosed with small fiber neuropathy and 180 patients diagnosed with fibromyalgia, including 73 with diagnosed intraepidermal nerve fiber density reduction. The severity of intraepidermal nerve fiber density reduction was compared between the 132 patients with small fiber neuropathy and the 73 with fibromyalgia-related small fiber pathology.

Results: We found that the reduction in intraepidermal nerve fiber density was significantly more severe in patients with small fiber neuropathy compared to those with diagnosed fibromyalgia-related small fiber pathology. ROC analysis showed that a reduction exceeding 38% relative to normative ranges, while having relatively low sensitivity (48%), had high specificity (94%) and positive predictive value (94%) for identifying small fiber neuropathy.

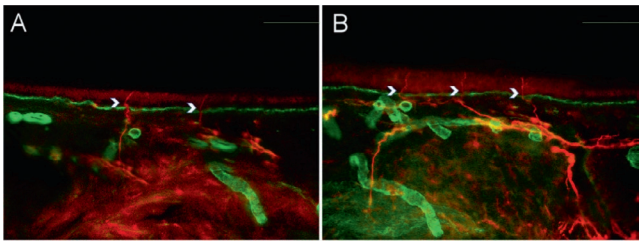

FIGURE 1 Intraepidermal nerve fiber density in small fiber neuropathy and small fiber pathology.

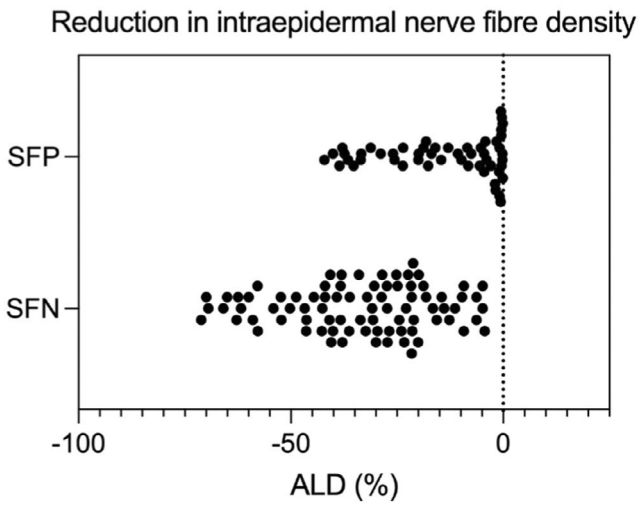

FIGURE 2 Reduction in intraepidermal nerve fiber density in patients with fibromyalgia and small fiber neuropathy.

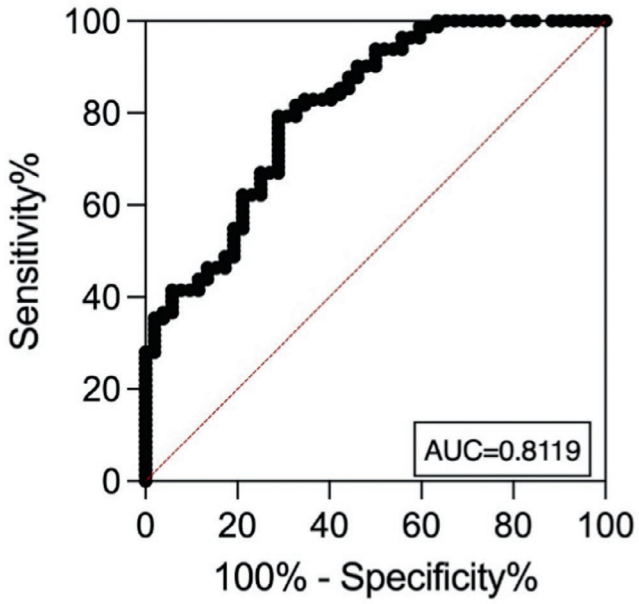

FIGURE 3 ROC curve for the accuracy of intraepidermal nerve fiber density reduction for distinguishing fibromyalgia-related small fiber pathology and small fiber neuropathy.

Conclusion: Our study demonstrated that intraepidermal nerve fiber density reduction is more severe in small fiber neuropathy than in fibromyalgia syndrome. A reduction exceeding 38% relative to normative ranges is a reliable indicator of small fiber neuropathy.

Disclosure: Nothing to disclose.

Headache 1

EPR-036 | Home-based biofeedback therapy for migraine prevention in episodic migraine: A randomized, waitlist-controlled trial

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Background and aims: This study evaluated the efficacy and safety of a new medical device for therapist-independent biofeedback for preventing episodic migraine in adults.

Methods: This was a nation-wide, open-label, randomized, waitlist-controlled multicenter trial in Norway. Participants were randomly assigned (1:1) to daily biofeedback sessions via the "Cerebri" medical device or waitlist control. The primary endpoint was the change in the mean number of migraine days from baseline to the last 28 days during the 12-week treatment phase. The primary analysis was conducted on the intent-to-treat population. ClinicalTrials.gov (NCT05616741).

Results: 279 were randomized to receive Cerebri treatment ($n=140$) or control ($n=139$). Mean age (female percentage) were 41.9 years (92.9%) in the biofeedback group, and 40.6 years (91.4%) in the control group. Baseline migraine days averaged 4.8 in the biofeedback group and 4.6 in the control group. At Weeks 9–12, the Cerebri group had a reduction of 0.9 days (95% CI -1.4 to -0.5), with no significant change in the control group (95% CI -0.5 to 0.4). The between-group difference was -0.9 days (95% CI -1.5 to -0.3, $p=0.002$). 30% responder rates were 44.3% for Cerebri versus 29.9% for control (OR 1.86, $p=0.033$). Among 140 participants, there were 139 treatment-emergent adverse events (AEs): 132 unrelated, 5 possibly related, and 2 causally related (pruritus, lightheadedness). Two unrelated serious AEs occurred (appendicitis, menorrhagia).

Conclusion: The "Cerebri" biofeedback treatment is a safe and effective non-pharmacological preventive treatment for adults with episodic migraine.

Disclosure: The Sponsor of the study is Nordic Brain Tech AS (contact information: info@nordicbraintech.com), a spin-off company from The Norwegian University of Science and Technology (NTNU) and St. Olavs Hospital in Norway. The company was founded in 2019 to commercialize a research-based intervention for treating migraines using remote biofeedback. The sponsor has no role in data collection, analysis, and interpretation of data and has no authority pertaining to publication of results. The coordinating investigator has access to the final trial data set. No contractual agreement limits this access. Data management according to the data management plan is conducted by the sponsor. Nordic Brain Tech AS, NTNU, and The Central Norway Regional Health Authority may benefit financially from the commercialization of the proposed treatment. A commercial license agreement exists between Nordic Brain Tech AS and NTNU Technology Transfer AS on the commercialization of the treatment. EAT, AO, AS are cofounders and shareholders of Nordic Brain Tech AS. EAT, AO, AS and ML hold a patent related to the Cerebri invention described in this study. In addition, EAT, AO, AS, and ML are coinventors of the proposed treatment in this study and may benefit financially from a license agreement between Nordic Brain Tech AS and NTNU. ACP, ESK, MHB, LRØ, ICKL, KGV and TWM have no ownership interest and does not own stocks of Nordic Brain tech AS or other companies developing biofeedback treatment.

EPR-037 | BIOmarkers of MIGraine response to erenumab (BIOMIGA project): Preliminary assessment of the structural MRI study

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Background and aims: The BIOMIGA project aimed to identify multimodal biomarkers predicting response to erenumab, an anti-CGRP monoclonal antibody, in subjects with migraine. To do a preliminary analysis of the structural neuroimaging data comparing healthy controls with people with migraine and, within, this latter group, responders with non-responders to ereneumab.

Methods: After preregistration (clinical trials: NCT04503083) data were collected in three European headache centers (Italy, Spain, Germany). T1 3D images were acquired with 3T MRI scanners at baseline and after a 3-month treatment with erenumab. Patients were classified as responders if a reduction ≥50% monthly headache/days was achieved. Matched healthy subjects were assessed as a control group. Images were analyzed with FreeSurfer to assess cortical thickness differences.

Results: The population consisted of 155 subjects living with migraine and 78 matched healthy subjects. At baseline, in the right hemisphere, people living with migraine exhibited a statistically significant increased cortical thickness in regions such as the subparietal sulcus, precuneus, and posterior ventral cingulate gyrus compared to controls. Similarly, in the left hemisphere, regions such as the intraparietal sulcus and precuneus showed significant cortical thickening, as presented in Table 1. After the 3-month treatment, no significant differences in cortical thickness were detected when comparing responders with non-responders.

Region	Mean Cortical thickness Healthy Controls	Mean Patients living with migraine	F-Value	p-Value	Effect Size
rh_S_subparietal_thickness	2,373	2,408	8,921	0,003	0,722
rh_G_precuneus_thickness	2,512	2,543	8,238	0,005	0,663
rh_G_cingul_Post_ventral_thickness	2,615	2,676	6,490	0,012	0,369
rh_S_oc_sup_and_transversal_thickness	2,128	2,166	5,737	0,017	0,531
rh_G_pariet_inf_Angular_thickness	2,709	2,719	5,086	0,025	0,578
rh_G_subcallosal_thickness	2,578	2,511	4,320	0,039	0,309
rh_G_oc_temp_med_Lingual_thickness	1,984	2,008	3,996	0,047	0,492
rh_S_oc_temp_med_and_Lingual_thickness	2,411	2,428	3,956	0,048	0,477
lh_S_intrapariet_and_P_trans_thickness	2,168	2,203	10,140	0,002	0,044
lh_G_precuneus_thickness	2,522	2,557	9,456	0,002	0,042
lh_G_pariet_inf_Angular_thickness	2,656	2,681	7,739	0,006	0,034
lh_G_cingul_Post_ventral_thickness	2,556	2,612	4,964	0,027	0,022
lh_G_oc_temp_med_Lingual_thickness	1,900	1,931	4,899	0,028	0,022
lh_S_subparietal_thickness	2,318	2,333	4,820	0,029	0,022
lh_Lat_Fis_ant_Vertical_thickness	2,421	2,467	4,514	0,035	0,020
lh_S_oc_sup_and_transversal_thickness	2,114	2,145	4,050	0,045	0,018

Table 1 - Cortical thickness comparison between HC (healthy controls) and people with migraine, regardless of the diagnosis or of treatment response rate. Only statistically significant p values are presented, uncorrected. rh=right hemisphere, lh= left hemisphere. S= sulcus; G= gyrus.

Table 1

Conclusion: Migraine is associated with structural alterations in widespread gray matter regions of the brain. Moreover, the results suggest that 3-month treatment with erenumab is not sufficient to induce structural changes in the cortical regions evaluated. Founding: Biomiga was funded by ERANet Neuron.

Disclosure: DM declares honoraria from Lundbeck and AbbVie HB declares honoraria from Novartis, Teva, Lundbeck and Eli Lilly P.P.-R. declares honoraria from AbbVie, Amgen, Dr Reddy's, Eli Lilly, Lundbeck, Medscape, Novartis, Organon, Pfizer and Teva Pharmaceuticals. Her research group has received research grants from AbbVie, AGAUR, EraNet Neuron, FEDER RIS3CAT, Instituto Investigación Carlos III, MICINN, Novartis, and Teva Pharmaceuticals, and has received funding for clinical trials from AbbVie, Amgen, Biohaven, Eli Lilly, Lundbeck, Novartis, Pfizer and Teva Pharmaceuticals. She is the Honorary Secretary of the International Headache Society,

is on the editorial board of Revista de Neurologia, is an associate editor for Cephalalgia, Headache, Neurologia, Frontiers of Neurology, and is an advisor of the Scientific Committee of the Editorial Board of The Journal of Headache and Pain. CT has received, in the last 3 years, personal fees for the participation in advisory boards or for speaking at sponsored symposia from AbbVie, Eli Lilly, Ipsen, Lundbeck, Medscape, Pfizer, and Teva. Her research group has received research grants from AbbVie, EraNet Neuron, Migraine Research Foundation and competitive grant from the Italian Ministry of Health. Her institution has received payments for clinical trials from AbbVie, Biohaven, Eli Lilly, Ipsen, Lundbeck, Pfizer and Teva. She is past-President of the International Headache Society, Associate Editor of Cephalalgia.

EPR-038 | Fremanezumab initiation at early disease stages may improve migraine outcomes: Post hoc analysis of the PEARL study

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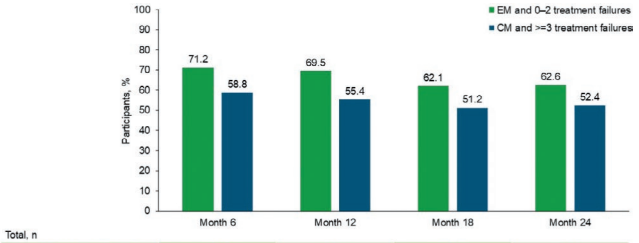
Background and aims: Due to reimbursement limitations, patients with migraine may only have access to preventive treatment with calcitonin gene-related peptide pathway monoclonal antibodies after multiple failures of traditional preventive treatments. PEARL (EUPAS35111) was a 24-month, prospective, observational study that evaluated the effectiveness and safety of fremanezumab for episodic and chronic migraine (EM, CM) prevention.

Methods: This post hoc analysis evaluated the impact of migraine type (EM, CM) and prior preventive treatment failures (0–2 or >=3) on the proportion of participants with a >=50% reduction in monthly migraine days (MMD) during the 6-month period following fremanezumab initiation (PEARL primary endpoint). In addition, a multivariate logistic regression model was used to identify independent variables associated with treatment response.

Results: Overall, 1128 participants (EM, $n=374$; CM, $n=754$) were included. During the 6-month treatment period, a >=50% reduction in MMD was achieved in 68.4% of participants with EM and 0–2 treatment failures, compared with 50.5% of participants with CM and >=3 treatment failures; this trend was observed over 24 months (Figure 1). Factors associated with a higher likelihood of achieving a 50% reduction in MMD were EM versus CM and no prior use of onabotulinumtoxinA (Table 1).



Total, n				
EM and 0–2 treatment failures	153	154	153	139
CM and >=3 treatment failures	500	500	492	441

CM, chronic migraine; EM, episodic migraine; MMD, monthly migraine days.
CM was defined as >=15 headache days/month for >3 months, >=8 of which meet migraine criteria; EM was defined as >=4 migraine days/month.
The drop in data at post-baseline time-points is due to participants who prematurely discontinued the study. Missing data are excluded.

Figure 1. Proportion of participants achieving >=50% reduction in MMD at Months 6, 12, 18 and 24 by migraine type and number of previous treatment failures

Variable	Odds Ratio	Lower 95% CI	Upper 95% CI	Wald Chi-Square	p-value
Migraine (EM/CM)	1.785	1.285	2.478	11.9646	0.0005
History of depression or anxiety (no/yes)	1.399	0.977	2.003	3.3664	0.0665
OnabotulinumtoxinA as premedication (no/yes)	1.542	1.125	2.113	7.2644	0.0070

CI, confidence interval; CM, chronic migraine; EM, episodic migraine; MMD, monthly migraine days.
A higher odds ratio indicates a stronger association with achieving a 50% reduction in MMD.

Table 1. Multivariate logistic regression with migraine type, depression or anxiety at baseline, and onabotulinumtoxinA premedication at baseline as independent variables

Conclusion: This analysis suggests a trend toward enhanced effectiveness of fremanezumab in patients with EM and fewer prior treatment failures, compared with CM and more treatment failures. Further prospective research is needed to fully interpret and confirm a true causal relationship.

Disclosure: MA: AbbVie, Amgen, AstraZeneca, Eli Lilly, GlaxoSmithKline, Lundbeck, Novartis, Novo Nordisk Foundation, Pfizer, Teva Pharmaceuticals. DDM: Allergan, Amgen, Bayer, Biogen, Cefaly, electroCore, Eli Lilly, Genesis Pharma, Merck Serono, Merz, Mylan, Novartis, Roche, Sanofi Genzyme, Specifar, Teva Pharmaceuticals. PPR: AbbVie, AGAUR, Amgen, Biohaven EraNet NEURON, Chiesi, Eli Lilly, Lundbeck Instituto Investigación Carlos III, MINECO, Novartis, Pfizer, RIS3CAT FEDER, Teva Pharmaceuticals. CT: AbbVie, Chordate, Dompé, Eli Lilly, Ipsen, Lundbeck, Novartis, Pfizer, Teva Pharmaceuticals, European Commission, Italian Ministry of Health, Migraine Research Foundation. PK, HA: Teva Pharmaceuticals. This study was funded by Teva Pharmaceuticals.

EPR-039 | Real-world effectiveness of fremanezumab in migraine prevention: Final outcomes of the Pan-European PEARL study

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Background and aims: PEARL (EUPAS35111) was a 24-month observational, prospective, Phase 4 study evaluating the real-world effectiveness and safety of fremanezumab for episodic and chronic migraine (EM, CM) prevention. Here we report effectiveness, and treatment adherence and persistence outcomes from the PEARL study after 24 months of follow up.

Methods: Eligible participants were adults with EM or CM receiving fremanezumab for migraine prevention, who maintained a daily headache diary prior to and throughout the study period. The primary endpoint was the proportion of participants with >=50% reduction in monthly migraine days (MMD) during the 6-month period after fremanezumab initiation. Secondary endpoints across Months 1–24 included mean change from baseline in MMD, and treatment adherence (participants who took their prescribed dose within ±5 days of the scheduled monthly/quarterly dosing regimen, per injection) and persistence.

Results: Of 1140 participants enrolled, 1129 were included in the effectiveness analysis (EM, 33.1%; CM, 66.9%; 87.2% female). In participants with available data, 56.5% (637/1128) achieved >=50% MMD reduction from baseline during the 6-month period after fremanezumab initiation (Figure 1). Proportions of participants reaching >=50% reduction in MMD were sustained across Months 1 to 24 (Figure 2), as were reductions in mean MMD (Figure 3). Adherence rates remained high throughout the study (~90%) and 75.6% (854/1129) of participants completed the study.

Participants, n	1128*	374	754

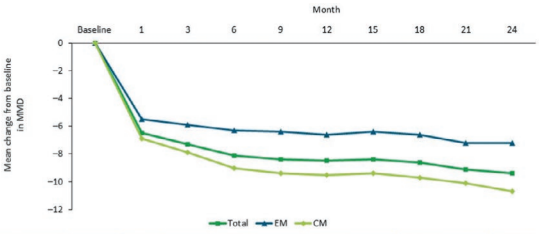
CM, chronic migraine; EM, episodic migraine; MMD, monthly migraine days.
*Of the 1140 enrolled participants, 11 were excluded from the effectiveness analysis set for one or more of the following reasons: baseline visit was unsigned, <4 migraine days in the baseline period were documented, <10 diary entries were documented after the first dose of fremanezumab. One participant from the effectiveness analysis set did not have data available for the primary endpoint.

Figure 1. Proportion of participants reaching >=50% reduction in MMD from baseline during the 6-month period after fremanezumab initiation (primary endpoint), by migraine type

Total participants, N	1125	1121	1115	1105	1111	1107	1100	1101	977
EM participants, n	374	372	372	371	372	373	371	370	327
CM participants, n	751	749	743	734	739	734	729	731	650

CM, chronic migraine; EM, episodic migraine; MMD, monthly migraine days.
The drop in data at post-baseline time-points is due to participants who prematurely discontinued the study. Missing data are excluded.

Figure 2. Proportion of participants reaching >=50% reduction in MMD from baseline at Months 1, 3, 6, 9, 12, 15, 18, 21 and 24, by migraine type



Total participants, N	1129	1125	1105	1062	1017	987	928	888	860	712
Participants with EM, n	374	374	364	351	341	336	321	310	302	255
Participants with CM, n	755	751	741	711	676	651	607	578	558	457

CM, chronic migraine; EM, episodic migraine; MMD, monthly migraine days.
The drop in data at post-baseline time-points is due to participants who prematurely discontinued the study. Missing data are excluded.

Figure 3. Mean change from baseline in the monthly average number of migraine days at Months 1, 3, 6, 9, 12, 15, 18, 21 and 24, by migraine type

Conclusion: These findings underscore the sustained effectiveness and robust adherence of long-term fremanezumab treatment in migraine prevention.

Disclosure: MA: AbbVie, Amgen, AstraZeneca, Eli Lilly, GlaxoSmithKline, Lundbeck, Novartis, Novo Nordisk Foundation, Pfizer, Teva Pharmaceuticals. DM: Allergan, Amgen, Bayer, Biogen, Cefaly, electroCore, Eli Lilly, Genesis Pharma, Merck Serono, Merz, Mylan, Novartis, Roche, Sanofi Genzyme, Specifar, Teva Pharmaceuticals. FMA: AbbVie, Eli Lilly, Lundbeck, Novartis, Pfizer, Teva Pharmaceuticals. CJS: AbbVie, Allergan, Almirall, Amgen, Eli Lilly, Grünenthal, Lundbeck, MindMed, Novartis, Pfizer, Teva Pharmaceuticals, Zynnon, Baasch-Medicus Foundation, Eye on Vision Foundation, German Migraine and Headache Society. GS: AbbVie, Lundbeck, Novartis, Pfizer, Teva Pharmaceuticals, Vinnova, Lund University, Swedish Neurological Association. PPR: AbbVie, Amgen, Biohaven EraNet NEURON, Chiesi, Eli Lilly, Lundbeck, Instituto Investigación Carlos III, MINECO, Novartis, Pfizer, RIS3CAT FEDER, Teva

Pharmaceuticals. PJD: AbbVie, electroCore, Eli Lilly, Lundbeck, Novartis, Pfizer, Teva Pharmaceuticals. TN: AbbVie, Amgen, Eli Lilly, Glenmark, Lundbeck, Neurocrine Novartis, Organon, Pfizer, Teva Pharmaceuticals, UCB. IPM: AbbVie, Allergan, Eli Lilly, Lundbeck, Novartis, Organon, Pfizer, Teva Pharmaceuticals. MLS: AbbVie, Eli Lilly, Lundbeck, Novartis, Pfizer, Teva Pharmaceuticals. CT: AbbVie, Chordate, Dompé, Eli Lilly, Ipsen, Lundbeck, Novartis, Pfizer, Teva Pharmaceuticals, European Commission, Italian Ministry of Health, Migraine Research Foundation. PK, VRC, HA, study funding: Teva Pharmaceuticals.

EPR-040 | Efficacy and safety of eptinezumab in chronic migraine: Randomized controlled trial in a predominantly Asian population

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Background and aims: This phase 3 clinical trial evaluated the efficacy and safety of eptinezumab for preventive migraine treatment in a predominantly Asian population with chronic migraine (CM).
Methods: SUNRISE (NCT04921384) comprised 4 periods: 28-day screening (baseline); 12-week double-blind, placebo-controlled; 12-week dose-blind extension; and 8-week safety follow-up. Adults (18-75y) diagnosed with CM were randomized 1:1:1 to IV eptinezumab 100mg, 300mg, or placebo at baseline. P-values are versus placebo.
Results: Of 983 participants randomized, 939 (95.5%) completed the placebo-controlled period. Participants were 63.5%/36.5% Asian/European with 17.4 mean monthly migraine days (MMDs) at baseline. Both eptinezumab doses met the primary and all key secondary efficacy endpoints. Primary endpoint: The mean change from baseline in MMDs (Weeks1-12) were 7.2 (100mg; $p < 0.0001$), 7.5 (300mg; $p < 0.0001$), and 4.8 (placebo). Key secondary endpoints: Eptinezumab demonstrated > 2-fold higher odds versus placebo for >= 50% (Weeks1-12, $p < 0.0001$) and >= 75% (Weeks1-4, $p < 0.0001$; Weeks1-12, $p < 0.0001$) reduction in MMDs, as well as lower Day 1 migraine rate ($p < 0.01$). Improvements across patient-reported outcomes showed better effect with eptinezumab than placebo. The rate of treatment-emergent adverse events (TEAEs) was comparable across groups (100mg, 37.6%; 300mg, 32.2%; placebo, 33.5%), with few serious TEAEs (<2%) or TEAEs leading to withdrawal (<2%). The most common TEAE was COVID-19 (100mg, 5.5%; 300mg, 4.6%; placebo, 4.3%).
Conclusion: Eptinezumab 100mg and 300mg demonstrated statistically significant greater reductions in monthly migraine days versus placebo in a predominantly Asian chronic migraine population, with efficacy observed as early as Day 1 and sustained through 12 weeks, with a well-tolerated safety profile consistent with previous trials.
Disclosure: Trial sponsored by Lundbeck

EPR-041 | Eptinezumab and patient education in chronic migraine and medication-overuse headache: The randomized RESOLUTION trial

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Background and aims: RESOLUTION was a phase 4 clinical trial to evaluate efficacy and safety of eptinezumab added to a Brief Educational Intervention in patients with chronic migraine (CM) and medication-overuse headache (MOH).
Methods: RESOLUTION (NCT05452239) comprised four periods: 28-day screening (baseline); 12-week double-lind, placebo-controlled; 12-week open-label extension; and 8-week safety follow-up. Adults (18-75y) with CM and MOH (excluding opioid-overuse headache) were randomized (1:1) to infusion with eptinezumab 100 mg or placebo, with all participants receiving Brief Educational Intervention about MOH prior to infusion. The primary endpoint was change from baseline in monthly migraine days (MMDs) across Weeks1-4.
Results: Of 608 participants randomized, 596 (98.0%) completed the placebo-controlled period. Mean MMDs, monthly headache days (MHDs), and monthly acute medication days (MAMDs) in the total population were 20.9, 21.7, and 20.1, respectively, at baseline. The eptinezumab arm met primary endpoint, with mean change from baseline in MMDs (Weeks1-4) of 6.9 versus 3.7 with placebo ($p < 0.0001$); it also met all key secondary endpoints (all $p < 0.0001$ vs. placebo): greater reductions in MMDs (Weeks1-12), MHDs (Weeks1-4, Weeks1-12), MAMDs (Weeks1-4, Weeks1-12), and average daily pain (Weeks1-2) and fewer participants still fulfilling CM and MOH criteria (Weeks1-4, Weeks1-12). The proportion of participants with treatment-emergent adverse events was similar between arms (eptinezumab, 41.9%; placebo, 36.9%).
Conclusion: Eptinezumab was superior to placebo in reducing monthly migraine days, headache days, and acute medication use in patients with CM and MOH also receiving Brief Educational Intervention. These effects were evident across Weeks1-4, sustained across Weeks1-12, and extended to all key secondary endpoints.
Disclosure: Trial sponsored by Lundbeck.

EPR-042 | Long-term safety and effectiveness of rimegepant for the preventive treatment of migraine in Japan

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Background and aims: The aim was to assess the long-term safety and effectiveness of rimegepant (RIM) 75 mg taken up to once daily for up to 40 weeks for migraine in Japan.

Methods: This open-label (OL) extension of a phase 3, randomized, double-blind (DB), placebo (PBO)-controlled study (NCT05399485) included adults in Japan with a history of 4–18 migraine attacks/month of moderate or severe pain intensity. After 12 weeks of DB treatment with RIM 75 mg or PBO every other day (EOD), participants could continue OL treatment for up to 40 weeks, taking RIM 75 mg EOD and additionally as needed on nonscheduled dosing days (maximum 1 dose of RIM 75 mg per calendar day).

Results: Of 496 participants who received DB treatment, 458 participants were treated with OL RIM for a mean (standard deviation) of 37.5 (6.3) weeks. The most common adverse events (AEs) were nasopharyngitis (25.1%) and COVID-19 (13.1%). The rate of AEs leading to RIM discontinuation was 1.3% and the rate of serious AEs was 0.9% (Table 1). There were no deaths. Aminotransferases > 3× the upper limit of normal (ULN) occurred in 4 participants (0.9%); none of these participants had concurrent elevations with total bilirubin > 2× ULN (Table 2). A mean reduction of 4.5 in monthly migraine days from the observation phase was observed through the overall OL phase (Table 3).

	DB RIM, OL RIM n=227	DB PBO, OL RIM n=231	Overall N=458
Any AE	162 (71.4)	175 (75.8)	337 (73.6)
AE occurring in ≥2% of participants			
Nasopharyngitis	51 (22.5)	64 (27.7)	115 (25.1)
COVID-19	32 (14.1)	28 (12.1)	60 (13.1)
Influenza	11 (4.8)	14 (6.1)	25 (5.5)
Back pain	15 (6.6)	9 (3.9)	24 (5.2)
Coronavirus infection	12 (5.3)	10 (4.3)	22 (4.8)
Oropharyngeal pain	11 (4.8)	10 (4.3)	21 (4.6)
Pyrexia	7 (3.1)	12 (5.2)	19 (4.1)
Constipation	9 (4.0)	8 (3.5)	17 (3.7)
Abdominal pain upper	7 (3.1)	8 (3.5)	15 (3.3)
Toothache	8 (3.5)	5 (2.2)	13 (2.8)
Gastroenteritis	6 (2.6)	7 (3.0)	13 (2.8)
Sinusitis	7 (3.1)	6 (2.6)	13 (2.8)
Dental caries	8 (3.5)	4 (1.7)	12 (2.6)
Abdominal pain	6 (2.6)	4 (1.7)	10 (2.2)
Diarrhoea	6 (2.6)	4 (1.7)	10 (2.2)
Stomatitis	6 (2.6)	3 (1.3)	9 (2.0)
Dysmenorrhoea	3 (1.3)	6 (2.6)	9 (2.0)
Alanine aminotransferase increased	4 (1.8)	5 (2.2)	9 (2.0)
Cystitis	4 (1.8)	5 (2.2)	9 (2.0)
Mild AE	127 (55.9)	141 (61.0)	268 (58.5)
Moderate AE	33 (14.5)	33 (14.3)	66 (14.4)
Severe AE	2 (0.9)	1 (0.4)	3 (0.7)
AE related to study drug	23 (10.1)	23 (10.0)	46 (10.0)
AE leading to study drug discontinuation	2 (0.9)	4 (1.7)	6 (1.3)
Serious AE	4 (1.8)	0	4 (0.9)
Serious AE related to study drug	2 (0.9)	0	2 (0.4)
Medication overuse headache AE	0	0	0
Hepatic-related AE	8 (3.5)	7 (3.0)	15 (3.3)
Hepatic-related AE leading to study drug discontinuation	2 (0.9)	1 (0.4)	3 (0.7)
Potential drug abuse AE	10 (4.4)	5 (2.2)	15 (3.3)
Cardiovascular AE	1 (0.4)	2 (0.9)	3 (0.7)
Suicidality AE	0	0	0
Hypertension AE	1 (0.4)	5 (2.2)	6 (1.3)
Raynaud's phenomenon AE	0	0	0

Participants n (%). OL RIM safety analysis set: participants taking ≥1 dose of OL RIM. DB RIM, OL RIM = participants who took RIM in both phases of the study. DB PBO, OL RIM = participants who were allocated PBO in the DB phase then took RIM during the OL phase.
AE=adverse event; DB=double-blind; OL=open label; PBO=placebo; RIM=rimegepant

Table 1: AEs on OL RIM

	DB RIM, OL RIM n=226	DB PBO, OL RIM n=231	Overall N=457
ALT			
>3× ULN	3 (1.3)	1 (0.4)	4 (0.9)
>5× ULN	0	0	0
AST			
>3× ULN	1 (0.4)	0	1 (0.2)
>5× ULN	0	0	0
ALT or AST			
>3× ULN	3 (1.3)	1 (0.4)	4 (0.9)
>5× ULN	0	0	0
TBL			
>1.5× ULN	1 (0.4)	2 (0.9)	3 (0.7)
>2× ULN	0	0	0
ALT or AST >3× ULN concurrent with TBL >2× ULN	0	0	0

Participants n (%) with liver function test data. OL RIM safety analysis set: participants taking ≥1 dose of OL RIM.
Concurrent is on the same collection date. DB RIM, OL RIM = participants who took RIM in both phases of the study.
DB PBO, OL RIM = participants who were allocated PBO in the DB phase then took RIM during the OL phase.
ALT=alanine aminotransferase; AST=aspartate aminotransferase; DB=double-blind; OL=open label; PBO=placebo; RIM=rimegepant; TBL=total bilirubin; ULN=upper limit of normal

Table 2: Liver function test elevations on OL RIM

	DB RIM, OL RIM		DB PBO, OL RIM		Overall	
	Mean (95% CI)	n	Mean (95% CI)	n	Mean (95% CI)	n
Observation phase	9.3 (3.1)[a]	226	9.1 (3.2)[a]	231	9.2 (3.1)[a]	457
Change from OP						
OL month 1 (study weeks >12 to ≤16)	−4.2 (−4.7, −3.7)	219	−4.3 (−4.9, −3.7)	226	−4.2 (−4.6, −3.8)	445
OL month 2 (study weeks >16 to ≤20)	−4.5 (−5.0, −4.0)	224	−4.5 (−5.0, −3.9)	229	−4.5 (−4.9, −4.1)	453
OL month 3 (study weeks >20 to ≤24)	−4.5 (−5.0, −4.0)	223	−4.7 (−5.3, −4.2)	228	−4.6 (−5.0, −4.2)	451
OL month 4 (study weeks >24 to ≤28)	−4.7 (−5.2, −4.2)	220	−4.6 (−5.1, −4.0)	226	−4.7 (−5.0, −4.3)	446
OL month 5 (study weeks >28 to ≤32)	−4.6 (−5.0, −4.1)	214	−4.3 (−4.9, −3.8)	226	−4.4 (−4.8, −4.1)	440
OL month 6 (study weeks >32 to ≤36)	−4.7 (−5.2, −4.3)	213	−4.5 (−5.1, −3.9)	223	−4.6 (−5.0, −4.2)	436
OL month 7 (study weeks >36 to ≤40)	−4.9 (−5.4, −4.4)	213	−4.7 (−5.2, −4.1)	220	−4.8 (−5.1, −4.4)	433
OL month 8 (study weeks >40 to ≤44)	−4.5 (−4.9, −4.0)	209	−4.8 (−5.4, −4.2)	217	−4.6 (−5.0, −4.3)	426
OL month 9 (study weeks >44 to ≤48)	−4.7 (−5.2, −4.3)	205	−4.8 (−5.4, −4.2)	215	−4.8 (−5.1, −4.4)	420
OL month 10 (study weeks >48 to ≤52)	−4.6 (−5.1, −4.1)	204	−4.8 (−5.3, −4.2)	213	−4.7 (−5.1, −4.3)	417
Overall OL	−4.6 (−5.0, −4.2)	226	−4.4 (−4.9, −3.9)	231	−4.5 (−4.8, −4.2)	457

OL RIM migraine analysis set: participants in both the DB migraine and OL RIM efficacy analysis sets with ≥14 days of eDiary efficacy data or non-scheduled OL RIM dosing (not necessarily consecutive) in ≥1 month (4-week interval) in the OL phase.
DB RIM, OL RIM = participants who took RIM in both phases of the study. DB PBO, OL RIM = participants who were allocated PBO in the DB phase then took RIM during the OL phase.
[a] Mean (SD).
DB=double-blind; OL=open label; PBO=placebo; RIM=rimegepant; SD=standard deviation

Table 3: Change in monthly migraine days on OL RIM

Conclusion: Sustained effectiveness was observed in the treatment with OL RIM 75 mg taken up to once daily for up to 40 weeks with a favorable safety profile.

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EPR-043 | Clinical predictors for efficacy of erenumab for migraine: A Registry for Migraine (REFORM) study

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Background and aims: Erenumab is effective for migraine prevention, but many patients experience variable outcomes or no benefit. This study aimed to identify clinical factors associated with therapeutic response to erenumab using data from a large cohort of patients with migraine.

Methods: A single-center, prospective study included 570 adults with ≥4 monthly migraine days, treated with 140 mg of erenumab monthly for 24 weeks. Participants recorded their responses in headache diaries, and outcomes were classified based on achieving a ≥50% reduction in monthly migraine days between weeks 13 and 24. Logistic regression analysis was used to identify clinical factors associated with response.

Results: Among participants, 298 (52.3%) were responders, and 272 (47.7%) were non-responders. Factors associated with a lower likelihood of response included chronic migraine (odds ratio [OR] 0.63), daily headache (OR 0.41), and failure of ≥3 preventive medications (OR 0.54). Conversely, higher age (10-year increase: OR 1.22) predicted better outcomes. Early responders (≥50% reduction within weeks 1–12) were less likely to have chronic migraine, had lower Migraine Disability Assessment Scores, more often experienced unilateral headache, and had lower allodynia scores compared to late responders.

Conclusion: In conclusion, chronic migraine, daily headache, and multiple preventive medication failures were associated with poorer responses to erenumab, while older age predicted better outcomes. Further research is needed to establish the optimal timepoint for evaluating efficacy of erenumab and to integrate novel clinical and biomarker data to enhance predictive accuracy.

Disclosure: WKK and HMA reports receiving personal fees from Lundbeck and Pfizer, outside of the submitted work. MA reports having been a consultant, speaker, or scientific advisor for AbbVie, Amgen, Astra Zeneca, Eli Lilly, GlaxoSmithKline, Lundbeck, Novartis, Pfizer, and Teva. MA also reports being a primary investigator for ongoing AbbVie and Pfizer trials. MA is supported through the Lundbeck Foundation Professor Grant (R310-2018-3711) and serves as an Associate Editor of the Brain and The Journal of Headache and Pain. RHC reports having received a travel grant from the Augustinus Foundation. HA reports receiving personal fees from Lundbeck, Pfizer, and Teva, outside of the submitted work.

EPR-044 | Profiles of migraine patients treated with triptan: A study based on data from the French Nationwide claims database

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Background and aims: Although recommendations for the diagnosis and management of migraine have been published, it is managed in a very heterogeneous way. Here, we describe the profiles and care pathways of migraine patients treated with triptan in France.

Methods: Retrospective cohort study of migraine patients treated with at least one triptan, identified in the 2/100th French Nationwide claims database (ESND) from 2016 to 2021 and analyzed from 2006 to 2022.

Results: Among the 37,884 migraine patients identified, we found that 76% were women. The mean age was 36.6 years at the first triptan. Annual mean number of general practitioner

consultations before and after the first triptan dispensing were 5.4 and 6.1, 2.5 and 3.3 in psychiatry, and 0.3 and 0.5 in neurology. Sick leave concerned 43% and 52% of patients. Preventive migraine treatments were dispensed to 9% of patients within the year before the first triptan dispensing and to 39% after. NSAIDs were dispensed to 52% of patients before and to 89% after. Triptan treatment was permanently stopped within 4 months of dispensing for 39% of patients, while 61% of patients continued it during the follow-up.

Conclusion: We highlight here the heterogeneous management of triptan users and the change of care pathways after the first triptan dispensing.

Disclosure: This research was conducted with support from Orion Pharma. The authors are members of Orion's advisory board XM has received personal fees from Allergan-Abbvie, Aptis Pharma, Biogen, BMS, Grünenthal, HAS, Lilly, Lundbeck, Teva, Merck-Serono, Novartis, Pfizer, Roche, and Sanofi-Genzyme / grants from APICIL, region Auvergne-Rhone-Alpes, contrat Interface Inserm / non-financial support from SOS Oxygène, not related to the submitted work MLM: Personal fees* and research support for FHU InovPain University Côte d'Azur° with: Abbvie/Allergan*, Amgen*°, Astellas*°, ATI*°, BMS°, Biogen°, Boehringer*°, Boston Scientific*, CoLucid°, Convergence°, Glaxo-SmithKline*, Grunenthal*°, Eli Lilly*°, IPSEN*, Lundbeck*°, Medtronic*°, Menari*, MSD*, Novartis*°, Orion Pharma*, Perfood*, Pfizer*°, ReckittBenckiser*, Saint-Jude*, Sanofi-Aventis*, Teva*°, UCB*°, UPSA*, Zambon*; Grants: DGOS (PHRC), ANSM, SFETD, Fondation APICIL, Migraine Foundation JM has received financial supports for boards and meeting presentations from Lilly, Abbvie, TEVA, Lundbeck, Pfizer, Orion Pharma / travel fees for congress from Ipsen Pharmaceuticals, Abbvie, Lundbeck, SOS Oxygen, Dr Reddy's CL has received personal fees from Allergan-Abbvie, Homeperf, Lilly, Lundbeck, Teva, Orion, Pfizer; Past President of the French Headache Society

Movement disorders 1

EPR-045 | Plasma neuronal biomarkers in Parkinson's disease with and without GBA1 mutations: A multicenter study

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Background and aims: Mutations in the GBA1 gene are the most significant genetic risk factor for Parkinson's disease (PD), contributing to lysosomal dysfunction and impaired glucocerebrosidase (GCase) activity, leading to alpha-synuclein accumulation. Limited studies have evaluated the effect of GBA1 mutations on plasma biomarkers of neurodegeneration and glial activation.

Methods: We enrolled 122 PD patients from two Italian centers, including 41 GBA1 mutation carriers and 81 non-carriers. Motor symptoms were assessed using MDS-UPDRS III, and non-motor symptoms with NMSS and MoCA. GCase activity and Lyso-GBA1 levels were measured in a subset of patients. Plasma levels of GFAP, NfL, and pTau181 were quantified using the SIMOA assay.

Results: No significant differences were found in motor features between groups. However, GBA1 carriers exhibited more severe hallucinations, mood disturbances, and cognitive impairment (NMSS domains 3 and 4, $p=0.005$, $p=0.008$). Plasma biomarker levels did not significantly differ between groups. In unadjusted analysis, MoCA scores negatively correlated with NfL and GFAP, with a stronger association in GBA1 carriers (GFAP, $p=0.001$, $\rho = -0.583$; NfL, $p=0.002$, $\rho = -0.542$) compared to non-carriers (GFAP, $p=0.017$, $\rho = -0.416$; NfL, $p=0.075$, $\rho = -0.309$).

Conclusion: GBA1 mutation carriers exhibited a more aggressive non-motor phenotype. However, plasma biomarker levels did not significantly differ between groups. The stronger correlation between clinical features and biomarkers in GBA1 carriers suggests a potential impact of the mutation on disease progression. Larger studies are needed to confirm these findings.

Disclosure: Nothing to disclose.

EPR-046 | Micrographia in Parkinson's disease: Automatic recognition through artificial intelligence

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Background and aims: Parkinson's disease (PD) leads to handwriting abnormalities primarily characterized by micrographia. Whether micrographia manifests early in PD, worsens throughout the disease, and lastly responds to L-Dopa is still under scientific debate. Owing to the biological complexity of human handwriting, innovative technological strategies are warranted to examine micrographia objectively in PD and fill the current knowledge gaps.

Methods: A total of 57 PD patients on chronic L-Dopa treatment were enrolled, including 30 patients in the early stages (H&Y≤2) and 27 in the mid-advanced stages (H&Y > 2), alongside 25 age- and sex-matched controls. Participants completed two standardized handwriting tasks in an ecological scenario. Handwriting samples were examined through clinically-based (i.e., perceptual) and artificial intelligence (AI)-based (automatic) procedures. Consistent (i.e., average stroke size) and progressive micrographia (sequential changes in stroke size) were both evaluated. Receiver operating characteristic (ROC) curves were used to evaluate the accuracy of the convolutional neural network (CNN) in classifying handwriting in PD and controls.

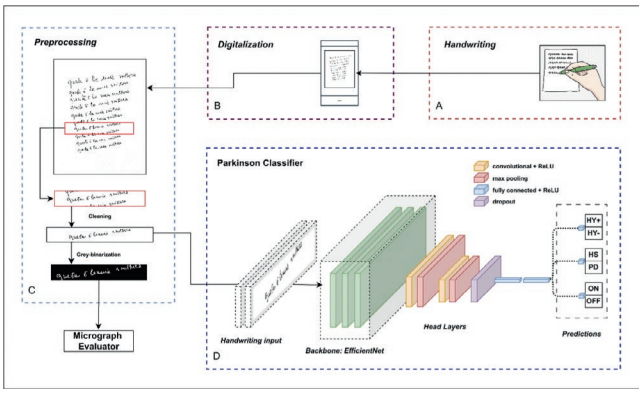

FIGURE 1 Dataset building: (A) Acquisition of handwriting samples. (B) Digitalization of the handwriting samples. (C) Preprocessing of the handwriting samples. (D) Model of deep learning architecture.

Results: Clinically and AI-based analysis revealed a general reduction in stroke size in PD supporting the concept of parkinsonian micrographia. Compared with perceptual analysis, AI-based analysis clarified that micrographia manifests early during the disease, progressively worsens and poorly responds to L-Dopa. The AI models achieved high accuracy in distinguishing PD patients from controls (91%), and moderate accuracy in differentiating early from mid-advanced PD (77%). Lastly, the AI model failed in discriminating patients in OFF and ON states.
Conclusion: AI-based handwriting analysis is a valuable tool for detecting and quantifying micrographia in PD.
Disclosure: Nothing to disclose.

EPR-047 | Optimal cut-off for the mini mental state examination and montreal cognitive assessment in multiple system atrophy

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Background and aims: Mild cognitive impairment (MCI) and dementia are reported in up to 44% and 7% of patients with Multiple system atrophy (MSA), respectively. No study has explored the sensitivity and discriminative power of Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MOCA) to detect MCI and dementia in MSA. We aimed to identify the optimal cut-off of MMSE and MOCA in order to distinguish MSA patients with MCI and dementia from patients with normal cognition (NC). The fluency item of MOCA was also assessed separately for the same purpose.
Methods: Sixty-two MSA patients underwent a comprehensive II level neuropsychological evaluation, in order to diagnose dementia, MCI or NC according to DSM-5. ROC analyses were used to establish the optimal cut-off scores for MMSE, MOCA and fluency item of MOCA for MCI and dementia, respectively.
Results: According to the II level neuropsychological evaluation, 4.8% of MSA patients were demented and 53,2% had MCI (Tab.1). The optimal cut-offs for MMSE to identify dementia (AUC = 0.915) and MCI (AUC = 0.698) were 20.5 and 26.5, respectively. The optimal cut-offs for MOCA to detect dementia (AUC = 0.919) and MCI (AUC = 0.702) were 14.0 and 19.5, respectively ROC analysis suggested that both tests were more accurate to identify MCI than dementia (Fig. 1; Fig. 2). The optimal cut-off for MOCA fluency item to identify MCI was 8.5 words (AUC = 0.717).

TABLE 1 Demographic and clinical characteristics of MSA patients Abbreviations: M, males; MCI, mild cognitive impairment; MMSE, Mini Mental State Examination; MOCA, Montreal Cognitive Assessment; N, number; NC, normal cognition; SD, standard deviation; UM.

(N=62)	
Age, years *(mean± SD)*	61.58±7.48
Education, years *(mean± SD)*	10.05±4.54
Sex, M (%)	31/62 (M,50%)
Disease duration, years *(mean± SD)*	4.61±2.85
UMSARS-I	24.49±7.65
UMSARS-II	24.53±7.58
UMSARS-IV	2.92±0.90
MMSE, *(mean± SD)*	25.42±3.73
MOCA, *(mean± SD)*	19.59±5.08
Cognitive diagnosis:	
- Dementia, %	4.8%
- MCI, %	53.2%
- NC, %	42%

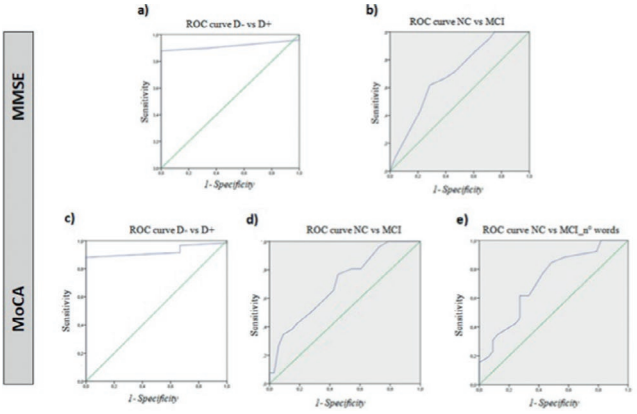

Figure 1 ROC curves for dementia (a) and MCI (a) for MMSE total score and MOCA total score (c, d) and number of words in fluency items (e) Abbreviations: D-, absence of dementia; D+, presence of dementia; MCI, mild cognitive impairment; MMSE, Mini mental.

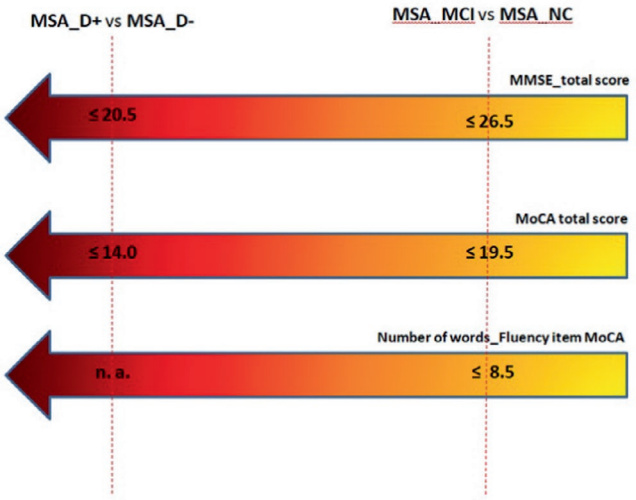

FIGURE 2 Optimal cut-offs for MMSE and MOCA to identify dementia and MCI in MSA. Abbreviations: D-, absence of dementia; D+, presence of dementia; MCI, mild cognitive impairment; MMSE, Mini mental state examination; MOCA, Montreal Cognitive Assessment; M

Conclusion: Our findings support MMSE and MOCA as easy and accurate instruments to detect MCI and dementia in MSA. MOCA fluency item is also a reliable tool to detect MCI in the same population.
Disclosure: Nothing to disclose.

EPR-048 | Prediction of motor progression in Parkinson's disease using clinical data and brain MRI-derived features

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Background and aims: The MDS-UPDRS-III is a standard tool for assessing motor symptoms in Parkinson's disease (PD) and is often employed as an endpoint in clinical trials. This study examines the progression in MDS-UPDRS-III scores among patients with early-stage PD. We hypothesize that baseline clinical data and brain MRI-derived features can predict motor progression in patients with early-stage PD.
Methods: Data from 519 patients with early-stage PD (Hoehn & Yahr stage < 2.5, MOCA > 22, mean age 62 ± 9 years, disease duration 1.3 ± 1.6 years) were retrospectively analyzed. Data originated from the PPMI database and Stanford University. Progression in motor signs between 1 and 3 years was evaluated using two criteria: (1) any increase (change > 0) in MDS-UPDRS-III scores from baseline, and (2) a clinically significant increase (change > = 5) in MDS-UPDRS-III scores from baseline. A Random Forest classifier was trained and validated using five-fold cross-validation. Input variables included baseline clinical data (Hoehn & Yahr stage, MDS-UPDRS-III, age) and head-size-normalized volumes of cortical lobes and subcortical structures (caudate nucleus, putamen, hippocampus, thalamus, and lateral ventricles) obtained with the icobrain software. Model performance was assessed using the mean and 95% confidence interval of the area under the receiver operating characteristic curve (AUC), accuracy, specificity, sensitivity, and precision.
Results: Table 1 summarizes the performance metrics, showing an AUC of 0.76 for predicting MDS-UPDRS-III change and 0.66 for predicting severe changes.

TABLE 1 The mean and 95% confidence interval of a random forest classifier's performance, trained on baseline clinical data and MRI-derived features to predict MDS-UPDRS-III changes. AUC = area under the receiver operating characteristic curve.

	Stable/ progressive	AUC	Accuracy	Sensitivity	Specificity	Precision
Any increase in MDS-UPDRS-III	138/381	0.76 (0.68 0.84)	0.72 (0.66 0.79)	0.77 (0.67 0.87)	0.59 (0.53 0.66)	0.84 (0.83 0.85)
Clinically meaningful increase in MDS-UPDRS-III	256/263	0.66 (0.62 0.7)	0.63 (0.59 0.67)	0.65 (0.59 0.72)	0.61 (0.56 0.65)	0.63 (0.59 0.67)

Conclusion: Baseline clinical data combined with MRI-derived features have the potential to predict future changes in motor symptoms in early-stage PD.
Disclosure: The author declares that financial support was received for the research by icometrix.

EPR-049 | Switching from placebo to opicapone in non-fluctuating Parkinson's disease patients: Findings from EPSILON study

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Background and aims: In the EPSILON study, opicapone (OPC) was more efficacious than placebo in improving motor impairments in levodopa-treated Parkinson's disease (PD) patients without motor complications. Findings from the open-label extension (OLE) phase are reported.
Methods: In the randomized, double-blind (DB), placebo-controlled EPSILON study, levodopa-treated PD patients without motor complications received OPC 50 mg or placebo for 24 weeks. After completing the DB phase, patients entered the OLE and received OPC 50 mg. Changes from OLE baseline to Week 52 in Movement Disorder Society-Unified PD Rating Scale (MDS-UPDRS)-Part III and Part IV (OLE key endpoint) scores were evaluated. Safety/tolerability were secondary endpoints.
Results: From OLE baseline to Week 52, there was a mean (standard error) reduction of -2.1 (± 7.9) in MDS-UPDRS-Part III score in patients transitioning from placebo to OPC (PLC-OPC

group, $N=155$), but those who received OPC in the DB phase (OPC-OPC, $N=151$) showed numerically greater improvements in the score at Week 52 (least-squares mean difference of -1.3 points [95%CI: -3.3,0.7; $p=0.196$] vs. PLC-OPC) (Figure 1). MDS-UPDRS-Part IV total scores remained low (Figure 2a), with a higher proportion of patients remaining free of motor complication (MDS-UPDRS-Part IV score = 0) in the OPC-OPC than in the PLC-OPC group (80.2% vs. 69.7%, Figure 2b). Time to fluctuations, dyskinesias and dystonia did not significantly differ between groups (Figure 2c). OPC was well-tolerated.

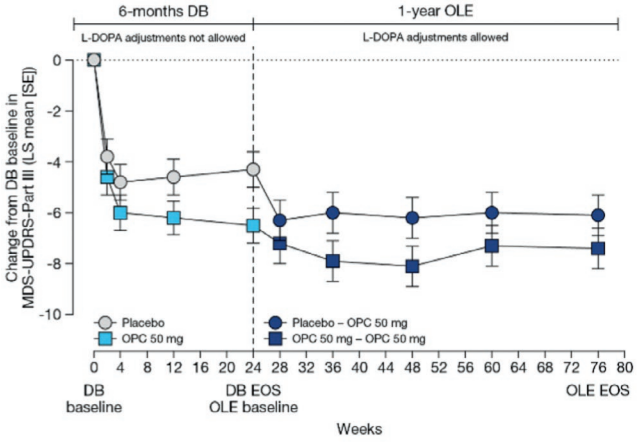

Figure 1. LS Mean (SE) change in MDS-UPDRS motor scores from DB baseline until the end of the OLE phase.

DB, double-blind; EOS, end of study; L-DOPA, levodopa; LS, least square; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; OLE, open-label extension; OPC, opicapone; SE, standard error.

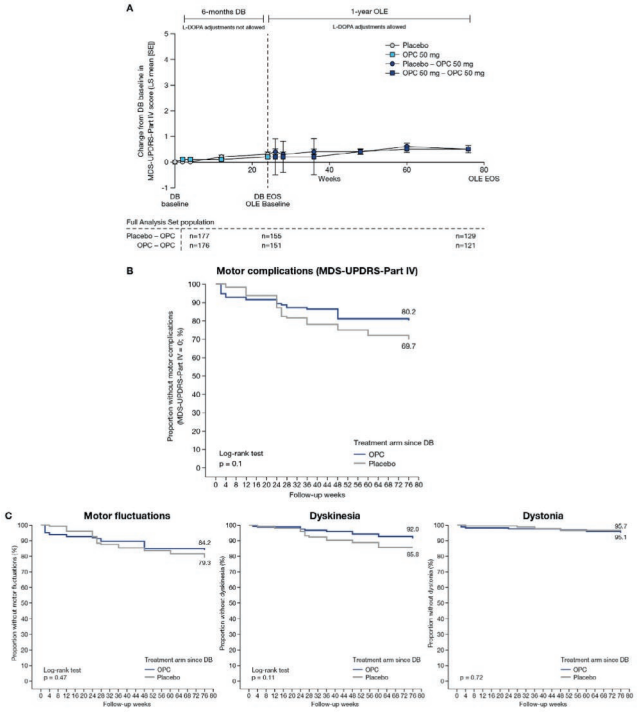

Figure 2. Motor complication throughout the study. A) LS Mean (SE) change from DB baseline in MDS-UPDRS-Part IV until the end of the OLE phase. **B)** Kaplan–Meier survival curve with proportion of patients free of motor complication (MDS-UPDRS-Part IV=0) from DB baseline until the end of the OLE phase; and **C)** Kaplan–Meier survival curve with proportion of patients free of motor fluctuations (MDS-UPDRS-Part IV, item 4.3 *Time spent in OFF state*=0), dyskinesia (MDS-UPDRS Part IV, item 4.1. *Time spent with dyskinesia*=0) and dystonia (MDS-UPDRS-Part IV, item 4.6 *Painful OFF-state dystonia*=0) from DB baseline until the end of the OLE phase.

DB, double-blind; EOS, end of study; L-DOPA, levodopa; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; OLE, open-label extension; OPC, opicapone.

Conclusion: OPC provided sustained motor benefits with a higher proportion of patients free of motor complications compared with those initially on placebo. These results support early OPC use in levodopa-treated PD patients without motor fluctuations.

Disclosure: JJF received grants/compensation from GlaxoSmithKline, Grunenthal, Fundação MSD, TEVA, MSD, Allergan, Novartis, Medtronic, GlaxoSmithKline, Novartis, TEVA, Lundbeck, Solvay, BIAL, Merck, Merz, Ipsen, Biogen, Acadia, Allergan, Abbvie, Sunovion Pharma, Zambon, Affiris and Angelini. OR has received compensation from AbbVie, Adamas, Acorda, Addex, AlzProtect, ApoPharma, AstraZeneca, Axovant, BIAL, Biogen, Britannia, Buckwang, CereSpir, Clevexel, Denali, INC Research, IPMDS, Lundbeck, Lupin, Merck, MundiPharma, NeurATRIS, NeuroDerm, Novartis, ONO Pharma, Osmotica, Parexel, Pfizer, Prexton Therapeutics, Quintiles, Roche, Sanofi, Servier, Sunovion, Theranexus, Takeda, Teva, UCB, Vectura, Watermark Research, XenoPort and Zambon; grants from CHU, France-Parkinson, INSERM, Michael J. Fox Foundation and Cure Parkinson UK. FS received honoraria from Lundbeck, UCB, Chiesi, Zambon, Britannia, Cynapsus, Sunovion, Kyowa, Abbvie, Neuroderm, Biogen and BIAL. AA received compensation/support from UCB, Boehringer Ingelheim, Britannia, AbbVie, Zambon, BIAL, NeuroDerm, Theravance Biopharma and Roche, Chiesi Pharma, Lundbeck and Horizon 2020. WP received fees/honoraria from Alterity, AbbVie, Affiris, AstraZeneca, Axovant, BIAL, Biogen, Britannia, Lilly, Lundbeck, NeuroDerm, Neurocrine, Denali Pharma, Orion Pharma, Roche, Stada, Sunovion, Takeda, UCB and Zambon; grant from Michael J. Fox Foundation, FP7 and Horizon 2020. GCF, HB, JM, FR, MMF and JH are employees of Bial. Study supported by Bial.

EPR-050 | Abstract withdrawn

EPR-051 | The OLE portion of the PROOF-HD trial shows persistent benefits of pridopidine on function, cognition, and motor in HD

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Background and aims: Pridopidine is a highly selective and potent S1R agonist in clinical development for Huntington's disease (HD) and ALS.

Methods: PROOF-HD was a Ph3, global, double-blind, placebo-controlled trial assessing pridopidine (45 mg bid) in early manifest HD. The double-blind (DBP) duration was 65-78wks, followed by an open-label period (OLE) (total 104weeks). Key endpoints include change from baseline through wk104 in functional capacity (TFC), progression (cUHDRS), cognition (SWR), and motor (Q-Motor). Prespecified subgroup analysis excluded participants on antidopaminergics (ADMs; VMAT2 inhibitors and antipsychotics).

Results: Pridopidine was well tolerated with a safety profile comparable to placebo. Pridopidine did not show significant benefits in all subjects. However, in prespecified subjects off ADMs, pridopidine was superior to placebo across key independent measures of HD progression, at all timepoints through the DBP. In subjects off ADMs treated with pridopidine during the DBP and OLE show persistent benefits lasting through wk104 across all endpoints compared to a propensity matched cohort from both the ENROLL-HD and TRACK-HD observational studies. Pridopidine demonstrated improvements in cUHDRS (ENROLL-HD: Δ0.90, $p < 0.0001$; TRACK-HD: Δ1.19, $p < 0.0001$), TFC (ENROLL-HD: Δ0.76, $p < 0.0001$; TRACK-HD: Δ0.71, $p = 0.0004$), SWR (ENROLL-HD: Δ6.47, $p < 0.0001$; TRACK-HD: Δ8.16, $p = 0.0003$), and Q-Motor FT IOI (ENROLL: did not assess Q-Motor; TRACK-HD: Δ-77.12 ms, $p < 0.0001$). Pridopidine inhibits CYP2D6 and its concomitant use with certain ADMs (CYP2D6 metabolized) increases exposure of ADMs. Participants on recommended adjusted doses of ADMs (per regulatory label guidance) maintain positive benefits of pridopidine.
Conclusion: Pridopidine shows consistent, sustained and clinically meaningful benefits across multiple endpoints of HD progression through 2 years.
Disclosure: This study was sponsored by Prilenia Therapeutics.

EPR-052 | Effect of 24-hour subcutaneous levodopa/carbidopa infusion (ND0612) on motor fluctuations in the Phase 3 BouNDless study

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Background and aims: Treatment with investigational ND0612 added 1.72h of Good ON-time over immediate-release levodopa/carbidopa (IR-LD/CD; $p < 0.0001$) in the phase 3 BouNDless study (NCT04006210). Patients who completed the double-blind phase of this study were eligible to enter into the ND0612 open-label extension (OLE) phase (<=54 months). Here, we report the effect of ND0612 on OFF and ON episodes, their duration, and transitions in the BouNDless study and 1-year OLE phase.
Methods: Data collection involved post hoc analysis of diary data and descriptive analysis of the number and duration of episodes spent in any PD motor state. The total number of transitions between motor states were analyzed by baseline-adjusted Poisson Regression. Analysis of OLE phase outcomes was performed until the last patient completed 1-year following OLE enrollment. Changes in diary states were measured from ND0612 initiation in the run-in phase of the study.
Results: At the end of the double-blind phase, ND0612 treatment led to fewer OFF episodes/day and shorter OFF duration (2.4 vs. 3.3; 3.8h vs. 5.2h), fewer episodes and prolonged duration of 'ON without dyskinesia' (2.7 vs. 3.1; 9.4h vs. 7.4h) and fewer daily transitions between OFF and ON (5.3 vs. 7.1) compared with IR-LD/CD ($p < 0.0001$). At the end of OLE Month 12, the LS mean ± SE changes in OFF-time (−1.86 ± 0.18h), Good ON-time (+1.96 ± 0.18h), and ON-time without any dyskinesia (+2.19 ± 0.26h) supported the sustained effect of ND0612 ($p < 0.0001$).
Conclusion: These data confirm the effectiveness of the ND0612 regimen in reducing OFF, improving ON, and reducing the transitions between them, compared to IR-LD/CD.
Disclosure: OR, ALE, RAH, FS, RP, JJF, KK, AA, NG and AJE were investigators in the study and they or their institutions report fees from NeuroDerm. LS, NS, LA, NV and NL are employed by NeuroDerm. JP is employed by Mitsubishi Tanabe Pharma America, Inc.

EPR-053 | Patient experience and satisfaction with once-daily deutetrabenazine for tardive dyskinesia: Age subgroup analysis

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Background and aims: Deutetrabenazine is approved by the United States Food and Drug Administration for the treatment of tardive dyskinesia (TD) and Huntington disease (HD)-related chorea. This analysis explored patient-reported ease of use, effectiveness, and satisfaction with once-daily (QD) deutetrabenazine extended-release tablets from participants with TD by age subgroup (<65 or ≥65 years).
Methods: This non-interventional, prospective, cross-sectional, institutional review board–approved survey included adults with TD or HD-related chorea taking deutetrabenazine QD. Participants in Shared Solutions patient support program who completed/were due for their 12-week nurse outreach phone call were eligible. Participants who consented received survey materials by mail/email.
Results: Among 209 participants with TD, 41.6% were aged ≥65 years. 73.6% of TD patients aged ≥65 years and 77.9% of those aged <65 years reported that their extra movements were very much/much improved with deutetrabenazine QD. Patients reported that these improvements led to positive impacts across several quality-of-life domains (Table 1). Nearly all (≥65 years: 98.9%; <65 years: 98.4%) reported that deutetrabenazine QD was very/somewhat easy to use. Satisfaction with deutetrabenazine QD was high; 86.2% of patients aged ≥65 years and 91.8% aged <65 years reported overall satisfaction with deutetrabenazine QD, and most (≥65 years: 95.4%; <65 years: 97.5%) strongly agreed/agreed that they will continue taking deutetrabenazine QD (Table 2).

TABLE 1 Participant-reported improvement and effects on quality-of-life domains.

n (%)	TD (n=209)		TD-Only Cohort (N=209)
	<65 years (n=122)	≥65 years (n=87)	
With respect to your extra movements, how would you describe yourself now compared to immediately before starting deutetrabenazine QD?			
Much improved/very much improved	95 (77.9)	64 (73.6)	159 (76.1)
Since starting deutetrabenazine QD, the reduction in my extra movements has…			
made me feel more comfortable in social settings, agree/strongly agree	97 (80.2)[a]	67 (77.0)	164 (78.8)[a]
improved my overall emotional well-being, agree/strongly agree	100 (82.0)	63 (74.1)[b]	163 (78.7)[b]
improved my overall physical health, agree/strongly agree	74 (61.2)[a]	46 (52.9)	120 (57.7)[a]
improved work or school life, including work at home, agree/strongly agree	69 (57.0)[c]	39 (45.9)[c]	108 (52.4)[c]
improved my ability to do household chores, agree/strongly agree	64 (52.9)[c]	32 (37.6)[c]	96 (46.6)[c]

[a]A response was not available for 1 participant in the <65 years subgroup and 1 participant in the overall population.
[b]A response was not available for 2 participants in the ≥65 years subgroup and 2 participants in the overall population.
[c]A response was not available for 1 participant in the <65 years subgroup, 2 participants in the ≥65 years subgroup, and 3 participants in the overall population.

TABLE 2 Participant-reported satisfaction and ease of use.

n (%)	TD (n=209)		TD-Only Cohort (N=209)
	<65 years (n=122)	≥65 years (n=87)	
Satisfaction			
I plan to continue taking deutetrabenazine QD, agree/strongly agree	119 (97.5)	83 (95.4)	202 (96.7)
Overall, I am satisfied with deutetrabenazine QD, agree/strongly agree	112 (91.8)	75 (86.2)	187 (89.5)
Ease of Use			
Overall ease of taking deutetrabenazine QD, very easy/somewhat easy	120 (98.4)	86 (98.9)	206 (98.6)
Remembering to take deutetrabenazine QD, very easy/somewhat easy	119 (97.5)	84 (97.7)[a]	203 (97.6)[a]
Understanding when to take deutetrabenazine QD, very easy/somewhat easy	119 (97.5)	84 (97.7)[a]	203 (97.6)[a]
Including deutetrabenazine QD in daily routine, very easy/somewhat easy	121 (99.2)	85 (98.8)[a]	206 (99.0)[a]

[a]A response was not available for 1 participant in the ≥65 years subgroup and 1 participant in the overall population.

Conclusion: Nearly all participants in both age subgroups reported overall satisfaction with deutetrabenazine QD, consistent with results in the overall population. Most participants reported improvements in their extra movements since starting deutetrabenazine QD, leading to positive impacts on several quality-of-life domains.

Disclosure: This study was funded by Teva Branded Pharmaceutical Products R&D, Inc.

MS and related disorders 1

EPR-054 | Serum neurofilament light chain as a biomarker for treatment efficacy of extended interval dosing in multiple sclerosis

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Background and aims: To evaluate serum neurofilament light chain (sNFL) levels as a biomarker for treatment efficacy in multiple sclerosis (MS) patients undergoing various disease-modifying therapies (DMTs), focusing on extended interval dosing (EID) regimens.

Methods: We conducted a single-center, cross-sectional study involving 125 MS patients at the University Hospital Cologne from April to September 2024. Patients had been on therapy for over two years without relapses in the past three months. They were categorized by current DMT regimen: low-efficacy DMTs (leDMTs; $N=8$), natalizumab EID (every 8 weeks; $N=39$), ofatumumab ($N=17$), ocrelizumab standard interval dosing (SID; $N=20$), ocrelizumab EID (every 9 months; $N=17$), and a no-DMT group ($N=19$). sNFL levels were measured using an electrochemiluminescence assay.

Results: The cohort primarily consisted of females (59%), with a median age of 42.0 years, median therapy duration of 3.73 years, median sNFL of 1.300 pg/mL, median EDSS of 3.0 and median disease duration of 7.0 years. Ofatumumab and natalizumab EID were associated with the lowest sNFL levels. Significantly lower sNFL levels were observed in patients receiving natalizumab EID, ofatumumab, ocrelizumab SID and EID compared to the no-DMT group, while no significant differences were noted among different DMT groups.

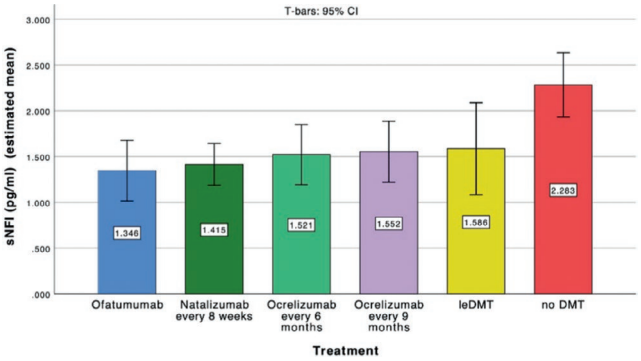

FIGURE 1 Estimated mean of serum neurofilament light chain (sNFL) levels (in pg/ml) in multiple sclerosis (MS) patients receiving various disease-modifying therapies (DMTs) with different dosing regimens, analyzed using Analysis of Covariance (ANCOVA).

Conclusion: In our cohort of MS patients receiving various monoclonal antibody therapies with different dosing regimens, sNFL levels showed no significant variation. Notably, EID regimens were not associated with elevated sNFL levels, indicating their potential to mitigate neuronal damage effectively. Further studies are warranted to investigate EID combined with sNFL monitoring as a strategy for de-escalating long-term immunotherapy in MS.

Disclosure: AK has received a study grant from Novartis. CW has received institutional support from Novartis, Alexion, Sanofi Genzyme, Biogen, Merck, Janssen, Bayer and Roche. He has received personal honoraria for teaching lectures from Biontech, Medpoint Medizinkommunikations, F&U confirm, Privatinstitut für Klinikmanagement,The Royal College Of Physicians, and for consulting from Wuesthoff+Wuesthoff and Bristows LLP. GRF, MS, WB and FS have nothing to disclose.

EPR-055 | Cognitive assessment of MOGAD and NMOSD patients: Preliminary results of a RIREMS group study

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Background and aims: Little is known about the impact of myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) and aquaporin-4-IgG-seropositive neuromyelitis optica spectrum disorder (NMOSD-AQP4+) on cognitive performance (CP). This ongoing multicenter longitudinal Italian study aimed to assess CP in adult MOGAD and NMOSD-AQP4+ patients compared to relapsing remitting multiple sclerosis (RRMS) cases.
Methods: As of 15/01/2025, 21 MOGAD (7F, mean age 42y), 20 NMOSD-AQP+ (18F, mean age 55y) and 19 RRMS patients (13F, mean age 37y) have been enrolled. CP is assessed using the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) battery corrected for sex, age and education, including Symbol Digit Modalities Test (SDMT), California Verbal Learning Test (CVLT-II) and Brief Visuospatial Memory Test-Revised (BVMT-R). Beck's Depression Inventory Scale (BDI-II) and Fatigue Scale for Motor and Cognitive Functions (FSMC) are also administered. Assessment is performed at baseline and after 18+/-6 months.
Results: At baseline, 5 (23.8%, CI:8.2-47.2%) MOGAD, 3 (15.0%, CI:3.2-37.9%) NMOSD and 3 (15.8%, CI:3.4-39.6%) RRMS patients show impairment in one or more BICAMS tests. However, no significant differences in median values of any of the tests have been observed among the groups. Mean FSMC score is significantly higher in MS (55.4+/-16.59) compared to MOGAD (38.3+/-17.19) and NMOSD-AQP4 patients (40.5+/-22.07, $p=0.009$). Follow-up assessments are currently ongoing.
Conclusion: To our knowledge, this is the first study assessing CP in MOGAD and NMOSD using BICAMS battery. Our preliminary data suggest that patients with MOGAD and NMOSD could show impairment in cross-sectional CP at similar rates of RRMS cases.

Disclosure: Massimiliano Calabrese received speaker honoraria from Biogen, Bristol Myers Squibb, Merck Serono, Novartis, and Roche and received research support from the Progressive MS Alliance and Italian Minister of Health and Biogen, Bristol Myers Squibb, Merck Serono, Novartis, and Roche. PA received honoraria for lecturing and participation in advisory boards, and/or travel expenses for attending congresses and meetings from Alexion, Almirall, Amgen, Biogen, BMS, Janssen, Lundbeck, Merck, Novartis, Roche, Sanofi-Genzyme, Teva and Viatris.

EPR-056 | Placental and breastmilk transfer of ocrelizumab from women with multiple sclerosis to infants: MINORE and SOPRANINO

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Background and aims: Conventional multiple sclerosis (MS) pregnancy and breastfeeding management focuses on infant safety, but discontinuing disease-modifying therapy increases the mother's risk of disease activity. Ocrelizumab (OCR) labeling advises contraception during treatment through 4 months post administration, but pregnancies may still occur. Prospective trials in women with MS assessed OCR transplacental (MINORE, NCT04998851) or breastmilk transfer (SOPRANINO, NCT04998851), and effects on infant B-cell levels.
Methods: MINORE enrolled 35 pregnant women with MS (gestational week [W] ≤30) whose last OCR infusion occurred ≤6 months prior to the last menstrual period or during the first trimester. Primary endpoint was proportion of infants with B-cell levels below lower limit of normal (LLN) at W6 of life. SOPRANINO enrolled 13 breastfeeding women receiving OCR (W2–24 at first postpartum infusion) and their infants. Coprimary endpoints were proportion of infants with B-cell

levels below LLN 30 days post-infusion and OCR average daily infant dose over the 60 days post-infusion.

Results: OCR was undetectable in most infant serum at birth in umbilical cord (33/35, 94.3%) and at W6 (32/33, 97.0%) (MINORE; Fig 1). OCR levels in breastmilk were negligible and undetectable in infant serum at 30 days post infusion (SOPRANINO). All infant B-cell levels exceeded age-specific LLN in MINORE (34/34) and SOPRANINO (10/10) (Fig 2). Maternal adverse events were typical of peripartum and the established OCR safety profile; infant adverse events were typical of infancy.

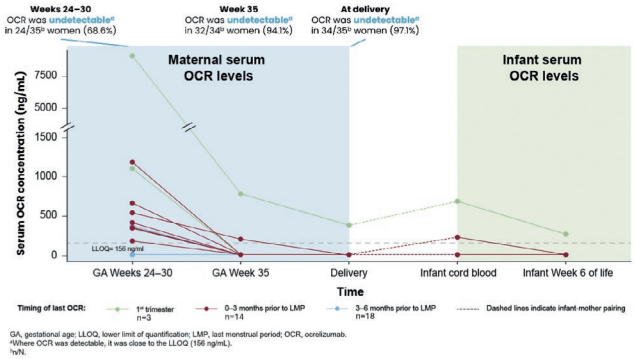
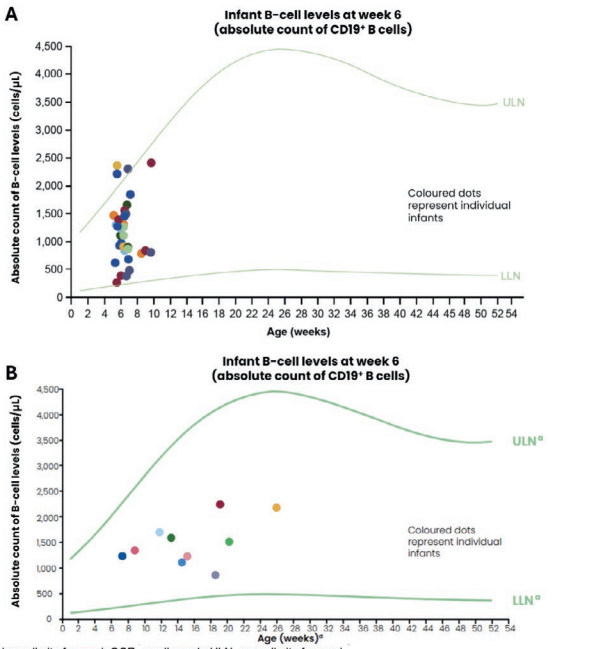


Figure 1. OCR in the Mother and Infant (MINORE)



LLN, lower limit of normal; OCR, ocrelizumab; ULN, upper limit of normal.
[a]Dynamic changes occur in the ULN and LLN of B-cell levels throughout the first year. A reduction in B-cell levels is observed from cord blood to the first week of life, followed by a rapid increase over the next 2 months. At ≈6 months of age maximum levels are attained, after which levels decrease progressively and stabilize at ≈1 year of age.

Figure 2. B Cells in Infants Exposed to OCR Via (A) Placental Transfer (MINORE) and (B) Breastmilk (SOPRANINO)

Conclusion: Pregnancy planning and breastfeeding are compatible with OCR treatment and provide an evidence basis for clinical management of women with MS.

Disclosure: Celia Oreja-Guevara, Sandra Vukusic, Riley Bove, Anna Shah, Edith L. Graham, Thomas McElrath, Carlo Pietrasanta, Ruth Dobson, Heidemarie Kletzl, Agne Kazlauskaite, Dusanka Zecevic, Catarina Raposo, Licinio Craveiro, Chien-Ju Lin, Noemi Pasquarelli and Kerstin Hellwig have disclosures. Elisabeth Maillart and Dina Jacobs have nothing to disclose. Full disclosures for each author will be provided at time of the presentation.

EPR-057 | Serum neurofilament light chain as a predictor of clinical and radiological outcomes: A post-hoc analysis of MAGNIFY-MS

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Background and aims: Serum neurofilament light chain (sNfL) is a biomarker reflecting neuroaxonal damage in multiple sclerosis (MS). We investigated associations of sNfL with radiological/clinical endpoints in cladribine tablets (CladT)-treated participants with relapsing MS in 2-year MAGNIFY-MS study (NCT03364036).

Methods: sNfL percentiles and Z-scores were derived based on a large reference dataset (Benkert et al., Lancet Neurol. 2022; 21:246–257). Changes in sNfL Z-score at month (M)12 and M24 were calculated versus baseline (BL). Associations between magnetic resonance imaging (MRI) parameters and Z-scores were explored using a multivariable linear regression model for repeated measures. Logistic regression was used for prediction analyses of no evidence of disease activity (NEDA-3) and no evidence of progression or active disease (NEPAD). Subgroup analysis: BL sNfL Z-score ≤1.5 and > 1.5.

Results: Of 270 participants, 180 (66.7%) were female, and 118 (43.7%) aged > 40 years. Mean sNfL Z-scores decreased after first CladT dose in most participants and remained stable until study end (Table 1). sNfL Z-score ≤1.5 subgroup: mean sNfL Z-scores decreased close to 0; sNfL Z-score > 1.5 subgroup: substantial decrease observed (Table 1). Higher BL sNfL Z-scores predicted more pronounced decrease in future T1 gadolinium-enhancing and active T2 lesion load between BL-M12: estimated coefficient of change -0.40, $p = 0.0005$ and -4.84, $p = 0.0002$, respectively. BL sNfL Z-scores could predict NEDA-3/NEPAD at M12 (Table 2). M12 sNfL Z-scores were not predictive for M24 results.

TABLE 1 sNfL Z-scores over the course of the study.

Visit	Total (N=270)		BL sNfL Z-score ≤1.5 (N=155)		BL sNfL Z-score >1.5 (N=106)	
	Mean (±SD)	Participants, n	Mean (±SD)	Participants, n	Mean (±SD)	Participants, n
BL	1.02 (1.48)	261	0.05 (1.05)	155	2.43 (0.64)	106
M12	0.18 (1.31)	235	-0.27 (1.21)	141	0.85 (1.14)	94
M24	0.40 (1.09)	213	0.07 (1.00)	125	0.86 (1.04)	88

BL, baseline; M, month; sNfL, serum neurofilament light chain; SD, standard deviation

TABLE 2 Effect of sNfL Z-scores on MRI parameters and clinical outcomes.

Time period	T1 Gd+ lesion count		Active T2 lesion count		NEDA-3		NEPAD	
	Estimated co-efficient (± SE)	p-value	Estimated co-efficient (± SE)	p-value	Estimated odds ratio (95% CI)	p-value	Estimated odds ratio (95% CI)	p-value
BL-M12	-0.40* (± 0.11)	0.0005	-4.84* (± 1.26)	0.0002	0.68* (0.51, 0.91)	0.0094	0.70* (0.53, 0.94)	0.0164

*adjusted (among other predictors) for sNfL Z-score at BL.

BL, baseline; CI, confidence interval; Gd+, gadolinium-enhancing; M, month; MRI, magnetic resonance imaging; NEDA-3, no evidence of disease activity; NEPAD, no evidence of progression or active disease; sNfL, serum neurofilament light chain; SE, standard error

Conclusion: CladT reduced sNfL levels in study participants, highlighting its neuroprotective effects. BL sNfL Z-scores can predict MRI activity, NEDA-3, and NEPAD in the first year of treatment.

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EPR-058 | Peripartum disease activity in women with multiple sclerosis: Ocrelizumab clinical trials and a noninterventional study

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Background and aims: Pre-pregnancy ocrelizumab (OCR) use in women with multiple sclerosis (MS) may help control disease activity during pregnancy and postpartum. Evidence on MS relapses around pregnancy from OCR interventional clinical trials (ICTs) can be complemented by real-world data from CONFIDENCE (ML39632, EUPAS22951), a noninterventional, prospective, multicenter study assessing long-term safety of OCR.

Methods: Women with MS across 13 OCR ICTs (as of Nov 2023) and CONFIDENCE (as of Nov 2024) who became pregnant (despite protocol requirements in ICTs) and had live births were included. Pre-pregnancy (up to 1 year), pregnancy and postpartum (up to 1 year) periods were analyzed, using annualized relapse rate (ARR) as the primary measure of disease activity.

Results: A total of 178 women with live births were analyzed, including 103 from ICTs and 75 from CONFIDENCE. The CONFIDENCE cohort was older and more active prior to pregnancy, with a longer MS disease duration, lower proportions of treatment-naive individuals and shorter duration of pre-pregnancy OCR (Table 1). CONFIDENCE participants resumed OCR postpartum at higher rates than ICT participants (48% vs. 31%). ARRs (95% CI) before, during and after pregnancy were 0.06 (0.02–0.14), 0.03 (0.00–0.09) and 0.04 (0.01–0.14) for the ICT cohort and 0.16 (0.08–0.29), 0.02 (0.00–0.11) and 0.17 (0.08–0.33) for the CONFIDENCE cohort, respectively (Table 2).

Conclusion: Low peri-pregnancy ARRs were observed across a broad and heterogenous population of childbearing women with MS. These data provide evidence on the pre-pregnancy use of OCR to maintain disease control during pregnancy and postpartum.

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TABLE 1 Participant Characteristics.

	Interventional Clinical Trials N=103	Noninterventional CONFIDENCE Study N=75
Age at OCR start, median [IQR], y	28.0 [25.0, 30.0]	31.0 [28.0, 33.5]
Time from MS diagnosis, median [IQR], y	0.4 [0.2, 2.2]	4.6 [1.8, 8.1]
Treatment naive, n (%)	70 (68.0)	15 (20.0)
Time from first OCR dose to LMP, median [IQR], mo	29.0 [15.6, 48.0]	22.2 [13.1, 34.9]
Time from last OCR dose[a] to LMP, median [IQR], mo	4.2 [2.2, 5.6]	4.0 [1.7, 6.0]
Received OCR after delivery, n (%)	32 (31.1)	36 (48.0)
Time from delivery to first OCR dose, median [IQR], mo	3.8 [1.9, 6.2]	2.4 [1.4, 8.1]

IQR, interquartile range; LMP, last menstrual period; MS, multiple sclerosis; OCR, ocrelizumab.
[a]OCR administered prior to LMP.

TABLE 2 ARRs in Peripregnancy Periods.

ARR (95% CI)	Interventional Clinical Trials N=103	Noninterventional CONFIDENCE Study N=75
Pre-pregnancy	0.06 (0.02–0.14)[a]	0.16 (0.08–0.29)
During pregnancy	0.03 (0.00–0.09)[b]	0.02 (0.00–0.11)[c]
Postpartum	0.04 (0.01–0.14)[d]	0.17 (0.08–0.33)[c]

ARR, annualized relapse rate; DMT, disease-modifying therapy; LMP, last menstrual period; OCR, ocrelizumab.
[a]n=101.
[b]n=103.
[c]n=67
[d]n=81.

EPR-059 | Ocrelizumab treatment in multiple sclerosis: 11-Year efficacy and safety clinical trial data

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Background and aims: Ocrelizumab (OCR) is approved for treating adult patients with relapsing multiple sclerosis (pwRMS) and primary progressive MS (pwPPMS). This study evaluated the long-term efficacy and safety of OCR up to 11 years through clinical trials (CTs) and their open-label extension (OLE) periods (up to November 2023).
Methods: Efficacy and safety outcomes were reported for pwMS treated with OCR in ongoing or completed CTs and their OLE follow-ups. Disability progression was assessed through 48-week confirmed disability progression (48W-CDP) on the Expanded Disability Status Scale (EDSS) and composite CDP. Rates per 100 patient years (PY) were recorded for adverse events (AEs), serious AEs, non-serious and serious infections.
Results: After 11 years on OCR, 91.7% of pwRMS and 79.5% of pwPPMS did not require a walking aid or wheelchair, respectively; 17.8% of pwPPMS remained free from composite CDP. Early OCR treatment significantly reduced risks of disability milestones compared with delayed treatment. Over an > 11-year follow-up period in clinical trials (with > 60% of patients who received > = 8 doses of OCR), no new safety concerns were observed. Infections were mostly of urinary and respiratory nature. Most patients with at least one recurrent (non-serious and serious) infection had one recurrency.

TABLE 1 48W-CDP–EDSS over 11 years with OCR.

	pwRMS	pwPPMS
Patients free from 48W-CDP–EDSS events (%)	74.9	33.5

48W-CDP, 48-week confirmed disability progression; EDSS, Expanded Disability Status Scale; OCR, ocrelizumab; pwPPMS, patients with primary progressive multiple sclerosis; pwRMS, patients with relapsing multiple sclerosis.

TABLE 2 OCR overall safety profile.

Adverse event[a] Rate per 100 PY (95% CI)	All RMS	All PMS
AE[b]	223 (221–225)	213 (210–216)
SAE	5.9 (5.6–6.2)	10.8 (10.1–11.5)
SI	1.7 (1.5–1.8)	3.7 (3.3–4.1)
NSI	63.8 (62.8–64.9)	57.1 (55.4–58.8)

[a]Excluding COVID-19 AEs; [b]Infections were the most common AE.
AE, adverse event; CI, confidence interval; COVID-19, coronavirus disease 2019; NSI, non-serious infection; OCR, ocrelizumab; PMS, progressive multiple sclerosis; PY, patient years; RMS, relapsing multiple sclerosis; SAE, serious adverse event; SI, serious infection.

Conclusion: Ocrelizumab demonstrated a stable and favorable long-term benefit–risk profile over 11 years. Disability progression and rates of AEs remained stable, supporting its continued use in treating MS.
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EPR-060 | Safety and efficacy of frexalimab in relapsing multiple sclerosis: 2-Year results from phase 2 open-label extension

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Background and aims: Frexalimab, a second-generation anti-CD40L antibody, blocks the CD40/CD40L pathway, which is important in regulating adaptive and innate immunity. During the 12-week (W) double-blind-period of the phase-2 trial (NCT04879628) in participants with relapsing multiple sclerosis (pwRMS), frexalimab was well-tolerated and efficacious, with the frexalimab-1200mg/intravenous (IV) arm showing an 89% reduction in new gadolinium-enhancing (Gd+) T1-lesions versus placebo. Here, we report W96 results in open-label extension (OLE).

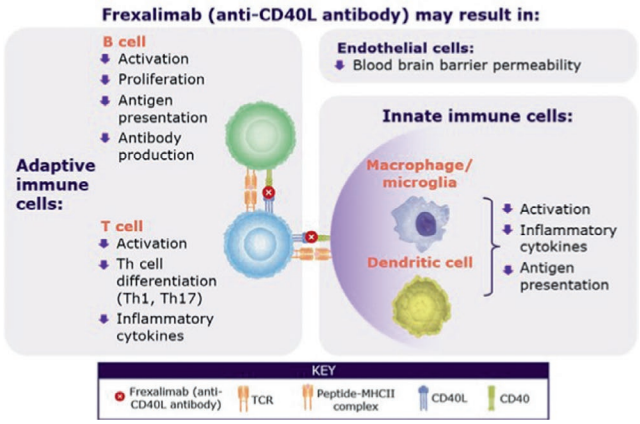

FIGURE 1 Proposed mechanism of action of frexalimab (anti-CD40L antibody) in multiple sclerosis

Methods: 129 participants were randomized (4:4:1:1) to frexalimab-1200mg/IV every-4-weeks (q4w) or frexalimab-300mg/subcutaneous (SC) q2w or matching placebo. At W12, participants receiving placebo switched to frexalimab. During OLE, SC dose was increased to 1800-mg q4w, resulting in similar frexalimab exposure as with frexalimab-1200mg/IV q4w dose; 36/57 participants in SC arms received this high-dose prior to W96 MRI. Key endpoints include safety and efficacy (Gd+ T1-lesions, new/enlarging T2-lesions, annualized relapse rate [ARR]).
Results: 106 participants (82%) remained on treatment at W96. Total number of Gd+ T1-lesions (mean [SD]) remained low in participants who continued receiving frexalimab and who switched to frexalimab at W12 (IV arms: frexalimab-1200mg/IV: 0.1 [0.5], placebo-IV/frexalimab-1200mg/IV: 0.1 [0.3]; all SC arms: 0.4 or below). New/enlarging T2-lesion monthly count remained low with frexalimab-1200mg/IV through W96. ARR (baseline–W96) was low (0.08 [95% CI, 0.03–0.18]) in the frexalimab-1200mg/IV arm; 92% of participants were relapse-free. Most common adverse events were nasopharyngitis, headache, and COVID-19. Lymphocyte counts were stable over W96.
Conclusion: Frexalimab continues to show favorable safety and sustained reduction in disease activity in pwRMS through W96, supporting its further development in phase-3 trials as a potential high-efficacy, non-lymphocyte-depleting therapy.
Disclosure: PV: Janssen, Biogen, Sanofi, Novartis (NVS), Teva, Merck, Roche, Imcyse, ABSci, BMS-Celgene (Cel), AdScientiam. CG: Actelion, NVS, Sanofi, GeNeuro, Roche, Siemens, Biogen, Teva, Merck, Janssen. YMD: Acorda, Bayer, Biogen, BMS-Cel, Chugai, EMDSerono(Ser), Genentech (Gene)-Roche, Horizon/Amgen, Janssen, NVS, Sanofi, Teva, NIAID, NIH NINDS, PCORI. GC: DSMB: APLT, AI, AMO, AZ, Avexis, Biolinerx, BrainStormCell, BMS-Cel, CSLBehring, Galmed, GreenValley, Horizon, Immunic, Karuna, Mapi, Merck, MitsubishiTanabe, Opko, Prothena, NVS, REGN, Sanofi, Reata, Teva, NHLBI, UTSouthwestern, UPenn, VTI; Alexion, Antisense, Biogen, ClinTrialSol, Entelexo, Sanofi, Gene, GW, Immunic, Immunosis, KleinBuendel, Merck/Ser, NVS, Perception, Protalix, REGN, Roche, SAB, UAB, Pythagoras. OK: Sanofi, Roche, Gene, Merck, NVS, GeNeuro, BMS-Cel, Mapi, VielaBio, Teva. IS: Sanofi, Ewo-Biogen, Shire, Gedeon-Richter, Teva, BI, Pfizer, Bayer, Roche, Mylan, Polpharma, Penumbra, Adapt, Merck, GL, Medochemie, NVS, Viatris, Nobel. MD: Sanofi. XM: Abbvie, Actelion, Alexion, Bial PD, Biogen, BMS-Cel, EMD Ser, Genzyme, Roche, Immunic, Janssen, MedDay, Medscape, Merck, Mylan, Nervgen, Neurax, NVS, Peervoice, Samsung-Biosys, Sandoz, Sanofi, Teva, TG, Excemed, ECTRIMS, MSIF, NMSS. SK: Biogen, EMDSer, Gene, Genzyme, Mallinckrodt, MedDay, NVS, Octave, Teva, TG. SS, XL, BS, BD, PT, EW: Sanofi Emp. GG: AbbVie, Actelion, Atara, Biogen, Canbex, Cel, EMD Ser, Japan Tobacco, Sanofi, Gene, GSK, GW, Merck, NVS, Roche, Synthon, Teva.

EPR-061 | Frexalimab reduces plasma neurofilament light chain in relapsing multiple sclerosis: Week 72 data from phase 2 trial

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Background and aims: Frexalimab, a second-generation anti-CD40L antibody, inhibits the CD40/CD40L pathway that regulates adaptive and innate immunity. During the double-blind period of a phase-2 trial (NCT04879628) in participants with relapsing multiple sclerosis (pwRMS), frexalimab showed an 89% reduction in new gadolinium-enhancing T1-lesions in the 1200mg/intravenous (IV) every-4-weeks (q4w) arm versus placebo at week (W) 12. This was accompanied by a reduction in neurofilament light chain (NfL), a biomarker of neuroaxonal damage. Treatment effect has been sustained in the open-label extension (OLE). Here, we describe changes in NfL through W72.
Methods: 129 pwRMS were randomized (4:4:1:1) to frexalimab-1200mg/IV q4w, frexalimab-300mg/subcutaneous (SC) q2w, or matching placebos. After W12, participants receiving placebo switched to respective frexalimab arms and entered the OLE ($n=125$). Plasma samples were collected from baseline through W72. NfL levels were measured using Quanterix Simoa® NF-LIGHT™ assay and summarized as geometric means.
Results: 111/125 participants remained on treatment at W72. Baseline NfL levels ($n=122$; geometric mean [SD]) were similar across groups ($F=0.10$, $p=0.96$): 11.8 [2.0], frexalimab-1200mg/IV; 12.6 [1.8], frexalimab-300mg/SC; 12.4 [1.9], placebo-IV/frexalimab-1200mg/IV; and 12.1 [1.8], placebo-SC/frexalimab-300mg/SC. At W72 ($n=106$), NfL levels reduced to 7.3 [1.6], 7.2

[1.9], 9.4 [1.7], and 7.1 [1.8] pg/mL, respectively. In participants with both baseline and W72 data ($n = 104$), there was a 40%, 45%, 25%, and 40% reduction in NfL geometric mean over time, respectively. Associations between the reduction in NfL and changes in MRI endpoints (baseline–W72) will be presented at the meeting.

Conclusion: The observed reduction in NfL through W72 indicates that frexalimab markedly reduces neuroaxonal damage in pwRMS.

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EPR-062 | Pediatric MS: Phenotypic characterization and pubertal influences on disease activity from the Danish MS Registry

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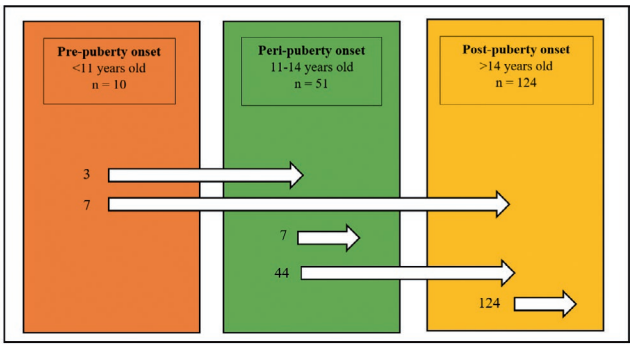
Background and aims: Pediatric-onset multiple sclerosis (POMS) constitutes ~5% of MS cases and presents distinct clinical and diagnostic challenges. Puberty, characterized by significant hormonal changes, may influence disease presentation, relapse rates, and long-term outcomes. This study aimed to investigate the impact of pubertal stages on clinical characteristics, relapse activity and disability progression in POMS using data from the Danish MS Registry (DMSR).

Methods: A nationwide cohort of 185 POMS patients included and s categorized into pre-pubertal (<11 years), peri-pubertal (11–14 years), and post-pubertal (>14 years) onset groups. Demographics, presenting symptoms, MRI findings, relapse rates, and Expanded Disability Status Scale (EDSS) scores were compared. Patients transitioning between pubertal stages ($n = 54$) were analyzed longitudinally for relapse rate.

Results: Pre-pubertal onset was associated with severe symptoms (cerebellar involvement, $p = 0.042$), greater lesion burden, higher 10-year disability (EDSS median = 3.75, $p = 0.039$), and lower relapse rates (ARR = 0.200). Male sex reduced relapse rates ($p = 0.013$). Female-to-male ratio increased from 1:1 pre-puberty to ~2:1 after puberty. Pre-pubertal patients transitioning to peri- or post-puberty showed increasing relapse rates, peaking during peri-puberty (ARR = 0.302).



Study population n=185; Total number of patients transitioned across at least two different pubertal epochs n=54.

FIGURE 1 Pre-, Peri- and Post puberty epochs by age of disease onset

TABLE 1 Relapse Risk and Key Determinants between Pubertal Groups compared to Post-puberty epoch.

	Total (N=185)	Pre-puberty onset (N=10)	Peri-puberty onset (N=51)	Post-puberty onset (N=124)	*p-value*
Median age at onset, [IQ range]	16 [14, 17]	9 [8, 10]	13 [12, 14]	16 [16, 17]	-
Female Sex, n (%)	124 (67.0)	5 (50.0)	35 (68.6)	84 (67.7)	-
Female-to-male ratio	2.03	1.0	2.19	2.10	*0.502*
Median disease duration at end of follow-up in years, [IQ range]	9.36 [4.1, 11.1]	12.3 [4.9, 17.9]	8.6 [4.7, 13.4]	7.65 [4.1, 10.3]	-
Median time from first clinical event to first visit in months, [IQ range]	10.8 [2.4, 26.4]	35.4 [16.8, 73.2]	14.4 [3.6, 30.6]	7.2 [2.4, 21.9]	-
Presenting symptoms at disease onset					
Visual, n (%)	31 (16.9)	*< 3*	7 (13.7)	22 (17.7)	*0.739*
Pyramidal, n (%)	26 (14.0)	3 (30.0)	6 (11.8)	17 (13.7)	*0.188*
Brainstem, n (%)	33 (17.8)	*< 3*	12 (23.5)	19 (15.3)	*0.400*
Sensory, n (%)	53 (28.6)	*< 3*	15 (29.4)	37 (29.8)	*0.496*
Cerebellar, n (%)	4 (2.2)	*< 3*	0 (0)	*< 3*	***0.042***[a]
Bowel and bladder, n (%)	*< 3*	0 (0)	*< 3*	0 (0)	*0.267*
Multifocal, n (%)	27 (14.6)	0 (0)	9 (17.6)	18 (14.5)	*0.415*
Unknown, n (%)	10 (5.4)	0 (0)	*< 3*	9 (7.3)	*0.408*
EDSS year 0					
Mean (SD)	1.76 (1.48)	2.6 (2.54)	1.62 (1.45)	1.75 (1.38)	
Median [IQR]	1.5 [1.0, 2.5]	2 [0.5, 4.125]	1.5 [0, 2.5]	1.5 [1, 2.5]	*0.437*
Missing N (%)	0 (0)	0 (0)	0 (0)	0 (0)	
EDSS year 2 ± 6 months					
Mean (SD)	1.43 (1.59)	3.50 (4.09)	1.54 (1.11)	1.07 (1.15)	
Median [IQR]	1.0 [0, 2.0]	2.50 [1.25, 5.25]	1.0 [1.0, 2.0]	1.0 [0, 1.50]	*0.340*
Missing N (%)	148 (80.0)	7 (70.0)	38 (74.5)	103 (83.1)	
EDSS year 5 ± 6 months					
Mean (SD)	1.34 (1.41)	1.50 (2.12)	1.35 (1.25)	1.32 (1.50)	
Median [IQR]	1.0 [0, 2.0]	1.50 [0.75, 2.25]	1.75 [0, 2.0]	1.0 [0, 2.0]	*0.933*
Missing N (%)	153 (82.7)	8 (80.0)	41 (80.4)	104 (83.9)	
EDSS year 10 ± 6 months					
Mean (SD)	1.39 (1.69)	4.12 (2.95)	1.23 (1.17)	0.92 (1.09)	
Median [IQR]	1.0 [0, 2.0]	3.75 [2.50, 5.38]	1.0 [0, 2.0]	0.50 [0, 2.0]	***0.039***[b]
Missing N (%)	150 (81.1)	6 (60.0)	40 (78.4)	104 (83.9)	
First disease-modifying therapy, n (%)					
Alemtuzumab, n (%)	5 (2.7)	*< 3*	*< 3*	3 (2.4)	-
Anti-CD20. n (%)	23 (12.4)	0 (0)	6 (11.8)	17 (13.7)	-
Natalizumab, n (%)	23 (12.4)	*< 3*	3 (5.9)	19 (15.3)	-
Orals, n (%)	108 (58.5)	4 (40.0)	36 (70.5)	68 (54.9)	-
Injectables, n (%)	21 (11.3)	4 (40.0)	4 (7.8)	13 (10.5)	-
Never treated, n (%)	5 (2.7)	0 (0)	*< 3*	4 (3.2)	-

[a] *Fisher exact test, p adj = 0.042;* [b] *Kruskal Wallis p.adj = 0.033.*
< 3 = The cell has been masked to ensure adherence to GDPR requirements.

Conclusion: Puberty significantly modulates disease course in POMS, emphasizing the need for early, sex-specific interventions, proactive monitoring, and further exploration of hormonal influences on disease progression and treatment response.

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Muscle and neuromuscular junction disorder 1

EPR-063 | Novel RRM2B gene variants associated with mitochondrial DNA deletions syndrome

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Background and aims: Mutations in the nuclear-encoded mitochondrial maintenance gene RRM2B are an important cause of familial mitochondrial disease in both adults and children and represent the third most common cause of multiple mitochondrial DNA deletions in adults. We report a series of six patients (four symptomatic cases) with novel RRM2B gene variants associated with mitochondrial DNA deletions syndrome and stress the relevance of muscle biopsy to sustain the diagnosis of primary mitochondrial dysfunction and, in cases like ours, to provide material for biochemical and molecular studies required to support the pathogenicity of novel variants.

Methods: Investigations included clinical and routine laboratory analyses, electrodiagnostic studies, muscle biopsy and molecular genetics.

Results: Evaluation of the clinical features of the symptomatic patients harboring pathogenic RRM2B variants showed that PEO associated with ptosis were universal. Neuromuscular features included proximal muscle weakness and fatigue (3 patients). Needle electromyography revealed a myopathic pattern. CK was occasionally elevated up to 380U/L. Muscle biopsy finding showed subsarcolemmal mitochondrial accumulation (ragged-red or ragged-blue fibers) after Gomori trichrome staining or SDH enzyme histochemistry (Figure 1.A&B). A multigene panel detected previously unreported heterozygous change in RRM2B gene, c.941del, p.(Asn314Thrfs*4) in one case and c.1045G > A, p.(Ala349Thr) in 5 patients. All patients who underwent muscle biopsy had multiple mitochondrial DNA deletions detectable either by long-range PCR assays or by Southern blot analysis (Figure 2).

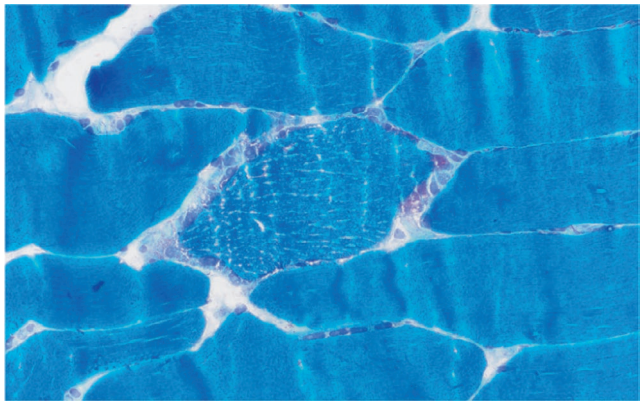

FIGURE 1A

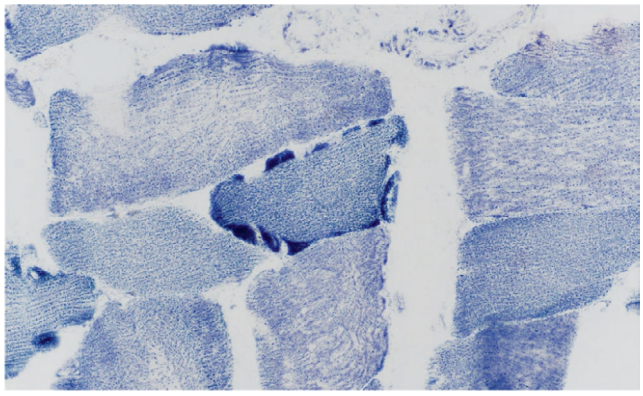

FIGURE 1B

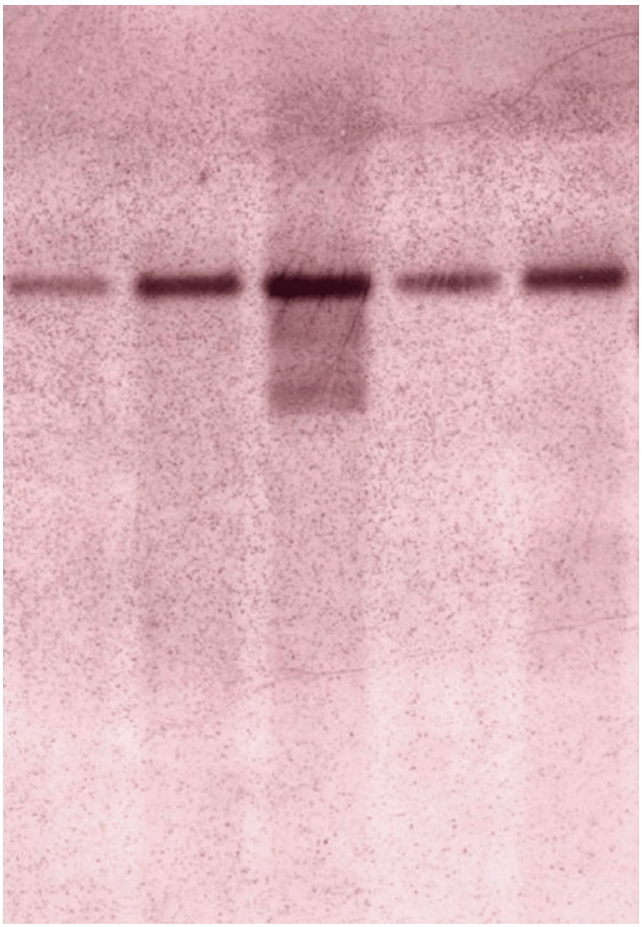

FIGURE 2

Conclusion: Our results support the pathogenicity of two novel RRM2B variants found in patients with multiple mtDNA deletions and highlights the utility of muscle biopsy in clarifying variants of unknown significance.
Disclosure: Nothing to disclose.

EPR-064 | Efgartigimod in pretreated patients with CIDP and progressive/relapsing or persistent disease activity

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Background and aims: In the ADHERE trial, subcutaneous (SC) efgartigimod PH20 (co-formulated with recombinant human hyaluronidase PH20) reduced relapse rate and was well tolerated in chronic inflammatory demyelinating polyneuropathy (CIDP). This post hoc analysis explores a pre-specified subgroup of participants with prior CIDP treatment and progressive/relapsing or persistent disease activity (CIDP Disease Activity Status ≥4).
Methods: Participants withdrew CIDP treatments during a ≤12-week run-in. Participants with active disease entered stage A and received weekly efgartigimod PH20 SC 1000 mg. Those with evidence of clinical improvement entered stage B and were randomized (1:1) to weekly efgartigimod PH20 SC 1000 mg or placebo for ≤48 weeks (Figure). Secondary efficacy outcomes and safety are reported.

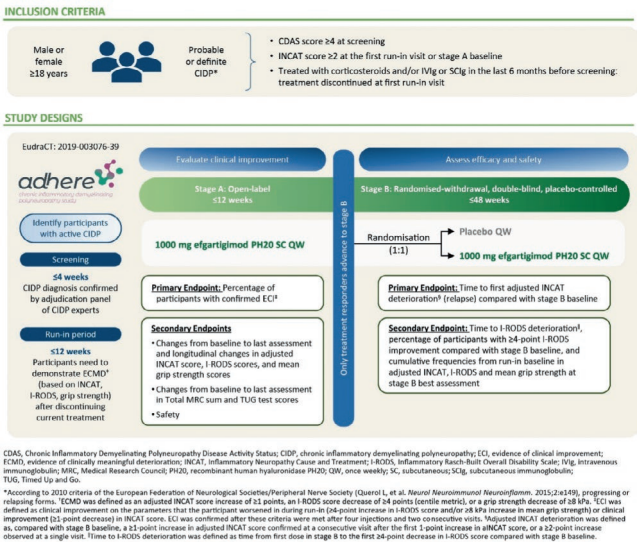

FIGURE 1 ADHERE study design, with inclusion criteria for the pre-specified subgroup of pretreated CIDP participants with persistent disease activity or progressive/relapsing active disease

Results: 139/322 participants met specified criteria and entered stage A; 95 were randomized and treated in stage B (efgartigimod PH20 SC: 48, placebo: 47). Mean Inflammatory Rasch-built Overall Disability Scale (I-RODS) score and mean grip strength (MGS) improved from stage (A and B) baseline to respective last assessment in efgartigimod-treated participants (Table 1). Mean I-RODS and MGS scores also improved from stage A-baseline to stage B-baseline. In efgartigimod-treated participants, improvements were maintained up to stage B-last assessment; scores deteriorated in placebo-treated participants in stage B. In stage B, efgartigimod PH20 SC reduced the I-RODS deterioration rate by 60% versus placebo (Table 1). Adverse events were mostly mild or moderate (Table 2). Results by CIDP treatment will be presented at the meeting.

TABLE 1 Secondary efficacy endpoints in the ADHERE trial in the pre-specified subgroup of pretreated CIDP participants with persistent disease activity or progressive/relapsing active disease.

	Stage A Efgartigimod PH20 SC (n=139)	Stage B Efgartigimod PH20 SC (n=48)	Stage B Placebo (n=47)
Mean (SE) change from baseline to last assessment*			
Adjusted INCAT score	−1.0 (0.16)	0.0 (0.16)	1.5 (0.30)
I-RODS score	9.1 (1.45)	1.3 (1.56)	−13.5 (3.14)
Grip strength (dominant hand), kPa	14.0 (1.66)	2.4 (1.98)	−14.3 (3.10)
Grip strength (non-dominant hand), kPa	13.3 (1.63)	3.5 (2.01)	−12.4 (3.38)
Total MRC sum score	3.9 (0.75)	−0.5 (0.71)	−5.7 (1.64)
TUG test score, s	−4.1 (1.08)	0.6 (0.46)	2.9 (0.98)
I-RODS decrease of ≥4 points, n (%)†		18 (37.5)	31 (66.0)
Hazard ratio (95% CI)		0.400 (0.218–0.734)	
Nominal *P* value		0.0031	
I-RODS improvement of ≥4 points, n (%)†		24 (50.0)	15 (31.9)
Odds ratio (95% CI)		2.433 (0.961–6.432)	
Nominal *P* value		0.0621	
Cumulative frequencies of stage B best assessment from run-in baseline, n (%)†			
Adjusted INCAT decrease of ≥1 points		32 (66.7)	20 (42.6)
I-RODS increase of ≥4 points		25 (52.1)	18 (38.3)
Mean grip strength increase ≥8 kPa in any hand		35 (72.9)	22 (46.8)

CI, confidence interval; INCAT, Inflammatory Neuropathy Cause and Treatment; I-RODS, Inflammatory Rasch-built Overall Disability Scale; MRC, Medical Research Council; PH20, recombinant human hyaluronidase PH20; s, second(s); SC, subcutaneous; SE, standard error; TUG, timed up and go.
*For stage A, this was the change from stage A baseline to stage A last assessment, and for stage B, this was the change from stage B baseline to stage B last assessment.
†Value thresholds representing minimal clinically important differences are utilised for these assessments (adjusted INCAT change of ≥1 point, I-RODS change of ≥4 points and mean grip strength change of ≥8 kPa in any hand).

TABLE 2 Incidence and event rates of adverse events in the pre-specified subgroup of pretreated CIDP participants with persistent disease activity or progressive/relapsing active disease

n (%) [event rate]	Stage A Efgartigimod PH20 SC (n=139; PYFU= 18.7)	Stage B Efgartigimod PH20 SC (n=48; PYFU= 24.2)	Stage B Placebo (n=47; PYFU= 12.9)
≥1 TEAE	92 (66.2) [14.5]	36 (75.0) [4.6]	27 (57.4) [5.2]
≥1 treatment-related TEAE*	43 (30.9) [5.1]	16 (33.3) [1.6]	12 (25.5) [1.5]
≥1 SAE	7 (5.0) [0.5]	1 (2.1) [0.04]	4 (8.5) [0.5]
≥1 treatment-related SAE*	2 (1.4) [0.1]	0	4 (8.5) [0.4]
≥1 AE of infections†	18 (12.9) [1.2]	21 (43.8) [1.1]	16 (34.0) [1.8]
Discontinued due to TEAEs	8 (5.8) [0.4]	0	1 (2.1) [0.07]
Deaths‡	2 (1.4) [0.1]	0	1 (2.1) [0.07]

AE, adverse event; CIDP, chronic inflammatory demyelinating polyneuropathy; PH20, recombinant human hyaluronidase PH20; PYFU, patient-year(s) of follow-up; SAE, serious adverse event; SC, subcutaneous; TEAE, treatment-emergent adverse event.
*Deemed treatment-related by the investigator. †Infections and infestations are grouped under System Organ Class (Medical Dictionary for Regulatory Activities v. 25.1).
‡Deemed to be not related to efgartigimod PH20 SC by the investigator.
Event rates were calculated as the number of events divided by the PYFU.
ADHERE+ data cut-off: 15 June 2023.

Conclusion: Efgartigimod PH20 SC provided clinical improvement and was well tolerated in pretreated patients with CIDP and progressive/relapsing or persistent disease activity.

Disclosure: TS: Alexion, Alnylam, argenx, Bayer Vital, Biogen, Bristol Myers Squibb, Celgene, Centogene, CSL Behring, EUROIMMUN, Grifols, Hexal AG, Horizon, Janssen-Cilag, Merck Serono, Novartis, Pfizer, Roche, Sanofi, Siemens, Swedish Orphan Biovitrum, Teva Pharmaceuticals, Viatris; JAA: Akcea Therapeutics, Alexion, Alnylam, Annexon Biosciences, argenx, CSL Behring, Grifols, Immunovant, ImmuPharma, J&J, Pfizer, Takeda; SR: Annexon Biosciences, argenx, CSL Behring, Dianthus Therapeutics, EXCEMED, Fresenius, Hansa Biopharma, Takeda, UCB; GL: Biogen, Chromocell, CSL Behring, Home Biosciences, Janssen, Lilly, Sangamo Therapeutics, Vertex Pharmaceuticals, Zambon; LQ: Alnylam, Annexon Biosciences, argenx, Avilar Therapeutics, Biogen, CSL Behring, Dianthus, Grifols, Janssen, LFB, Lundbeck, Merck, Novartis, Octapharma, Roche, Sanofi, UCB; LM: Alexion, Alnylam, argenx, Biogen, CSL Behring, LFB, Novartis, Pfizer, Roche, Sanofi; ADR, BVH, EH, GI: argenx; MS: argenx, Bayer, Biogen Idec, Biotest, CSL Behring, Genzyme, Grifols, Immunovant, Kedrion, Merck, Novartis, Octapharma, Roche, Sanofi-Aventis, Teva Pharmaceuticals, UCB; RAL: Alexion, Annexon Biosciences, argenx, Avilar Therapeutics, BioCryst, Boehringer Ingelheim, CSL Behring, Dianthus Therapeutics, Grifols, Immunovant, Intellia Therapeutics, J&J, Nervosave Therapeutics, Novartis, Nuvig Therapeutics, Sanofi, Seismic Therapeutic, Takeda, TGTX; PAvD: Annexon Biosciences, argenx, Grifols, Hansa Biopharma, Octapharma, Roche, Sanofi, Sanquin, Takeda

EPR-065 | Myasthenic crises, exacerbations, and corticosteroid use in US patients receiving Ravulizumab or Efgartigimod

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Background and aims: Ravulizumab (terminal complement inhibitor) and efgartigimod (neonatal Fc receptor blocker) are approved to treat anti-acetylcholine receptor antibody-positive generalized myasthenia gravis (gMG). However, real-world data comparing outcomes with these treatments remains limited. This study evaluated pre- and post-treatment initiation hospitalizations due to crises or exacerbations and corticosteroid use among patients with gMG receiving ravulizumab or efgartigimod.

Methods: Physician-abstracted medical records were included for adults with gMG in Cardinal Health's Neurology Provider Extended Network initiating first targeted immunotherapy on/after 01Dec2021. Hospitalizations due to crises or exacerbations were evaluated in the 6 months pre- and post-treatment initiation; corticosteroid use was evaluated throughout treatment.

Results: In total, 45 patients received ravulizumab (female, 35.6%; mean ± SD age at initiation: 61.5 ± 13.6), and 107 received efgartigimod (54.2%; 57.0 ± 16.6). Pre-initiation, 5 ravulizumab and 3 efgartigimod patients had crises-related hospitalizations; post-initiation, zero hospitalizations for crises occurred in either group. Pre-initiation, 9 patients in both groups experienced exacerbation-related hospitalization; post-initiation, zero ravulizumab patients and 2 efgartigimod patients experienced exacerbation-related hospitalization. Mean exacerbation-related hospitalizations per patient per month decreased from 0.17 to 0 among ravulizumab patients and increased from 0.19 to 0.25

among efgartigimod patients. Among patients taking oral corticosteroids (OCS) at initiation, 17/19 (89.5%) ravulizumab patients and 33/46 (71.7%) efgartigimod patients reduced/discontinued their OCS dose post-initiation.
Conclusion: After initiation of either ravulizumab or efgartigimod, fewer patients were hospitalized due to crises or exacerbation, and both treatments were associated with OCS sparing. However, patients receiving ravulizumab trended toward fewer event-related hospitalizations and a greater reduction in steroid use compared with those receiving efgartigimod.
Disclosure: CAS has received compensation for medical advisory board membership and/or serving as a speaker for Alexion, AstraZeneca Rare Disease, argenx, CSL Behring, and UCB. SPM has served as a consultant for Abbvie, Alexion, argenx, Catalyst, Grifols, KabaFusion, Supernus, and UCB. NS is a paid speaker for Alexion and Catalyst. KSY is an employee of Alexion, AstraZeneca Rare Disease, and holds stock or stock options in AstraZeneca and Takeda. JL, JCY, MB, EW, and NN are employees of Alexion, AstraZeneca Rare Disease and hold stock or stock options in AstraZeneca. DG, JS, and PP are employees of Cardinal Health, which received funding to conduct this research. MTP has received compensation for medical advisory board membership or regional advisory board participation from Alexion, AstraZeneca Rare Disease, Amgen, argenx, Catalyst, CSL Behring, Immunovant, and UCB.

EPR-066 | Comprehensive analysis of motor endplate pathology in AChR-Ab-positive myasthenia gravis

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Background and aims: Since the 1970s, it has been established that complement deposition at the neuromuscular junction (NMJ) in AChR-ab+ myasthenia gravis (MG), leads to motor endplate destruction. However, no in-depth studies have been conducted since these early observations. We aimed to re-examine the NMJ in AChR-ab+ MG, motivated by the rapid effects of novel therapies which suggest that complete NMJ destruction is unlikely.
Methods: Intercostal muscle (ICM) biopsies from 30 AChR-ab+ MG patients are analyzed by histology, electron microscopy (EM), transcriptomic and proteomic analysis, and compared to non-myasthenic controls.
Results: Histological analysis revealed C5b-9-deposition at ~75% (interindividual range of 33-100%) of all NMJs investigated. EM studies showed postsynaptic simplification and shortened clefts, though not all NMJs showed endplate destruction. There was notable inter- and intraindividual variability in endplate destruction despite overall high rates of complement deposition. Transcriptomic analysis revealed upregulation of immune cell markers with TNFA, STAT3 and IL6 showing the strongest expression. Proteomic analysis are pending. Additionally, we will investigate a potential correlation between NMJ destruction and disease severity.
Conclusion: Our findings demonstrate variability in complement deposition and NMJ destruction in AChR+ MG, indicating that not all NMJs are equally affected. Histologic and transcriptomic analyses suggest a critical role of macrophages, which could promote future therapeutic strategies.
Disclosure: Project supported by Janssen Pharmaceutica NV, a Johnson and Johnson company

EPR-067 | Real world study in Italian public hospital with Efgartigimod in patients affected by generalized myasthenia gravis

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Background and aims: Myasthenia gravis (MG) is an autoimmune neuromuscular disorder caused by IgG autoantibodies targeting the neuromuscular junction. Recycling of IgG is mediated by the neonatal Fc receptor (FcRn). Efgartigimod, an Fc fragment of human IgG1, has demonstrated efficacy in MG; however, the clinical characteristics of patients with the highest response remain unclear.
Methods: Twelve patients with AChR-positive generalized MG were treated with two cycles of Efgartigimod over one year, and nine patients completed a third cycle. Clinical evaluation was conducted using MG-ADL at four time points and QMG at the beginning and end of each cycle. MG-ADL and QMG scores were further subdivided into ocular (O), bulbar (B), and generalized (G) symptom subdomains, and patients were classified as predominantly ocular (pO), bulbar (pB), or generalized (pG) based on symptom prevalence.
Results: Significant improvements were observed in MG-ADL and QMG from baseline across all symptom subdomains. Baseline AChR antibody levels correlated with MG-ADL improvement ($p < .04$). Thymectomized patients demonstrated superior outcomes, with MG-ADL improving by 62% versus 22% ($p < .01$) and QMG by 45% versus 3.5% ($p < .01$) during the first two cycles. Patients with pO symptoms responded less to therapy, with generalized symptoms contributing most to the minor response.

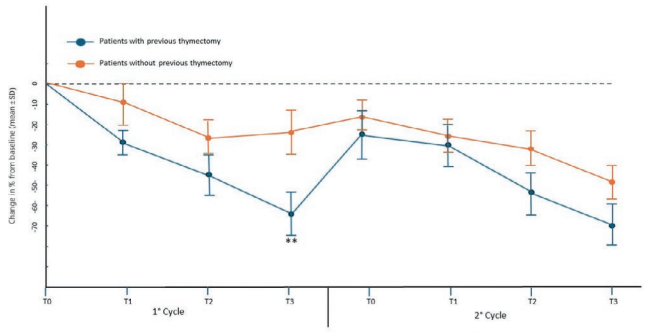

Fig 1 Percentage change from baseline in MG-ADL

FIGURE 1 Change of mean MG-ADL (SD) from baseline (T0 of 1°cycle) of patients with previous thymectomy or not. ** $p < .01$ with *U*-Mann–Whitney test

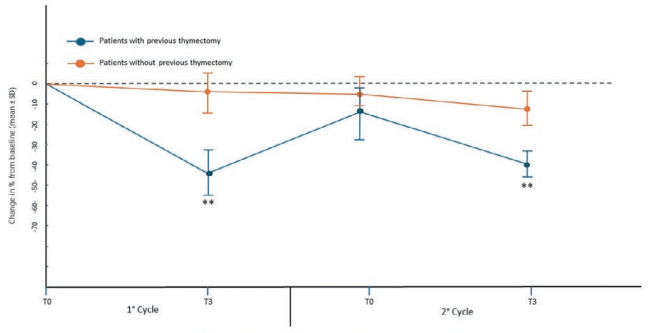

Fig 2 Percentage change from baseline in QMG

FIGURE 2 Change of mean QMG (SD) from baseline (T0 of 1°cycle) of patients with previous thymectomy or not. ** $p < .01$ with *U*-Mann–Whitney test.

Conclusion: Our findings suggest that patients with high baseline AChR antibody titers, previous thymectomy, and non-ocular symptom predominance respond better to Efgartigimod. These results underscore the need for larger studies to validate these observations and optimize patient selection.
Disclosure: Nothing to disclose.

EPR-068 | Pulmonary manifestations in adult patients with Dermatomyositis (DM): Effect of intravenous immunoglobulins

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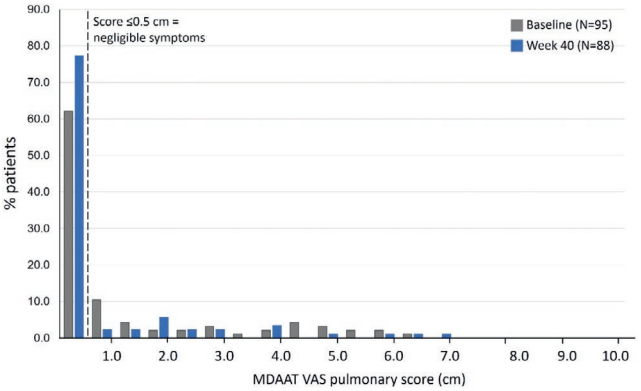
Background and aims: Pulmonary manifestations (e.g., interstitial lung disease) are a major cause of morbidity and mortality in patients with dermatomyositis (DM). The ProDERM trial was designed to evaluate the efficacy and safety of intravenous immunoglobulin (IVIg) in adult DM patients.

Methods: The ProDERM trial was a placebo-controlled, double-blind, Phase 3 study. We present a post-hoc analysis of the ProDERM data on the effect of IVIg on pulmonary symptoms. Investigators assessed pulmonary symptoms at baseline and all subsequent visits by using the Myositis Disease Activity Assessment Tool (MDAAT). Visual analog scales (VAS) were scored over 10 cm to quantify overall pulmonary disease activity (higher score indicating worse disease). Physicians also reported presence/absence of dysphonia, dyspnea or cough from active reversible ILD, and dyspnea from respiratory muscle weakness on MDAAT.
Results: At baseline 59/95 patients (62.1%) had a pulmonary VAS ≤0.5 cm (Figure 1), indicating no myositis lung involvement. By Week 40, the number of patients with a VAS ≤0.5 cm increased to 68 of the 88 patients with available data (77.3%; $p = 0.007$). At week 16 (end of placebo-controlled phase) data of patients with VAS > 0.5 cm showed a mean decrease in the IVIg group of 1.15 cm ($n = 12$; 37.7%; $p = 0.001$) versus 0.17 cm (6.5%) in patients on placebo ($n = 21$; $p = 0.50$). The percentage of patients with dysphonia decreased from 20% at baseline to 8% at Week 40 ($p = 0.04$).



MDAAT = myositis disease activity assessment tool; VAS = visual analog scale

FIGURE 1 MDAAT pulmonary VAS score at baseline and Week 40.

Conclusion: IVIg may have favorable effects on active pulmonary manifestations of DM. Future studies should include pulmonary outcomes.
Disclosure: J. Schessl: Pfizer, Octapharma C. Charles-Schoeman: Pfizer, Octapharma, AbbVie, Bristol Myers Squibb, Boehringer Ingelheim, Recludix, Galapagos, Sana Biotechnology, Immunovant, Pfizer, Alexion, Priovant, CSL Behring, E. Clodi: Employee of Octapharma R. Aggarwal: Boehringer Ingelheim, Bristol Myers Squibb, EMD Serono, Janssen, Priovant, Pfizer, Alexion, ANI Pharmaceutical, Argenx, Artasome, AstraZeneca, CabalettaBio, Capella, Capstanx, Corbus, CSL BEhring, Glaapagos, Horizontal Therapeutics, I-Cell, Immunovant, Kezar, Kyverna, Lilly, Manta Medicines, Novartis, Nuvig Therapeutic, Nakarta, Octapharma, Teva, Tourmaline Bio & Verismo Therapeutics

EPR-069 | Association of recent infection and subsequent myasthenia gravis: A nationwide case-control study from 1985 to 2020

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Background and aims: Infections have been suggested to trigger myasthenia gravis (MG) onset. We determined the association between recent infections and the subsequent development of MG.
Methods: We used nationwide health registers from 1985 to 2020 to identify MG patients by linking individual-level data across registers. Each patient was matched to 10 controls from the general population based on age, sex, and diagnostic index date. Using conditional logistic regression, we computed matched odds ratios (ORs) with 95% confidence intervals to assess the relative risk of developing MG following recent infection. Analyses were adjusted for baseline comorbidities.
Results: We identified 2,110 MG patients and 21,100 matched individuals from the general population, with 27.4% aged 50 years or younger. In the year preceding MG diagnosis (excluding the month before diagnosis), 4.9% of MG patients experienced a hospital-diagnosed infection, compared to 2.8% in the general population, with an OR of 1.8 (95% CI: 1.5–2.2). The strongest associations were observed for lower respiratory tract and ear, nose, and throat infections. Comorbidity-adjusted analyses did not alter the results (OR 1.7, 95% CI 1.4-2.2).
Conclusion: MG patients have a 1.8-fold higher infection risk in the year prior to diagnosis compared to the general population, likely due to unrecognized respiratory and bulbar dysfunction or infections triggering MG development. Clinical awareness of this association could enable early prevention and intervention strategies.
Disclosure: Nothing to disclose.

EPR-070 | Ulviprubart pharmacokinetics, pharmacodynamics (PK/PD), and safety: Inclusion body myositis (IBM) phase 1 study results

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Background and aims: IBM is a rare, progressive disease characterized by invasion of muscle by highly differentiated cytotoxic CD8+ T cells. Ulviprubart, a monoclonal antibody, selectively depletes cytotoxic CD8+ KLRG1+ T cells by targeting KLRG1 expressed on most IBM-muscle–infiltrating T cells. Here, we describe PK/PD and safety of ulviprubart in patients with IBM.
Methods: In this phase 1, open-label study (NCT04659031), initial patients received subcutaneous ulviprubart (0.1, 0.5, or 2.0 mg/kg) as a single dose prior to dosing every 8 weeks (Q8W) ~6–12 months later, while later patients received 2.0 mg/kg Q8W; patients received ulviprubart for up to 18 months. PK/PD and safety with ulviprubart were assessed.
Results: Nineteen patients (mean age, 66 years; 79% male) were enrolled (0.1 mg/kg: $n=3$; 0.5 mg/kg: $n=3$; 2.0 mg/kg: $n=13$). Ulviprubart displayed a long absorption phase, slow clearance, and 21-day half-life. Peripheral CD8+ KLRG1+ and CD4+ KLRG1+ T-cell depletion was achieved, with mean CD8+ KLRG1+ T-cell maximum depletions of 69%, 97%, and 98% after single doses of 0.1, 0.5, and 2.0 mg/kg, respectively. Effector CD8+ T-cell populations (T-cell effector memory [TEM] and TEMs expressing CD45RA [TEMRA]) were depleted to the extent of their KLRG1 expression. Regulatory T cells and B cells were preserved. No serious adverse events (AEs) or discontinuations due to AEs were reported.
Conclusion: In patients with IBM, ulviprubart led to sustained selective depletion of peripheral blood CD8+ KLRG1+ T cells and had a favorable safety profile.
Disclosure: M Needham, RD Henderson, and C Liang: Abcuro, Inc. — Consultant D Soler-Ferran and HJ Wilkins: Abcuro, Inc. – Employment S Greenberg: Abcuro, Inc. – Founder; Consultant

EPR-071 | Clinical outcome of myasthenic crisis: A multicenter prospective study

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Background and aims: Myasthenic crisis (MC) affects 15-20% of patients with MG (Myasthenia gravis) and remains a major clinical challenge, with high mortality and significant economic burden. With advances in disease monitoring and rescue therapies, the in-hospital mortality for MC reduced significantly. However, studies regarding the long-term outcomes post-MC are limited.
Methods: This observational multicenter cohort study with prospective collected patients diagnosed with MC or impending MC between December 2018 and October 2024 (NCT04837625). Outcome measures included all-cause mortality,1-year MGFA postintervention status (PIS), and long-term complications associated with MG.

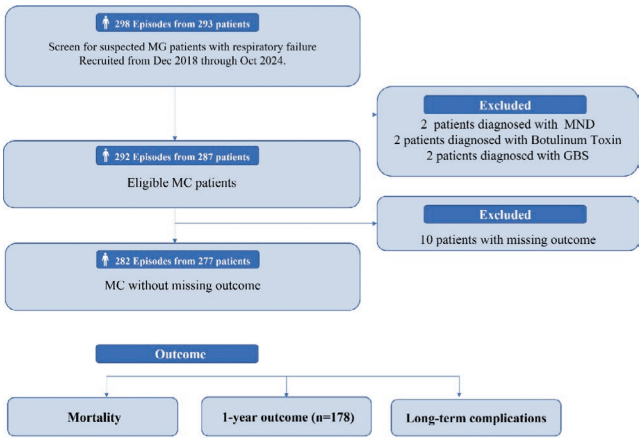

FIGURE 1 Flowchart of the study cohort.

Results: In this cohort, we included 282 episodes of myasthenia gravis (MG) with an average follow-up time of 26.13 ± 23.5 months and 923 clinical assessments. The all-cause mortality rate was 14.9% (42/282), with an in-hospital mortality rate of 4.96% (14/282). The primary causes of death were infectious shock (42.9%), multiple organ failure (16.2%), myocarditis (16.2%), and thymoma recurrence (8.1%). Kaplan–Meier survival curves indicated that patients with thymoma-associated myasthenia gravis (TAMG) had a significantly lower survival rate compared to those with late-onset (LOMG) and early-onset myasthenia gravis (EOMG) throughout the observation period ($p < 0.001$). Among 178 patients with consecutive 1-year follow-up, 44.9% (80/178) achieved minimal manifestation (MM) status or better. Long-term complications included recurrent infections (11.0%), gastrointestinal ulcers (8.2%), metabolic abnormalities (8.2%), osteoporosis (4.9%), and chronic pain (4.4%).

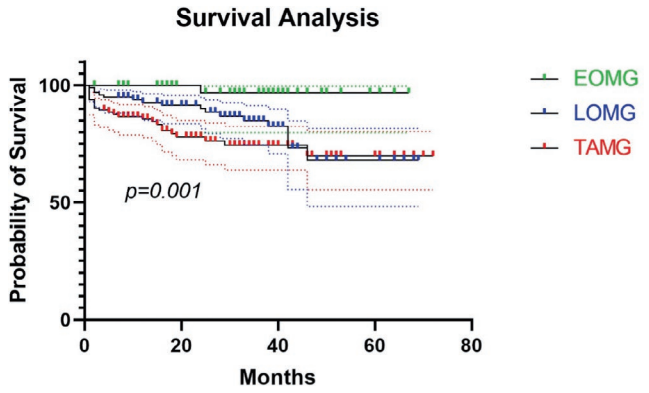

FIGURE 2 Kaplan–Meier survival analysis of thymoma-associated myasthenia gravis, late-onset and early-onset myasthenia Gravis

Conclusion: This is the first prospective cohort study to report the long-term outcomes of MG patients post-MC, highlighting the importance of disease monitoring and timely intervention in improving the life quality of MG.
Disclosure: Nothing to disclose.

EPR-072 | Expanding the genotype-phenotype spectrum of KCNA2-related disorders

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Background and aims: The aim of this study was to refine the genotype and phenotypic spectrum of KCNA2-related disorders.
Methods: We collected phenotypic data of patients with electrophysiologically characterized KCNA2 variants through literature search, an international network of epilepsy and genetic centers.
Results: 122 patients (52 novel, 70 published) harboring KCNA2 pathogenic variants were collected. Inheritance was: de novo = 65, familial = 20, unknown = 37. Functional studies revealed: Loss-Of-Function (LOF) in 71/122, Gain-Of-Function (GOF) 38/122, GOF-LOF 13/122. Mean age at epilepsy onset was 3.5 months in GOF-LOF patients, around 10 months in both the LOF and GOF groups. Seizure types in the three functional groups are described in the table below. Febrile seizures occurred more frequently in LOF patients. Intellectual disability was mild in 23/54 LOF, 6/38 GOF, 1/13 GOF-LOF, moderate in 10/54 LOF, 8/38 GOF, 2/13 GOF-LOF, severe/profound in 8/54 LOF, 3/38 GOF, 6/13 GOF-LOF. Most common neurological features were ataxia and tremor. 1/3rd of GOF-LOF subjects had spasticity. MRI showed as the most common feature cerebellar atrophy, with predominance in GOF-LOF.

TABLE 1 Seizure types in the three functional groups.

Seizure Type	LOF (n=63)	GOF (n=35)	GOF-LOF (n=13)
Focal	10	1	0
Absences	21	21	5
Generalized Tonic-Clonic	36	23	6
Myoclonic	16	9	10

Conclusion: The largest cohort of patients with KCNA2-related-disorders to date is described in this study. Our data confirm genotype-phenotype correlations with LOF variants featuring a higher proportion of milder phenotypes, whereas the

most severe clinical presentations were observed in the GOF-LOF group.
Disclosure: Nothing to disclose.

EPR-073 | Restoration of neurodegeneration in SCA3 via modulation of the insulin/IGF-1 signaling pathway using astragaloside IV

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Background and aims: The pathogenesis of Spinocerebellar ataxia type 3 (SCA3) is associated with dysregulation of the Insulin/IGF-1 signaling (IIS) pathway. Astragaloside IV (AST), a potent antioxidant, has demonstrated properties that enhance IIS activity.
Methods: This study investigated the therapeutic effects of AST (25 mg/kg and 50 mg/kg) on motor deficits, degradation of the SCA-84Q mutant protein, IIS pathway modulation, mitochondrial function, and expression levels of phosphorylated IGF1R (p-IGF1RTyr1135/1136) and IRS1 (p-IRS1Ser307) in transgenic SCA-15Q/84Q mouse models.

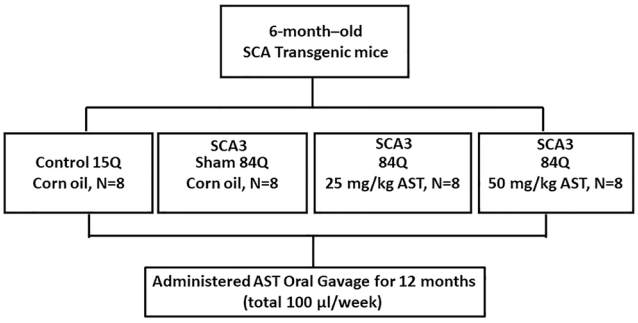

FIGURE 1 Flow chart of Astragaloside IV(AST) therapy in SCA3 transgenic mice

Results: AST treatment improved motor performance, enhanced mitochondrial function in the cerebellum, and promoted Purkinje neuron survival. It also modulated the IIS pathway by upregulating Ins2 gene expression, increasing p-IGF1RTyr1135/1136, and suppressing p-IRS1Ser307 in the cerebellum of SCA-84Q mice.

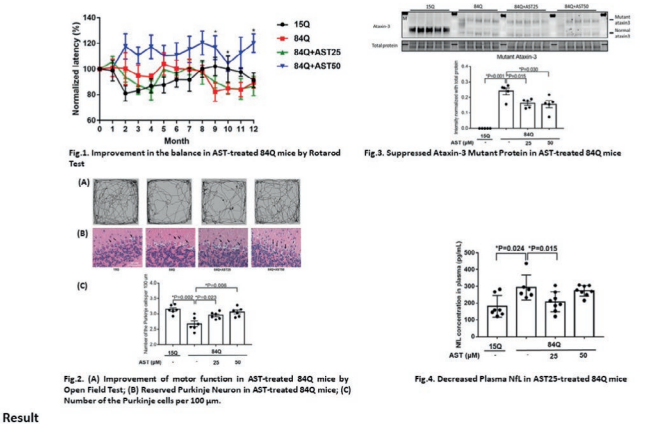

FIGURE 2

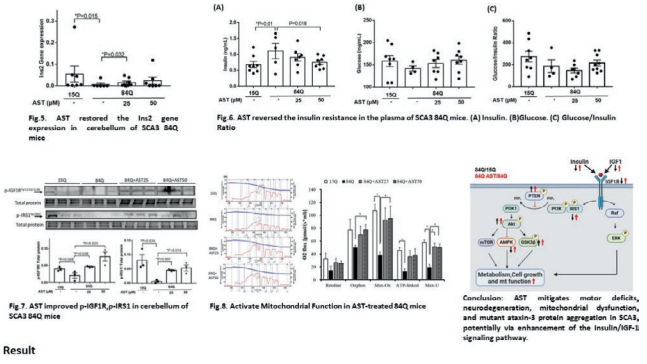

FIGURE 3

Conclusion: AST mitigates motor deficits, neurodegeneration, mitochondrial dysfunction, and mutant ataxin-3 protein aggregation in SCA3, potentially via enhancement of the IIS pathway.
Disclosure: Nothing to disclose.

EPR-074 | Genetic findings through whole exome sequencing (WES) in dystonia patients

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Background and aims: Dystonia is a hyperkinetic movement disorder characterized by abnormal repetitive movement and/or postures. Exome sequencing (ES) studies have shown a diagnostic yield of 20%, with higher rates in young onset, generalized and combined/complex dystonia, suggesting genetic testing only in selected patients. We evaluated diagnostic yield of genetic testing in an Italian dystonia cohort.
Methods: Cohort of 100 dystonic patients (45% males, mean age at evaluation 46 ± 19 years), ES, neurological examination, disease history collection, brain MRI.
Results: Childhood-onset dystonia was documented in 31% of the cohort, adult-onset in 51%; mean age at onset was 24.6 ± 19 years. Family history was positive in 53%. Overall, 38% had generalized dystonia, 26% multifocal, 19% focal, 17% segmental. 52% had isolated dystonia, 29% complex (mainly associated with intellectual disability), and 19% combined. Myoclonus was the most frequently associated movement disorder, followed by Parkinsonism. Genetic diagnosis was reached in 26% of cases, the most frequent genes being KMT2B (4 cases), VPS16 (3), GNAL (2) and GCH1 (2). Diagnostic yield was higher in complex phenotypes (41%), generalized dystonia (39%) and childhood onset (35%), although a genetic cause was found also in 15% of isolated dystonia, 21% of focal dystonia and 20% of adult-onset dystonia. Unlike family history, brain MRI (iron deposition, basal ganglia alterations, cortical or cerebellar atrophy, leukopathy) provided helpful diagnostic clues in 38% of patients with a positive genetic diagnosis.

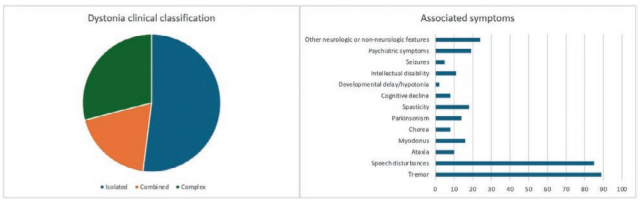

FIGURE 1 Distonia classification and associated clinical features in the cohort.

Conclusion: ES is a powerful tool for genetic diagnosis in dystonia, with better results in complex phenotypes, young patients and suggestive alterations at brain MRI.
Disclosure: Nothing to disclose.

EPR-075 | Development of a gene panel for Parkinson's disease and repeat expansion disorders using long-read adaptive sampling

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Background and aims: Long-read sequencing has improved the detection of structural variants and repeat expansions. We are now able to delineate complex structural rearrangements, repeat expansions, and low-complexity regions with long-reads. However, whole genome sequencing is still costly for genetic diagnostics. Herein, we created a neurodegenerative gene panel on the Oxford Nanopore Technologies (ONT) adaptive sampling platform that targets PD-related and repeat expansion genes. We investigated the genetic diagnostic utility of this newly designed panel.
Methods: The long-read gene panel consisted of 565 genes selected from genetic diagnostic panels for neurodegeneration (CeGat), MDS TaskForce genes, PD GWAS loci, and genes related

to repeat expansion disorders. We tested the panel's diagnostic utility on patients with 1) known pathogenic variants in LRRK2, PRKN, SNCA, and RAB32 ($n=6$); 2) idiopathic PD negative for known genetic causes ($n=3$); 3) known repeat expansions in the genes ATXN1, ATXN2, ATXN3, C9orf72, DAB1, FGF14, HTT, RFC1, TAF1, and ZFHX3 ($n=12$).
Results: A mean coverage of 25X and a mean Q-score of 18.8 was obtained across all genes and individuals with an average read length of 10kb. Thus far, using an EPI2ME workflow and the software NCRF, we accurately detected four PRKN deletions, a missense variant in LRRK2, and repeat expansions in ATXN2, ATXN3, FGF14, and RFC1. However, an SNCA triplication was not detected.
Conclusion: This type of panel design has the potential to be a more efficient genetic diagnostic tool for structural variant detection. Further validation of the panel with a larger and more diverse patient cohort would strengthen its potential.
Disclosure: Nothing to disclose.

EPR-076 | Phenotypic-genetic spectrum of STUB1-related disorders: Insights into the severe end with neurodevelopmental disorder

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Background and aims: Pathogenic variants in STUB1 are associated with a broad spectrum of neurodegenerative disorders, including spinocerebellar ataxias-16 and 48. Additionally, biallelic STUB1 variants have been reported in only four patients with neurodevelopmental disorders characterized by global developmental delay (GDD) and variable intellectual disability (ID). STUB1 encodes an E3 ubiquitin ligase that is crucial for maintaining protein homeostasis, yet the full phenotypic and allelic spectrum remains poorly understood.
Methods: Ten probands from eight consanguineous families with STUB1 variants were identified using exome sequencing and international data sharing platforms. Clinical phenotypes and brain magnetic resonance imaging were analyzed. Zebrafish STUB1 knockout embryos by CRISPR/Cas9 were generated and the role of STUB1 on brain morphology and motor function was characterized.
Results: We describe homozygous missense and predicted loss-of-function STUB1 variants in ten patients presenting with a neurodevelopmental phenotype characterized by GDD/ID, dysmorphic facial features, movement disorders, and ataxia. Brain imaging revealed two distinctive patterns: one of cerebellar atrophy; and the other of enlargement of the frontoparietal extra-axial subarachnoid spaces, with compensatory lateral ventricle enlargement and thinning of the corpus callosum. Comparative studies in stub1 knockout zebrafish revealed early medulla size reduction, late-onset cerebellar and dendritic defects, and motor abnormalities, without significant impact on overall brain structure. There was also slow growth.
Conclusion: This study not only consolidates the association of STUB1 defects with a neurodevelopmental phenotype but also expands the understanding of STUB1-related disorders as part of an emerging group of conditions with a broad spectrum ranging from neurodevelopmental disorders to neurodegeneration.
Disclosure: Nothing to disclose.

EPR-077 | Resting-state EEG analysis defines the signature of CACNA1A and GAA-FGF14 related channelopathies

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Background and aims: CACNA1A variants and GAA-FGF14 ataxia share overlapping neurological phenotypes, including chronic cerebellar signs and episodic ataxia. Sparse evidence linking CACNA1A mutations to altered resting-state electroencephalogram (EEG) patterns exists, with no data for GAA-FGF14. This study aimed to compare EEG metrics among these groups and healthy controls (HC).

Methods: Resting-state EEGs were analyzed in 29 CACNA1A, 15 GAA-FGF14 ataxia patients, and 30 HC. EEGs were recorded using the 10-20 system, bandpass-filtered (0.5–40 Hz), and segmented into 2-second epochs. Artifacts were removed via independent component analysis. Relative bandpower was calculated using Welch's method, and functional connectivity was assessed via weighted Phase-Lag Index (wPLI) and Minimum Spanning Tree (MST) metrics. Bayesian linear regression evaluated genotype effects, adjusting for age and sex differences. Priors were informed by separate healthy cohort data.

Results: Results are summarized in Table 1. Relative delta and theta power were increased in CACNA1A patients compared to both GAA-FGF14 patients and HC (Figure 1a-c). FGF14 patients consistently exhibited higher relative beta and gamma power than CACNA1A patients and HC (Figure 1d,e). Functional connectivity analysis revealed significantly increased overall wPLI in the theta and delta bands in CACNA1A patients compared to HC (Figure 2a). Additionally, MST Maximum Degree Centrality and in the delta band was increased in CACNA1A patients indicating higher degree of centralization (Figure 2b).

TABLE 1 Summary of significant differences. Mean differences (MD) and the 95% Highest-density intervals (95%HDI) are shown for each value. Significant p-values ($p < 0.05$) are shown in bold.

experiment	band	Location/ Measure	CACNA1A vs. HC MD [95%HDI]	p	FGF14 vs. HC MD [95%HDI]	p	CACNA1A vs. FGF14 MD [95%HDI]	p
Relative Power	delta	frontal	-0.09 [-0.17, -0.02]	**0.02**	-0.08 [-0.19, 0.02]	0.12	-0.01 [-0.11, 0.1]	0.78
	theta	overall	0.03 [0.0, 0.05]	**0.02**	-0.01 [-0.04, 0.02]	0.47	0.04 [0.01, 0.07]	**0.01**
		frontal	0.02 [-0.0, 0.04]	0.11	-0.01 [-0.04, 0.02]	0.39	0.03 [0.0, 0.06]	**0.04**
		central	0.04 [0.02, 0.07]	**<0.01**	-0.01 [-0.04, 0.03]	0.63	0.05 [0.02, 0.08]	**<0.01**
		parietal	0.03 [0.01, 0.06]	**<0.01**	-0.0 [-0.03, 0.02]	0.75	0.04 [0.01, 0.07]	**0.01**
		occipital	0.01 [-0.01, 0.04]	0.25	-0.02 [-0.06, 0.01]	0.15	0.04 [0.0, 0.07]	**0.02**
	beta	overall	0.0 [-0.03, 0.04]	0.71	0.06 [0.0, 0.1]	**0.03**	-0.05 [-0.1, 0.0]	0.05
		frontal	0.03 [-0.01, 0.07]	0.16	0.07 [0.02, 0.12]	**0.01**	-0.04 [-0.09, 0.01]	0.09
		parietal	-0.01 [-0.05, 0.03]	0.59	0.06 [0.01, 0.12]	**0.02**	-0.07 [-0.13, -0.02]	**0.01**
		occipital	-0.04 [-0.08, 0.01]	0.11	0.03 [-0.03, 0.09]	0.3	-0.06 [-0.12, -0.0]	**0.04**
	gamma	overall	0.01 [-0.01, 0.02]	0.33	0.02 [0.0, 0.04]	**0.02**	-0.01 [-0.03, 0.0]	0.1
		frontal	0.03 [0.01, 0.04]	**0.01**	0.04 [0.02, 0.06]	**<0.01**	-0.01 [-0.04, 0.01]	0.3
		parietal	-0.01 [-0.02, 0.0]	0.12	0.01 [-0.0, 0.02]	0.16	-0.01 [-0.02, -0.0]	**0.01**
		occipital	-0.04 [-0.06, -0.02]	**<0.01**	-0.01 [-0.04, 0.02]	0.6	-0.03 [-0.06, 0.0]	0.06
Connectivity	delta	wPLI	0.06 [0.02, 0.1]	**<0.01**	0.04 [-0.02, 0.09]	0.2	0.03 [-0.02, 0.08]	0.28
		MDC	0.06 [0.01, 0.11]	**0.01**	0.03 [-0.02, 0.1]	0.26	0.03 [-0.04, 0.09]	0.44
	theta	wPLI	0.06 [0.01, 0.12]	**0.03**	0.01 [-0.05, 0.08]	0.69	0.05 [-0.02, 0.12]	0.16

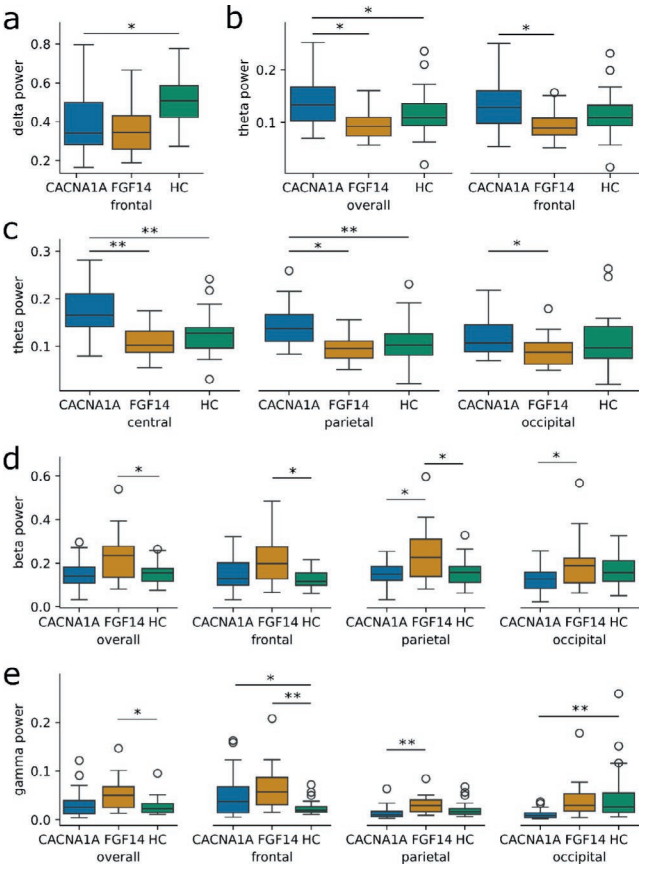

FIGURE 1 Relative bandpower measures. The y-axis represents the relative bandpower for each frequency band, while the x-axis displays the groups, with the measurement locations indicated below. Panels show: (a) relative delta power, (b,c) relative theta.

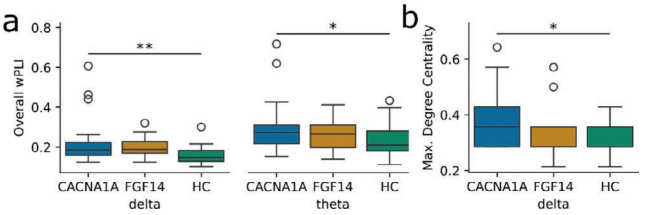

FIGURE 2 Connectivity measures. The y-axis represents the respective connectivity measure, while the x-axis displays the groups, with the bands indicated below. Panels show: (a) Overall weighted Phase-Lag Index (wPLI), and (b) Multiple Spanning Tree (MST).

Conclusion: Distinct resting-state EEG alterations characterize CACNA1A and GAA-FGF14 ataxias, reflecting unique network-level effects of P/Q-type calcium channel dysfunction. Advanced EEG analysis shows potential as a biomarker for calcium channelopathies.

Disclosure: This study was supported by the intramural funding program of the Medical University of Innsbruck for young scientists MUI-START, Project 2022-1-3.

EPR-078 | Biallelic variants in alkaline ceramidase 3 cause infantile and early childhood onset neurodegeneration

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Background and aims: Biallelic variants in Alkaline Ceramidase 3 (ACER3) have recently been linked to early-onset leukodystrophy in 3 case reports describing 5 families with 7 patents. Here we describe previously unreported 57 patients from 54 unrelated families with biallelic variants in ACER3 and cumulatively delineate the phenotypic spectrum of ACER3-related.
Methods: Exome sequencing, data sharing, screening the genetic databases of several international genetic laboratories, and GeneMatcher were used to identify the patients here. ACER3 enzyme activity, lipidomics in patient fibroblasts, mutagenesis, functional assays, and protein modeling were performed.
Results: The cohort is composed of 64 patients from 59 families including 34 females and 30 males. 45 individuals are currently alive with a mean age of 6.6 ± 4.9 years (range 1.4-18). 19 patients (30%) died between the ages of 3 and 19 years due to the rapidly progressive disease. The disease presents with predominantly infantile-onset (86%), moderate (52%) and rapidly (39%) progressive neurological deficit manifesting with global developmental delay (71%) or developmental regression (98%)/stagnation (83%) commonly resulting in limbs spasticity (93%), limb dystonia (72%) and axial hypotonia (73%) with invariable posterior gradient white matter signal changes and diffuse cerebral volume loss (73%) on neuroimaging (Figure 1). ACER3 variants are presented in Figure 2. Functional studies reveal significantly reduced ceramide hydrolysis. Mutant analysis identifies functional hot spots, with in vitro assays showing a 2–40% decrease in ceramidase activity. Lipidomic analysis confirms a 50% increase in ceramide and sphingomyelin levels, alongside reduced sphingosine (Figure 3).

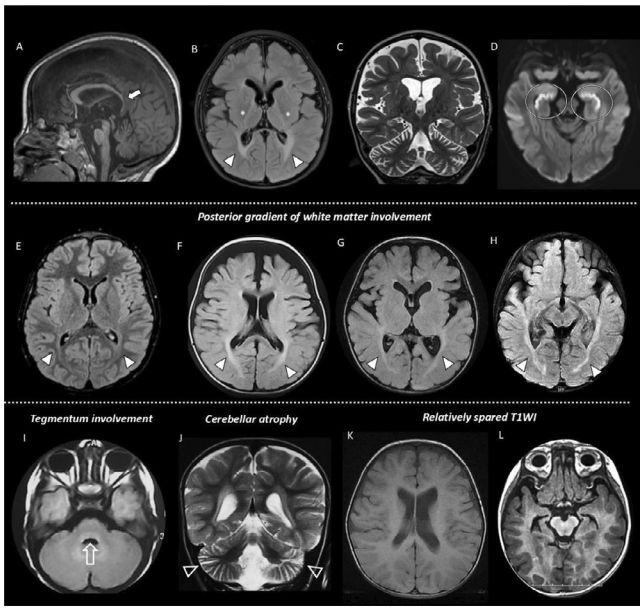

FIGURE 1 Brain MRIs of the cohort showing white matter abnormalities.

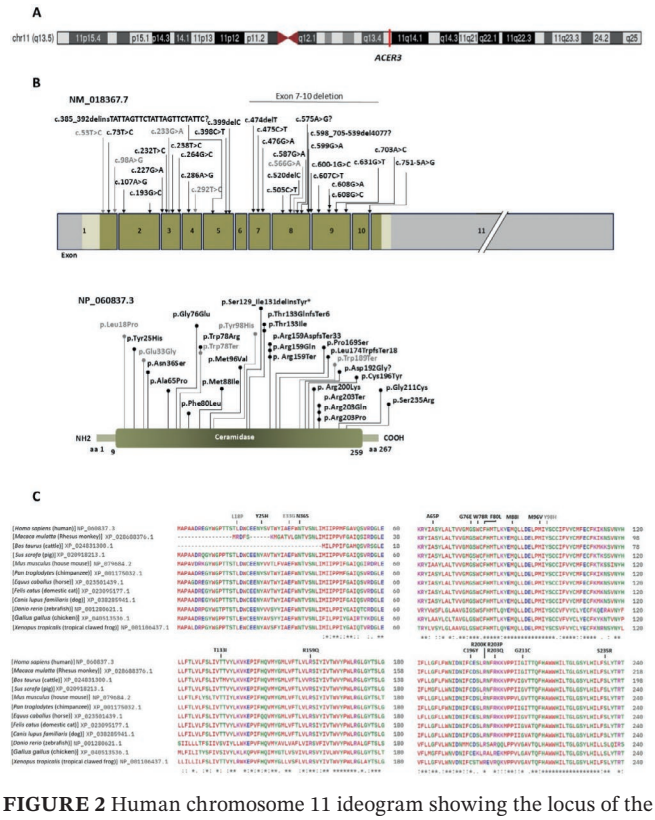

FIGURE 2 Human chromosome 11 ideogram showing the locus of the ACER3 gene on Chr11q13.5. Schematic representation of ACER3 MAEN transcript (NM_018367.7) and protein. M (NP_060837.3) indicating the approximate positions of the variants identified in the families.

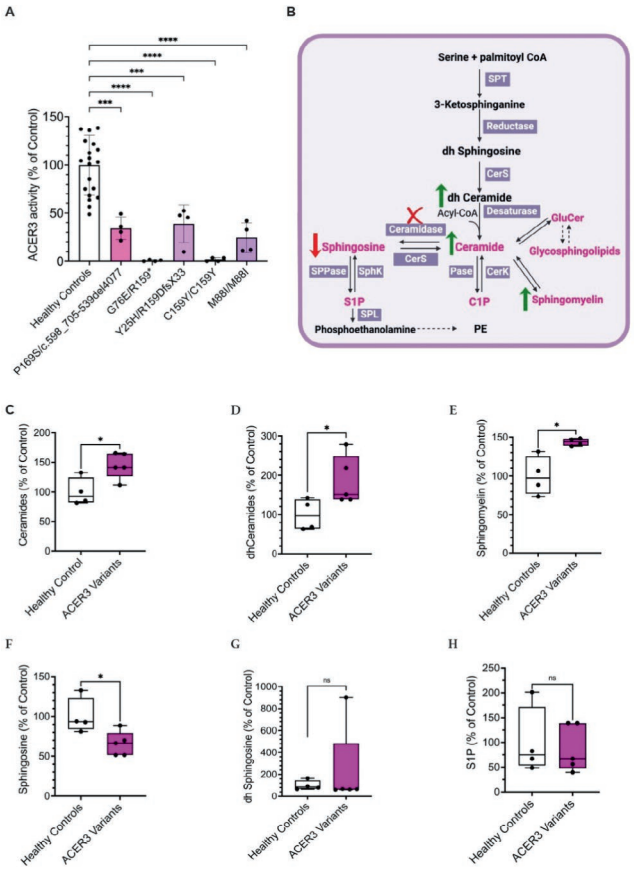

FIGURE 3 ACER3 ceramidase enzyme activity was determined from skin fibroblasts from four healthy controls and five separate patient skin fibroblast cell lines

Conclusion: Biallelic variants in ACER3 are associated with infantile/childhood-onset neurodegeneration with progressive leukodystrophy.
Disclosure: Nothing to disclose.

EPR-079 | NBIA diagnosis: Lessons from ten years experience in a French reference lab

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Background and aims: Neurodegeneration with Brain Iron Accumulation (NBIA) is a group of inherited disorders characterized by abnormal iron accumulation in brain's basal ganglia.
Methods: The DNA of 319 patients with clinical and MRI characteristics compatible with a diagnosis of NBIA was examined. A brain MRI was requested for each patient and clinical dataware was collected. A panel Next Generation Sequencing of 9 genes was performed, including: ATP13A2, CP, DCAF17, FA2H, FTL, C19orf12, PANK2, PLA2G6, and WDR45. For patients with negative NBIA panel, a trio exome or genome analysis has been requested.
Results: The molecular diagnosis of NBIA could be established for 72 (23 %). For each subtype, the age of onset of the first symptoms, the nature of these symptoms, and the main clinical manifestations were evaluated. Actually, 4 families presented with dominant MPAN, including mosaic carriers of the familial variant displayng late onset presentation in two of them. They are the only demonstrated mosaic cases reported to date in the C19ORF12 gene (3). Post-zygotic mosaicism could also explain the presence in our cohort of two male monozygotic twins, where only one of them is symptomatic for a WDR45 variant. We have also identified an atypical form of Woodhouse Sakati syndrome, with a patient carrying composite heterozygous variants with the first description of a missense variant, in trans with a classical non sense variant, and an attenuated phenotype.

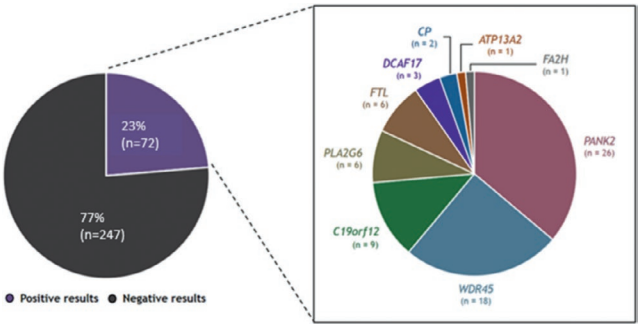

FIGURE 1 Table

Conclusion: Our work aimed to provide a precise description of patients affected by NBIA, and to identify new genetic causes of iron accumulation.
Disclosure: Nothing to disclose.

EPR-080 | Trio-WES in pediatric-onset epilepsy: Assessing diagnostic yield and widening genotypic landscape

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Background and aims: Whole-exome sequencing (WES) is a cost-effective genetic test for epilepsy with an expected diagnostic yield of ~32%. We aimed to assess the diagnostic yield of trio-based WES in pediatric-onset epilepsy, identify novel variants associated with epilepsy, and evaluate the clinical impact of genetic diagnosis.
Methods: 30 patients with pediatric-onset epilepsy were enrolled in EPIEXOME, a prospective monocentric study on

genetic epilepsies, and underwent trio-WES. The variants were classified according to ACMG criteria.
Results: The cohort included 11 patients with isolated epilepsy and 19 with cognitive and/or motor disturbances. Epilepsy was focal in 15/30 and generalized in 15/30 cases. Mean age at onset was 5.75 years [0-16]. Trio-WES resulted positive in 11/30 (37%, table 1), uncertain in 8/30, and negative in 11/30 cases. Among positive cases, 7 variants were de novo, one variant was inherited in autosomal dominant fashion by an affected father, 3 cases were recessive.

TABLE 1 Variants identified in positive cases. Abbreviations: P = Pathogenic; LP = Likely pathogenic; VUS = variant of uncertain significance.

ID	Gene	Transcript	Variants	Status	ACMG
1	*SLC6A1*	ENST00000287766.4	c.1070C>T p.Ala357Val	Heterozygous (de novo)	P
5	*GABRB1*	ENST00000295454.3	c.841A>G p.Thr281Ala	Heterozygous (de novo)	LP
9	*TUBA1A*	ENST00000301071.7	c.97G>A p.Asp33Asn	Heterozygous (de novo, mosaicism)	LP
13	*KCNT1*	ENST00000298480.5	c.2800G>A p.Ala934Thr	Heterozygous (de novo)	P
15	*SON*	ENST00000290239.6	c.6064dup p.Thr2022AsnfsTer8	Heterozygous (de novo)	P
19	*NEXMIF*	ENST00000055682.6	c.1441C>T p.Arg481*	Heterozygous (de novo)	P
20	*CACNA1A*	ENST00000360228.5	c.3946G>A p.Asp1316Asn	Heterozygous (affected father)	LP
22	*QARS1*	ENST00000306125.6	c.799C>T p.Arg267Trp c.1304A>G p.Tyr435Cys	Compound heterozygous	VUS LP
24	*KMT2E*	ENST00000311117.3	c.1725_1726delAA p.Thr575=fs	Heterozygous (de novo)	P
29	*KCNJ10*	ENST00000368089.3	c.557T>C p.Val186Ala c.886G>A p.Val296Met	Compound heterozygous (likely)	LP LP
30	*PEX7*	ENST00000318471.5	c.120C>G p.Tyr40* c.347G>T p.Ser116Ile	Compound heterozygous	P LP

Conclusion: In a monocentric cohort, trio-WES achieved a diagnostic result in 37% of the cases. The high representation of de novo variants stresses the relevance of trio analysis in epilepsy. We link GABRB1 gene with two novel epileptic phenotypes (EIMFS and Lennox-Gastaut Syndrome) and report a case of steroid-responsive para-infectious acute encephalopathy in a patient with biallelic QARS1-variants. The clinical impact of genetic diagnosis included personalized therapeutic possibilities (KCNT1, CACNA1A, QARS1), reverse phenotyping (SON), and adhesion to patient advocacy groups (SLC6A1).
Disclosure: Nothing to disclose.

Neuroimmunology 1

EPR-081 | Single institution experience with efgartigimod in patients with GFAPA: Treatment response and adverse events

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Background and aims: Autoimmune glial fibrillary acidic protein astrocytopathy (GFAPA) is a novel autoimmune central nervous system (CNS) disorder, some patients respond poorly to conventional immunotherapy. Our study revealed a real-world experience with efgartigimod in treating GFAPA, which is expected to provide safety and effectiveness data for efgartigimod.
Methods: We conducted a retrospective analysis of 36 patients diagnosed with GFAPA from Jan 2021 to July 2024. Patients were divided into two groups: those who received efgartigimod treatment ($n = 16$) and those who did not ($n = 20$). Clinical outcomes were assessed via the modified Rankin Scale (mRS), Clinical Assessment Scale in Autoimmune Encephalitis (CASE), clinical symptoms, and Glasgow Coma Scale (GCS), along with analysis of treatment-emergent adverse events (TEAEs), cerebrospinal fluid (CSF) total protein, leukocyte, and antibody titers, and blood serum IgG levels.
Results: Compared with the control, efgartigimod treatment group was associated with clinical improvement, as evidenced by significantly greater reductions in CASE scores at discharge ($p < 0.05$) and apparent decreases in CASE scores at follow-up ($p = 0.08$), improvements in GCS scores at discharge and follow-up. Additionally, patients receiving efgartigimod presented significant reductions in CSF total protein, leukocyte, and anti-GFAP antibody titers and serum IgG levels. The most common TEAEs were mild to moderate infections, with no significant safety concerns identified.
Conclusion: Efgartigimod was generally safe for patients with GFAPA and appeared to accelerate the recovery of clinical symptoms and neurological function. However, further prospective randomized studies with larger patient cohorts are needed to confirm the safety and efficacy of efgartigimod.
Disclosure: Nothing to disclose.

EPR-082 | Super-refractory Anti-NMDAR encephalitis: Clinical features, risk factors and prognostic outcomes

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Background and aims: Anti-NMDAR encephalitis (NMDARE) is the most common autoimmune encephalitis, typically responding well to immunotherapy. Frequency, risk factors, and outcomes associated with severe clinical status after second-line immunotherapy are unknown. This study aimed to define and characterize super-refractory NMDARE.
Methods: Retrospective study including patients diagnosed with non-herpetic NMDARE at the French national reference center between October 2007 and February 2022, with admission to ICU. Super-refractory NMDARE was defined as ICU hospitalization lasting more than 90 days after second-line immunotherapy, excluding those deceased within 90 days of treatment. Favorable outcome was defined as mRS < 2 at 24 months of onset. Clinical and paraclinical features were compared between super-refractory and ICU-admitted NMDARE.
Results: Of 219 NMDARE patients admitted to the ICU, 26 (11.45%) met criteria for super-refractory (92% females, median

age 24 years). Non-Caucasian ethnicity was more prevalent (56% vs. 35%, $p = 0.040$) in super-refractory patients, who presented more frequent intubation (62% vs. 100%, $p < 0.001$), seizures (87% vs. 100%, $p = 0.051$), movement disorders (82% vs. 100%, $p = 0.018$) and dysautonomia (62% vs. 85%, $p = 0.023$). Cerebrospinal fluid pleocytosis [cell-count > 70 (46% vs. 21%, $p = 0.008$)], extreme delta brush pattern (21% vs. 7.1%, $p = 0.041$) and ovarian teratomas (62% vs. 22%, $p < 0.001$) were also more frequent. This group received earlier first and second-line immunotherapy ($p < 0.05$) despite poorer outcomes (72% vs. 39%, $p = 0.004$) and higher mortality (19% vs. 6.7%, $p = 0.046$).
Conclusion: Super-refractory NMDARE represents a distinct, high-risk subgroup, marked by a severe clinical presentation, high prevalence of ovarian teratoma and poorer outcomes. Early identification and targeted management strategies are essential for improving its prognosis.
Disclosure: Nothing to disclose.

EPR-083 | Distinguishing primary angiitis of the central nervous system from its histopathological mimics

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Background and aims: Primary angiitis of the central nervous system (PACNS) has a challenging anatomopathological diagnosis due to its heterogeneity and secondary vascular inflammation present in other conditions. This study aimed to compare PACNS with histologically mimicking conditions, identifying features that may aid in differential diagnosis.
Methods: Retrospective case-control study including 9 PACNS and 12 mimicking conditions (CNS infections, inflammatory diseases, or systemic affections). Using digital pathology (QPath), we analyzed CD3, CD20, and CD45 stains. Granulomas, fibrinoid necrosis, and microglial nodules were assessed. The five most inflamed medium-sized vessels (excluding meningeal) were selected, creating three concentric zones: transmural, intermediate, and outer (fixed size). Lymphocyte densities were compared using *U*-Mann–Whitney and mixed linear regression (accounting repeated measures). CD3 lymphocyte transmural density was analyzed with a ROC curve.
Results: PACNS presented granulomas more frequently (56.0% vs. 8.3%; $p = 0.046$), tending to exhibit higher transmural inflammation (lymphocytes/mm^2) in CD3 staining [median: 5237 (IQR: 3958–6440) vs. 3410 (IQR: 3078–3559), $p = 0.059$], CD20 [median: 2215 (IQR: 1428–3618) vs. 473 (IQR: 0.00–2205), $p = 0.117$], and total lymphocytes [median: 7475 (IQR: 5892–10569) vs. 4183 (IQR: 3629–6115), $p = 0.091$]. Mixed analysis highlights higher transmural density respect other regions in PACNS (CD3: $p = 0.0198$; CD20: $p = 0.1199$; total: $p = 0.0553$). The ROC curve showed an AUC of 77.78%, with an optimal cutoff at 3509.48 CD3 transmural density (sensitivity: 0.88; specificity: 0.67) to discriminate PACNS from mimics.
Conclusion: Despite no significant differences in inflammation patterns between groups, granuloma presence, and transmural inflammation, predominantly CD3 lymphocytes, was greater in the PACNS, which may aid in histological diagnosis.
Disclosure: Nothing to disclose.

EPR-084 | Efgartigimod in the treatment of anti-NMDAR encephalitis compared with IVIG and SPA-IA during acute attacks

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Background and aims: The purpose of this study was to evaluate the efficacy of Efgartigimod (EFG) in anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis patients during acute attacks.
Methods: A case-control study was designed to compare 26 anti-NMDAR encephalitis patients who were treated with EFG, and 15 patients with intravenous immunoglobulin (IVIG), and 23 patients with immunoadsorption with staphylococcal protein A column (SPA-IA) treatment.
Results: At baseline, no significant differences in mRS scores were observed among the EFG, IVIG, and SPA-IA groups of anti-NMDAR encephalitis patients. When compared with the IVIG group, patients treated with EFG had significantly decreased serum IgG levels ($p = 0.002$). Compared with the SPA-IA group, EFG-treated patients had lower CSF anti-NMDAR antibody titers at admission ($p = 0.039$) and higher post-treatment IgG levels ($p = 0.002$). In the EFG and SPA-IA groups, there was a significant reduction in anti-NMDAR antibody titers in both CSF and serum ($p < 0.01$), while no remarkable decrease was found in the IVIG group ($p > 0.05$). Additionally, serum IgG levels significantly decreased in both the EFG and SPA-IA groups at baseline and during the 1-month follow-up. By the third month of follow-up, IgG levels in the blood of both groups remained below the baseline levels.
Conclusion: EFG could be an elegant alternative to both IVIG and SPA-IA therapies for anti-NMDAR encephalitis during acute attacks. It has a better effect on reducing antibody titers than IVIG and is comparable to SPA-IA therapy, and no serious adverse events were observed during infusion.
Disclosure: The authors declare that they have no competing interests.

EPR-085 | Safety and efficacy of riliprubart in chronic inflammatory demyelinating polyneuropathy: 76-week phase 2 trial results

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Background and aims: Riliprubart, a first-in-class humanized IgG4-monoclonal antibody, selectively inhibits activated-C1s in the classical-complement pathway (Figure) and can be self-administrated subcutaneously via an auto-injector. Preliminary results from an ongoing Phase-2 trial evaluating riliprubart in participants with chronic inflammatory demyelinating polyneuropathy (CIDP; NCT04658472) suggested encouraging clinical-benefits and safety-profile up to 48-weeks. Here, we report efficacy and safety results of riliprubart at Week-76.

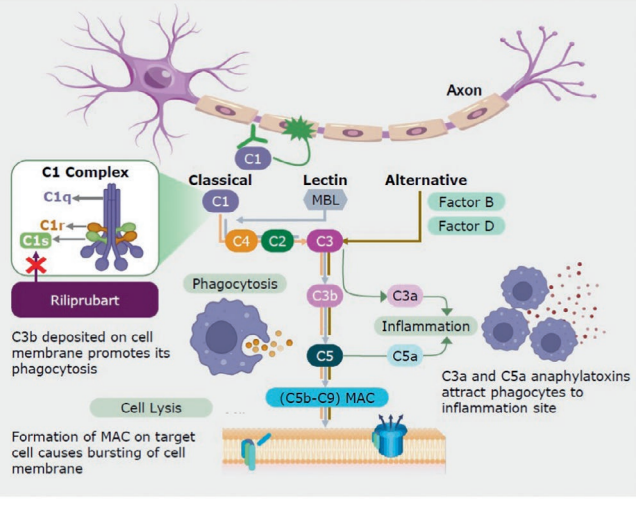

FIGURE 1 Riliprubart targeting C1s and the classical complement pathway.

Methods: This open-label, Phase-2 trial evaluates riliprubart across three groups: Standard-of-care (SoC)-Treated, SoC-Refractory, and SoC-Naïve. Participants undergo 24-week treatment (Part-A), followed by an optional treatment-extension (Part-B: 52-weeks). Primary-endpoint (Part-A) is %-participants relapsing (SoC-Treated) or responding (SoC-Refractory/Naïve), defined as ≥1-point change in adjusted-Inflammatory Neuropathy Cause and Treatment (INCAT) disability score. Part-B evaluates safety and efficacy-durability based on %-relapse-free participants (SoC-Treated) or with sustained-response (SoC-Refractory/Naïve), defined as no-increase in adjusted-INCAT score ≥2-points at Week-76 relative to Week-24. Exploratory-endpoints include additional efficacy measures (INCAT, IRODS, MRC-SS, grip-strength), change in total-complement, and plasma neurofilament-light chain-levels.

Results: As of August-2024, in SoC-Treated group, 81.3% (N=39/48) participants entered Part-B, including 47.9% (N=23/48) completed Part-B treatment-period (ongoing:27.1%; discontinued:6.3%). In SoC-Refractory and SoC-Naïve groups, 72.2% (N=13/18) and 50% (N=6/12) participants, respectively, entered Part-B, including 61.1% (N=11/18) in SoC-Refractory (ongoing:0%; discontinued:11.1%) and 16.7% (N=2/12) in SoC-Naïve group (ongoing:8.3%; discontinued:25%) completing Part-B. Updated full Part-B efficacy and safety data up to Week-76 will be presented at meeting.

Conclusion: Mature Week-76 results may suggest potential for riliprubart to demonstrate sustained clinical effect in participants who experience failure/inadequate response/residual disability despite SoC therapy, supporting its development in Phase-3, and potentially offering new treatment option for CIDP.

Disclosure: LQ-Research grants: Instituto de Salud Carlos III–Ministry of Economy and Innovation (Spain), CIBERER, Fundació La Marató, GBS-CIDP Foundation International, UCB, Grifols. Received speaker/expert testimony honoraria: CSL Behring, Novartis, Sanofi, Merck, Annexon, Alnylam, Biogen, Janssen, Lundbeck, argenx, UCB, Dianthus, LFB, Avilar Therapeutics, Octapharma, Roche. Serves:Clinical Trial Steering Committee for Sanofi, Principal Investigator: UCB's CIDP01 trial. RAL-Consultant: CSL Behring, BioCryst, Dianthus, Grifols, Nuvig, Pfizer, Sanofi (Steering Committee), Annexon, Alexion, Avilar, argenx, J&J, Takeda, Boehringer Ingelheim (DSMB), Intellia (DSMB), Nervosave, TGTX, Seismic and medical advisory board GBS-CIDP Foundation International. Receives royalties: UptoDate; speaker: Medscape. HPH-Consultant: Sanofi, Octapharma. Received fees:serving on Steering and Data Monitoring Committees from Biogen, BMS Celgene, GeNeuro, Merck, Novartis, Octapharma, Roche TG Therapeutics. PAvD-Consultant: Annexon, argenx, Hansa Biopharma, Immunic, Octapharma, Roche, Sanofi (Institutional research fund received all honoraria), grants: Prinses Beatrix Spierfonds, Sanquin, Grifols. JL-None. AD-Received honoraria: argenx and Alexion for conference, ad board. SA-Consultant:Alexion, argenx, UCB, Janssen, Hansa Biopharma, Roche, Sanofi, Amicus, LFB, Alnylam, Astrazeneca, Pfizer, Biogen. EW,KA,YL,MAA,NA-Employees of Sanofi, may hold shares and/or stock options in company. RACH-Consultant: Hansa Biopharma, Sanofi.

EPR-086 | Efficacy of Riliprubart in chronic inflammatory demyelinating polyneuropathy: Phase 2 subgroup analyses

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Background and aims: Riliprubart, a first-in-class humanized IgG4-monoclonal antibody, selectively inhibits activated-C1s in the classical complement pathway (Figure) and can be self-administrated subcutaneously, via an auto-injector. In a Phase-2 trial (NCT04658472), riliprubart treatment suggested encouraging clinical benefits and safety profile across a broad spectrum of participants with chronic inflammatory demyelinating polyneuropathy (CIDP). Here, we report subgroup efficacy analyses from this ongoing trial.

Methods: This open-label, Phase-2 trial evaluates riliprubart across three groups: Standard-of-care (SoC)-Treated, SoC-Refractory, and SoC-Naïve. Participants underwent 24-week treatment (Part-A), followed by an optional treatment extension (Part-B: 52-weeks). In Part-A, post-hoc analyses were performed in the standard-of-care (SoC)-Treated and SoC-Refractory groups, and all participants. Response rate for endpoints (INCAT, I-RODS, MRC-SS, grip strength) were evaluated in subgroups defined by standard demographics and clinical characteristics, possibly predictive for the overall outcome (age, sex, CIDP subtype, time since start of therapy/diagnosis, previous therapies, immunoglobulin [Ig] dose, baseline plasma neurofilament-light chain [NfL], and INCAT score).

Results: As of April-2024, preliminary interim data from 48 SoC-Treated and 18 SoC-Refractory participants (who completed or discontinued 24-week treatment) were analyzed. In the overall population, the INCAT response rates were similar across all analyzed subgroups, indicating clinically meaningful benefits regardless of baseline characteristics. Consistent trends were observed across other efficacy measures. Available data of these results will be presented at the meeting.

Conclusion: The results suggest consistent clinical effects of riliprubart across a range of baseline characteristics and assessment scores for people living with CIDP who experience failure/inadequate response or residual disability despite SoC treatment.

Disclosure: RAL-Consultant: CSL Behring, BioCryst, Dianthus, Grifols, Nuvig, Pfizer, Sanofi (Steering Committee), Annexon, Alexion, Avilar, argenx, J&J, Takeda, Boehringer Ingelheim (DSMB), Intellia (DSMB), Nervosave, TGTX, Seismic and medical advisory board GBS-CIDP Foundation International. Receives royalties: UptoDate; speaker: Medscape. LQ-Research grants: Instituto de Salud Carlos III–Ministry of Economy and Innovation (Spain), CIBERER, Fundació La Marató, GBS-CIDP Foundation International, UCB, Grifols. Received speaker/expert testimony honoraria: CSL Behring, Novartis, Sanofi, Merck, Annexon, Alnylam, Biogen, Janssen, Lundbeck, argenx, UCB, Dianthus, LFB, Avilar Therapeutics, Octapharma, Roche. Serves: Clinical Trial Steering Committee for Sanofi, Principal Investigator: UCB's CIDP01 trial. HPH-Consultant:Sanofi, Octapharma. Received fees:serving on Steering and Data Monitoring Committees from Biogen, BMS Celgene, GeNeuro, Merck, Novartis, Octapharma, Roche TG Therapeutics. PAvD-Consultant: Annexon, argenx, Hansa Biopharma, Immunic, Octapharma, Roche, Sanofi (Institutional research fund received all honoraria), grants: Prinses Beatrix Spierfonds, Sanquin, Grifols. JL-None. AD-Received honoraria: argenx and Alexion for conference, ad board. SA-Consultant: Alexion, argenx, UCB, Janssen, Hansa Biopharma, Roche, Sanofi, Amicus, LFB, Alnylam, Astrazeneca, Pfizer, Biogen. EW, YL, MAA, NA-Employees of Sanofi, may hold shares and/or stock options in company. RACH-Consultant: Hansa Biopharma, Sanofi.

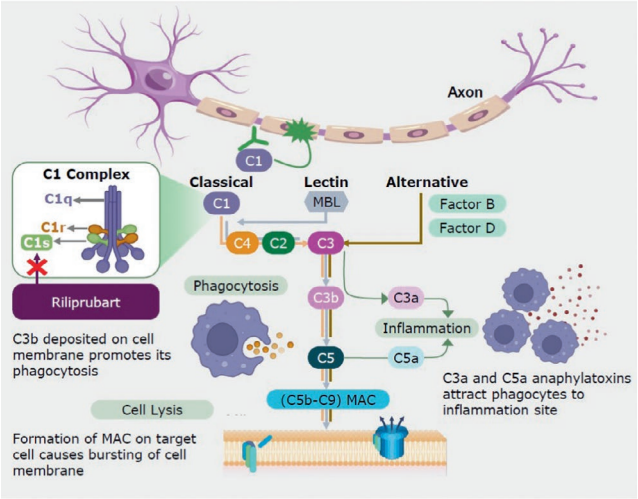

FIGURE 1 Riliprubart targeting C1s and the classical complement pathway

EPR-087 | Healthcare resource utilization and costs associated with exacerbation or crisis in generalized myasthenia gravis

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Background and aims: Exacerbation and crisis are experienced by 38.5% and 2.1% of patients with generalized myasthenia gravis (gMG), respectively.1 While the overall burden of gMG is documented, the impact of exacerbation/crisis remains unclear, hindering efforts to address unmet healthcare needs.
Methods: Adults with incident gMG (MG diagnosis by a neurologist; 12-month washout before the first MG diagnosis) and >=1 clinical event (exacerbation: primary MG diagnosis in an inpatient or emergency setting or any exacerbation-related diagnosis; or crisis: intubation) were identified from Komodo Research Database (01/2017-09/2023). Index date was the first clinical event following gMG. Patients had >=12 months of insurance coverage pre- and post-index. Monthly per-patient healthcare resource utilization (HRU) and costs were described 12 months pre- and post-index.
Results: Among 2,657 patients (mean age: 61.1 years; female: 47.5%), the first clinical event (exacerbation: 98.2%; crisis: 1.8%) were reported predominantly in the outpatient setting (55.2%) and, on average, 3.8 months after gMG diagnosis. Mean monthly inpatient days (0.75 vs. 0.29) and outpatient visits (3.44 vs. 2.47) increased post-index compared to pre-index. Mean monthly total healthcare costs increased twofold ($7,985 vs. $2,939), driven by pharmacy ($3,711 vs. $723) and inpatient costs ($2,420 vs. $943). HRU and costs peaked during the first month post-index; reaching $19,325, 3.21 inpatient days, and 4.88 outpatient visits and remained elevated compared to pre-index.

TABLE 1 Monthly HRU and costs (2023 USD) pre- and post-index clinical event.

	Patients with a clinical event, N=2,657		
	12 months pre-index	First month post-index	12 months post-index
	n (%) or mean ± SD [median]		
Had ≥1 inpatient admission	692 (26.0)	989 (37.2)	1,400 (52.7)
Number of admissions	0.03 ± 0.07 [0.00]	0.41 ± 0.56 [0.00]	0.08 ± 0.11 [0.08]
Number of inpatient days	0.29 ± 0.95 [0.00]	3.21 ± 6.28 [0.00]	0.75 ± 1.82 [0.17]
Had ≥1 emergency visit	1,479 (55.7)	542 (20.4)	1,382 (52.0)
Number of emergency visits	0.13 ± 0.41 [0.08]	0.28 ± 0.79 [0.00]	0.12 ± 0.42 [0.08]
Had ≥1 outpatient visit	2,646 (99.6)	2,521 (94.9)	2,652 (99.8)
Number of outpatient visits	2.47 ± 2.49 [1.83]	4.88 ± 4.26 [4.00]	3.44 ± 2.91 [2.75]
Had ≥1 other visit	1,556 (58.6)	628 (23.6)	1,772 (66.7)
Number of other visits	0.21 ± 0.41 [0.08]	0.42 ± 1.15 [0.00]	0.46 ± 0.91 [0.17]
Total healthcare costs	2,939 ± 5,364 [1,382]	19,325 ± 32,041 [7,499]	7,985 ± 12,794 [3,760]
Pharmacy costs	723 ± 3,075 [91]	2,872 ± 10,632 [140]	3,711 ± 10,614 [386]
Ig	257 ± 1,798 [0]	1,924 ± 7,124 [0]	1,694 ± 5,078 [0]
C5i	90 ± 1,981 [0]	418 ± 7,676 [0]	1,207 ± 8,743 [0]
MAb	6 ± 129 [0]	51 ± 1,054 [0]	54 ± 437 [0]
FcRni	0 ± 0 [0]	18 ± 916 [0]	288 ± 2,412 [0]
Medical costs	2,216 ± 4,177 [1,006]	16,452 ± 30,561 [3,750]	4,274 ± 5,971 [2,312]
Inpatient costs	943 ± 3,641 [0]	13,604 ± 30,441 [0]	2,420 ± 4,605 [758]
Emergency costs	165 ± 344 [27]	503 ± 2,201 [0]	149 ± 337 [12]
Outpatient costs	1,050 ± 1,570 [584]	2,241 ± 4,516 [987]	1,563 ± 2,711 [807]
Other costs	58 ± 211 [2]	105 ± 469 [0]	142 ± 419 [14]

C5i=Complement-5 inhibitor, **FcRni**=Neonatal Fc receptor antagonist, **HRU**=healthcare resource utilization, **Ig**=Immunoglobulin, **MAb**=Monoclonal antibody, **USD**=United States Dollar.

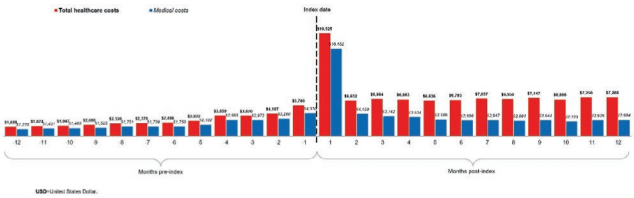

FIGURE 1 Distribution of mean total healthcare and medical cost (2023 USD) pre- and post-index.

Conclusion: Clinical events associated with gMG are resource-intensive, with both acute and long-term impacts. Findings underscore the importance of more effective and earlier treatments to achieve optimal disease control and reduce risk of crises/exacerbations.

Disclosure: This study was sponsored by Johnson & Johnson Innovative Medicine. Nicholas J. Silvestri and Kavita Grover have received personal compensation for serving as consultants for Johnson and Johnson. Kavita Gandhi, Antoine C El Khoury, Maria Ait-Thiyaty and Zia Choudhry are employees of Johnson and Johnson and may hold stock/stock options of Johnson and Johnson. Martin Cloutier, Maryia Zhdanava, Porpong Boonmak, Anabelle Tardif-Samson and Yuxi Wang are serving as employees of Analysis Group, Inc. Geoffroy Coteur is contractor for Johnson and Johnson.

EPR-088 | Clinical phenotypes of glycine receptor antibody encephalitis

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Background and aims: Glycine receptor (GlyR) antibodies have initially been described in progressive encephalomyelitis with rigidity and myoclonus (PERM), and few reports have been published since of this rare entity with similar, but also different phenotypes. This study aimed to describe the clinical characteristics of patients with GlyR antibodies who were referred to our center.
Methods: Within our ERN-accredited nationwide referral center, we included all patients who tested positive for GlyR antibodies in serum and/or cerebrospinal fluid (CSF), using an in-house live cell-based assay (serum 1:80, CSF 1:2). Patients were classified into the following phenotypes: PERM, rhombencephalitis, status epilepticus (SE), and chronic, focal epilepsy.
Results: We identified 20 patients with GlyR antibodies. One result was deemed clinically irrelevant (alternative diagnosis genetic leukodystrophy). Twelve patients (63%) were males, and median age was 56 (IQR 35, range 12-83). PERM was the most common phenotype ($n=12$, 63%), while two, two, and three patients had rhombencephalitis, SE, and epilepsy, respectively. Two patients had co-existing phenotypes (the first being predominant): rhombencephalitis and PERM; PERM and SE. Brain imaging was often normal or non-specific (14/17, 82%). Immunotherapy was effective in 9/13 assessable patients, five by first-line immunotherapy (corticosteroids and intravenous immunoglobulins), and four after addition of rituximab. Two patients had underlying cancer, including mesothelioma treated with pembrolizumab, and sigmoid adenocarcinoma.
Conclusion: While patients with GlyR antibodies present largely with PERM, other phenotypes such as rhombencephalitis, status epilepticus, and chronic, focal epilepsy are also observed. Patients generally respond well to immunotherapy making an adequate and timely diagnosis essential.
Disclosure: S. Abu Hassan is an awardee of the Singhealth Health Manpower Development Plan by the Ministry of Health, Singapore that is funding her fellowship at Erasmus MC. The other authors have nothing to disclose.

EPR-089 | An open-label trial of IVIg in autoimmune-associated seizures: The AMICE study

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Background and aims: Autoimmune-associated seizures (AAS) are most frequently refractory to anti-epileptic drugs but often respond to immunotherapy. We assessed the efficacy of IVIg in AAS.
Methods: In this prospective open label trial with IVIg, we included patients with AAS ≥16 years, experiencing ≥1 seizure/week, and confirmed antibodies. All patients received two courses of IVIg (0.4 grams/kg/day day 1-5 and 22-26). The primary outcome measure was the proportion of patients with a seizure frequency reduction > 50% and the proportion achieving seizure freedom in Weeks 6–8. The secondary outcomes were clinical improvement, relapse rate and ≥50% seizure reduction at Weeks 16–18.
Results: Twenty-six patients were included: 13 with antibodies against extracellular antigens (extracAE; $n=11$ anti-LGI1, $n=1$ anti-NMDAR, $n=1$ anti-Caspr2) and 13 with intracAE (all anti-GAD, concentration > 10,000IU/ml). After IVIg, 14/26 (54%) had > 50% seizure frequency reduction, more frequent in extracAE patients (10 [77%] vs. 4 [31%], $p=0.024$). Four extracAE patients achieved seizure freedom in Weeks 6–8, compared to zero intracAE patients ($p=0.048$). ExtracAE patients had a 94% median reduction of seizure severity versus 4% in intracAE patients ($p=0.002$). Still, 4/13 of the latter had > 50% seizure reduction after IVIg, while being refractory to anti-seizure medication before. Recurrence of seizures was seen in 17/26 patients, necessitating renewed immunotherapy. At Week 18, 12 (92%) extracAE and 10 (77%) intracAE patients had > 50% seizure reduction.

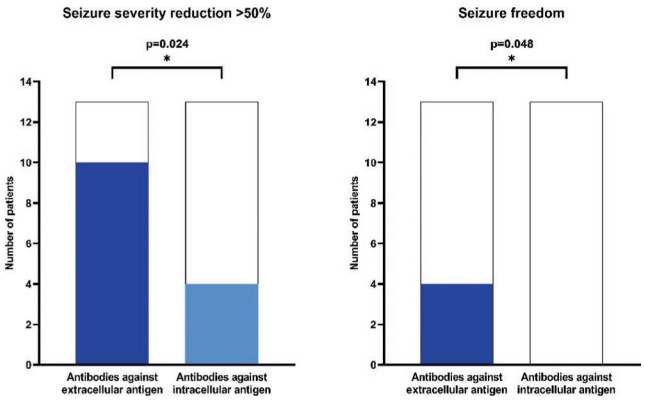

FIGURE 1 Seizure freedom and > 50% seizure reduction in Weeks 6–8 compared to baseline. Number of patients with respectively > 50% seizure severity reduction and with seizure freedom in Weeks 6–8 (Days 36–56), compared to baseline.

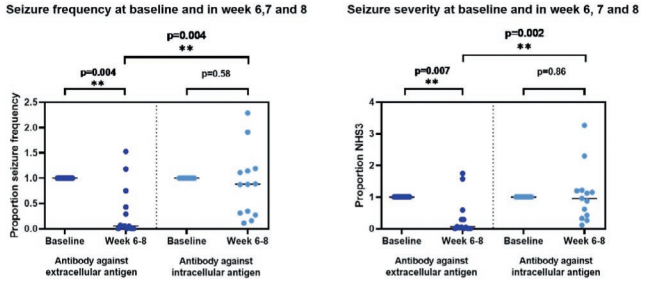

FIGURE 2 Seizure frequency and severity at baseline and in Weeks 6–8. Respectively seizure frequency and seizure severity at baseline compared to Weeks 6–8, shown in proportions compared to baseline, and compared between patients with extra- and intracAE.

	Patients with antibodies against extracellular antigen (n=13)	p-value	Patients with antibodies against intracellular antigen (n=13)	p-value	p-value (extra-cellular vs. intracellular)
Baseline (3 weeks before start of IVIg)					
Seizure frequency per week, median (IQR, range)	50.3 (18.5-232.8, 1-6583)	-	3.7 (3-27.5, 2.3-73.7)	-	**0.007**
Seizure severity score[a] per week, median (IQR, range)	69.3 (29-256.2, 4-663)	-	9.0 (4.5-61.7, 3.3-198.7)	-	**0.010**
Primary outcome - weeks 6-8[b]					
Seizure frequency per week, median (IQR, range)	3.3 (0-24.2, 0-552)	-	3.3 (1.3-12.3, 0.3-84)	-	0.28
Frequency compared to baseline, median % (IQR, range)	5.6 (0-58.9, 0-152.9)	**0.004**	88.0 (29.0-116.7, 11.1-228.6)	0.58	**0.004**
Seizure severity score[a] per week, median (IQR, range)	5.3 (0-24.2, 0-582)	-	12 (2.7-42.8, 1-170.7)	-	0.074
Severity compared to baseline, median % (IQR, range)	5.6 (0-44.0, 0-175)	**0.007**	96.0 (37.4-121.1, 11.1-327.3)	0.86	**0.002**
Seizure severity reduction >50% compared to baseline	10 (77%)	-	4 (31%)	-	**0.024**
Seizure freedom	4 (31%)	-	0 (0%)	-	**0.048**
Late follow-up - weeks 16-18[c]					
Seizure frequency per week, median (IQR, range)	0.0 (0.0-67.5, 0.0-169)	-	5.0 (2.5-23.5, 0.0-97.0)	-	0.18
Frequency compared to baseline, median % (IQR, range)	0.0 (0.0-8.6, 0.0-257.1)	**0.010**	36.4 (18.4-54.1, 0.0-200.0)	**0.011**	**0.007**
Seizure severity score[a] per week, median (IQR, range)	0.0 (0.0-69.0, 0.0-304.0)	-	11.0 (3.5-54.0, 0.0-198.0)	-	0.12
Severity compared to baseline, median % (IQR, range)	0.0 (0.0-8.5, 0.0-416.4)	**0.010**	28.6 (16.3-55.6, 0.0-200)	**0.011**	**0.004**
Seizure severity reduction >50% compared to baseline	12 (92%)	-	10 (77%)	-	0.30
Seizure freedom	7 (54%)	-	2 (15%)	-	**0.048**
Seizure recurrence before week 18[d]	9 (69%)	-	8 (62%)	-	1.00
Additional immunotherapy weeks 1-8[e]	7 (54%)		0 (0%)		**0.003**
Study day, median (IQR, range)	22.0 (14.0-23.0, 12-26)		n.a.		n.a.
Type of immunotherapy					
ivMP only	5/7 (71%)		0 (0%)		
ivMP and oral prednisone	1/7 (14%)		0 (0%)		
ivMP, rituximab and oral prednisone	1/7 (14%)		0 (0%)		

Abbreviations: IQR = interquartile range; IVIg = intravenous immunoglobulins; ivMP = intravenous methylprednisolone.

[a] The seizure severity score is determined using the National Hospital Seizure Severity Scale (NHS3).
[b] Day 36 to 56.
[c] Day 106 to 126.
[d] Day 1 to 126.
[e] Day 1 to 56.

Table 1. Follow-up characteristics

Conclusion: In patients with AAS, IVIg lead to reduction of seizures and seizure freedom, most pronounced in extracAE. Recurrence after waning effects of IVIg is common, supporting the need for longer-lasting immunotherapies.

Disclosure: This study was funded by the Dutch Epilepsy foundation (EpilepsieNL, project 19-08) and the Interlaken Leadership Award, an unrestricted research grant from CSL Behring.

Neuropathies

EPR-090 | Nitrous oxide polyneuropathy: The new trend

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Background and aims: The prevalence of recreational use of nitrous oxide (N2O) is increasing among young people. NO2 is thought to alter neuronal membrane glutamate or gamma aminobutyric acid receptors, producing its effect within seconds of inhalation. N2O interferes with the metabolism of vitamin B12 and methionine, resulting in an increase in homocysteine concentration. Clinical manifestations include sensorimotor polyneuropathy, ataxia, myelopathy, and megaloblastic anemia, among others. Neurotoxicity is potentially reversible with vitamin B12 supplementation and N 2 O abstinence. Frequent findings on complementary tests include sensory/motor axonal involvement on electroneurography (ENG) or cervical spinal cord hyperintensity on MRI.

Methods: Description of three clinical cases (two males and one female) with a mean age of 48 years NO2 consumption.

Results: In this paper we discuss three clinical cases of three NO2-consuming patients. Patient 1 reports frequent consumption, and 2 and 3 daily consumptions. All of them started with a similar clinical manifestation. On admission, laboratory tests were requested to evaluate vitamin deficiencies, as well as electroneurography tests, which revealed axonal polyneuropathy in all of them, either sensory or motor, or both. In patient 2, cervical MRI showed T2 enhancement at this level indicative of subacute combined spinal cord degeneration. The description of the case series is shown in table 1.

TABLE 1 Case series description.

	Patient 1	Patient 2	Patient 3
Age and gender	24, female	23, male	40, male
Reason for consultation	Gait disturbance, manipulative clumsiness and leg paresthesias of subacute and progressive onset over months of evolution	Paresthesias in hands and feet with ascending progression, manipulative clumsiness and difficulty in walking of months of evolution	Ascending distal paraesthesias of the lower limbs and hands and difficulty walking for the last year. Manipulative clumsiness
Physical examination on admission	-Tremor of trunk and limbs. -Pulsion to the left with eyes closed. - Hyperreflexia -Alteration of distal arthrokinetic sensitivity in lower limbs. -Tactile hypoaesthesia of lower limbs -Impossible gait	-Distal tetraparesis hands and feet 4/5 -Global hyporeflexia -Hipopalaesthesia upper limbs -Distal palaesthesia in feet -Abolished arthrokinetics. Steppage gait with increase of base of support -Distal palpex in feet	- Arreflexia -Hypoaesthesia in glove and up to the knees - Abolished apalaesthesia and positional -Ataxic gait
Laboratory tests	- Vit B12: 243 pg/ml - Homocysteine: 52.10 mcmol/l - Methylmalonic acid: 0.69 mcmol/l - Hb: 13 g/dl - MCV:105	- Vit B12: 256 pg/dl - Homocysteine: pending - Methylmalonic acid: pending - Hb: 16 g/dl -MCV: 96.4	- Vit B12: 235 pg/dl - Homocysteine: pending - Methylmalonic acid: pending - Hb: 15 g/dl - MCV: 109
ENG/EMG	Severe axonal sensory PNP of lower limbs	Severe symmetrical axonal motor PNP of the lower limbs with acute denervating activity at the distal level of MMII.	Sensory-motor axonal PNP (mild sensory in upper limbs and severe sensory-motor of lower limbs)
MRI Spine	Anodyne	Homogeneous cervical spinal cord enhancement	Pending
Treatment	Daily intramuscular vitamin B12	Daily intramuscular vitamin B12	Daily intramuscular vitamin B12
Physical examination on discharge	- Achilles reflex not evocable, rest present - Gait ataxic but possible unaided.	- Strength 4+/5 lower limbs -Mild distal hypopalaesthesia -Arthrokinetics with faults -Gait without alterations	-Hyperalgesia -Hyperalgesia feet to knee -Arreflexia - Dysmetria in heel-knee manoeuvre -Minimally ataxic gait

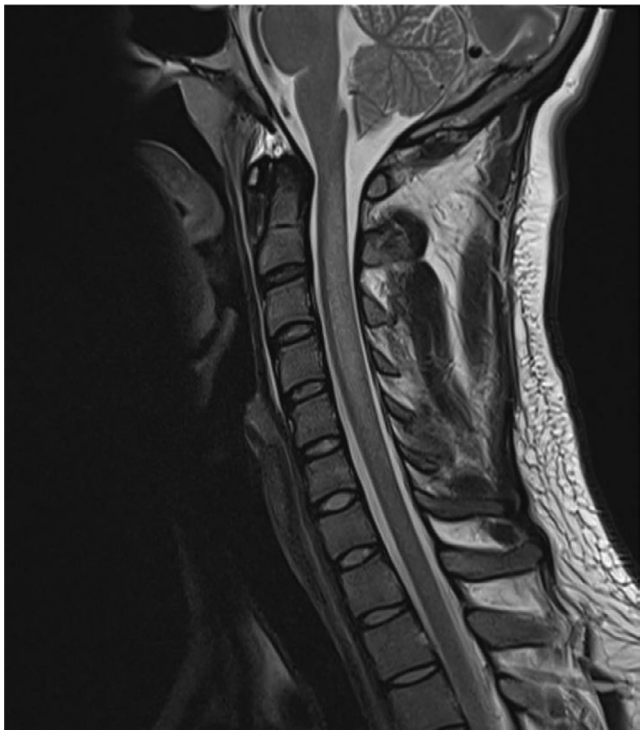

FIGURE 1 Cervical MRI. T2 hyperintensity is observed at cervical level, corresponding to patient 2.

Conclusion: Clinical suspicion is essential in patients with these clinical manifestations as it has been shown that initiation of treatment and cessation of NO2 consumption improves patient recovery. This case report aimed to contribute to the scientific literature for the knowledge and early recognition of this entity.
Disclosure: Nothing to disclose.

EPR-091 | Minimally invasive resection of first rib for treatment of thoracic outlet syndrome: Technique and outcomes

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Background and aims: Thoracic outlet syndrome (TOS), first described by Peet et al. in 1956,1 refers to symptoms caused by the compression of the neurovascular bundle within the thoracic outlet which extends from the supraclavicular fossa to the axilla between the clavicle and first rib.2 Various approaches to a first rib resection, including the supraclavicular, infraclavicular, and trans-axillary approach, offer distinct advantages and limitations.3,4 This report presents a minimally invasive infraclavicular approach to a first rib resection that improves visualization and access to the posterior first rib while allowing for neurovascular protection.3,5.
Methods: We retrospectively analyzed patient outcomes of TOS patients who received the minimally invasive infraclavicular approach to a first rib resection from 2020 through 2023. We assessed both intraoperative and postoperative metrics including blood loss, complications, fluids, pain, weakness, and numbness.
Results: Thirteen patients underwent the minimally invasive first rib resection procedure performed exclusively by the presenting surgeon. Intraoperative results found mean blood loss to be 59.1 cc, 1.3L of crystalloid fluid, and 3 minor complications. Postoperative outcomes showed that numbness improved in 85% (11 of 13 subjects) of patients. VAS neck and arm pain scores decreased 15% and 30%. Additionally, upper extremity weakness improved in 4 of the 5 with preoperative symptoms. A case illustration will be presented to highlight these significant improvements.
Conclusion: This novel minimally invasive infraclavicular approach to a first rib resection offers a clear and direct approach to the posterior first rib, enhancing neurovascular protection while also providing the patient with significant relief of their TOS symptoms.
Disclosure: Nothing to disclose.

EPR-092 | The impact of CIDP on patients' employment: Results from a real-world multinational survey

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Background and aims: The objective of this secondary analysis is to highlight the impact of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), an immune-mediated rare disease that causes increasing weakness and sensory symptoms, on patients' work situation.
Methods: As part Adelphi's CIDP Disease Specific Programme™, a cross-sectional real-world survey, matched physician- and patient-reported data were collected in the US, the UK, France, Germany, Italy, Japan and Spain between September 2022 and April 2023. Neurologists submitted demographics through electronic record forms, while some patients voluntarily provided employment data and completed the Work Productivity & Activity Impairment (WPAI) questionnaire.
Results: Mean patient age was 54.4 (SD 12.6, $N = 310$), with 59% being male. Many patients were out of full-time employment: 21% were retired, 10% unemployed, 8% working part-time, and 6% on long term sick leave. In nearly half these cases, patients indicated CIDP was the reason for their current employment status. Out of 292 patients, 48% reported their disease had impacted their career (past or present): 15% had work responsibilities reduced, 14% stopped working, 12% needed flexible working hours, 11% had/needed unplanned time off work, and 9% experienced a reduction in income. Almost a third (32/118) of patients that were employed either full- or part-time had missed time from work in the last 7 days because of CIDP (mean 6.8 hours, SD 7.0). The mean WPAI percentage for overall work impairment, encompassing absenteeism and presenteeism, was 33.6 (SD 25.4, $n = 106$).
Conclusion: CIDP has a substantial impact on patients' employment, often hindering or completely preventing them from working.
Disclosure: SP and CA are employees of argenx and have stock in argenx, the sponsor of the study. JW, YT and RS are employees of Adelphi Real World which received honoraria from argenx for access to data from Adelphi's Disease Specific Programme. FB, LV and SD were commissioned by and received honoraria from argenx.

EPR-093 | Baseline characteristics of the first 200 study participants with multifocal motor neuropathy in the iMMersioN study

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Background and aims: Multifocal motor neuropathy (MMN) is a rare, peripheral, chronic neuropathy characterized by progressive and disabling asymmetric limb weakness without sensory loss, caused by immune-mediated complement activation, motor nerve conduction block, and axonal degeneration. The global, prospective, longitudinal iMMersioN study (NCT0598 8073) will characterize disease course, management, and burden of MMN on adult patients with new/existing diagnoses, receiving standard of care treatments. Baseline characteristics of the first 200 participants are reported.
Methods: Outcome measures (MMN-Rasch-built Overall Disability Score [MMN-RODS]; modified MRC-10 [mMRC-10]) and the impact on health-related quality of life (Rasch-Transformed Fatigue Severity Scale [RT-FSS]; chronic acquired polyneuropathy patient-reported index [CAP-PRI]; Patient Global Impression of Severity [PGI-S]) will be assessed for up to 24 months. Site visits coincide with existing treatment visits (approximately every 3 months), with an optional visit 7–14 days after study start.
Results: At enrolment closure, 413 participants have been enrolled. Of the first 200 participants, 76.9% had definite, 11.6% probable, and 11.6% possible MMN. Mean (SD) age was 55.4 (12.8) years; 37% were female, 68% white, and 76.5% European. 46.0% of participants had 3 or 4 limbs affected. Mean (SD) time since initial symptoms and diagnosis were 13.6 (10.0) and 9.6 (8.3) years, respectively. Mean (SD) baseline scores were 74.0 (16.0) for MMN-RODS centile, 90.7 (10.9) for mMRC-10, 11.0 (6.5) for RT-FSS, and 10.7 (6.3) for CAP-PRI. Most participants ($n = 80$) had a PGI-S score of 4 (moderate disease).
Conclusion: iMMersioN is the first, global study to detail the impact of MMN and MMN treatment on patients in a real-world setting.
Disclosure: KC: Alnylam, Amicus, argenx, Biogen, CSL Behring, Ipsen, Janssen, Lupin, Pfizer, Roche, Sanofi-Genzyme, Vertex, UCB CH: argenx, Biogen, Lupin, Roche, UCB SP: ADOC, argenx, Berlin-Chemie Menarini, Kedrion, Mylan, Octapharma, Pfizer, Roche, Salveo, Sanofi Genzyme, Teva Actavis, Wörwag LQ: Annexon, Alnylam, argenx, Avilar Therapeutics, Biogen, CIBERER, CSL Behring, Dianthus, Fundació La Marató, GBS-CIDP Foundation International, Grifols, Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), Janssen, LFB, Lundbeck, Merck, Novartis, Octapharma, Roche, Sanofi, UCB SA: Nothing to disclose IVdW, EP, IVH, MV, OVdS and CA-B: Employees of argenx GS: Employee of PPD, part of Thermo Fisher Scientific, consultant for argenx SC: Employee of PPD, part of Thermo Fisher Scientific, consultant for argenx JAA: Akcea therapeutics, Alexion, Alnylam, Annexon, argenx, CSL Behring, Grifols, Immunovant, Immupharma, Johnson & Johnson, Pfizer, Takeda

EPR-094 | Hereditary neuropathies in Serbian population

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Background and aims: Hereditary neuropathies encompass a genetically and phenotypically diverse group of disorders. This study aimed to determine final diagnoses in patients referred from a Serbian tertiary referral center under suspicion of hereditary neuropathy.
Methods: Patients referred for genetic testing from the Neurology Clinic, University Clinical Center of Serbia (2009–2023) were included. Among 778 suspected cases of hereditary neuropathy, 229 patients were either lost to follow-up or presented with conditions mimicking neuropathy.
Results: Of 549 evaluated patients, 48 (8.7%) had hereditary neuropathy with liability to pressure palsies (HNPP) with PMP22 deletion, and 56 (10.2%) had non-hereditary compressive neuropathies. Charcot-Marie-Tooth disease (CMT) subtype 1A (CMT1A) accounted for 91 (16.6%) cases (3 with point mutations). Other subtypes included X-linked CMT (CMTX) (2.9%), HINT1 (2.7%), and 37 (6.7%) with rarer CMT forms. The most common distal motor neuropathy (dMN) subtype was HSPB1 (0.55%). Hereditary sensory autonomic neuropathy (HSAN) was identified in 2 cases. Polyneuropathy associated with other genetic syndromes was found in 29 (5.2%) patients, while 3.0% had inconclusive WES findings and 6.4% lacked mutations. Acquired neuropathy was diagnosed in 157 (28.6%) patients.
Conclusion: In line with other populations, CMT1A was the most common cause of hereditary neuropathy in Serbia. A notable presence of CMTX and HINT1 neuropathy is specific for Serbian population. These findings highlight the importance of targeted genetic analysis in diagnosing hereditary neuropathies in certain population.
Disclosure: Nothing to disclose.

EPR-095 | Healthcare resource utilization and caregiver burden in CIDP: Results from a real-world multinational survey

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Background and aims: Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is a rare, immune-mediated disease that causes progressive weakness and sensory symptoms. This analysis highlights medical and non-medical resources required by CIDP patients.
Methods: CIDP-treating neurologists completed surveys for Adelphi's Disease Specific Programme™ (September 2022-April 2023), capturing demographics, healthcare resource utilization, caregiver support, and mobility aids usage across the UK, the US, France, Germany, Italy, Japan and Spain.
Results: Mean patient age was 54.8 (SD 12.6, $N = 936$) years; 63% were male and 47% used mobility aids, usually a cane/walking stick (36%). The mean number of healthcare professional types involved in disease management was 2.4 (SD 1.4); patients most often saw a neurologist (81%), followed by a physical therapist (41%) and family doctor/GP (38%). Patients attended a mean 7.8 (SD 13.4) consultations in the last 12 months ($n = 914$). Among 750 patients, 14% were hospitalized in the last 12 months; for their most recent hospitalization, 55% were admitted through the ER, and 9% spent time in the ICU. Out of 840 patients, 3% received professional caregiver support, while 25% relied on

informal caregivers, usually a partner/spouse (84% out of 219 patients). Patients with informal caregiver(s) ($n = 211$) received a mean 28.7 (SD 33.3) hours of care per week. Consequently, caregivers ($n = 157$) reduced working hours (22%), stopped working (11%) or worked from home (10%). Participation in activities like social events (50%), physical activity/exercise (33%) and going on holiday (29%) was reduced or avoided altogether.
Conclusion: CIDP patients require many resources, including mobility aids, hospitalizations and assistance from healthcare professionals and caregivers.
Disclosure: SP and CA are employees of argenx and have stock in argenx, the sponsor of the study. JW, YT and RS are employees of Adelphi Real World which received honoraria from argenx for access to data from Adelphi's Disease Specific Programme. FB, LV and SD were commissioned by and received honoraria from argenx.

EPR-096 | CIDP patients' journey to diagnosis: Results from a real-world multinational survey

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Background and aims: This secondary analysis aimed to characterize the diagnostic journey of patients suffering from Chronic Inflammatory Demyelinating Polyneuropathy (CIDP), a rare and severe immune-mediated disease associated with progressive limb weakness and sensory symptoms.
Methods: Adelphi's CIDP Disease Specific Programme™ collected point-in-time data through surveys of CIDP-treating neurologists between September 2022 and April 2023. This real-world, multinational study captured demographics and journey to diagnosis data for CIDP patients in the US, the UK, France, Germany, Italy, Japan and Spain.
Results: In the total sample ($N = 936$), 63% of patients were male, with the mean age being 54.8 (SD 12.6) years. The mean period of time between patients' ($n = 660$) symptom onset and first consultation with a healthcare professional ($n = 903$), usually a general neurologist (56%) or family doctor/GP/PCP (27%), was about 7.0 (SD 15.7) months. Another 6.0 (SD 15.0) months would typically pass before patients were diagnosed with CIDP, predominantly by a general neurologist (76% of 934 patients). The mean number of diagnostic tests undergone by patients was 19.2 (SD 10.1). Neurological examination (98%), a review of the patient's medical history (88%) and an electromyogram (EMG) (85%) were most often used to aid diagnosis. Out of 740 patients, 34% were initially misdiagnosed with one or more condition(s). Patients were most frequently misdiagnosed with Guillain–Barré syndrome (33%), diabetic polyneuropathy (15%), and fibromyalgia (12%).
Conclusion: Patients suffering from CIDP experience a substantial burden securing their diagnosis. The journey to diagnosis is, on average, longer than a year, and over a third were initially misdiagnosed.
Disclosure: SP and CA are employees of argenx and have stock in argenx, the sponsor of the study. JW, YT, and RS are employees of Adelphi Real World which received honoraria from argenx for access to data from Adelphi's Disease Specific Programme. FB, LV and SD were commissioned by and received honoraria from argenx.

EPR-097 | A comparison of treatment satisfaction in CIDP across 5 countries: Results from a real-world multinational survey

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Background and aims: Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) is an immune-mediated disorder affecting sensory function and strength. This study compares patient and physician satisfaction with treatment across five countries.
Methods: Point-in-time data were collected in the UK, France, Germany, Italy, and Spain via physician and patient surveys as part of Adelphi's CIDP Disease Specific Programme™ (September 2022-April 2023). This real-world study captured demographics, as well as treatment history and satisfaction data. Treatment satisfaction data were not collected for UK patients.
Results: In all countries, patients ($n = 542$) were predominantly male; mean (SD) age ranged between 51.9 (10.9) and 56.6 (13.8). At time of survey, the majority of patients were receiving treatment: the UK ($n = 54$) reported the largest proportion (94%), while Spain ($n = 120$) reported the lowest (80%). Despite treatment, around half of patients in most countries experienced moderate-to-severe symptoms; exceptions were Spain (38%) and the UK (78%). The proportion of patients less than satisfied with overall treatment were 21% (Germany, $n = 81$), 33% (Spain, $n = 27$), 35% (Italy, $n = 26$), and 45% (France, $n = 18$). Inversely, 4% (Italy), 10% (Germany), 11% (France), and 25% (Spain) of patients were very satisfied with treatment. For treatment efficacy and treatment convenience, Spanish patients again reported the highest rates of satisfaction, and German patients the lowest rates of dissatisfaction. Physicians of these patients were more positive: 33% (France, $n = 18$), 42% (Italy, $n = 26$), 48% (Spain, $n = 27$), and 58% (Germany, $n = 81$) were very satisfied with overall treatment.
Conclusion: Across countries, CIDP patients were less satisfied with treatment than their physicians; around half reported moderate-to-severe symptoms despite treatment.
Disclosure: SP and CA are employees of argenx and have stock in argenx, the sponsor of the study. JW, YT and RS are employees of Adelphi Real World which received honoraria from argenx for access to data from Adelphi's Disease Specific Programme. FB, LV and SD were commissioned by and received honoraria from argenx.

EPR-098 | Autonomic nervous system impairment in patients with chronic demyelinating polyneuropathies

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Background and aims: In chronic demyelinating polyneuropathies more attention is often paid to motor and sensory functions, and autonomic functions are usually overlooked. The aim of our study was to examine autonomic dysfunction in patients with different types of chronic demyelinating polyneuropathies, acquired and hereditary.
Methods: Following diagnoses were included: chronic inflammatory demyelinating polyneuropathy (CIDP, $n=98$), polyneuropathy associated with monoclonal gammopathy of undetermined significance (MGUS-PN, $n=51$), Charcot-Marie-Tooth disease type 1A (CMT1A, $n=51$), hereditary neuropathy with liability to pressure palsies (HNPP, $n=18$) in comparison to healthy controls (HCs, $n=125$), SCOPA-AUT questionnaire was used, comprising questions related to the function of the cardiovascular, gastrointestinal and urinary systems, as well as thermoregulation and sexual functions.
Results: Mean SCOPA-AUT score was 13.6 ± 11.1 in CIDP, 18.4 ± 8.4 in MGUS-PN, 14.1 ± 9.5 in CMT1A, 11.7 ± 8.6 in HNPP versus 7.4 ± 7.3 in HCs. All patient groups, except for HNPP, differed in comparison to HCs ($p<0.01$). Gastrointestinal, urinary and cardiovascular scores were worse in MGUS-PN compared to HCs (3.3 ± 3.6 vs. 1.4 ± 1.7, 4.5 ± 3.0 vs. 2.3 ± 2.6 and 1.1 ± 1.4 vs. 0.5 ± 1.0, respectively, $p<0.05$). Thermoregulation was worse in all patient groups compared to HCs ($p<0.05$). Male sexual dysfunction was noticed in CIDP and MGUS-PN, and female sexual dysfunction in CIDP, MGUS-PN and CMT1A.
Conclusion: Among patients with chronic demyelinating polyneuropathies, autonomic dysfunction was most pronounced in patients with MGUS-PN. Patients with HNPP presented the least autonomic impairment.
Disclosure: Nothing to disclose.

Sleep-wake disorders

EPR-099 | Obstructive sleep apnea in amyotrophic lateral sclerosis: Diagnostic challenges and predictive modeling

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a neurodegenerative disorder characterized by motor and non-motor symptoms, including sleep disturbances. Despite their clinical significance, sleep-related issues remain underexplored in ALS clinical assessments. We aimed to investigate sleep disorders' prevalence, characteristics, and impact in ALS patients.
Methods: We conducted a prospective study enrolling ALS patients followed by the Neuromuscular Disorders Service of the University Hospital of Parma, Italy. Disease severity, cognitive performances, sleep quality, daytime sleepiness, and quality of life were specifically assessed. Full-night cardiorespiratory monitoring (CRM) was performed to diagnose sleep-related breathing disorders. Correlations between sleep disturbances, ALS severity, and patient outcomes were explored. Logistic regression was used to develop a predictive model for OSA.
Results: Among 22 ALS patients (70.57 ± 10.8 years), 86.4% reported sleep disturbances, including leg cramps (55%), insomnia (20%), and restless leg syndrome (15%). 57.1% of patients were affected by OSA: male patients were more frequently affected by OSA (72.7% vs. 40%) and generally presented more severe manifestations ($p=0.010$). A novel predictive score incorporating BMI, PSQI, sex, and bulbar involvement showed 87.5% specificity and 80% accuracy for OSA detection (Fig. 1). Elevated apnea indices correlated with reduced 12-month survival (67% vs. 100% for lower indices) (Fig. 2).

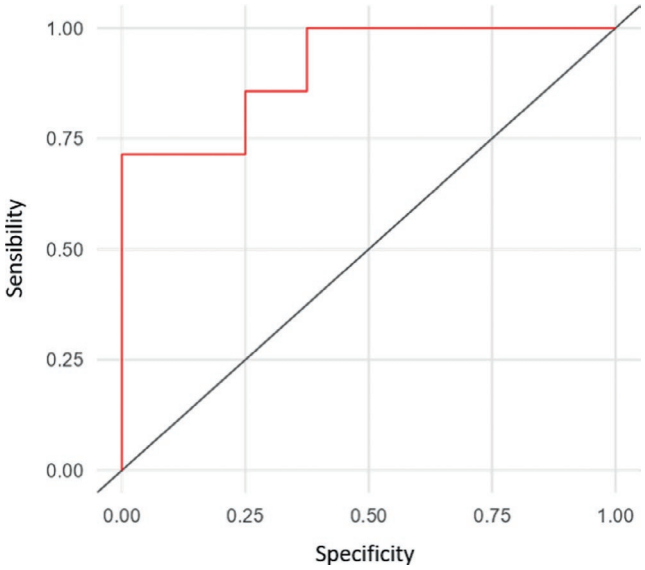

FIGURE 1 ROC curve representing the reliability in predicting the presence of OSA in the study population using a model with four variables: Body Mass Index, Pittsburgh Sleep Quality Index total score, gender, and presence of pseudobulbar symptoms.

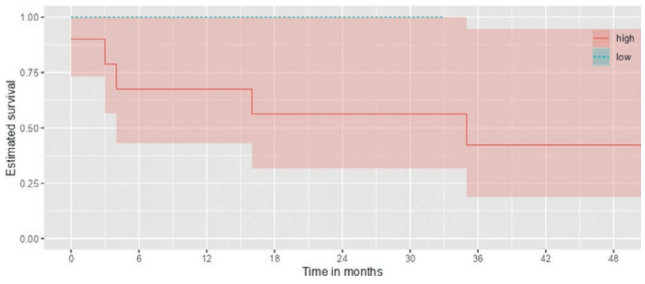

FIGURE 2 Graphical representation (Kaplan–Meier method) of the estimated survival in relation to AHI values in the sample. The red line represents patients with an AHI > 3.8 events/h, the blue dotted line represents those with an AHI.

Conclusion: Our findings reveal a high prevalence of sleep disorders in ALS patients, emphasizing the limitations of standard OSA screening tools. The OSAPS model demonstrated superior accuracy for OSA prediction in this population. Comprehensive sleep assessments may improve patient management and

outcomes. Further multicenter studies are warranted to validate these findings.

Disclosure: Each Author has no relevant financial or non-financial interests to disclose. All authors have reviewed and approved the manuscript for submission and affirm that the work was conducted independently without external influence.

EPR-100 | The burden of insomnia and excessive daytime sleepiness: Switzerland's pilot study preliminary results

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Background and aims: Excessive daytime sleepiness (EDS) and insomnia (IN) significantly impact individuals and society, yet their specific needs and broader socioeconomic effects remain underexplored. To address this gap, a pilot trial for a multistage, European-wide, multicenter research study commenced in Switzerland in mid-2023.

Methods: This prospective, national cohort observational study aimed to evaluate the burden and progression of EDS and IN over 12-month post-initial assessment. Recruitment is conducted by nine primary care providers, aiming for completion by June 2024. The primary goal is to assess study feasibility, with secondary goals of determining EDS/IN prevalence in primary care and their correlation with health-related quality of life (QoL) using validated tools. Patients screened positive for EDS/IN are invited to join the online study, featuring standardized questionnaires.

Results: Of 632 screened subjects, 238 (44%) reported subjective EDS/IN, 135 expressed interest, and 92 participated in the online segment (64% female, mean age 47.4 years, BMI 24.8 kg/m^2). Of these, 38% had EDS (ESS > 10) and 70% had IN symptoms (ISI > 7), though only 4.9% were diagnosed with a sleep/wake disorder at baseline. Over half reported distress in social, occupational, and educational areas. QoL assessment with SF-12 showed reduced scores (normalized score: 0.66), primarily due to the mental component (0.57).

Conclusion: Excessive daytime sleepiness (EDS) and insomnia (IN) symptoms are highly prevalent in primary care settings and apparently underdiagnosed. Our findings highlight a significant decline in quality of life (QoL) among patients with these conditions.

Disclosure: This study was supported by the European Academy of Neurology.

EPR-101 | Discriminative value of psychomotor vigilance and sustained attention to response tests in identifying hypersomnolence

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Background and aims: Attention deficits are key symptoms of central disorders of hypersomnolence (CDH), such as narcolepsy. Sustained Attention to Response Test (SART) and Psychomotor Vigilance Test (PVT) are common tools to assess attention deficits, but their discriminative value for CDH remains unclear. This study aimed to identify the most discriminative outcome measures of SART and PVT and calculate their cut-off values to distinguish CDH from healthy controls (HC).

Methods: This study is a subproject of the international Swiss Primary Hypersomnolence and Narcolepsy Cohort Study (iSPHYNCS). Participants (CDH patients and HC) completed SART (3 sessions: 11am, 1pm, 5 pm) and PVT (1 session: 3pm). Reaction time (RT), standard deviation of RT (SD), lapses (both tests), commission errors (SART), and fastest/slowest 10% of RT

(F10 and S10, respectively) for PVT) were analyzed. ROC and PCA analyses were performed, and cut-off values calculated.
Results: SART (CDH, $n = 132$; HC, $n = 31$) showed higher SD and lapses in patients ($p < 0.05$). For PVT (CDH, $n = 119$; HC, $n = 31$), all outcomes except F10 were worse in patients ($p < 0.005$). ROC analysis showed SART's lapses and SD achieved AUCs of 0.66 and 0.65, respectively, with cut-offs of 0 lapses and 67 ms for SD of RT. PVT's SD and S10 yielded higher AUCs of 0.79 and 0.76, with cut-offs of 47 ms and 410 ms, respectively. PCA-based combination of parameters did not enhance accuracy.

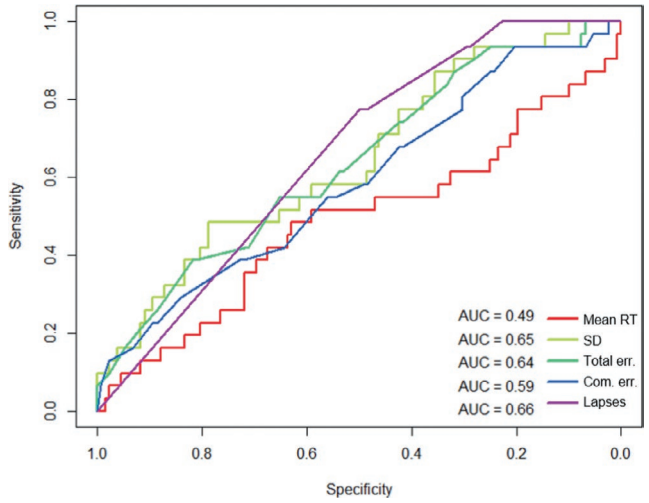

FIGURE 1 ROC curves for SART outcomes distinguishing CDH patients from HC. "Com. err." denotes commission errors, and "Total err." represents the sum of commission errors and lapses.

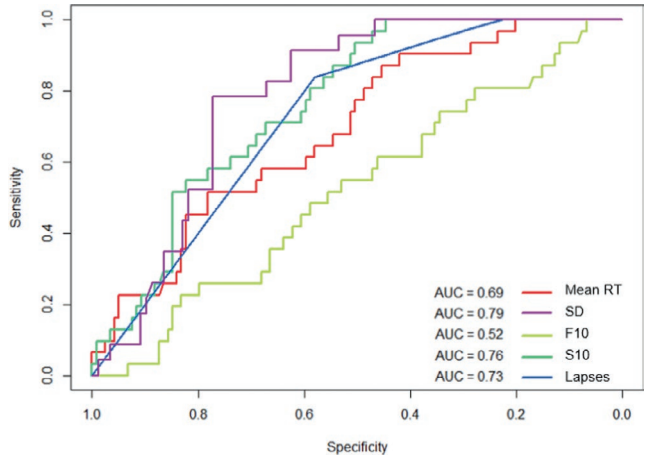

FIGURE 2 ROC curves for the PVT outcomes to distinguish CDH patients from HC.

Conclusion: The PVT appears more accurate than the SART for identifying attention deficits in CDH. Reliable cut-offs ensure proper test interpretation and support SART and PVT use for treatment monitoring.
Disclosure: The authors declare no conflict of interest. The study is supported by the Swiss National Science Foundation (SNF 320030_185362; SNF 32003B_215721).

EPR-102 | Glucagon-like 1 analogs and sleep-related eating disorder—A new hope?

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Background and aims: Sleep-related eating disorder (SRED) is a syndrome characterized by periods of involuntary eating after arousal during sleep, with partial or complete loss of awareness. The current therapeutic options have limited efficacy. Glucagon-like peptid-1 (GLP-1) analogs might be a possible treatment.
Methods: We report 3 cases of patients with SRED resolution after introducing GLP-1 analogs.
Results: The first case is a 44-year-old woman who seeks medical attention due to initial insomnia and sleep fragmentation due to unaware arousals to consume high-calorie and "bizarre" foods, causing a 40 kg weight gain in 20 years. SSRIs, topiramate, and zonisamide were tried without efficacy. After beginning liraglutide, complete and sustained remission was observed. The second case is a 47-year-old man evaluated for multiple night-eating arousals since age 18. He was given ropinirole, topiramate and APAP, with partial improvement. SRED subsided with the introduction of semaglutide. The last case is a 56-year-old woman with SRED associated with zolpidem abuse. The patient reduced her zolpidem intake but still had SRED episodes. After starting semaglutide, complete control of symptoms was observed.
Conclusion: The effects of GLP-1 analogs on appetite suppression have been extensively studied and may be due to effects on the digestive tract or central nervous system (such as on the infralimbic cortex). These have shown promise in treating addictions, such as smoking or drug use. These are the first reported SRED cases improved by GLP-1 analogs, which may present a new hope for the treatment of this treatment-resistant condition.
Disclosure: Nothing to disclose.

EPR-103 | Incidence and burden of narcolepsy in France using the Système National des Données de Santé (SNDS)

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Background and aims: Narcolepsy is a rare, chronic, central nervous system disorder of hypersomnolence characterized by excessive daytime sleepiness. The study objective was to estimate the incidence and burden of narcolepsy in France.
Methods: Retrospective population-based cohort study using anonymized healthcare data among 66 million people from the SNDS database (2014-2019). Incident narcolepsy cases (INCS) were matched to non-narcolepsy controls.
Results: 1,650 INCS were identified, with annual incidence rates varying from 0.45 to 0.55 per 100,000 person years. INCS were young (50% < 24.5 years) and predominantly female (54.7%).

Other sleep disorders (e.g., sleep apnea; 26.8% vs. 0.71%), psychiatric (e.g., depression, anxiety; 8.2% vs. 3.5%) and nervous system (e.g., migraine, epilepsy; 8.3% vs. 1.6%) comorbidities were more frequent in INCS versus controls. The frequency of outpatient and inpatient visits were significantly higher for INCS than controls, including general practitioners (incidence rate ratio [IRR] [95% CI] 1.77 [1.74-1.79]) any specialists (2.71 [2.67-2.75]), neurologists (29.96 [27.91-32.16]), psychiatrists (5.23 [5.07-5.40]), and all-cause in-patient admissions (3.87 [3.76-3.98]). Approximately 80% of INCS received narcolepsy medication within 7 months of diagnosis: 73.0% first received modafinil monotherapy. Other treatments included: methylphenidate 32.4%, venlafaxine 19.5%, and pitolisant 17.6% at any time after the index date (date of narcolepsy diagnosis). Most patients (93%) started on monotherapy and up to 47.6% subsequently received combination therapy. Overall medication persistence of narcolepsy-specific medications for INCS was 19-28% at 6 months and 8-15% at 12 months.
Conclusion: This study provides a robust estimation of narcolepsy incidence and presents evidence for high healthcare burden compared with controls.
Disclosure: SC and SG are employees of Takeda Development Center Americas, Inc. BP and AA are employees of OXON Epidemiology, who were contracted by Takeda for this work. YD received funds for seminars, board engagements and travel to congresses from Avadel, Bioprojet, Idorsia, Jazz, Orexia, and Takeda. Takeda Development Center Americas, Inc., provided funding to Excel Medical Affairs for support in writing this abstract.

EPR-104 | The relationship between glymphatic function and disease duration in isolated rapid eye movement sleep behavior disorder

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Background and aims: Isolated rapid eye movement sleep behavior disorder (iRBD) is commonly recognized as a prodromal stage of alpha-synucleinopathies, such as Parkinson's disease, multiple system atrophy, and dementia with Lewy bodies. Dysfunction of the glymphatic system was observed in these neurodegenerative disorders using diffusion tensor imaging along the perivascular space (DTI-ALPS) method. This study aimed to evaluate the association between the ALPS-index and the duration of iRBD.
Methods: In this study, we included 51 patients (67.00 ± 7.0 years [mean age ± SD]) with an iRBD diagnosis confirmed by polysomnography. The patients reported the onset of their dream enactment symptoms during interview. Glymphatic function was evaluated with the DTI-ALPS method by obtaining diffusion parameters near the top of the lateral ventricles and calculating age-adjusted ALPS-indices. We performed a correlation analysis between the ALPS-index and the duration of iRBD since the onset of the first symptoms.
Results: We identified a statistically significant positive correlation between the ALPS-index and the duration of iRBD dream enactment (Spearman's rho = 0.357, $p = 0.010$). Regression analysis revealed statistical significance ($p = 0.005$), with the summary model showing R = 0.387, R^2 = 0.150.
Conclusion: Preserved function of the glymphatic system was associated with longer duration of iRBD. These findings suggest that the glymphatic system may serve as a protective factor preserving the prodromal stage of the disease and can potentially be used as a biomarker for delayed conversion into fully pronounced neurodegenerative disease.
Disclosure: Nothing to disclose.

EPR-105 | Sleep-disordered breathing is associated with adverse short- and long-term outcomes after acute ischemic stroke

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Background and aims: Sleep-disordered breathing (SDB) is common after stroke and is associated with poor outcomes, but data from large cohort studies are sparse.
Methods: This retrospective cohort study, from the Bern Sleep – Stroke Registry, was conducted at the Inselspital Bern. Acute ischemic stroke/TIA patients underwent respiratory polygraphy within 72h of admission. SDB severity was categorized based on apnea-hypopnea index (AHI), with thresholds defining mild (AHI≥5h), moderate (AHI≥15h), and severe (AHI≥30/h) cases. Evaluated outcomes including poor functional outcome (mRS≥3 at 3-month), all-cause mortality, and MACE over an 84-month follow-up period. Cox and logistic regression models, adjusted for age, sex, BMI, hypertension, diabetes, dyslipidemia, atrial fibrillation, and initial stroke severity (NIHSS), were employed.
Results: We included 1083 patients, (678 (63%) males, mean age 66.0 ± 14.5y, 982 (91%) ischemic stroke), 29), of whom 819 (76%) had SDB (AHI≥5/h), sub-categorized as mild 323 (29.8%), moderate 248 (23%), and severe 248 (23%). Central sleep apnea was observed in 6.4%. The initial mean NIHSS was 4.4 ± 5.5. All-cause mortality was associated with severe SDB (adjusted HR, 2.74 [95%CI, 1.19-6.34]). MACE were significantly associated with mild (adjusted HR, 1.47 [95%CI, 1.06-2.04]), moderate (adjusted HR, 2.01 [95%CI, 1.43-2.82]) and severe SDB (adjusted HR, 1.53 [95%CI, 1.07-2.18]). Poor functional outcome was associated with severe SDB (adjusted OR, 2.50 [95%, 1.45-4.38]).
Conclusion: Results reveal a significant association between SDB and adverse short- and long-term stroke outcomes, with the impact varying by SDB severity. Further investigation is needed to refine stroke risk profiles and optimize post-stroke management strategies.
Disclosure: None

EPR-106 | The Bern Sleep–Wake Registry (BSWR): From raw polysomnographic data to clinical outcomes

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Background and aims: The combined availability of clinical outcomes and polysomnography (PSG) raw data offers novel data driven approaches toward patient characterization and the identification of new digital biomarkers. With the Bern Sleep – Wake Registry (BSWR), we aimed to provide a continuously growing respective data collection.

Methods: Data including clinical records, electrophysiological measures and questionnaire scores from patients assessed at the sleep–wake center of the University Hospital Bern since 2000 are continuously transferred into a REDCap database. Median (IQR) values are reported.

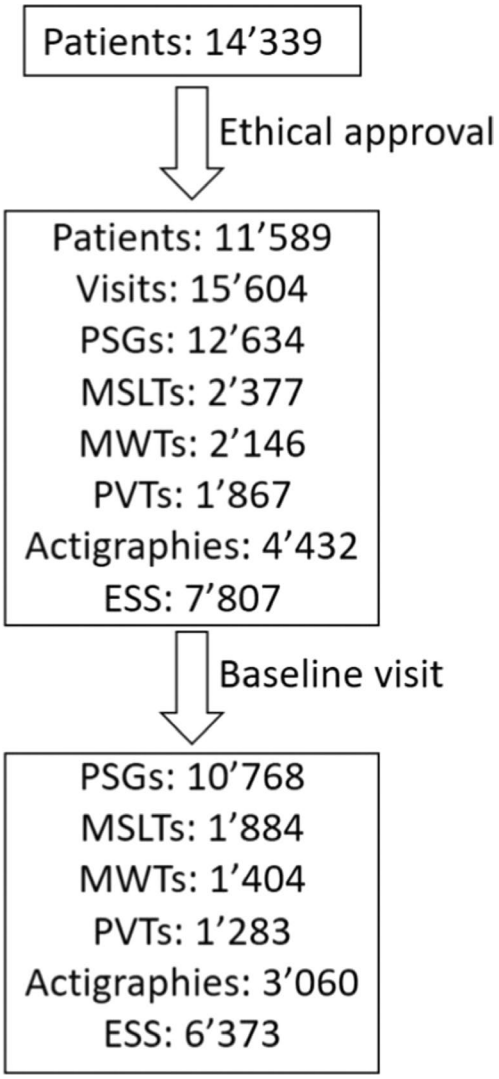

FIGURE 1 Flowchart on availability of multi-modal data.

Results: A total of 11,589 patients from the BSWR were included for scientific evaluation according to general consent based ethical approval (KEK- 2022-00415). At first consultation, age was 50 (36, 61) years, with male over-representation (65%), BMI was 26 (23, 30), Epworth sleepiness scale was 10 (6, 14), PSG-derived sleep efficiency was 88% (77, 94), AHI was 12 (4, 28). Moderate to severe sleep apnea and periodic limb movements (AHI / PLMI > 15), were prevalent (44% and 23%, respectively). The most common diagnoses included sleep disordered breathing (62%), central disorders of hypersomnolence (12%) and insomnia (7%). We found marked differences between disorders, gender and age across multiple parameters in the multi-modal data set, often with interdependent effects (e.g., an age-dependent enhancement of the Epworth sleepiness scale in women as compared to men). From 2,162 patients, follow-up visits are available.

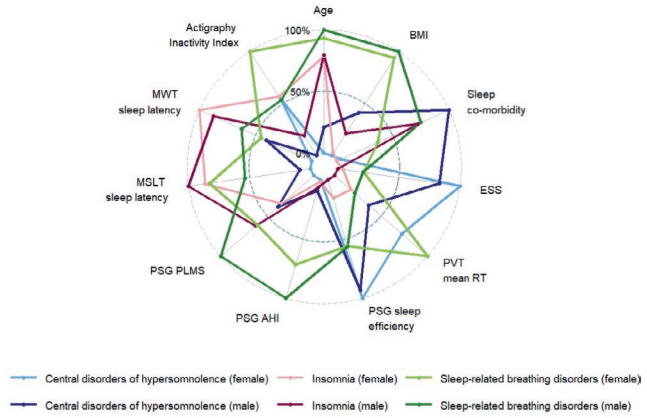

FIGURE 2 Spider-plot of multi-modal data for most prevalent primary sleep disorders (baseline visit).

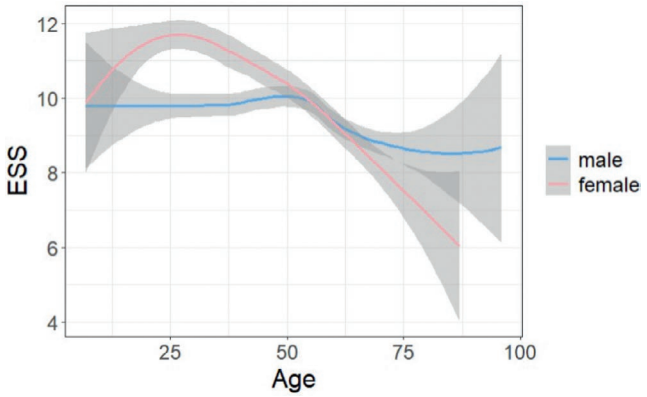

FIGURE 3 Age-dependent daytime sleepiness peak in women (baseline visit).

Conclusion: The BSWR is to date the largest patient registry covering the full sleep disorder spectrum, providing an invaluable source for validating digital biomarkers and diagnostic criteria.

Disclosure: The authors declare no conflicts of interest. This work was supported by the Inselspital MB-Neuro Grant "A digital reference network platform for clinical and experimental neuroscience—deep phenotyping and data integration".

EPR-107 | Effect of orexin agonist on wakefulness in NT1 during MWT and baseline comparison of microsleeps between NT1 and NT2

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Background and aims: The Maintenance of Wakefulness Test (MWT) assesses excessive daytime sleepiness (EDS) in clinical trials, primarily using mean sleep latency (SL) as the endpoint. However, SL does not capture quality of wakefulness (QoW) before sleep. Microsleeps—brief sleep episodes (3-15 seconds) occurring before sleep onset—may serve as a sensitive biomarker for EDS. This study compares baseline microsleep features between NT1 and NT2 participants in Phase 2 randomized trials NCT05687903 and NCT05687916. Additionally, we examined microsleep changes in NT1 patients receiving orexin receptor 2-selective agonist TAK-861 in NCT05687903.

Methods: Baseline MWT, ESS, and microsleep features were compared between 112 NT1 and 71 NT2 participants. In NCT05687903, NT1 participants received TAK-861 (placebo: $n=22$; 0.5mg/0.5mg: $n=23$; 2mg/2mg: $n=21$; 2mg/5mg: $n=23$; 7mg: $n=23$). Four 40-minute MWT sessions were conducted at baseline and after 28 and 56 days of treatment. Microsleeps were manually scored from MWT data. Changes in microsleep rates and time-to-first microsleep were assessed using mixed-effect models.

Results: At baseline, NT1 participants had significantly ($p<0.05$) shorter mean SL (4.72 ± 6.46 vs. 9.75 ± 8.95 minutes), higher ESS scores (18.51 ± 2.99 vs. 17.14 ± 3.59), and higher microsleep rate (8.01 ± 7.26 vs. 2.82 ± 4.09) than NT2 participants. In NT1 participants, TAK-861 reduced microsleep rates from >6 (baseline) to <2 (day 56) minutes per 10 minutes and delayed time-to-first microsleep for all treatment arms. Placebo-treated NT1 participants showed minimal changes.

Conclusion: At baseline, QoW, measured by microsleep features, differed between NT1 and NT2 participants. TAK-861 significantly reduced microsleep rates and delayed microsleep onset in participants with NT1. Future analyses will explore microsleep dynamics in NT2 participants.

Disclosure: All authors are employees of Takeda Development Center Americas, Inc. Takeda Development Center Americas, Inc., provided funding to Excel Medical Affairs for support in writing this abstract.

Sunday, June 22, 2025

Ageing and Dementia 2

EPR-108 | A cost-efficient tool to screen patients for anti-amyloid immunotherapies in memory clinics: The FRAPI score

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Background and aims: Determining amyloid status is crucial for identifying patients eligible for anti-amyloid therapies. This study aimed to develop a cost-effective predictive tool that integrates neuropsychological tests and brain atrophy scales to assess amyloid status in a cohort potentially eligible for anti-amyloid treatment.

Methods: We retrospectively analyzed 101 consecutive patients from the Dementia Unit at the University Hospital of Parma. Participants met the FDA eligibility criteria for Lecanemab and underwent amyloid-PET assessment for suspected AD, complete cognitive tests, and MRI/CT scans. Binomial logistic regression

evaluated the predictive accuracy of cognitive tests and visual atrophy scales individually and in combination.

Results: The Free and Cue Selective Reminding Test (FCSRT) Immediate Free Recall (IFR) subtest demonstrated the highest predictive accuracy (AUC = 0.68; 95% CI = 0.56–0.80), followed by the Recall of Rey's figure (AUC = 0.66; 95% CI = 0.54–0.78). Among visual rating scales, the antero-posterior index (API) was the most accurate (AUC = 0.68; 95% CI = 0.59–0.80). Combining these measures into the FRAPI score (FCSRT, IFR ≤17 = 2 points; Recall of Rey's Figure: ≤13 = 1 point; API: ≥1 = 2 points) yielded the highest predictive accuracy (AUC = 0.77; 95% CI = 0.67–0.87), with notable performance in patients with > 8 years of education (AUC = 0.96; 95% CI = 0.91–1).

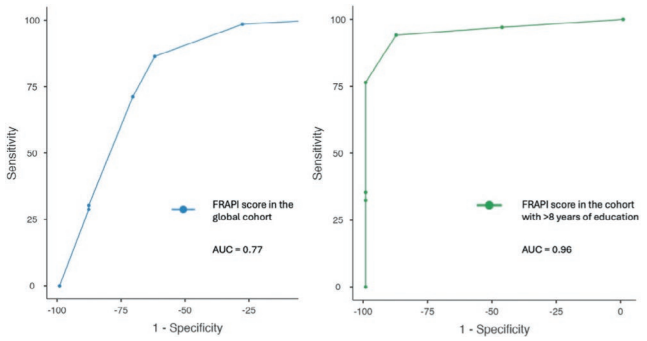

FIGURE 1 ROC curves of the FRAPI (F: FCSRT; R: Recall of Rey's figure; API: Antero-posterior index) score in the global cohort and among patients with education > 8 years.

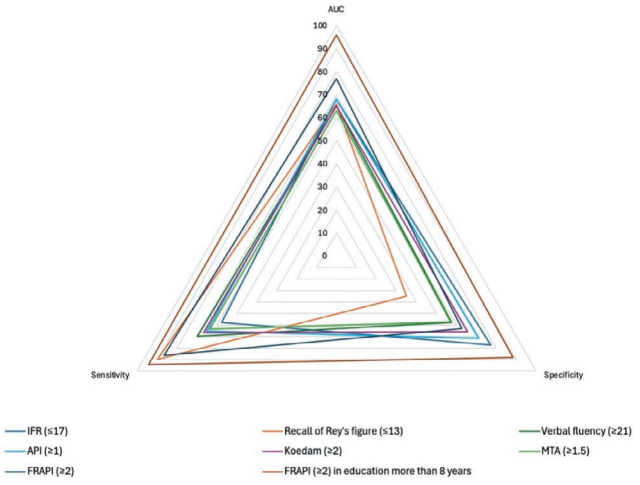

FIGURE 2 Predictive performance of the main neuropsychological, visual rating scores, and the novel FRAPI (F: FCSRT; R: Recall of Rey's figure; API: Antero-posterior index) score. The cut-offs displayed are those with the highest Youden index.

TABLE 1 Predictive performance of the FRAPI (F: FCSRT; R: Recall of Rey's figure; API: Antero-posterior index) score in the global cohort and in patients with education > 8 years.

Global cohort						Education > 8 years					
Cutpoint	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC (95% CI)	Cutpoint	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC
≥1	98.5%	28.6%	72.2%	90.9%	0.77 (0.67-0.87)	≥1	97.0%	47.0%	78.5%	88.9%	0.96 (0.91-1)
≥2	86.3%	62.8%	81.4%	70.9%	-	≥2	94.1%	88.2%	94.1%	88.2%	-
≥3	71.2%	71.4%	82.4%	56.8%	-	≥3	76.4%	100%	100%	68%	-
≥4	30.3%	88.5%	83.3%	40.2%	-	≥4	35.3%	100%	100%	43.6%	-
≥5	28.8%	88.5%	82.6%	39.7%	-	≥5	32.3%	100%	100%	42.5%	-

Conclusion: The FRAPI score is a practical, cost-effective tool for screening patients eligible for anti-amyloid treatment, especially those with higher education, to obtain biological confirmation of AD in primary and secondary memory clinics.

Disclosure: Nothing to disclose.

EPR-109 | Water-soluble QTY variant of the gamma-secretase complex provides insights into amyloid precursor protein recognition

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Background and aims: The Amyloid Precursor Protein (APP), when processed by gamma-secretase complex, is cleaved into various peptides, including the Amyloid Beta 42 fragments. These fragments are prone to oligomerization, and the resulting oligomers subsequently self-assemble into amyloid plaques. This process is believed to initiate a cascade of events involved in Alzheimer's disease. Thus, targeting APP recognition could be a viable therapeutic and diagnostic approach.

Methods: We engineered a water-soluble presenilin-1 subunit of the gamma-secretase complex utilizing the QTY-code. QTY-code is a method to generate water-soluble variants of membrane proteins without the use of detergents. The APP fragment (PDB ID: 6IYC) complexes with the QTY-variant were generated using AlphaFold3. All-atom molecular dynamics simulations and binding free energy calculations were conducted to elucidate the interaction patterns with APP.

Results: Our findings reveal that the water-soluble QTY-variant of presenilin-1 subunit demonstrates structural resemblance to presenilin-1 (Figure 1). The QTY-variant demonstrated water-solubility (Figure 2), with its hydrophilic surface. Subsequently, simulations in aqueous solvent indicate that the system stabilizes after 30ns, with the MMGBSA binding free energy around -200 kcal/mol (Figure 3). The conserved binding interfaces suggest that APP is effectively captured by the water-soluble variant, with key residues contributing to the interaction being uncovered.

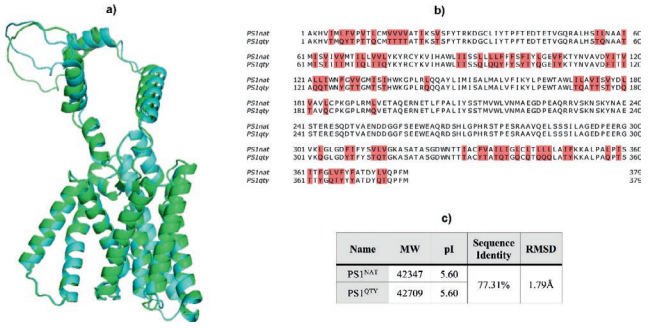

FIGURE 1 Bioinformatics analysis of the QTY variant of presenilin-1. a) Superposed structures of the QTY-variant (cyan) and presenilin-1 (green). Sequence alignment (b) with variations highlighted, and their sequence characteristics (c).

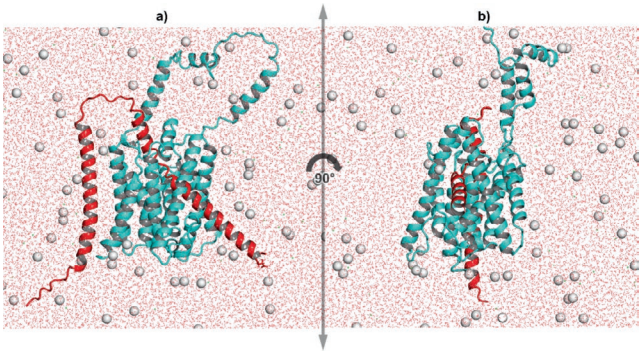

FIGURE 2 The water-soluble QTY-variant of presenilin-1 (cyan) complexed with APP fragment (red). The equilibrated complex is in solution with Monte-Carlo placed K+ CL− ions (neutralizing, concentration = 0.15 M).

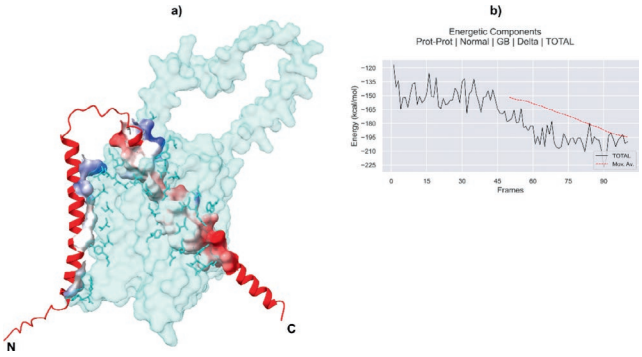

FIGURE 3 Binding interface of the APP fragment and QTY-variant complex. a) The QTY-variant (cyan) and the APP (red) with the contributing residues mapped. b) MMGBSA binding energy calculations of the complex through 50ns equilibrated simulation.

Conclusion: These insights into APP binding reveal another aspect of the underlying interaction mechanism. Our findings establish a framework for studying the early molecular development of Alzheimer's disease. The water-soluble QTY-variant can be utilized as a diagnostic tool and for efficiently analyzing drug targets in an aqueous environment.
Disclosure: Nothing to disclose.

EPR-110 | Impact of the COVID-19 pandemic on dementia diagnoses in Sweden: Trends from 2015 to 2023

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Background and aims: The COVID-19 pandemic has influenced the diagnosis and management of dementia. This study explores trends in dementia diagnoses across Sweden from 2015 to 2023, examining regional, gender, and diagnostic differences. The analysis focuses on the pandemic's impact (2020–2022) and the post-pandemic period (2023).
Methods: This is a retrospective cohort study. Age standardized diagnosis rates were collected from specialized in- and outpatient care obtained from the National Patient Registry. Diagnoses were vascular dementia, Alzheimer's disease, unspecified dementia, and other dementias. Diagnosis rates were averaged across pre-pandemic (2015–2019), pandemic (2020–2022), and post-pandemic (2023) periods. Logistic regression modeling was used to determine expected outcome without pandemic influence which was compared to actual outcome. Student t-test was used to determine significant differences.
Results: Vascular dementia showed a 31.9% reduction ($p < 0.01$), unspecified dementia declined by 25.5% ($p < 0.01$), and Alzheimer's disease fell by 11.1% ($p < 0.01$). Post-pandemic (2023) trends varied: Alzheimer's disease exhibited partial recovery, increasing by 6.0% from pandemic levels ($p < 0.05$), vascular and unspecified dementia rates declined by 2.8% ($p < 0.05$) and 3.4% ($p < 0.05$), respectively. Across all diagnoses, 2023 rates remained below pre-pandemic levels by -33.8%.
Conclusion: The COVID-19 pandemic significantly disrupted dementia diagnoses in Sweden. Vascular dementia appears more vulnerable than other diagnoses groups. Post-pandemic recovery has been uneven, with some diagnoses, such as Alzheimer's disease, showing signs of improvement, while others continue to decline. Possible explanations could include higher diagnostic burden in primary care and less resources for diagnosis of complex dementia disorders.
Disclosure: No disclosures.

EPR-111 | Apraxic deficits predict general cognitive impairment in patients with biomarker-verified Alzheimer's pathology

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Background and aims: Apraxia represents a core feature of Alzheimer's disease (AD), a neurodegenerative disorder characterized by the accumulation of β-amyloid plaques and tau deposition. However, systematic descriptions of apraxic deficits in AD patients remain scarce. Here, we comprehensively investigate apraxia profiles and their link with cognitive impairment in patients with biomarker-verified Alzheimer's pathology.
Methods: We characterized the frequency and patterns of apraxic deficits in patients with biomarker-verified Alzheimer's pathology using a battery of standardized apraxia tests. Demographic variables and apraxia scores were related to patients' general cognitive impairment using hierarchical regression analysis.
Results: Apraxic deficits were found in 68% of patients with biomarker-verified Alzheimer's pathology ($n = 66$). AD patients were more impaired in imitating finger gestures (than hand

gestures: 89.0% vs. 78.9%, $p<0.001$) and imitating complex hand movements (than single hand movements: 97.4% vs. 77.9%, $p<0.001$), even when controlling for general cognitive impairment. Apraxia assessments explained about 60% of the variance in dementia severity, with performance in the KAS subtest of pantomiming object use (beta coefficient: 0.44, $p=0.001$) and the DATE subtest for limb apraxia (beta coefficient: 0.38, $p=0.002$) constituting significant predictors of general cognitive impairment.

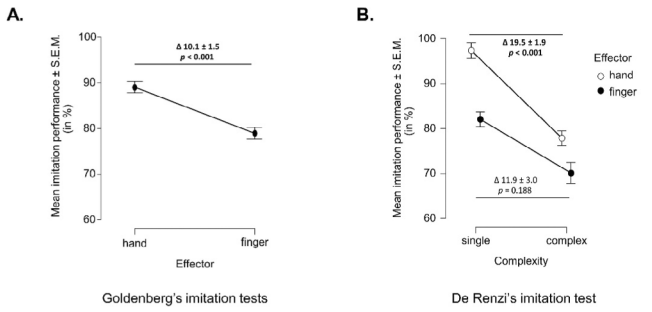

FIGURE 1 Differential patterns of apraxic imitation deficits in the patients with biomarker-verified Alzheimer's pathology

Conclusion: These findings emphasise the relevance of apraxia in patients with biomarker-verified Alzheimer's pathology, revealing that praxis deficits predict general cognitive impairment in AD. Further research is warranted into the role of apraxia as a potential early diagnostic criterion in AD.
Disclosure: Nothing to disclose.

EPR-112 | Photophobia discriminates between Alzheimer's disease and dementia with Lewy bodies patients

F. Millet Barros[1]; J. Durães[1]; M. Tábuas Pereira[1]; P. Faustino[1]; C. Bernardes[1]; R. Pancas[2]; M. Lima[3]; I. Baldeiras[4]; C. Cavadas[5]; I. Santana[1]
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Background and aims: Visual photosensitivity has recently been suggested as a common and possibly specific symptom in dementia with Lewy bodies (DLB), including in prodromal phases. It is, however, not an easily quantifiable symptom, as there are currently no validated scales for assessing photophobia in DLB. In this study, we aimed to assess the ability of the Visual Light Sensitivity Questionnaire-8 (VLSQ-8) to discriminate between DLB and Alzheimer's Disease (AD) patients.
Methods: We included 94 dementia patients - 52 with DLB and 42 with AD - diagnosed according to the most recent international criteria, who underwent CSF-AD biomarker analysis, as well as cognitive (MMSE), dysautonomia (SCOPA-AUT), cognitive fluctuations (DCFS-R), hallucinations (NEVHI), and photophobia (VLSQ-8) evaluations.
Results: Mean VLSQ8 was significantly higher in DLB patients (12.3 ± 5.9) than in AD (9.6 ± 3.1). VLSQ8 was correlated with dysautonomia (measured by SCOPA-AUT, $r=0.38$, $p<0.001$), the presence of simple hallucinations (measured by NEVHI, $r=0.24$, $p=0.020$) and fluctuations (measured by DCFS-R, $r=0.24$, $p=0.019$). In a binary logistic regression adjusted for age, age of onset, sex, education and MMSE, VLSQ8 was associated with the diagnosis of DLB (OR: 1.172, 95%CI = [1.048, 1.311], $p=0.005$).
Conclusion: In our cohort of dementia patients, a quantitative assessment for photophobia using the VLSQ8 was able to discriminate between AD and DLB patients. It correlated with dysautonomia, fluctuations and visual hallucinations, suggesting common underlying mechanisms.
Disclosure: None.

EPR-113 | Dysautonomia and fluctuations in dementia with Lewy bodies

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Background and aims: Cognitive fluctuations are a core clinical finding in Dementia with Lewy Bodies (DLB), yet their underlying causes remain poorly understood. Our aim was to evaluate whether dysautonomia is associated with cognitive fluctuations in DLB.
Methods: We included DLB patients with mild dementia from our memory clinic. Diagnosis was made according to the most widely accepted criteria and supported by extensive characterization, including DaTScan, Amyloid-PET and/or CSF biomarkers. Cognitive fluctuations were assessed with the Mayo Fluctuations Scale (MFS) and dysautonomia with the SCOPA-AUT questionnaire. Motor function was assessed with the Movement Disorder Society-Unified Parkinson's Disease Rating Scale, Part III (MDS-UPDRS III) and behavioral symptoms with the Neuropsychiatric Inventory (NPI). Patients with mild dementia (CDR=1) were selected to warrant a homogeneous cohort with the core symptoms. Univariate and multivariable analyses were conducted to assess the relationship between cognitive fluctuations (MFS) and other variables.
Results: Our cohort included 61 patients, 37 of which (60,7%) were male. The mean age was $76.3(\pm5.5)$ years and the mean of disease duration was $4.1(\pm2.4)$ years. Average MMSE was $21.8(\pm3.8)$, mean MFS was $2.2(\pm1.2)$, mean MDS-UPDRS III was $30.6(\pm23.7)$, mean NPI was $19.7(\pm13.7)$ and mean

SCOPA-AUT was 16.4(±9.0). On univariate analysis, MFS correlated with SCOPA-AUT (r = 0.27, $p = 0.038$) and NPI (r = 0.48, $p < 0.001$). On multivariable analysis (table 1), MFS was only associated with SCOPA-AUT (β = 0.039, 95%CI = [0.004, 0.074], $p = 0.029$).
Conclusion: Our study suggests an association between dysautonomia and cognitive fluctuations in DLB, highlighting potential novel therapeutic targets. Understanding this relationship may uncover new pharmacological and non-pharmacological treatments to better manage DLB.
Disclosure: Nothing to disclose.

EPR-114 | Natural language processing distinguishes Italian individuals with nonfluent/agrammatic from logopenic variants of PPA

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Background and aims: Differentiating between logopenic (lvPPA) and nonfluent/agrammatic (nfvPPA) variants of Primary Progressive Aphasia relies on expert evaluations of speech and language production. An effortful production of sentences (including morphosyntactic and phonological errors) can be present in both variants for different reasons. Connected speech analysis greatly supports the phenotypical classification of PPA, targeting abnormal language production.
Methods: 19 Italian patients with PPA (nfvPPA = 9; lvPPA = 10) underwent an audio-recorded picture description task from the SAND battery. The speech data were analyzed using computational methods with the CLAN software, allowing the extraction of linguistic features. Using a Mann-Whitney non-parametric test corrected for false discovery rate (FDR), we analyzed 45 linguistic features of four linguistic levels. A machine-learning (ML) model was trained to classify nfvPPA versus lvPPA.
Results: We identified ten features belonging to 4 linguistic levels differentiating nfvPPA from lvPPA. These included, at the phonetic and phonological level: silent pause ratio; at the lexico-semantic level: noun, adverb, article, and determiner ratios; at the morphosyntactic level: total number of utterances and utterance error ratio; and at the pragmatic/discourse level: total words, total morphemes, and idea density. The ML model reached a sensitivity and specificity > 90%.
Conclusion: We implemented natural language processing to perform a machine-learning classification based on connected speech samples of Italian-speaking subjects. This approach has been applied for the first time to Italian PPA and demonstrated that key linguistic markers can be identified and compared across the two variants.
Disclosure: Nothing to disclose.

EPR-115 | AI-based staging, causal hypothesis and progression of subjects at risk of Alzheimer's disease: A multicenter study

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Background and aims: In 2024, eleven European scientific societies/organizations and one patient advocacy association have defined a biomarker-based diagnostic workflow evaluating neurocognitive disorders. This study evaluated the clinical performance of an AI-tool using neuropsychological assessment and neuroimaging for staging, diagnosis, and progression prediction in individuals at risk of Alzheimer's disease (AD).
Methods: This multicentric study enrolled 796 subjects: 705 from ADNI and 91 from three Italian centers. Participants were staged as healthy (HS), subjective cognitive impairment (SCI), mild cognitive impairment (MCI), or AD-dementia at baseline and 24-month follow-up. Patients were clinically profiled based on cognitive and neuroimaging findings, with first-line biomarkers measured. The AI-tool TRACE4AD™ (DeepTrace Technologies S.R.L.) analyzed neuroimaging and neuropsychological data to perform staging, clinical profiling, and predicting AD-dementia conversion. AI-human staging agreement was assessed using Cohen's kappa, and AI performance was evaluated by sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), area under curve (AUC), and accuracy.
Results: For the staging classification the inter-rater AI-humans agreement was substantial for both HS/SCI versus rest (Cohen's κ = 0.81) and MCI (κ = 0.70) classification, almost perfect for MSD versus rest (κ = 0.90) classification. For the causal hypothesis classification, the AI performance versus biomarker-based diagnosis was: PPV 91%, NPV 100%, and accuracy 91%. For the binary classification of progression to AD-dementia at 24-month, the AI performance was: sensitivity 89%, specificity 82%, accuracy 85%, and AUC 83%.
Conclusion: The AI-tool demonstrated its usefulness in supporting the clinical treatment of AD patients by assisting with staging, clinical profiling, and progression.

Disclosure: S.A., R.N., M.Z., G.S., D.C., M.A., P.V., E.G.B., V.F., L.B., G.M., P.B., F.S., F.B.P., declares no conflict of interest. I.C. and C.S. declare to own DeepTrace Technologies S.R.L shares. C.S. declares to be CEO of DeepTrace Technologies SRL. the Alzheimer's Disease Neuroimaging Initiative, Data used in preparation of this article were obtained from the Alzheimer's Disease Neuroimaging Initiative (ADNI) database (adni.loni.usc.edu). As such, the investigators within the ADNI contributed to the design and implementation of ADNI and/or provided data but did not participate in analysis or writing of this report. A complete listing of ADNI investigators can be found at: http://adni.loni.usc.edu/wpcontent/uploads/how_to_apply/ADNI_Acknowledgement_List.pdf

EPR-116 | CSF LDH is strongly associated with CSF Alzheimer's disease biomarkers: A real-world cohort data

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Background and aims: Disturbances in glucose transport mechanisms, oxidative stress, and impaired mitochondrial function are pathophysiological contributors to Alzheimer's disease (AD). We aimed to investigate the association of CSF LDH with established CSF AD biomarkers.
Methods: A retrospective single-center observational study that included 265 patients with the diagnosis of AD at the stage of mild cognitive impairment and dementia, with confirmatory CSF biomarkers. We studied the relationship between CSF parameters (glucose, lactate dehydrogenase - LDH, protein, chloride) and blood analytical parameters (glucose, proteins, albumin, C-reactive protein) with AD CSF biomarkers levels.
Results: 265 patients were included, 56,6% were females. Mean age of onset was 63.77 ± 8.06 years. The mean MMSE score was 16.4 ± 7.54 points. Multiple regression, with AD CSF biomarkers levels, adjusted for age, MMSE, sex and education level showed that CSF LDH was positively correlated with CSF total tau ($\beta = 0.66$, p-value < 000.1) and CSF p-tau ($\beta = 0.67$, p-value < 0.001) and negatively correlated with Aβ40/42 ratio ($\beta = -0.58$, p-value < 0.001), with no correlation with Aβ42 level ($\beta = 0.20$, p-value $= 0.135$). Multiple regression between CSF AD biomarkers and the rest of the analytical parameters didn't show other significant associations.
Conclusion: LDH levels are increased in patients with acute brain injury and might reflect neuronal destruction. The positive correlation with the AD biomarkers for neurodegeneration might reflect impaired glucose metabolism, a key contributor to AD, but it can also be related to the loss of integrity of the neuronal membrane and more severe neurodegeneration. More studies are necessary to define the role and prognostic value of this biomarker in AD.
Disclosure: Nothing to disclose.

Infectious diseases

EPR-117 | Meningoencephalitis caused by serratia marcescens in a 74-year-old patient with no significant medical history

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Background and aims: We present a case of meningoencephalitis caused by Serratia marcescens and review the literature.
Methods: Case presentation
Results: A 74-year-old female patient with no significant medical history was hospitalized in the Neurology Department due to fever up to 40°C, confusion, and expressive aphasia. She also reported a few episodes of diarrhea within the previous 24 hours. The neurological examination revealed significant neck stiffness, a positive Kernig sign, and mild right hemiparesis. Based on these findings, a central nervous system (CNS) infection was suspected, and a lumbar puncture was performed. The analysis of the CSF revealed 5000 cells, with 96% neutrophills, elevated protein levels, and low glucose levels. Gram-staining microscopy revealed a Gram-negative bacillus. Cultures of the CSF grew Serratia marcescens. The patient was treated with 21 days of intravenous ceftazidime with excellent clinical and laboratory response.
Conclusion: Serratia marcescens is an extremely rare pathogen that causes acute CNS infection in adults. The majority of cases in the literature refer to patients who have recently undergone neurosurgical procedures. A few cases of this infection in intravenous drug users and neonates have also been reported. The is the first reported case of spontaneous CNS infection caused by Serratia marcescens in a patient with no significant medical history. As an enteropathogen, this case is considered an opportunistic infection with hematogenous spread, likely triggered by the intestinal inflammation that preceded the symptoms of the CNS infection.
Disclosure: Nothing to disclose.

EPR-118 | Fatal hemorrhagic leukoencephalitis following VZV infection in an immunocompetent host: A case report

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Background and aims: Varicella Zoster Virus (VZV) is a neurotropic virus primarily linked to neurological complications in immunocompromised individuals but rarely in immunocompetent hosts. This case report describes a fatal instance of hemorrhagic leukoencephalitis following VZV infection in an immunocompetent patient, emphasizing atypical neuroradiological features and negative cerebrospinal fluid (CSF) polymerase chain reaction (PCR) results.
Methods: Case description, literature review.
Results: A 76-year-old immunocompetent male with coronary artery disease on dual antiplatelet therapy (DAPT) and Parkinson's disease presented with transient loss of

consciousness. Examination revealed mild extrapyramidal symptoms and right periocular crusting, consistent with recent Herpes Zoster treated two weeks earlier. Brain CT showed bilateral white matter hypodensities. Within hours, he deteriorated to coma. MRI revealed extensive T2/FLAIR hyperintensities in deep white matter, including the capsular, thalamic, and mesencephalic regions, rapidly extending with hemorrhagic transformation. Acyclovir, Methylprednisolone, and intravenous immunoglobulin were initiated. Delayed lumbar puncture showed elevated protein and pleocytosis, but VZV PCR was negative. Serum VZV PCR and serology were positive. Despite treatment, the patient succumbed.

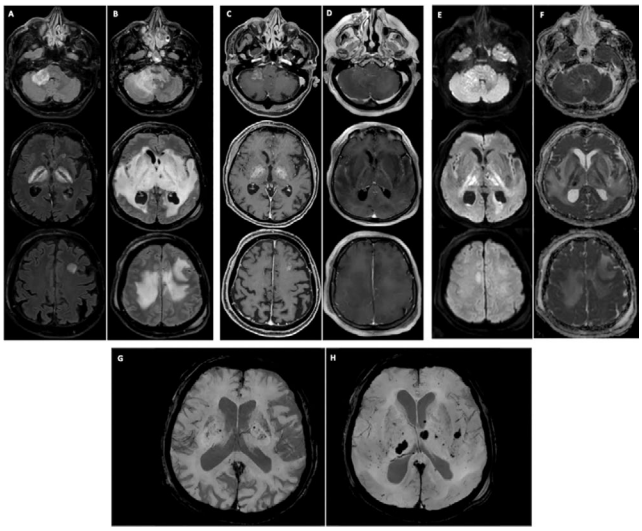

FIGURE 1 Brain MRI of the patients at ER arrival and at follow-up five days later.

Conclusion: This case highlights an atypical leukoencephalitic VZV presentation in an immunocompetent host, suggesting an immune-mediated mechanism alongside direct viral effects. The symmetric white matter involvement with hemorrhagic transformation is reminiscent of acute hemorrhagic encephalomyelitis. Negative CSF PCR complicates diagnosis, underscoring the need for early recognition and combined immunomodulatory and antiviral therapy.

Disclosure: The authors have no disclosures related to the present work

EPR-119 | Clinical features and outcomes of neurocysticercosis patients in Thailand

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Background and aims: Neurocysticercosis (NCC) is a life-threatening disease with significant morbidity. This study evaluates clinical characteristics, risk factors, and outcomes among NCC patients in Northern Thailand.
Methods: A retrospective analysis was conducted on 106 NCC patients categorized into seizure ($n=74$) and non-seizure groups ($n=32$). Demographics, clinical features, imaging findings, and treatment outcomes were compared using statistical analyses.
Results: The mean age was 48.3 ± 16.7 years, with seizure patients being younger than non-seizure patients (45.4 ± 16.4 vs. 55.0 ± 15.8 years, $p=0.007$). Males accounted for 64.2% of the cohort. Non-seizure patients showed significantly higher rates of sensory deficits (28.1% vs. 10.8%, $p=0.04$), intraventricular lesions (18.8% vs. 4.1%, $p=0.02$), and hydrocephalus (34.4% vs. 5.4%, $p<0.001$). Surgical intervention was more frequent in the non-seizure group (21.9% vs. 6.8%, $p=0.04$). Hospital stays tended to be longer in the non-seizure group (median: 12 vs. 7 days, $p=0.07$). Overall mortality was 0.9%, with no significant difference between groups.
Conclusion: Non-seizure NCC patients exhibit distinct clinical characteristics, including higher rates of sensory deficits, intraventricular lesions, and hydrocephalus. These findings suggest a different disease phenotype, highlighting the need for tailored diagnostic and management strategies.
Disclosure: Nothing to disclose.

EPR-120 | Substantia Nigra encephalitis and post-viral parkinsonism: case report and literature review

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Background and aims: Viral infections such as influenza, Coxsackie, Epstein-Barr viruses, and Japanese encephalitis virus have been incriminated as rare causes of secondary parkinsonism due to their tropism for mesencephalon and diencephalon, leading to severe nigral cell loss and, consequently, to

a broad spectrum of symptoms, from Parkinsonism to signs of widespread neuronal damage. We present a literature review of Substantia Nigra (SN) encephalitis starting from a case report.
Methods: We perform a literature review regarding potential causes of SN encephalitis. We present one such case admitted in our clinic.
Results: A 40-year-old female was admitted to our clinic with altered consciousness, GCS = 8 points(E2V2M4), flaccid tetraplegia and tonic-clonic seizures. Lab results and vitals indicated septic shock, with pathogen screening returning positive blood culture for E.Coli. Extensive serologic and CSF screening detected the presence of Anti Cytomegalovirus IgG and IgM. Head MRI revealed bilateral, symmetrical T2/FLAIR hyperintensities involving the substantia nigra, suggesting a possible CMV SN encephalitis. The patient progressed to atypical post-viral parkinsonism with a mild improvement under Levodopa/Carbidopa, before infectious complications led to her death. Cases of SN encephalitis have been documented since the encephalitis lethargica outbreak after the 1918 influenza epidemic, but they have been also linked to numerous other viral infections that had a tropism for SN due to numerous hypothesized mechanisms that were based on neurovirulence.

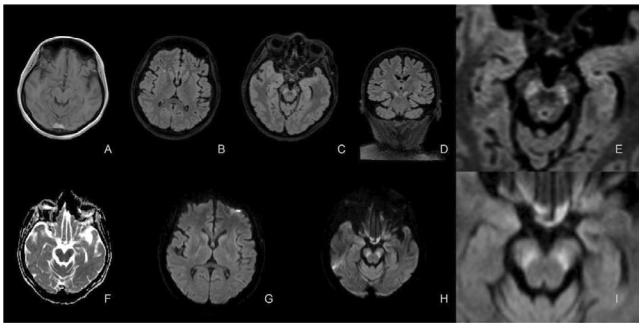

FIGURE 1 Cerebral MRI showing bilateral extensive substantia nigra lesions, with hyperintense signal in T2/FLAIR and restriction of diffusion on DWI.

Conclusion: SN encephalitis is a rare complication of viral infections. This case highlights diagnostic challenges, the impact of viral infections upon SN inflammation and the severe outcome many of these patients face
Disclosure: Nothing to disclose.

EPR-121 | Clinical characteristics and treatment outcomes in herpes simplex type I encephalitis

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Background and aims: Herpes simplex virus type 1 (HSV-1) is leading cause of sporadic infectious encephalitis. The mortality rate of HSV-1 encephalitis (HSV1E) has been reported below 20% but survivors still have a significant morbidity rate of 60~70%. We reviewed clinical characteristics and treatment outcomes of HSV1E in single center in South Korea.
Methods: We analyzed 12 patients of PCR positive HSV1E who were admitted to Department of Neurology at Hallym Medical Center (2017~2022).
Results: The mean age was 51.7 years. Presenting symptoms were headache (58%), fever (58%), seizure (50%), confusion (33%), and aphasia (33%). CSF study showed lymphocytic pleocytosis (185.7 ± 215.4 cells/μL) and mildly elevated protein (60.1 ± 25.9 mg/dL) but CSF glucose was not decreased. Brain MRI demonstrated typical unilateral or asymmetric edematous lesions in medial and anterior temporal areas (11 patients), also in insular cortex (7 patients), inferior frontal lobe (2 patients), and thalamus (3 patients). Brain MRI was negative in 1 patient. All patients were treated with intravenous acyclovir (10 mg/kg every 8 hours) at least for 14 days. Corticosteroid was given in 8 patients (66.7%). There was no significant difference in outcomes of patients with or without corticosteroid. Two patients developed antibody-negative autoimmune encephalitis and the time of onset after HSV1E was 14 days and 180 days each. After 6 months, no one died but 5 patients (41.6%) had a moderate to severe disability.
Conclusion: The outcome of this case series is better than previous reports. Early suspicion and early empiric acyclovir therapy could reduce mortality and morbidity.
Disclosure: Nothing to disclose.

EPR-122 | Therapeutic approaches for ramsay hunt syndrome affecting multiple nerves: A systematic literature review

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Background and aims: Ramsay Hunt syndrome (RHS) involves reactivation of the varicella-zoster virus in the geniculate ganglion, affecting the facial nerve (CN7) [1]. This leads to ipsilateral facial paralysis and may extend to nearby cranial nerves, causing symptoms like hearing loss, tinnitus, or vertigo [2]. Even with the unusualness of this, there´s no description of treatments and outcomes in these patients. This study aimed to highlight the interplay between cranial nerve dysfunction and posterior recovery, based on treatment regime.
Methods: We conducted a systematic literature review following PRISMA protocols, emphasizing abnormal presentations. PubMed database was searched until 2014 using keywords: "Ramsay-Hunt Syndrome", and "Nerve". 45 studies found. We evaluated age, cranial nerve involvement, and outcome.

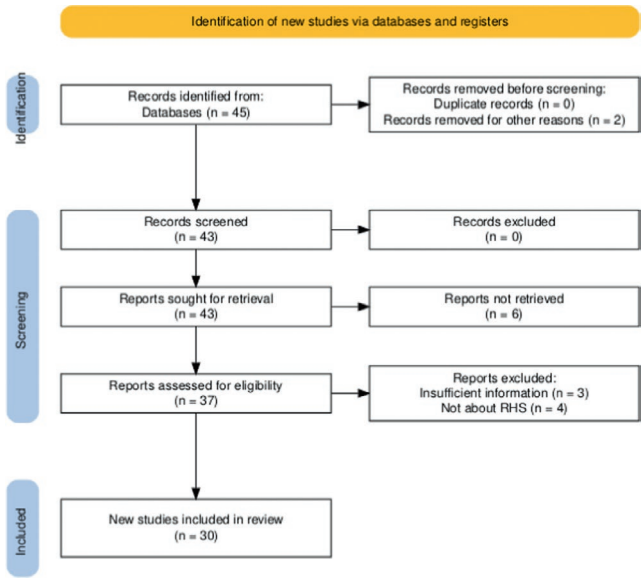

FIGURE 1 PRISMA flowchart presenting the process of inclusion of studies for systematic review

Results: We included 30 studies, reporting 33 patients with a mean age of 56 years. Of which, 10 (30%) were female, and 23 (60%) male. 91% of patients presented CN7 involvement, 48.4% with vestibulocochlear, 36% trigeminal, and 27% vagus. 60% of patients treated with valacyclovir didn´t recover their functionality in nerves besides the CN7, compared to 47.6% of those treated with acyclovir. 43.7% of patients with vestibulocochlear involvement presented better prognosis using acyclovir, while valacyclovir obtained fewer results. Both treatments presented better recovery when administered with corticosteroids.

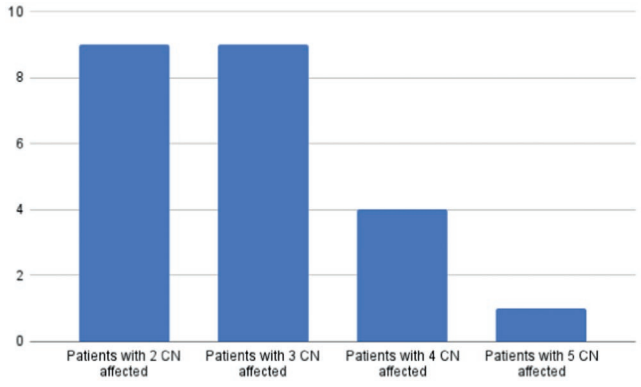

FIGURE 2 Patients based on the number of structures affected

Conclusion: Although rare, cranial nerve involvement is a challenge in rehabilitation of RHS patients. This study provides a list of cases where the use of acyclovir showed a better prognosis when other cranial nerves are affected, contrasting with literature around CN7 involved alone, which might be inconclusive or opposite [3].
Disclosure: Nothing to disclose.

EPR-123 | Focal deficits mimicking stroke in post-malaria neurological syndrome

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Background and aims: Post-malaria neurological syndrome (PMNS) is a rare but clinically significant complication emerging after resolution of acute malaria, particularly with Plasmodium falciparum, appearing days to weeks post-treatment. Although only a few dozen cases are reported, actual incidence may be underrecognized.
Methods: Clinical case.
Results: A 60-year-old male, who had emigrated to Angola without malaria prophylaxis, was first admitted with persistent fever and altered consciousness requiring mechanical ventilation. He was diagnosed with severe Plasmodium falciparum malaria, presenting neurological, hematological, renal, and cardiovascular dysfunction. Following antimalarial therapy, he fully recovered. Several weeks later, he presented with sudden right hemispheric dysfunction, including left facial droop and hemiparesis. Brain imaging showed no large-vessel occlusion, but CT-perfusion revealed right hemispheric hypoperfusion. Tenecteplase was given. Subsequently, he developed fever and altered consciousness. Tests for malarial parasites and antigens were negative. Lumbar puncture revealed 47 cells (83% lymphocytes) with normal protein and negative meningitis/encephalitis panel. Electroencephalography showed focal slow theta activity in the right temporal region, without epileptiform discharges. Magnetic resonance imaging demonstrated multifocal lobar microhemorrhages. PMNS was presumed, and high-dose steroids led to full recovery in 15 days.
Conclusion: Despite underdiagnosis in endemic regions, PMNS may appear in non-endemic settings due to global travel. Recognizing this condition is crucial for timely diagnosis and management, as it responds to corticosteroids and may be self-limiting. Investigation is warranted to clarify pathophysiological mechanisms, particularly in endemic areas, where exposure to Plasmodium might modulate immune responses and influence clinical outcomes.
Disclosure: Nothing to disclose.

EPR-124 | Balint's syndrome as a manifestation of post-varicella acute disseminated encephalomyelitis in adults

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Background and aims: Balint's syndrome (BS) is a rare neurological disorder characterized by a triad of simultanagnosia, optic ataxia, and oculomotor apraxia. It is typically associated with bilateral parieto-occipital lesions and, in rare cases, can be an initial manifestation of acute disseminated encephalomyelitis (ADEM).

Methods: A 55-year-old man with a history of varicella 20 days before admission, presented with bilateral visual acuity decline, and speech impairment. On admission, the patient was disoriented in time and space, neurological examination revealed severe optic ataxia, simultaneous agnosia, oculomotor apraxia, and cerebellar syndrome. Ophthalmologic examination revealed a profound loss of visual acuity. Brain magnetic resonance imaging (MRI) revealed multiple patchy and nodular lesions in the bilateral parieto-occipital regions, with ring enhancement after gadolinium injection. Laboratory results were unremarkable. The patient received intravenous methylprednisolone for five days, followed by oral corticosteroid therapy for three months, leading to progressive clinical improvement and complete resolution of the MRI lesions after eight months. A final diagnosis of BS associated with ADEM was confirmed.

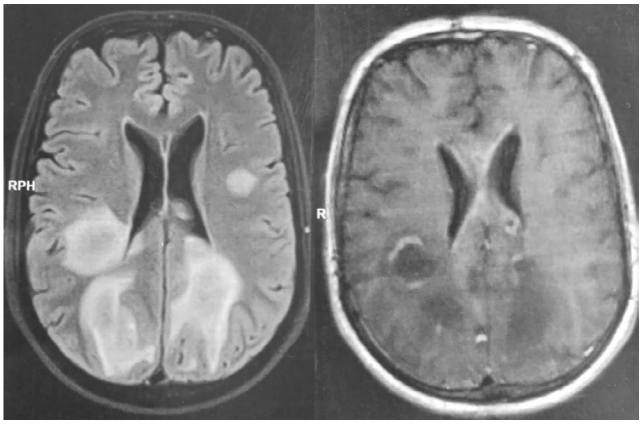

FIGURE 1 Brain magnetic resonance imaging (T1 GADO and Flair) showed multiple patchy and nodular lesions in the bilateral parieto-occipital regions, with ring enhancement after gadolinium injection

Results: ADEM is an acute demyelinating disease of the central nervous system that often occurs after a viral infection, particularly in children. It presents with diverse symptoms and atypical presentations such as BS. The precise mechanisms linking ADEM and BS remain unclear but suggest that extensive demyelination leads to a disconnection between posterior visual association areas and the motor regions of the prefrontal cortex.
Conclusion: The association between BS and ADEM is extremely rare. This case underscores the importance of recognizing complex visual disturbances in atypical ADEM presentations.
Disclosure: Nothing to disclose.

Cerebrovascular diseases 2

EPR-125 | Capillary index score in mechanical thrombectomy: Predicting functional outcomes and identifying no-reflow risk

A. Scartezzini[1]; M. Plebani[2]; C. Zivelonghi[1]; N. Mandruzzato[2]; M. Cappellari[1]; B. Petralia[2]; B. Bonetti[1]; N. Micheletti[1]
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Background and aims: Despite advances in mechanical thrombectomy (MT), futile recanalization remains a major challenge, affecting nearly 50% of successfully recanalized patients. The no-reflow phenomenon (NRP), a form of persistent microvascular dysfunction, is thought to contribute significantly. The Capillary Index Score (CIS), an angiographic marker based on procedural digital subtraction angiography (DSA), may help assess microvascular integrity, but its prognostic role in acute ischemic stroke (AIS) remains underexplored. We aimed to evaluate the predictive role of CIS before MT (pre-CIS) and after MT (post-CIS) for functional outcomes (mRS at 90 days) and hemorrhagic transformation (HT) in AIS patients treated with MT.
Methods: A single-center, retrospective-prospective study included 117 AIS patients with anterior circulation large vessel occlusions treated with MT. CIS was assessed pre- and post-procedurally. Univariate and multivariate logistic regression identified predictors of unfavorable outcomes (mRS ≥3) and HT. ROC curves and ANOVA likelihood ratio tests evaluated model performance.
Results: A favorable pre-CIS (>2) was an independent predictor of functional independence (OR 0.17, 95% CI 0.08–0.88, $p=0.03$), confirming its role as an early marker of microvascular integrity. Pre-CIS improved predictive model performance ($p=0.034$). Post-CIS reflected persistent microvascular dysfunction and showed a trend toward higher HT rates ($p=0.071$), suggesting its role in identifying patients at risk of no-reflow.
Conclusion: Pre-CIS is confirmed as an early predictor of functional outcomes, while post-CIS highlights persistent no-reflow and its potential link to HT. CIS may enhance prognostic models, potentially serving as a tool for decision-making, though further validation in larger cohorts is warranted.
Disclosure: Nothing to disclose.

EPR-126 | CD177null genotype on neutrophils predicts poor neurological outcome in ischemic stroke patients

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Background and aims: Neutrophils are important contributors to ischemic brain injury. In preclinical rodent studies, the lack of the neutrophilic surface molecule Ly6G was associated with exacerbated stroke damage. Ly6G is thought to represent an "eat me" signal on neutrophils that ensures neutrophil phagocytosis. Human neutrophils do not express Ly6G, but an analogue, CD177. CD177 is lacking in ~5% of the general population. The consequences of the CD177null genotype for stroke recovery were unknown.
Methods: In a prospective study, patients with first-time ischemic strokes are recruited at the University Hospital Essen. Peripheral blood samples are taken. CD177 and various other immune cell markers are analyzed by flow cytometry. Clinical examinations and interviews are conducted to assess vascular

risk factors and neurological impairments. Patients are examined on three time-points: T1 = < 72h, T2 = ≥72h–144h, T3 = 3 months post-stroke.

Results: From October 18th, 2022 to October 20th, 2024, 236 stroke patients were included. By flow cytometry, 10 patients were CD177null and 226 CD177WT genetopes. CD177null and CD177WT patients showed similar vascular risk factor profiles except that CD177null patients exhibited more often a history of TIA (20% vs. 0.4%, $p=0.073$), carotid dissection (33.3% vs. 5.4%, $p=0.015$) and regular sports activity ($p=0.024$) (Figure 1). Compared with CD177WT patients, CD177null patients had higher neurological deficits in the National Institutes of Health Stroke Scale at all time-points examined, most prominently at T2 and T3, and a higher disability in the modified Rankin Scale at T3 (Figures 2, 3).

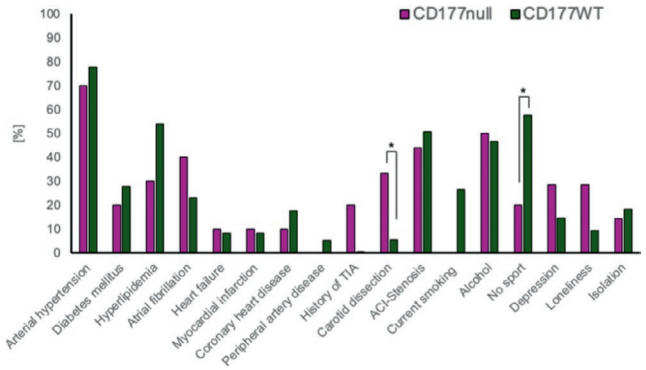

FIGURE 1 Vascular risk profiles in CD177null and CD177WT stroke patients. Percentages of each vascular risk factor are shown.

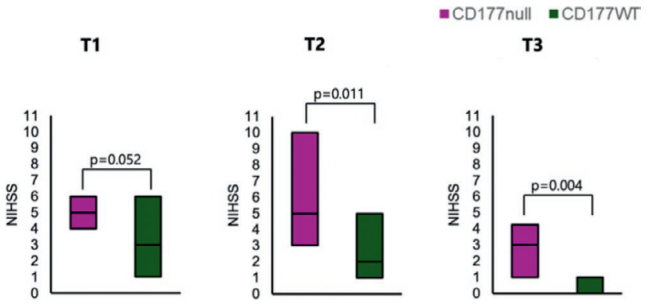

FIGURE 2 National Institutes of Health Stroke Scale score in CD177null and CD177WT stroke patients. Median, Q1 and Q3 are shown.

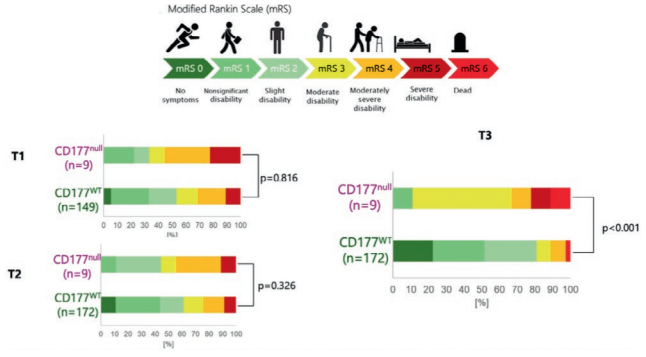

FIGURE 3 Modified Rankin scale scores in CD177null and CD177WT stroke patients. Percentages of each score are shown.

Conclusion: CD177 deficiency is associated with poor neurological outcome in ischemic stroke patients.

Disclosure: Supported by DFG TRR332 (449437943).

EPR-127 | Predictors of intracranial non-stenosing vulnerable atherosclerotic plaques in ESUS: A risk stratification model

F. Mazzacane[1]; B. Del Bello[1]; C. Asteggiano[1]; E. Rognone[2]; F. Ferrari[1]; A. Persico[3]; A. Costa[1]; R. De Icco[1]; A. Morotti[4]; A. Pichiecchio[1]; A. Cavallini[3]

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Background and aims: Intracranial vulnerable non-stenosing atherosclerotic plaques (vNSPs) are emerging as potential causes of Embolic Strokes of Undetermined Source (ESUS). While Vessel Wall MRI (VWMRI) is a valuable tool for detecting vNSPs, its limited availability and high technical complexity necessitate the identification of high-risk patients for targeted imaging.

Methods: A prospective cohort of 80 single-territory ESUS patients undergoing VWMRI was analyzed. A multivariable logistic regression model including the clinical predictors of vNSPs was developed. Model performance was evaluated using the area under the curve (AUC) of the receiver operating characteristic (ROC) curve, specificity, sensitivity, positive predictive value (PPV), and negative predictive value (NPV).

Results: Age (adjusted odds ratio [aOR] 1.12, 95% confidence interval [CI] 1.05–1.23, $p=0.04$) and smoking exposure (aOR 8.48, 95% CI 2.32–40.6, $p=0.003$) were independently associated with culprit vNSPs. The model, incorporating these two variables, demonstrated good discriminatory performance (AUC 0.84, 95% CI 0.76–0.92). Specificity, sensitivity, NPV, and PPV were 0.70, 0.91, 0.95, and 0.55, respectively.

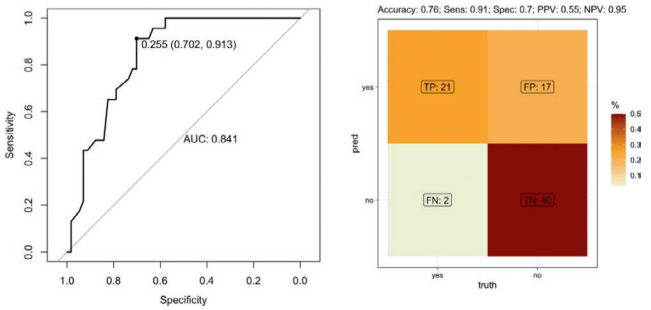

FIGURE 1 Panel A: ROC curve for the predicted probability of the presence of a culprit vNSP. Panel B: confusion matrix. TP, true positives; FP, false positives; TN true negatives; FN, false negatives.

Conclusion: This simple clinical model shows promise in stratifying ESUS patients for VWMRI, with high NPV aiding in excluding low-risk patients thus optimizing the diagnostic yield and resource utilization. However, the low PPV highlights the need for additional predictive factors, such as imaging and blood biomarkers, to refine risk stratification. In conclusion, a model

based on simple clinical features demonstrated good performances in in identifying ESUS patients at risk for intracranial culprit vNSPs. Further studies and external validation are essential to confirm these results.

Disclosure: Funding: "Ricerca Corrente 2022-2024" granted to IRCCS Mondino Foundation.

EPR-128 | Spatial transcriptomics of dopaminergic neuron degeneration in rat ventral tegmental area after motor-cortical stroke

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Background and aims: For motor learning, the integrity of dopaminergic (DAergic) pathways from the ventral tegmental area (VTA) to the cortex is essential. Secondary degeneration of DAergic VTA-neurons after stroke, however, impedes relearning of lost motor skills. To study the time-dependent impact of ischemic cortical stroke on the microenvironment of this complex brain region, we traced the cell type-specific dynamics of DAergic degeneration in the VTA of adult rats, along with the response in the peri-infarct cortex.

Methods: Adult Sprague-Dawley rats (n = 2) received a photothrombotic stroke in the motor-cortical area. Fresh-frozen, OCT-embedded samples from the midbrain and cortex were collected at post-stroke days 3 and 7. Spatial transcriptomics (50 µm spots) was performed and integrated using deep learning and deconvolution techniques to profile the spatially resolved gene expression patterns at an inferred cellular level in the tissue. DAergic neuron degeneration was further validated via tyrosine hydroxylase-positive (Th+) immunostaining.

Results: We analyzed the ventral midbrain including the substantia nigra and VTA for changes in cell type composition. Progressive degeneration of DAergic VTA-neurons was observed, with the ipsilateral/contralateral ratio decreasing from 0.96 on day 3 to 0.76 on day 7 post-stroke ($p < 0.03$). This reduction was independently validated through Th+ immunostaining ($p < 0.0001$). Additionally, reactive astrocytes marked by Gfap ($p < 1e\text{-}10$) increased at day 3 in the ipsilateral midbrain hemisphere.

Conclusion: Our preliminary findings suggest spatiotemporal gene expression patterns of DAergic neurodegeneration in the midbrain, providing a robust model for exploring strategies to support post-stroke recovery. Currently, we are complementing the data with additional time-points and single-nucleus sequencing.

Disclosure: Nothing to disclose.

EPR-129 | Early nutrition support enhances recovery after endovascular thrombectomy: A prospective study with historical control

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Background and aims: We investigated the effectiveness of a comprehensive nutritional intervention provided by a multidisciplinary healthcare team on outcomes in acute stroke patients undergoing endovascular thrombectomy (EVT).

Methods: This prospective cohort study examined acute stroke patients undergoing EVT and achieved successful recanalization with comprehensive nutritional intervention, compared to a propensity-matched historical control group. A total of 70 patients were prospectively enrolled between April 2022 and March 2024. The historical control group consisted of 427 consecutive patients treated between January 2015 and December 2020. After propensity matching, 42 pairs were included. The intervention protocol utilized a multidisciplinary healthcare team, including physicians, nurses, dietitians, speech-language pathologists, and pharmacists to achieve targeted nutrition, aiming to initiate within two days and reach requirements (30 kcal/kg and 1.5 g/kg protein) within one week, with success defined as reaching ≥70% of targets. The primary outcome was the modified Rankin Scale (mRS) at 90 days.

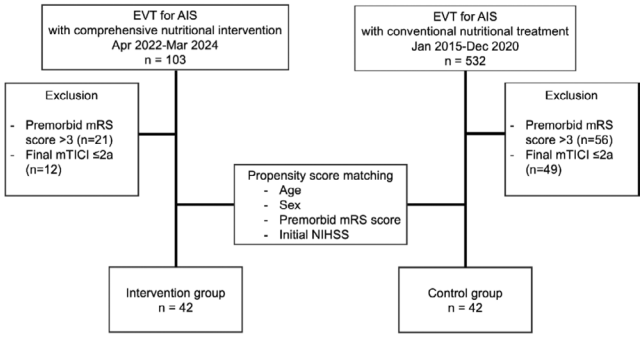
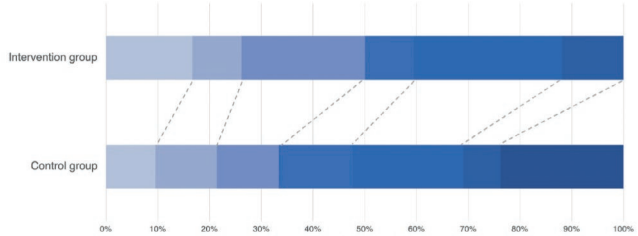


FIGURE 1 Patient selection.

Results: The matched cohort (median age 78.0 years, 53.3% male) showed comparable baseline and EVT-related characteristics. Nutritional therapy was initiated within two days in 92.8% and 78.5% of the intervention and control groups, respectively ($p = 0.126$). The intervention group showed favorable effects on 90-day mRS scores (adjusted common odds ratio: 2.280, 95% CI 1.040-5.080, $p = 0.041$). Target nutrient intake achievement was higher in the intervention group (95.2% vs. 76.1%, $p = 0.025$). No significant differences were observed in complications including aspiration pneumonia, diarrhea, and hyperglycemia.



mRS	0	1	2	3	4	5	6
Intervention group (n=42)	7(16.6)	4 (9.5)	10 (23.8)	4 (9.5)	12 (28.5)	5 (11.9)	0 (0)
Control group (n=42)	4 (9.5)	5 (11.9)	5 (11.9)	6 (14.2)	9 (21.4)	3 (7.1)	10 (23.8)

FIGURE 2 Distribution of mRS scores at 90 days following EVT.

Conclusion: Comprehensive nutritional intervention in the acute phase improved functional outcomes in EVT patients, suggesting its potential benefit in post-stroke care management.
Disclosure: Nothing to disclose.

EPR-130 | Low fibrinogen after intravenous thrombolysis: a possible predictor of hemorrhagic intracranial complications?

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Background and aims: Current Czech guidelines for treatment with intravenous thrombolysis (IVT) include the examination of coagulation parameters, including fibrinogen levels, before IVT, 6 hours and 24 hours after IVT, but there is no official recommendation on when to substitute fibrinogen, and whether to do so at all. Substitution is available in hospitals (Hemocomplettan i.v.). Fibrinogen substitution may be a way to prevent the development of bleeding complications during IVT treatment. The aim of this study was to evaluate whether a decrease in fibrinogen levels below the reference range of 1.8 g/l is associated with a higher likelihood of intracranial hemorrhage in patients with ischemic stroke treated with IVT.
Methods: This multicenter retrospective study was conducted in 7 Czech centers. The study population consists of 280 patients enrolled in the observational group (divided into subgroups according to the type of hemorrhagic complication after IVT) and the control group (without hemorrhagic complication) according to the model 1:1 principle (same NIHSS, age, sex).
Results: In all treatment groups (all observational subgroups as well as the control group), a decrease in fibrinogen levels was noted after IVT administration, with varying degrees of signification. A statistically significant difference ($p=0.0394$) was found at 6 h after IVT administration in patients with the most clinically serious form of bleeding (parenchymal hematoma type 2), fibrinogen value 1.84 g/l versus 2.53 g/l.

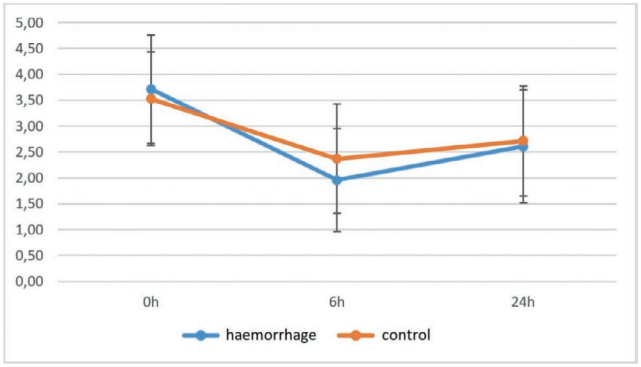

FIGURE 1 Fibrinogen level in subgroup "parenchymal hematoma 2" and its control before IVT, 6 hours and 24 hours after IVT.

Conclusion: Patients with the clinically most severe form of hemorrhagic complication (parenchymal hematoma type 2) had significantly lower fibrinogen levels than those in the control group 6 hours after IVT administration.
Disclosure: Nothing to disclose.

EPR-131 | Outcomes of early vs. delayed anticoagulant Initiation in stroke patients + atrial fibrillation: Updated meta-analysis

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Background and aims: Large randomized trials show direct oral anticoagulants (DOACs) reduce ischemic stroke risk in atrial fibrillation (AF) patients by ~2/3, with low intracranial hemorrhage risk. However, limited data exist on long-term outcomes of early versus delayed NOAC/DOAC therapy, particularly within 90 days post-stroke.
Methods: We conducted a systematic review and meta-analysis by searching PubMed and the Cochrane database for randomized controlled trials (RCTs) and observational studies comparing early (≤4 days after stroke onset) versus delayed NOAC/DOAC therapy in ischemic stroke patients with AF. Outcomes included (1) recurrent ischemic stroke (IS), (2) intracranial bleeding (IB), and (3) all-cause mortality (AM). Heterogeneity was assessed using the I^2 statistic.
Results: Six studies (3 RCTs, 3 observational; n = 8,892) were included, with 4,076 patients receiving early NOACs. At 90 days, there were no significant differences in recurrent IS (RR 1.07; 95% CI 0.64–1.77; $p=0.80$), IB (RR 0.90; 95% CI 0.47–1.70; $p=0.74$), or AM (RR 0.79; 95% CI 0.52–1.20; $p=0.26$). Subgroup

analysis of RCTs alone showed consistent results, including the new OPTIMAS trial, published in November 2024. When hypothetically excluding OPTIMAS, early NOAC initiation significantly reduced recurrent IS risk (RR 0.63; 95% CI 0.41–0.98; $p = 0.04$).

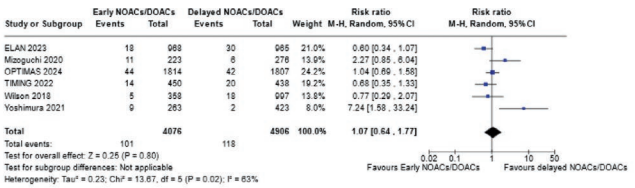


Figure 1A. There were no noticeable differences between the early and delayed initiation of NOAC/DOAC treatment in stroke patients regarding the risk of recurrent ischemic stroke within 90 days. The Relative Risk (RR) was 1.07 (95% CI: 0.64–1.77; p = 0.80).

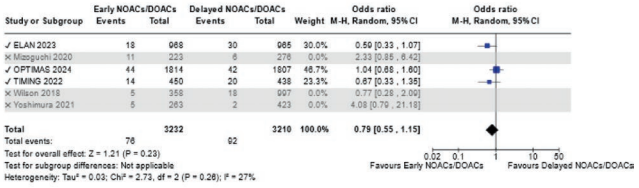
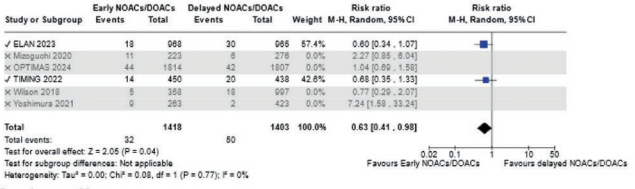


Figure 1A. No significant differences were found between early and delayed NOAC/DOAC initiation in stroke patients for the risk of recurrent ischemic stroke within 90 days (RR: 0.79, 95% CI: 0.55–1.15; p = 0.23). This contrasts with previous meta-analyses showing significant results. We suspect the inclusion of the recently published OPTIMAS trial (November 2024) influenced this finding. Reanalyzing with only the two RCTs from earlier meta-analyses yielded different results.

Figure 1A. Randomied Controlled Trials Subgroup Analysis Of Recurrent Ischemic Stroke.



Supplement 1A.

Figure 1A. Recurrent Ischemic Stroke Within 90 Days.

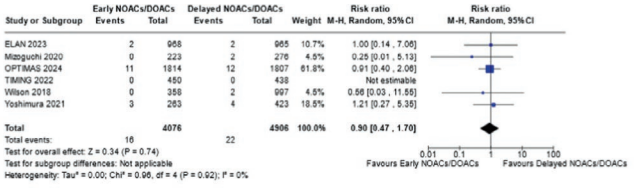


Figure 1B. No significant differences were observed between the early and delayed initiation of NOAC/DOAC treatment in stroke patients concerning the risk of intracranial bleeding within 90 days. The risk ratio (RR) was 0.9 (95% CI: 0.47–1.70; p = 0.74).

Figure 1B. Intracranial Bleeding At 90 days.

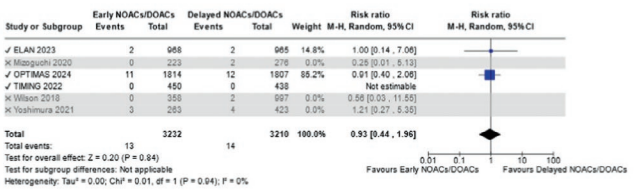


Figure 1B. The subgroup analysis of randomized controlled trials (RCTs) revealed no considerable differences between the early and delayed initiation of NOAC/DOAC treatment in stroke patients regarding the risk of intracranial bleeding within 90 days. The risk ratio (RR) was 0.93 (95% CI: 0.44–1.96; p = 0.84).

Figure 1B. Randomied Controlled Trials Subgroup Analysis Of Intracranial Bleeding.

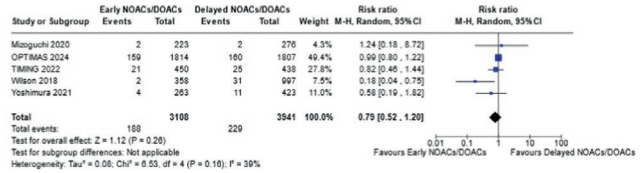


Figure 1C. No significant differences were observed between the early and delayed initiation of NOAC/DOAC treatment in stroke patients concerning the risk of all-cause mortality within 90 days. The risk ratio (RR) was 0.79 (95% CI: 0.52–1.20; p = 0.26).

Figure 1C. All-cause Mortality at 90 days.

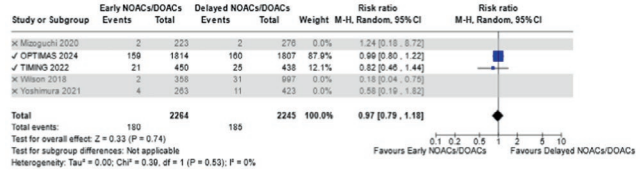


Figure 1C. The subgroup analysis of randomized controlled trials (RCTs) revealed no considerable differences between the early and delayed initiation of NOAC/DOAC treatment in stroke patients regarding the risk of all-cause mortality within 90 days. The risk ratio (RR) was 0.97 (95% CI: 0.79–1.18; p = 0.74).

Figure 1C. Randomied Controlled Trials Subgroup Analysis Of All-cause Mortality.

Conclusion: These findings suggest no significant differences in safety or efficacy between early and delayed NOAC/DOAC initiation within 90 days in stroke patients with AF. While current evidence supports the non-inferiority of early therapy, further RCTs are needed to establish the long-term superiority of early treatment.

Disclosure: Nothing to disclose.

EPR-132 | Safety and efficacy of CEA and IVT in acute stroke and occluded cervical internal carotid artery

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Background and aims: In acute ischemic stroke (AIS) and acute cervical internal carotid artery (cICA) occlusion, intravenous thrombolysis (IVT) represents a standard treatment, and emergent carotid endarterectomy (CEA), used alone or in combination with IVT, is an experimental alternative. The aim was to assess the safety and efficacy of IVT, emergent CEA, and IVT+CEA in AIS patients with acute cICA occlusion.

Methods: In a retrospective, multicenter study, the IVT group consisted of 41 patients (26 males; median age 72 [60–79] years), the IVT+CEA group of 31 patients (26 males; median age 70 [63–77] years), and the CEA group of 61 patients (45 males; median age 68 [61–75] years). 3-month outcomes were assessed using a modified Rankin Scale (mRS), with good outcomes defined as 0–3.

Results: The following results were observed in the IVT, IVT+CEA, and CEA groups: recanalization rate 17.1%, 77.4%, and 88.5%, resp.; good 3-month clinical outcomes 56.1%, 74.2%, and 89.8%, resp.; 3-month mortality 22.0%, 19.4%, and 6.8%, resp. ($p < 0.05$ in all cases for IVT vs. CEA comparison). The use of CEA alone was identified as an independent positive predictor of good 3-month clinical outcomes (OR 5.185, 95% CI: 1.973–13.63; $p = 0.0009$), and an independent negative predictor of 3-month mortality (OR 0.295, 95% CI: 0.07112–0.8754; $p = 0.0329$).

Conclusion: In this retrospective, multicenter study, using an emergent CEA alone in patients with AIS and acute cICA occlusion was associated with a higher recanalization rate and the achievement of good 3-month clinical outcomes, and lower 3-month mortality compared to IVT.

Disclosure: Disclosure: Roman Herzig: Supported by STROCZECH within the CZECRIN Large Research Infrastructure (No. LM2023049) funded by the state budget of the Czech Republic, Ministry of Health of the Czech Republic (Grant No. DRO—UHHK 00179906), and Charles University, Czech Republic (Cooperation Program, research area NEUR). Igor Guňka: Nothing to disclose. Svatopluk Ostrý: Nothing to disclose. Jiří Fiedler: Nothing to disclose. Vladimír Přibáň: Nothing to disclose. Martin Kovář: Nothing to disclose. Petr Štádler: Nothing to disclose. Ondřej Škoda: Nothing to disclose. Jiří Neumann: Nothing to disclose. Veronika Kunešová: Supported by STROCZECH within the CZECRIN Large Research Infrastructure (No. LM2023049) funded by the state budget of the Czech Republic.

EPR-133 | burden and distribution of cerebral microbleeds and stroke recurrence and prognosis in cerebral hemorrhage

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Background and aims: To investigate the relationship between the burden and distribution of cerebral microbleeds and the recurrence of ischemic and hemorrhagic stroke in survivors of spontaneous intracerebral hemorrhage (ICH) and their impact on prognosis.

Methods: Patients with first-onset spontaneous ICH between January 1, 2019, and October 31, 2023, were consecutively enrolled from the stroke registry of Xianyang Hospital of Yan'an University. Patients were divided into a non-severe CMBs group (< 10 microbleeds) and a severe CMBs group (≥10 microbleeds) based on magnetic susceptibility-weighted imaging findings. Follow-up assessments were conducted via telephone for a period of 12 months post-discharge. The primary outcomes were recurrent stroke and type of recurrent stroke, while the secondary outcome was long-term (1-year) functional prognosis. Cox proportional hazards models were used to assess the risk of stroke recurrence. Logistic regression analysis was used to determine the independent association between CMBs and poor functional prognosis 1 year after cerebral hemorrhage.

Results: Among the 412 patients enrolled, 278 had detectable CMBs, including 80 in the severe CMBs and 198 in the non-severe CMBS, with 22 cerebral hemorrhages and 35 cerebral infarctions occurring during a median follow-up of 28.5 months. Severe CMBs burden was associated with recurrent hemorrhagic stroke (HR = 4.592, 95% Cl: 1.943–10.848) and was an independent risk factor for poor prognosis at 1 year (OR = 2.190, 95% Cl: 1.205–3.982) as well.

TABLE 1 Endpoint events during follow-up in subgroups with different burden and distribution of cerebral microhemorrhage.

Variables	Recurrent cerebral haemorrhage	Recurrent cerebral infarction
Cerebral micro haemorrhage load subgroup		
CMBs count < 10	10 (3.0)	25 (7.5)
CMBs count ⩾ 10	12 (15.2)	10 (12.7)
Cerebral microhaemorrhage distribution subgroups		
Presence of Lobar CMB	2 (5.9)	5 (14.7)
Presence of Non-Lobar CMB	20 (5.3)	30 (7.9)

TABLE 2 Multivariate cox proportional-hazards model of hemorrhagic stroke recurrent

Variables	Wald	P	HR	95%CI
Smoking	1.659	0.198	1.767	0.743-4.204
Presence of Lobar ICH	2.442	0.118	2.109	0.827-5.378
Presence of Lobar CMBs	0.107	0.743	1.279	0.293-5.589
CMBs count≥10	12.073	0.001	4.592	1.943-10.848

TABLE 3 Univariate and multivariate logistic regression analysis affecting prognosis

Variables	poor prognosis (n=84)	good rognosis (n=197)	Univariate			Multivariate		
			OR	P	95%CI	OR	P	95%CI
Age（mean）	65.90±9.84	57.84±10.85	1.079	<0.001	1.053-1.107	1.081	<0.001	1.052-1.111
Male	64（64.0）	200（64.1）	1.004	0.985	0.628-1.606			
Hypertension	77（77.0）	239（76.6）	1.023	0.935	0.599-1.745			
Diabetes mellitus	21（21.0）	40（12.8）	1.808	0.047	1.007-3.243			
Coronary artery disease	18（18.0）	60（19.2）	0.922	0.785	0.515-1.651			
Hyperlipidemia	35（35.0）	103（33.1）	1.087	0.729	0.677-1.747			
Prior ischemic stroke	36（36.0）	123（39.4）	0.864	0.541	0.542-1.379			
Smoking	33（33.0）	79（25.3）	1.453	0.134	0.891-2.368			
Alcohol consumption	11（11.0）	24（7.7）	1.478	0.309	0.697-3.136			
Antiplatelet medication	24（24.0）	59（18.9）	1.354	0.271	0.790-2.322			
Serum low-density lipoprotein	2.53（2.06，2.97）	2.35（1.91，2.87）	1.325	0.069	0.978-1.794			
Total serum cholesterol	3.91（3.39,4.63）	3.95（3.38,4.53）	1.054	0.669	0.829-1.339			
Admission NHISS score	7（4,12）	5（2,8）	1.102	<0.001	1.058-1.148	1.121	<0.001	1.071-1.173
Statin use	68（68.7）	178（57.1）	1.651	0.041	1.022-2.669	1.774	0.04	1.025-3.068
Presence of Lobar ICH	12（12.0）	48（15.4）	0.750	0.405	0.381-1.476			
CMBs count≥10	30（30.0）	49（15.7）	2.300	0.002	1.360-3.890	2.190	0.010	1.205-3.982
Presence of Lobar CMBs	13（13.0）	21（6.7）	2.071	0.051	0.996-4.305	2.296	0.052	0.994-5.302

Conclusion: Our findings indicate that patients with severe CMBs have a high risk of recurrent hemorrhagic stroke following ICH and a poor prognosis.
Disclosure: Nothing to disclose.

Child neurology/developmental neurology

EPR-134 | Lentiviral hematopoietic stem cell gene therapy (atidarsagene autotemcel) for late juvenile metachromatic leukodystrophy

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Background and aims: Metachromatic leukodystrophy (MLD) is a rare lysosomal disease due to arylsulfatase A (ARSA) deficiency. Atidarsagene autotemcel (arsa-cel), an ex-vivo hematopoietic stem cell gene therapy, has shown favorable outcomes in early-onset MLD. A phase III trial (NCT04283227) evaluates arsa-cel in pre-symptomatic or early-symptomatic Late Juvenile MLD (LJ-MLD) patients. This report presents interim engraftment, pharmacodynamic and safety data.
Methods: Six patients (4 pre-symptomatic, 2 early-symptomatic) were treated. Median age at treatment was 10.4 years (range: 2.7-15.5 years). Stem cell source was mobilized peripheral blood. The infused drug product median dose was 23.1×10^6 CD34+ cells/kg (range: 16.0-28.9×10^6 CD34+ cells/kg), with a vector copy number (VCN)/cell range of 2-5.
Results: Median follow-up was 27.8 months (range: 12.6 to 34.3 months). All patients are alive. Five remained neurologically stable; one early-symptomatic patient experienced disease progression, followed by stabilization up to 30 months post-treatment. Short-term adverse events were consistent with busulfan's safety profile. No malignancies, clonal expansion, or immune responses against ARSA occurred. All treated patients showed rapid engraftment of transduced cells. At 1-year post-treatment, five patients with available data showed median VCN in peripheral blood mononuclear cells (PBMCs) of 0.3/cell (range 0.2-0.9) with a transduction rate in bone marrow progenitor cells ranging from 18.8% to 85.4%. ARSA activity reached supra-normal levels in PBMCs and normal levels in cerebrospinal fluid at latest follow-up.
Conclusion: Early results with arsa-cel show safety and pharmacodynamics efficacy in LJ-MLD, consistent with those seen in early-onset MLD. Continued monitoring will assess clinical endpoints and long-term safety.
Disclosure: Valeria Calbi, Francesca Fumagalli, Vera Gallo have occasionally received consultant fees and reimbursement for travel costs and participation fees from Orchard Therapeutics. JB, PN, NDG, and LC are current employees of Orchard Therapeutics. AS is a former employee of GSK and clinical consultant for Orchard Therapeutics. Atidarsagene autotemcel was licensed to GlaxoSmithKline (GSK) in 2014 and GSK became the clinical trial sponsor. In 2018 MLD development rights were transferred to Orchard Therapeutics (OTL) and OTL became the clinical trial sponsor

EPR-135 | Long-term medical and social outcomes in children and adolescents with Lennox Gastaut syndrome

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Background and aims: Lennox Gastaut syndrome (LGS) is a severe, chronic epilepsy that begins in childhood and continues into adulthood, causing persistent seizures and neurocognitive impairment. This study aimed to assess epilepsy, neurodevelopmental outcomes, and quality of life (QoL) in individuals with LGS and identify predictors of these outcomes.
Methods: A cross-sectional evaluation was conducted at a tertiary-care center in South India between June 2023 and March 2024. The cohort included 96 patients (aged 2-25 years, diagnosed before 18), assessed for epilepsy severity, motor functional status, social quotient, behavioral comorbidities, quality of life, and caregiver burden using various standardized scales.
Results: The study involved 96 participants (63.5% boys) with at least 1-year of regular follow-up. Mean (+ S.D.) age of the cohort was 10.3 (5.8) years. 56.3% had a structural etiology. Long-term outcomes showed ongoing epilepsy in 73 patients, unfavorable motor status in 77, moderate to severe socio-adaptive deficits in 68, autism spectrum disorder in 47, ADHD in 39, impaired QoL in 78, and significant caregiver burden in 79. Generalized paroxysmal fast activity on inter-ictal EEG was associated with ongoing epilepsy ($p = 0.01$). Better epilepsy control was linked to improved motor and cognitive outcomes.

Conclusion: The study revealed a predominance of structural etiology, with ongoing epilepsy and significant impacts on QoL and caregiver burden in more than two-third of patients in last follow-up. With improved survival rates in children and adolescents with LGS, better epilepsy control could lead to improved neurocognitive outcomes, enhanced QoL, and reduced caregiver burden.
Disclosure: Nothing to disclose.

EPR-136 | Long-term 24-month findings of N-acetyl-L-leucine for Niemann-Pick disease type C

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Background and aims: The IB1001- 301 clinical trial was a Phase III, double-blind, randomized, placebo-controlled trial comparing N-acetyl-L-leucine (NALL) with placebo for the treatment of neurological signs and symptoms in Niemann-Pick disease type C (NPC) after 12 weeks. The primary Scale for the Assessment and Rating of Ataxia (SARA) endpoint was reduced −1.97 points with NALL and −0.60 with placebo ($p < 0.001$). Extended follow-up data were obtained in an open-label Extension Phase (EP) to evaluate the long-term, neuroprotective effects of NALL for NPC.
Methods: Patients received treatment with orally administered NALL 2–3 times per day (patients 4- 12 years receiving weight-based doses (2 to 4 g per day), those ≥13 years 4 g per day). The primary endpoint was the modified 5-domain NPC Clinical Severity Scale (5-Domain NPC- CSS) (range 0–25 points; lower score representing better neurological status). Comparisons were made to the expected annual trajectory of disease decline established in published natural history studies. Exploratory endpoints included the 15-domain NPC- CSS (excluding hearing) and SARA.
Results: 54 patients aged 5–67 years were treated in the EP. After 24 months, the mean (±SD) change from baseline on the 5-domain NPC-CSS was -0.24 (±2.69) on NALL, compared to +3.0 (±6.32) in the historical cohort: mean difference -3.24 (95% Confidence Interval (CI) -5.59 to -0.89; $p = 0.009$). The result of the 15-domain NPC- CSS was supportive of the primary analysis and the improvements in neurological status demonstrated in the Parent Study's primary SARA endpoint were sustained over the 24-month long-term follow-up.
Conclusion: Treatment with NALL after 24 months was associated with a statistically significant and clinically meaningful reduction in disease progression and consistent with a neuroprotective, disease-modifying effect.
Disclosure: Marc Patterson, Janelle Raymond, Beth Zanrucha, and Asante Hatcher are all employees of IntraBio the study sponsor. Tatiana Bremova- Ertl received speaker's honoraria and consultancy fees from Actelion, Sanofi- Genzyme and Zevra as well as blinded video- rater fees from Intrabio.

EPR-137 | Quantitative sleep EEG biomarkers in Rett Syndrome: Sleep as a window to understand synaptic dysfunction

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Background and aims: Rett Syndrome (RTT) is a neurodevelopmental disorder caused by mutations in the MECP2 gene, with sleep disturbances affecting ~80% of individuals. Dysregulation of thalamocortical connectivity and synaptic dysfunction in RTT may contribute to abnormalities in sleep spindles and slow waves, as observed in other neurological disorders. This study investigates the role of quantitative sleep EEG analysis in uncovering neural circuit abnormalities in RTT, comparing findings with MECP2-deficient animal models.
Methods: We enrolled 14 females with typical RTT and MECP2 mutations, alongside age-matched controls. Using overnight polysomnography and quantitative EEG analysis, we assessed spindle density and slow-wave parameters (power, slope, amplitude) via custom MATLAB scripts. Spearman's correlation analysis was applied for clinical insights, and Wilcoxon tests compared RTT patients with controls.

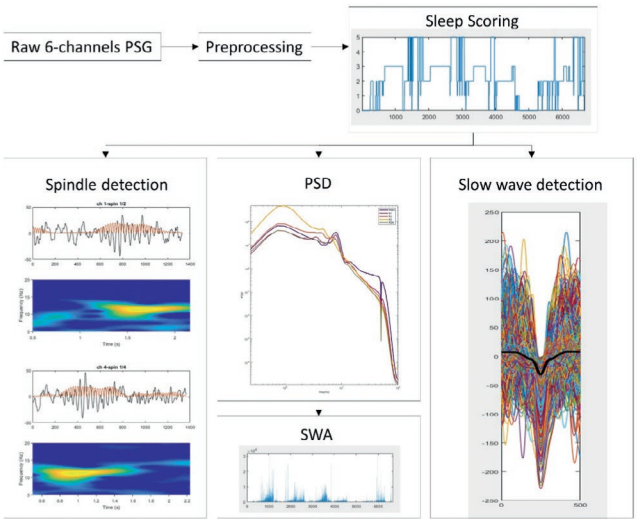

FIGURE 1 Pipeline of analysis

Results: Our analysis identified two key findings. First, spindle density (spindles per minute) was significantly reduced in RTT patients compared to controls. Second, slow-wave parameters exhibited a diminished nocturnal decrease in RTT patients, suggesting disrupted sleep-dependent synaptic homeostasis and impaired cortical synaptic plasticity.

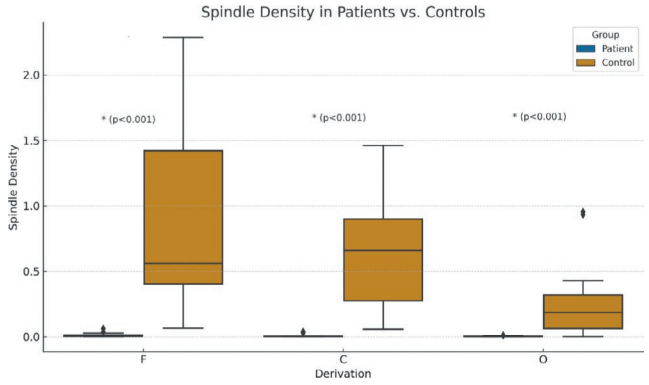

FIGURE 2 Spindle density, patients versus controls

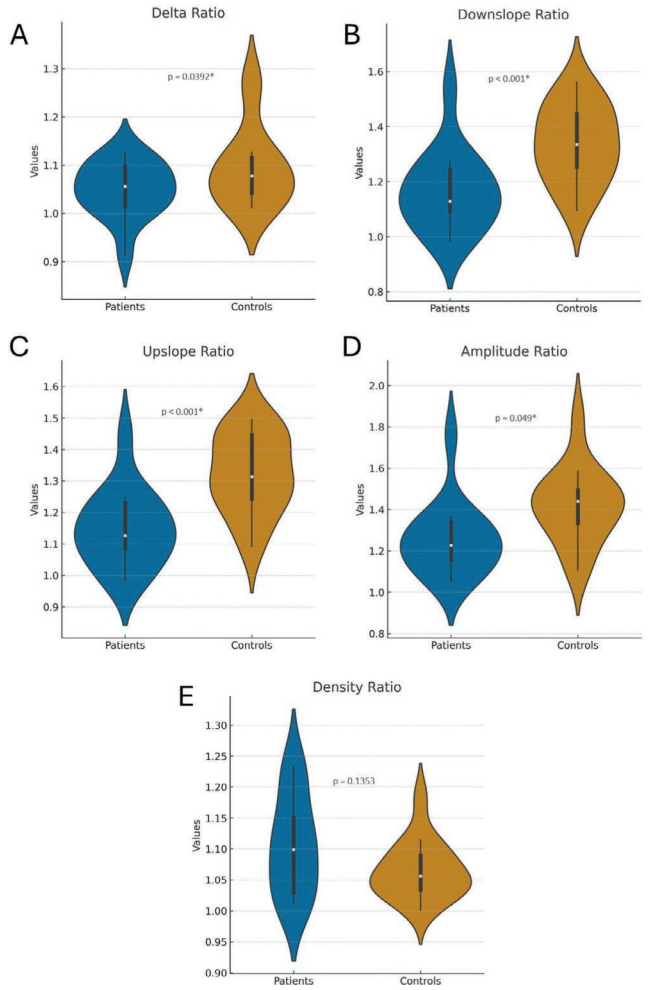

FIGURE 3 Delta Power and Slow Waves parameters ratios between 1st and 2nd half of NREM

Conclusion: This study demonstrates decreased spindle density and altered slow-wave parameters in RTT patients, consistent with findings in animal models. These electrophysiological biomarkers provide insights into sleep-dependent synaptic dysfunctions and neural circuit abnormalities in RTT. Further exploration of quantitative sleep EEG biomarkers may offer valuable prognostic and therapeutic opportunities for RTT.

Disclosure: Nothing to disclose.

EPR-138 | Investigating the neuroprotective effects of MgSO4 in children at risk of preterm birth: Meta-analysis of 20109 infants

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Background and aims: Preterm birth, which is defined as the delivery of babies before 37 gestational weeks are completed, is still a serious global-health issue. One of the major challenges among preterm birth infants is the prevalence of neurological disorders. In order to prevent the complications related to preterm birth, many interventions and agents have been utilized such as magnesium sulfate (MgSO4). The aim of this study was to investigate the neuroprotective effects of MgSO4 in children at risk of premature birth.

Methods: PubMed, WOS, Scopus, and Embase databases have been searched for relevant articles. The main outcomes assessed were cerebral palsy (CP), and any other available data. The random effects model was utilized to estimate odds ratio (OR).

Results: 55 studies involving more than 20,000 preterm infants were included. The analysis performed on the MgSO4 effectiveness on CP showed an OR suggesting a reduced risk of CP compared to the placebo group [OR = 0.74, 95% CI = (0.64; 0.86), I2 = 16%] (Fig. 1). The analysis performed on the effectiveness on preventing intraventricular hemorrhage showed an OR suggesting a reduced risk of CP compared to the placebo group [OR = 0.85, 95% CI = (0.76; 0.94), I2 = 66%] (Fig. 2). Side effects thought to be associated with MgSO4 such as necrotizing enterocolitis and patent ductus arteriosus didn't show any significant difference between MgSO4 and placebo groups [OR = 1.08, 95% CI = (0.88; 1.32), I2 = 51%; OR = 1.11,95% CI = (0.83; 1.48), I2 = 5%; respectively] (Fig. 3).

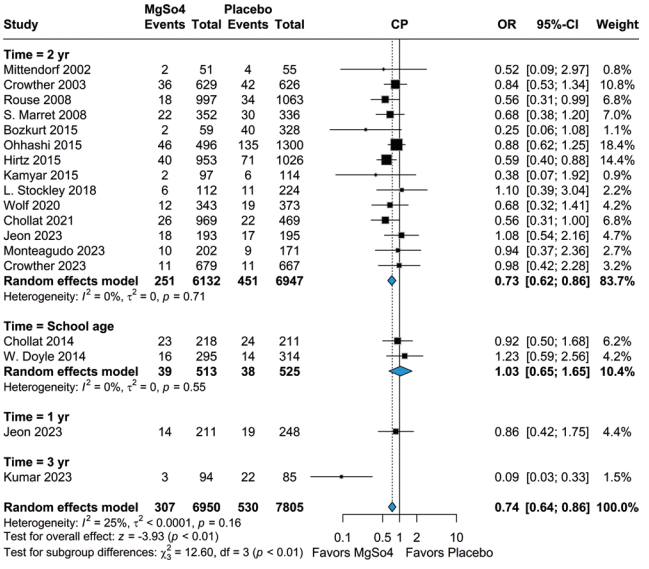

FIGURE 1 Effectiveness of magnesium sulfate in reducing cerebral palsy risk in preterm infants.

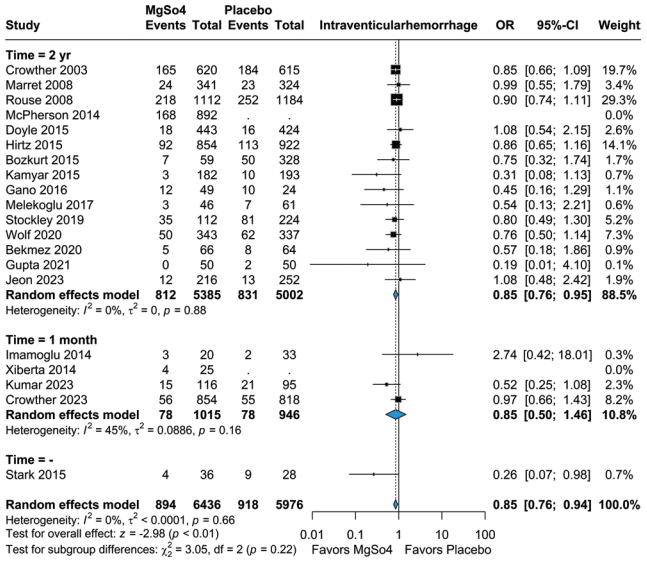

FIGURE 2 Effectiveness of Magnesium Sulfate in Preventing Intraventricular Hemorrhage in Preterm Infants.

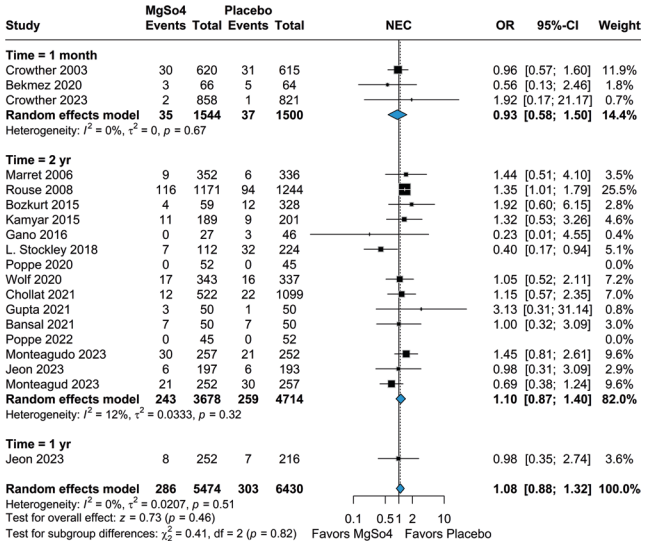

FIGURE 3 Comparison of necrotizing enterocolitis (NEC) and patent ductus arteriosus (PDA) rates among included preterm infants with or without MgSO4 administration.

Conclusion: MgSO4 has a neuroprotective potential and is recommended to be used for preterm infants.
Disclosure: Nothing to disclose.

EPR-139 | Exploring the associations of lesion metrics and neurological functions on cognitive outcomes in pediatric stroke

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Background and aims: The prevalence of cognitive problems after pediatric stroke is high and various risk factors such as stroke-related variables, demographic, neurological and cognitive factors may affect the cognitive long-term outcome. Whether and how these risk factors are associated with cognitive outcome is still incompletely understood. This study investigated how lesion volume, lesion location and neurological functions at discharge, 6-month and 2-year after pediatric stroke contribute to long-term cognitive outcome.
Methods: This observational study included patients after pediatric arterial ischemic stroke. Cognitive long-term outcome (intelligence, processing speed, working memory) was assessed at least one year after stroke. Neurological functions were measured using the pediatric stroke outcome measure at discharge, at 6-month and 2-year follow-up. Magnetic resonance imaging at stroke manifestation was applied to determine acute to subacute lesion metrics (volume & location).
Results: 43 patients aged 6 to 23 years were enrolled in the study. Cognitive functions were significantly associated with lesion volume and lesion location. Processing speed and working memory were worse if the left caudate nucleus was involved. Further, cognitive long-term outcome correlated significantly with neurological functions at discharge, 6-month and 2-year follow-up.
Conclusion: Cognitive long-term outcome was associated with lesion volume, lesion location and neurological functions. Our study adds to the determination of risk factors for cognitive long-term rehabilitation and highlights the need for the combined evaluation of neurological and cognitive performance.
Disclosure: Nothing to disclose.

EPR-140 | AI in pediatric TBI outcome prediction: A systematic review

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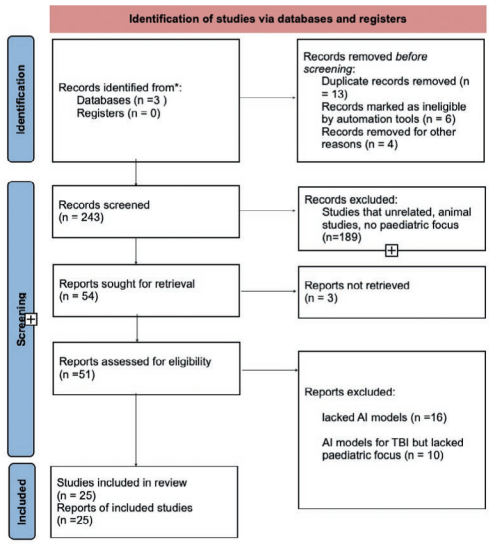
Background and aims: Pediatric TBIs is a leading cause of mortality and long term disabilities in children. Approximately half a million children go into American hospitals every year due to a TBI, showing the extent to which this is an issue within the medical world. In order to prevent the more dangerous outcomes it is crucial that there is early intervention along with tailored care given how sensitive the system is. AI can provide an easier solution to this - it can analyze the complex personalized datasets and provide accurate prognostic insights. This would reinforce or possibly show better ways to treat pediatric patients with TBIs and prevent harmful outcome.
Methods: A systematic search of PubMed, Embase, and Scopus databases was conducted for studies published in the last 10 years. Inclusion criteria were original peer-reviewed research focusing on pediatric TBIs, utilizing AI for outcome predictions, and reporting performance metrics. Articles were screened, and data on AI model type, accuracy (e.g., AUC, sensitivity, specificity), and clinical applicability were extracted.



PRISMA 2020 flow diagram for new systematic reviews which included searches of databases and registers only

FIGURE 1

Results: Of 243 initial articles, 25 met the inclusion criteria. Most studies used machine learning algorithms, with several incorporating imaging and clinical data. Predictive accuracy for long-term outcomes ranged from AUC 0.80 to 0.93. However, limitations included small, heterogeneous datasets and a lack of external validation. Few studies focused specifically on pediatric populations, limiting generalizability.
Conclusion: AI demonstrates potential in predicting outcomes in pediatric TBI but requires further validation. Developing standardized pediatric datasets and improving model transparency could enhance clinical adoption
Disclosure: Nothing to disclose.

EPR-141 | Neuroendoscopic lavage for the early management of posthemorrhagic hydrocephalus in neonates: A meta-analysis

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Background and aims: Posthemorrhagic hydrocephalus (PHH) is a significant complication of neonatal intraventricular hemorrhage (IVH). Neuroendoscopic lavage (NEL) is an emerging treatment option, but its efficacy compared to traditional management remains unclear. We aimed to access the available evidence on the effectiveness and safety of NEL versus traditional management for the early treatment of PHH in neonates.
Methods: A comprehensive search of electronic databases (PubMed, Embase, Google Scholar, and Web of Science) was conducted to identify studies exploring the effectiveness of NEL. The analysis was performed using random-effects models. The primary outcome was ventriculoperitoneal (VP) shunt dependency. Secondary outcomes included infection rates, multiloculated hydrocephalus, and mortality.
Results: Seven studies involving 237 neonates met the inclusion criteria. The pooled analysis revealed a shunt dependency rate of 50% (95% CI: 35.34-65.02%) with significant heterogeneity (I^2 =83%). The infection rate was 11.12% (95% CI: 5.73-16.52%), while the incidence of multiloculated hydrocephalus was 6% (95% CI: 0.52-11.52%). Mortality showed a low rate of 4.38% (95% CI: 1.44-7.32%). These findings suggest that while NEL is associated with promising safety outcomes and low VP shunt dependency, the variability found underscores the need for standardization and further research.

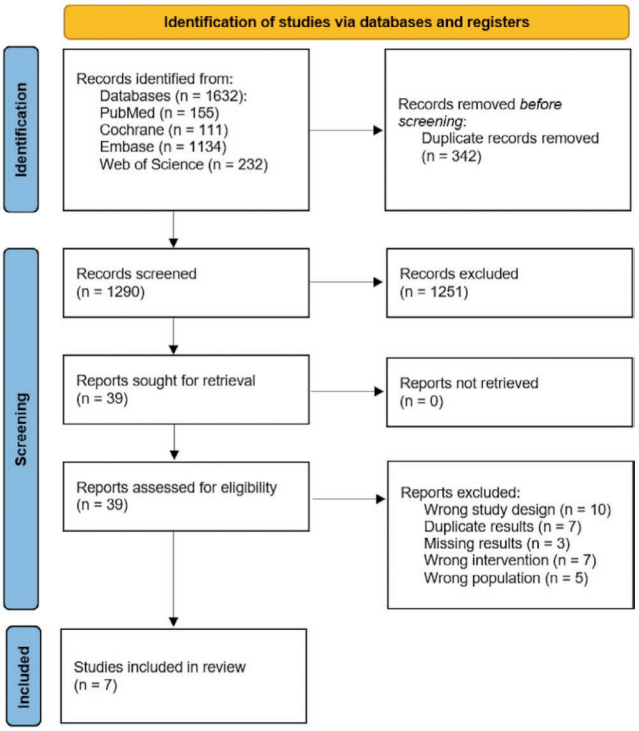

FIGURE 1 Forest plots of results.

Conclusion: This meta-analysis of NEL for neonatal PHH found low shunt dependency rates, moderate infection rates, and low mortality. Significant variability was observed across studies. Further research, including well-designed randomized controlled trials, is needed to determine the true effectiveness and safety of NEL compared to traditional treatments.
Disclosure: Nothing to disclose.

EPR-142 | Institutional cohort characteristics of patients with AVMs

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Neurology Department. Diomid Gherman Institute of Neurology and Neurosurgery. Moldova, Chisinau.

Background and aims: Arteriovenous malformations (AVM) can develop within the brain or spine, with hemorrhage representing their most significant potential risk.
Methods: a retrospective evaluation of electronic medical records was conducted at the Diomid Gherman Institute of Neurology and Neurosurgery, from 2017 to 2024. Data were extracted using ICD-10 codes, followed by manual review.
Results: The cohort included 76 patients, with a mean age of 43.7 ± 14.56 years; 51.3% were male. The most common clinical manifestations were headache (89.7%), neurological deficits (48.6%), convulsive seizures (35.5%), general weakness (34.2%), consciousness disturbances (32.8%), vertigo (32.8%), speech disorders (25%), visual disturbances (14.4%), cranial nerve palsies (13.1%), dizziness and nausea (12%), cerebellar syndrome (11.8%), and disease-related mortality (5.2%). Of the AVMs, 95.5% were cerebral and 4.5% were spinal. Diagnostic methods utilized included digital subtraction angiography (91.2%), computed tomography angiography (75%), cerebral/spinal MRI (57.3%), and plain computed tomography (42.6%). Complications were 39.47% - hemorrhagic stroke and 4.11% ischemic stroke. Surgical approaches were tailored individually, with a mean of 1.76 ± 1.48 interventions per patient (range: 0–7). Embolization emerged as the most frequently employed treatment following its implementation at the institution.
Conclusion: This cohort represents the largest series of AVM patients in the country. The clinical characteristics align with international findings, and patients were diagnosed and treated using state-of-the-art techniques. These results underscore the importance of a multidisciplinary approach in managing AVM cases.
Disclosure: Institutional research grant.

Headache 2

EPR-143 | Treatment pattern and reasons for discontinuing preventive treatment in cluster headache. A prospective cohort study

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Danish Headache Center, Department of Neurology, University of Copenhagen, Rigshospitalet-Glostrup, Glostrup, Denmark

Background and aims: Pharmacological prevention of cluster headache aimed to reduce attack frequency and intensity, but its long-term effectiveness and tolerability remain unknown. Despite recent innovations for mi-graine, treatments for cluster headache have seen little progress since the 1990s. We aimed to quantify the discontinuation rates of verapamil and other prevention due to side effects and assess the proportion of verapamil responders who maintain effectiveness at follow-up.
Methods: In total, 596 patients with cluster headache according to the ICHD-criteria completed a semi-structured interview between 2017 and 2023, with 430 being followed up for another interview after a median of 4.6 years (IQR: 2.8).
Results: Of the 457 patients (77%) who have tried prevention, 121 (26%) discontinued due to intolerable side effects. Discontinuation rate for the first-line treatment, Verapamil, was 18%. Proportionally, second-line treatments lithium and topiramate had higher discontinuation rates, with cessation due to tolerability in nearly half of the participants. The odds of discontinuing lithium or topiramate were four times higher than for verapamil ($p < 0.0001$). At follow-up, only 33% were on a current prevention. Of the initial 137 verapamil responders, 76% continued use of verapamil or discontinued due to remission. Only half of these were 50%-responders. 23% had discontinued verapamil due to side effects, with fatigue and dizziness most frequently reported.

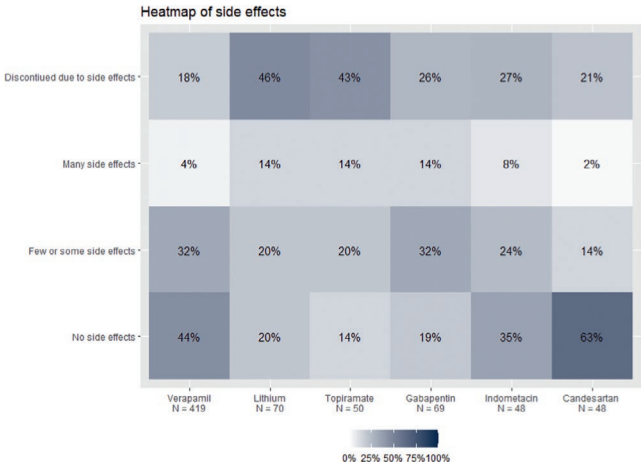


FIGURE 1 Heatmap of discontinuation rates

Conclusion: Effective therapeutic prevention of cluster headache is hindered by intolerability and insufficient efficacy. Verapamil remains effective for most initial responders over time, but our findings under-score the need for more tolerable and effective longterm preventive treatments for cluster headache.
Disclosure: This study was funded by H. Lundbeck A/S but had no influence on design or execution of the study nor drafting of the abstract.

EPR-144 | Impact of atogepant on achieving best possible quality of life among patient global impression of change responders

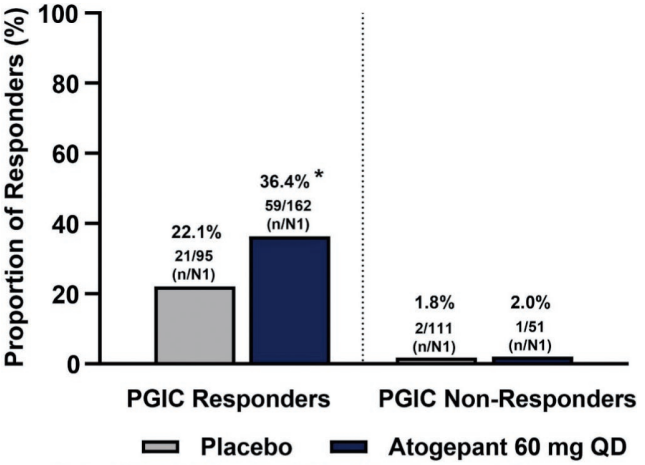
C. Tassorelli[1]; P. Gandhi[2]; M. Duan[2]; K. Carr[2]; K. Umashankar[2]; J. Stokes[2]; G. Forde[3]; T. Bilchik[4]; R. Halker Singh[5]
[1]University of Pavia, Pavia, Italy; [2]AbbVie, North Chicago, IL, USA; [3]North American Partners in Pain Management, North New Hyde Park, NY, USA; [4]Department of Neurology, Yale School of Medicine, New Haven, CT, USA; [5]Mayo Clinic, Phoenix, AZ, USA

Background and aims: We evaluated the impact of atogepant, an oral calcitonin gene-related peptide receptor antagonist used for migraine prevention, on participants reporting best possible

quality of life (QoL) based on Migraine-Specific Quality of Life Questionnaire among responders and non-responders to Patient Global Impression of Change (PGIC).

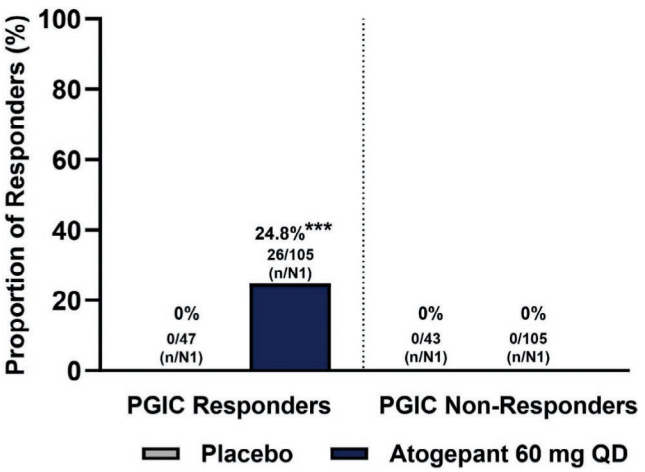
Methods: ADVANCE, ELEVATE, and PROGRESS were phase 3, multicenter, randomized, double-blind, placebo-controlled, 12-week trials that included adults with episodic migraine (EM), EM with prior inadequate responses to 2-4 oral preventive treatments, and chronic migraine (CM), respectively. This post hoc analysis evaluated the proportion of participants who achieved a score of 100 for all 3 MSQv2.1 domain scores at Week 12 based on their PGIC response (responders and non-responders). PGIC is a 7-point single question scale measuring participant impression of change in migraine symptoms since first dose of treatment. MSQv2.1 is a 3-domain questionnaire composed of 14 items designed to assess how migraine limits social and work activities, prevents social and work activities, and what emotions are associated with migraine. A score of 100 indicates the best possible QoL, with less disruption from migraine.

Results: In PGIC responders, a higher proportion of EM participants treated with atogepant 60mg once daily achieved MSQv2.1 scores of 100 in all 3 domains compared with placebo [ADVANCE($p <= .05$); ELEVATE($p <= .001$)(Figure 1,2)], and numerically higher proportion in CM atogepant-treated participants [PROGRESS($p >= .05$)(Figure 3)].



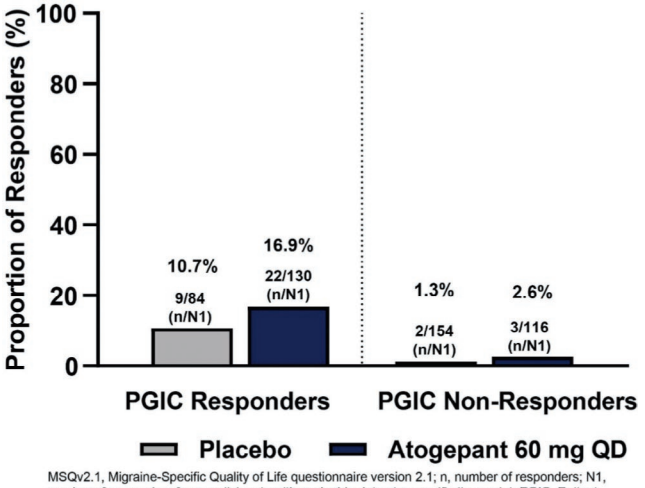
*P value ≤ .05; MSQv2.1, Migraine-Specific Quality of Life questionnaire version 2.1; n, number of responders; N1, number of responders from participants with evaluable data at a specific time point; PGIC, Patient Global Impression of Change; QD, Once Daily. PGIC responders are defined by a response of "much better" or "very much better". PGIC non-responders are defined by a response of "minimally improved", "no change", "minimally worse", "much worse", or "very much worse".

Figure 1: Proportion of Participants Achieving a Score of 100 Based on MSQv2.1 Among PGIC Responder/Non-Responders at Week 12 of ADVANCE Trial



***P value ≤ .001; MSQv2.1, Migraine-Specific Quality of Life questionnaire version 2.1; n, number of responders; N1, number of responders from participants with evaluable data at a specific time point; PGIC, Patient Global Impression of Change; QD, Once Daily. PGIC responders are defined by a response of "much better" or "very much better". PGIC non-responders are defined by a response of "minimally improved", "no change", "minimally worse", "much worse", or "very much worse".

Figure 2: Proportion of Participants Achieving a Score of 100 Based on MSQv2.1 Among PGIC Responder/Non-Responders at Week 12 of ELEVATE Trial



MSQv2.1, Migraine-Specific Quality of Life questionnaire version 2.1; n, number of responders; N1, number of responders from participants with evaluable data at a specific time point; PGIC, Patient Global Impression of Change; QD, Once Daily. PGIC responders are defined by a response of "much better" or "very much better". PGIC non-responders are defined by a response of "minimally improved", "no change", "minimally worse", "much worse", or "very much worse".

Figure 3: Proportion of Participants Achieving a Score of 100 Based on MSQv2.1 Among PGIC Responder/Non-Responders at Week 12 of PROGRESS Trial

Conclusion: A greater proportion of atogepant-treated EM and CM participants who are PGIC responders reported best possible QoL with lower disruption from migraine, compared with placebo.

Disclosure: Cristina Tassorelli has participated in advisory boards or has lectured for AbbVie, Dompé, Eli Lilly, Ipsen, Lundbeck, Medscape, Pfizer and Teva. She is principal investigator or collaborator in clinical trials sponsored by AbbVie, Eli Lilly, Ipsen, Lundbeck, Pfizer and Teva. She has received research grants from the European Commission, the Italian Ministry of Health, the Italian Ministry of University, the Migraine Research Foundation, and the Italian Multiple Sclerosis Foundation. Grace Forde has received personal

compensation from AbbVie. Rashmi Halker Singh has served as a consultant for AbbVie, Impel, Pfizer, Supernus, and Teva. She has provided editorial services for Current Neurology and Neuroscience Reports, Headache, and Medscape, and has received grants for research support from Amgen, Eli Lilly, and Gore Pharmaceuticals. Tanya Bilchik has participated in an advisory board for AbbVie. She is a clinical trial investigator for AbbVie. PG, KC, MD, KU, and JS are AbbVie employees and may hold AbbVie stock.

EPR-145 | BIOmarkers of MIGraine response to erenumAb (BIOMIGA): Preliminary assessment of clinical and biomolecular markers

D. Martinelli[1]; E. Caronna[2]; H. Basedau[3]; M. Pocora[4]; E. Ballante[1]; R. Greco[1]; V. Gallardo López[2]; L. Asskour[2]; E. Giné Ciprés[2]; A. Alpuente[2]; M. Torres-ferrus[2]; A. Zanaboni[1]; J. Mehnert[3]; G. Castellazzi[1]; A. May[3]; P. Pozo-Rosich[2]; C. Tasssorelli[4]

[1]1IRCCS C. Mondino Foundation, Pavia, Italy; [2]Headache and Neurological Pain Research Group, Vall d'Hebron Research Institute, Department of Neuroscience, Universitat Autònoma de Barcelona, Barcelona, Spain; Neurology Department, Hospital Universitari Vall d'Hebron, Barcelona, Spain; [3]University Medical Center Hamburg-Eppendorf,Institute of Systems Neuroscience, Hamburg, Germany; [4]IRCCS C. Mondino Foundation, Pavia, Italy; University of Pavia, Brain and Behavioral Science Department, Pavia, Italy

Background and aims: The BIOMIGA project aimed to identify multimodal biomarkers predicting response to erenumab an anti-CGRP monoclonal antibody in subjects with migraine. Here we present the preliminary analysis of the clinical and biomolecular data of the BIOMIGA population.

Methods: After preregistration (clinicaltrials: NCT04503083) data were collected in three European headache centers (Italy, Spain, Germany). Participants were clinically phenotyped at baseline. Plasma levels and gene expression in peripheral blood mononuclear cells (PBMCs) were assessed for α-CGRP, IL-1β, and TNF-α levels and relative at baseline and after a 3-month course of treatment with erenumab. Subjects were defined as responders if they achieved a ≥50% reduction in monthly headache/days(MHD) at month 3.

Results: Of the 164 participants enrolled, 137 (83.5%) were female, median age 42 years, 38% had a diagnosis of chronic migraine (CM), and 62% of highly frequent episodic migraine (HFEM). The median MHD at baseline was 13 [8-25 95% non-parametric C.I.]. At month 3, 47.5% of subjects qualified as "responders". CM was more prevalent among non-responders ($p=0.024$) and responders generally had fewer baseline MHDs. At baseline, responders had higher α-CGRP plasma levels (433 vs. 361 pg/ml; $p=0.017$), especially CM subjects ($p=0.039$). IL1β expression was higher in responders ($p=0.033$), notably in EM subjects ($p=0.029$). At month 3, CM non-responders exhibited a persistent higher CGRP expression in PBMCs ($p=0.018$) compared to responders.

Conclusion: Clinical and molecular profiles could become treatment response biomarkers. Elevated baseline plasma CGRP and IL-1β expression may help identify patients more likely to benefit from erenumab. Funding: This study was funded by ERANet Neuron.

Disclosure: DM declares honoraria from Lundbeck and AbbVie HB declares honoraria from Novartis, Teva, Lundbeck and Eli Lilly P.P.-R. declares honoraria from AbbVie, Amgen, Dr Reddy's, Eli Lilly, Lundbeck, Medscape, Novartis, Organon, Pfizer and Teva Pharmaceuticals. Her research group has received research grants from AbbVie, AGAUR, EraNet Neuron, FEDER RIS3CAT, Instituto Investigación Carlos III, MICINN, Novartis, and Teva Pharmaceuticals, and has received funding for clinical trials from AbbVie, Amgen, Biohaven, Eli Lilly, Lundbeck, Novartis, Pfizer and Teva Pharmaceuticals. She is the Honorary Secretary of the International Headache Society, is on the editorial board of Revista de Neurologia, is an associate editor for Cephalalgia, Headache, Neurologia, Frontiers of Neurology, and is an advisor of the Scientific Committee of the Editorial Board of The Journal of Headache and Pain. CT has received, in the last 3 years, personal fees for the participation in advisory boards or for speaking at sponsored symposia from AbbVie, Eli Lilly, Ipsen, Lundbeck, Medscape, Pfizer and Teva. Her research group has received research grants from AbbVie, EraNet Neuron, Migraine Research Foundation and competitive grant from the Italian Ministry of Health. Her institution has received payments for clinical trials from AbbVie, Biohaven, Eli Lilly, Ipsen, Lundbeck, Pfizer and Teva. She is past-President of the International Headache Society, Associate Editor of Cephalalgia.

EPR-146 | Patterns of referral to a headache unit: A gender perspective

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Background and aims: No major differences have been described regarding levels of care based on gender in migraine. Despite this, it has been proposed that women are more likely than men to receive treatment for migraine. We aimed to analyze differences regarding referral to a headache unit from a gender perspective.

Methods: In January 2008, an outpatient headache unit was set up in a tertiary hospital. Patients were referred mainly from general practitioners (GP) and, also, from general neurologists and other specialties. All patients were prospectively registered. Variables gathered in each patient were diagnosis, referral source, age at inclusion, time from onset of headache, gender, and previous therapies.

Results: In January 2025, 9940 patients had been included in the registry. Among them, 6220 patients (4956, 79.7% female) with migraine. Age at first consultation (39.93 ± 15.02 vs. 37.07 ± 15.52 years, p:0.004) and latency in years from onset of migraine to referral (18.11 ± 14.83 vs. 14.95 ± 14.19, $p < 0.0001$), were higher in female patients. Considering previous therapy, women had previously received more frequently triptans as symptomatic therapy (28.6% vs. 21.5%, $p < 0.001$) and at least one preventive (39.5% vs. 31.8%, $p < 0.001$) When considering only patients referred from GP, age at first consultation

(39.32 ± 15.06 vs. 36.02 ± 15.28 years, $p < 0.001$) and latency from onset (17.73 ± 14.82 vs. 13.73 ± 13.28 years, $p < 0.0001$), were also higher among women, and they also previously received more frequently triptans (29.4% vs. 21.6%, $p < 0.001$) and preventive therapy (34.7% vs. 25.7%, $p < 0.001$).

Conclusion: Regardless of the referral source, women are referred to a headache unit later but having received more treatment.

Disclosure: Nothing to disclose.

EPR-147 | Optimization and validation of a new score in diagnosing spontaneous intracranial hypotension

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Xuanwu Hospital, Capital Medical University, Beijing, China

Background and aims: Diagnosis of spontaneous intracranial hypotension (SIH) relies on detecting cerebrospinal fluid (CSF) leak by myelography and opening pressure by lumbar puncture. However, these intrusive examinations limit the early diagnosis. We developed a new scoring system using magnetic resonance imaging (MRI) based on the Bern score to assist in diagnosing SIH.

Methods: This study was conducted from November 2018 to October 2022. SIH patients were diagnosed by ICHD-3 and with CSF leak detected by myelography. Cerebral venous disease (CVD) patients and healthy controls were also included for differentiation. Six signs from the Bern score were evaluated. The new scoring system was developed from the items of the Bern score using binary logistic regression analysis. Its likelihood of the diagnosis was compared to that of the Bern score and the restricted Bern score.

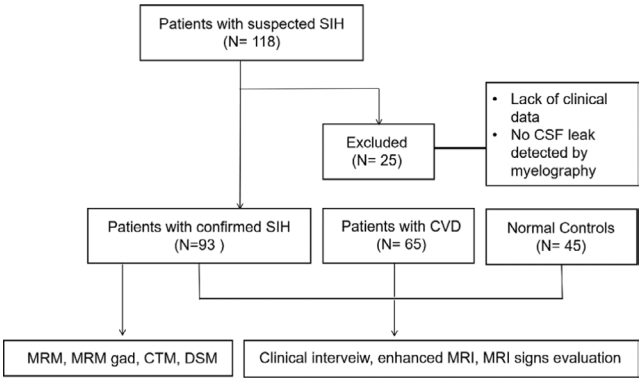

FIGURE 1 Study flowchart of the patient inclusion and clinical evaluation

Results: A total of 93 SIH patients, 65 CVD patients and 45 healthy controls were studied. Three qualitative signs were selected. Pachymeningeal enhancement and subdural fluid were weighted major (2 points each), and venous sinus distention was weighted minor (1 point). The cut-off value was 0.5 on a scale of 5 points. The new score showed better discriminatory value compared to the Bern score and restricted Bern score by the McNemar test ($p < 0.001$), sensitivity (93.5%), specificity(96.4%), and AUC(0.97). It also showed consistent diagnostic value as disease duration varied.

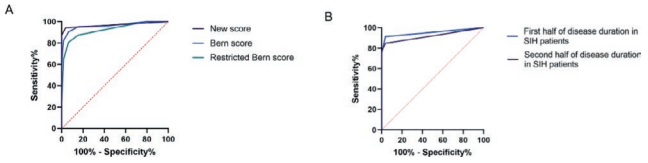

FIGURE 2 Receiver operator characteristic (ROC) curve of the Bern score, restricted Bern score, the new score and the new score in different disease duration

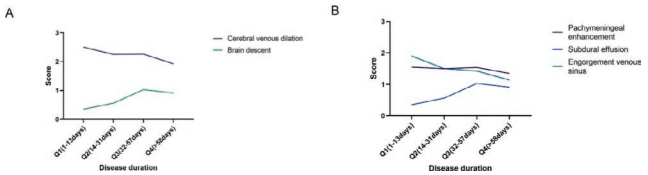

FIGURE 3 Time-dependent variation of MRI findings

Conclusion: The new MRI-based scoring system effectively predicts SIH diagnosis using qualitative signs, making it more practical for clinical use and facilitating earlier identification and diagnosis of SIH.

Disclosure: Nothing to disclose.

EPR-148 | Inhibiting PAC1 receptor internalization and ERK activation may reduce hyperalgesia in a chronic migraine model

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Background and aims: Pituitary adenylate cyclase-activating polypeptide (PACAP) and its PAC1 receptor are implicated in migraine, but their exact role in migraine pathogenesis remains unclear.

Methods: A chronic migraine (CM) rat model was induced by repeated nitroglycerin (NTG) injections. Mechanical and thermal pain thresholds were assessed using von Frey filaments and the hot plate test. c-Fos, CGRP, PACAP, PAC1, PKA, and phosphorylated ERK levels were analyzed via western blot and immunofluorescence. PAC1 receptor internalization was visualized by fluorescence and confocal microscopy.

Results: NTG or PACAP administration increased c-Fos and CGRP expression. Pitstop2 significantly reduced hyperalgesia in CM rats, whereas PACAP6-38 had no effect. Pitstop2 blocked PAC1 receptor internalization and prevented PKA and ERK pathway activation, while PACAP6-38 did not.

Conclusion: Inhibiting PAC1 receptor internalization alleviates allodynia in CM rats by suppressing ERK signaling. Modulating receptor internalization offers a novel approach for understanding PACAP signaling in the trigeminal vascular system and migraine pathogenesis.

Disclosure: Nothing to disclose.

EPR-149 | Neurovascular demand-supply mismatch of visual network underpins aura phenomenon ignition in patients with migraine

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Background and aims: Although neuroimaging investigations have demonstrated that "hyperresponsive" and "hyperconnected" visual cortices may represent the functional substrate of cortical spreading depolarization in patients with migraine with aura (MWA), the mechanisms underpinning the brain "tendency" to ignite the aura phenomenon are still matter of debate. Since triggers able to induce aura increase brain increase energy demand, a vascular supply unable to satisfy the increased energy requirement could be hypothesized.

Methods: We recruited 23 patients with MWA, 25 patients with migraine without aura (MWoA) and 20 healthy controls (HC). All patients and HC underwent a 3-Tesla MRI in order to obtain both cerebral blood flow and local functional connectivity maps. Finally, regional neurovascular coupling was estimated from the correlation coefficient between ReHo map and cerebral blood flow maps.

Results: A significantly higher regional cerebral blood flow across the visual cortex of both hemispheres was detected in MWA patients compared to patients with MWoA. Concomitantly, a reduced neurovascular coupling in the primary visual cortex parcel of the visual network was observed in the left hemisphere of MWA patients, compared to patients with MWoA and HC.

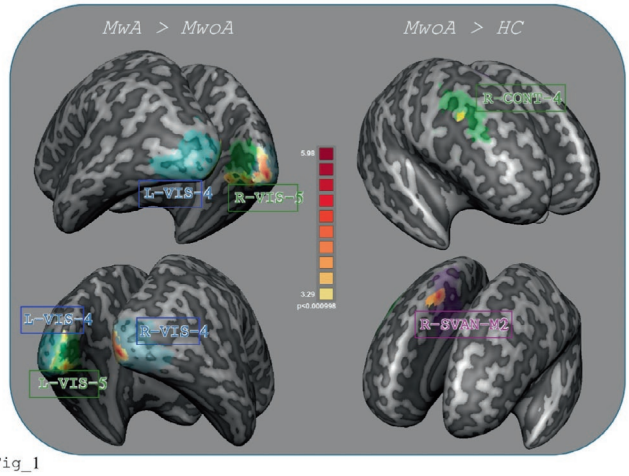

Fig_1

FIGURE 1 Significant differences in voxel-based CBF maps ($p < 0.05$ – TFCE corrected) between MwA and MwoA patients (left) and between MwoA patients and HCs (right).

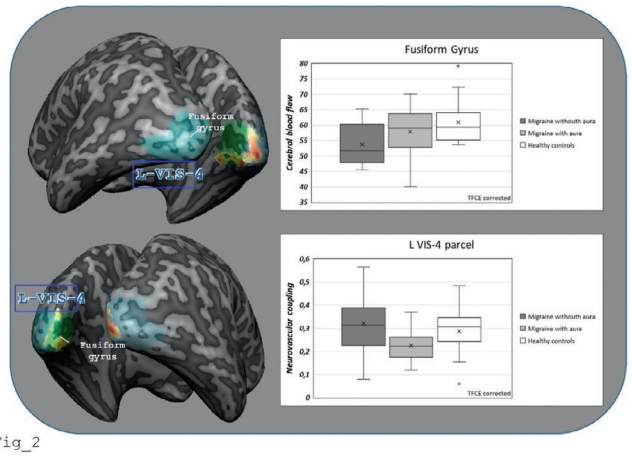

Fig_2

FIGURE 2 Significant differences in visual areas CBF maps and VIS-4 parcel neurovascular-coupling according to Schaefer atlas (ref. 28) (TFCE corrected) showed on inflated brains and by box-plots in patients with MwA, patients with MwoA and HC.

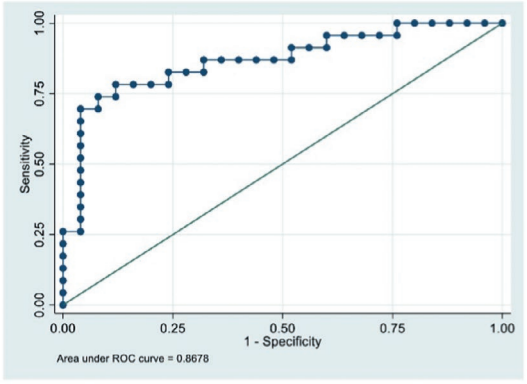

Fig_3

FIGURE 3 ROC curve analysis of logistic regression model considering the rCBF of primary and secondary right visual cortices and neurovascular-coupling of VIS-4 parcel from Schaefer atlas (ref. 28).

Conclusion: Visual cortex neurovascular "decoupling" might represent the "link" between trigger exposure and aura phenomenon ignition. While vascular oversupply may compensate neurovascular demand-supply at rest, it becomes inadequate in case of increased energy demand (as in response to aura triggers), paving the way to the aura phenomenon ignition in MWA. Whether preventive treatments may restore energy demands and cerebral blood flow trade-off within the visual network should be further investigated.

Disclosure: Nothing to disclose.

EPR-150 | Identifying comorbidity profiles in migraine patients: results from the REFINE study

S. Avaltroni[1]; R. Ornello[1]; V. Caponnetto[2]; A. Onofri[1]; C. Rosignoli[1]; M. Braschinsky[3]; O. Šved[3]; R. Gil-Gouveia[4]; C. Lampl[5]; J. Paungarttner[5]; P. Martelletti[6]; W. Wells-Gatnik[6]; I. Martins[7]; D. Mitsikostas[8]; L. Apostolakopoulou[8]; G. Nabaei[9]; A. Ozge[10]; D. Narin[10]; P. Pozo-Rosich[11]; A. Muñoz-Vendrell[11]; M. Prudenzano[12]; M. Gentile[12]; K. Ryliskiene[13]; J. Vainauskiene[13]; S. Sacco[1]

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Background and aims: Migraine is a leading cause of disability among young individuals worldwide. While preventive treatments improve outcomes for many, resistant and refractory migraine cases often fail to respond. This study aimed to identify specific comorbidity patterns in patients with resistant and refractory migraine.

Methods: The REFINE study included 689 patients classified as resistant, refractory, or non-resistant/non-refractory migraine according to European Headache Federation criteria. A Latent Class Analysis (LCA) was conducted using eight comorbidities associated with migraine—obesity, autoimmune/rheumatological disorders, psychiatric diseases, cardiovascular disorders, gastrointestinal conditions, chronic pain, allergic/respiratory conditions, and musculoskeletal disorders—and the EHF diagnosis as variables.

Results: The three-class model provided the best fit (BIC = 6065.292). Class 1 comprised 30.99% of patients, with the highest prevalence of resistant (22.8%, vs. 13.9% in Class 2 and 14.6% in Class 3) and refractory migraine (33.2%, vs. 5.2% in Class 2 and 4.1% in Class 3). Class 1 also showed the highest prevalence of chronic pain (77.8%), psychiatric disorders (85.9%), and allergic/respiratory conditions (32.2%). Obesity was present in 100% of Class 1 and Class 3 but absent in Class 2. Autoimmune/rheumatological disorders affected 32.2% of Class 1 patients. Cardiovascular (27.9%) and gastrointestinal conditions (5.7%) were less frequent in Class 1.

Conclusion: LCA identified a class with a higher prevalence of obesity, psychiatric disorders, and chronic pain, significantly associated with resistant and refractory migraine, suggesting the need for tailored management strategies.

Disclosure: Nothing to disclose.

EPR-151 | Glymphatic dysfunction in migraine mice model

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Background and aims: The glymphatic system is crucial for waste removal in the central nervous system, facilitated by aquaporin-4 (AQP4) at astrocytic ends. While it is involved in several neurological disorders, the link between the glymphatic system and migraine remains unclear.

Methods: Using a nitroglycerin-induced migraine model in C57BL/6 mice, we examined glymphatic function by assessing cerebrospinal fluid (CSF) tracer influx. AQP4 expression and polarization were also measured. To investigate the role of glymphatic dysfunction, mice were treated with TGN-020, an AQP4 blocker.

Results: In the migraine model, glymphatic CSF influx was reduced, and AQP4 expression and polarization were impaired, indicating glymphatic dysfunction. Further inhibition of glymphatic function with TGN-020 worsened migraine-related pathology in mice.

Conclusion: The findings suggest that glymphatic dysfunction may exacerbate migraine pathology. These results highlight the potential role of the glymphatic system in migraine, offering new targets for prevention and treatment.

Disclosure: Nothing to disclose.

Movement disorders 2

EPR-152 | Characteristics of patients with Parkinson´s disease treated with a device-aided therapy. A comparative analysis

D. Santos García[1]; Á. Solleiro[1]; G. González-Ortega[2]; P. Mir[3]; N. López-Ariztegui[4]; R. García-Ramos[5]; I. Legarda[6]; A. Planas-Ballvé[7]; D. Alonso-Modino[8]; P. Sánchez Alonso[9]; I. Cabo[10]; M. Blázquez Estrada[11]; f. Escamilla[12]; E. Cubo[13]; J. Hernández Vara[14]; Á. Sánchez Ferro[15]; S. DATs-PD GETM Spanish Registry[16]

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Background and aims: New device-aided therapies (DATs) have emerged to treat people with Parkinson's disease (PwP). Our aim was to know which DATs were indicated by the neurologist and to compare the characteristics of the patients treated in Spain under real clinical practice in 2024.

Methods: Data collected in the DATs-PD GETM Spanish Registry were used (REDCap). This is a descriptive, observational, prospective, multicenter, clinical registry with progressive inclusion of PwP treated with a DAT in daily clinical practice conditions in more than 40 centers from Spain for 10 years. For this proposal, only data from visits V1 (indication of DAT) and V2 (initiation of DAT) were analyzed but no follow-up data. All patients with information on DAT received until 31/DEC/2024 were included.

Results: A total of 313 PD patients (66.7 ± 9.6 years old at V2; 61.7% males) were treated with a DAT. The most frequent was subcutaneous foslevodopa/foscarbidopa (fLD/fCD) (47%) followed by deep brain stimulation (DBS) (20.1%) and continuous subcutaneous apomorphine infusion (CSAI) (19.8%) (Figure 1A). Up to 23.6% had received at least one previous DAT (Figure 1B) and 47% an on-demand therapy (Figure 1C). Differences in age, time with fluctuations and other aspects (motor status, quality of life, activities of daily living, etc.) were observed between different DAT groups (Table 1 and Figure 2).

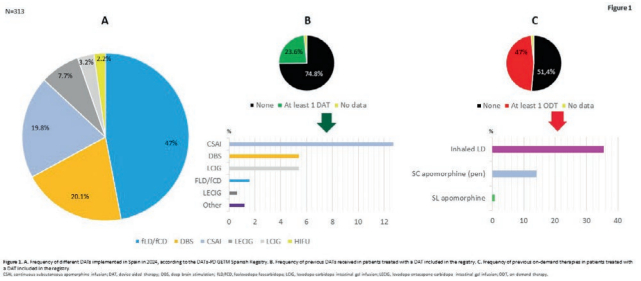

Figure 1. A. Frequency of different DATs implemented in Spain in 2024, according to the DATs-PD GETM Spanish Registry. B. Frequency of previous DATs received in patients treated with a DAT included in the registry. C. Frequency of previous on-demand therapy in patients treated with a DaT included in theregistry.

FIGURE 1

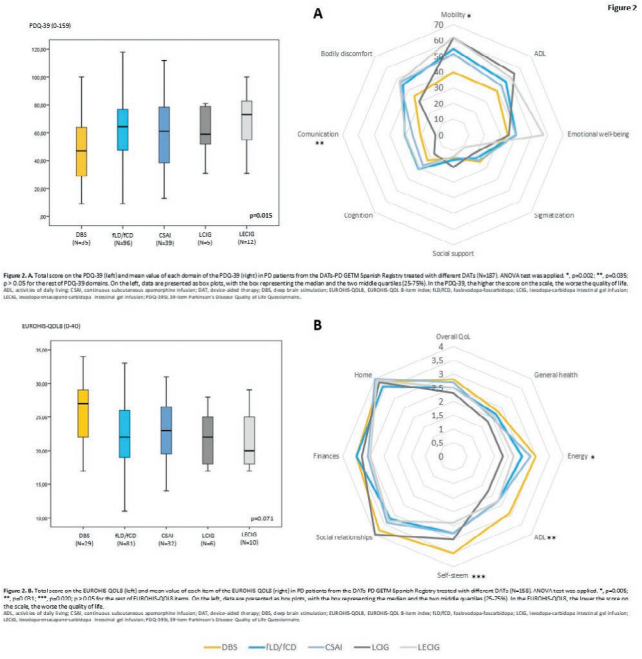

Figure 2. A. Total score on the PDQ-39 (left) and mean value of each domain of the PDQ-39 (right) in PD patients from the DATs-PD GETM Spanish Registry treated with different DATs (N=187). ANOVA test was applied. *, p=0.002; **, p=0.035; p > 0.05 for the rest of PDQ-39 domains. On the left, data are presented as box plots, with the box representing the median and the two middle quartiles (25-75%). In the PDQ-39, the higher the score on the scale, the worse the quality of life. ADL, activities of daily living; CSAI, continuous subcutaneous apomorphine infusion; DAT, device-aided therapy; DBS, deep brain stimulation; EUROHIS-QOL8, EUROHIS- QOL 8-item index; fLD/fCD, foslevodopa-fosacarbidopa; LCIG, levodopa-carbidopa intestinal gel infusion; LECIG, levodopa-entacapone-carbidopa intestinal gel infusion; PDQ-39SI, 39-item Parkinson's Disease Quality of Life Questionnaire.

B. Total score on the EUROHIS QOL8 (left) and mean value of each item of the EUROHIS QOL8 (right) in PD patients from the DATs PD GETM Spanish Registry treated with different DATs (N=358). ANOVA test was applied. *, p=0.005; **, p=0.051; ***, p=0.035; p > 0.05 for the rest of EUROHIS/QOL8 items. On the left, data are presented as box plots, with the box representing the median and the two middle quartiles (25-75%). In the EUROHIS/QOL8, the lower the score on the scale, the worse the quality of life.

ADL, activities of daily living; CSAI, continuous subcutaneous apomorphine infusion; DAT, device-aided therapy; DBS, deep brain stimulation; EUROHIS-QOL8, EUROHIS- QOL 8-item index; fLD/fCD, foslevodopa-fosacarbidopa; LCIG, levodopa-carbidopa intestinal gel infusion; LECIG, levodopa-entacapone-carbidopa intestinal gel infusion; PDQ-39SI, 39-item Parkinson's Disease Quality of Life Questionnaire.

FIGURE 2

Characteristics	DBS N=63	fLD/fCD N=147	CSAI N=62	LCIG N=10	LECIG N=24	HIFU N=7	Entire cohort N=313	p
Age at initiation of DAT	60.8 ± 6.6	67.8 ± 9.2	68.7 ± 9.4	65.7 ± 14.2	70 ± 9.3	69.6 ± 9.4	66.7 ± 9.6	<0.0001
Gender (males) (%)	71.4	61.2	53.2	60	61.2	71.4	61.7	0.437
Weight (kg)	78.4 ± 15.6	71.1 ± 14.6	74.9 ± 15.8	74.6 ± 12.9	70.6 ± 8.5	N.A.	73.5 ± 14.7	0.126
BMI	26.4 ± 3.9	26.4 ± 4.2	27.1 ± 4.3	25.9 ± 3.7	24.9 ± 2.5	N.A.	26.4 ± 4.1	0.433
Principal caregiver (%):	29	61	59.7	100	47.8	0	53.2	<0.0001
Comorbidities (%):								
- Arterial hypertension	25.4	38.4	49.2	30	43.5	42.9	38.1	0.150
- Diabetes mellitus	9.7	11.1	18	10	17.4	0	12.4	0.549
- Dyslipemia	22.2	31.5	36.1	20	29.2	28.6	29.9	0.618
- Atrial fibrillation/arritmia	6.3	7.5	9.8	0	4.3	0	7.1	0.799
- Ischemic cardiopathy	0	4.1	6.6	10	0	8.7	4.2	0.133
- Lung disease	4.8	11.6	4.9	0	4.3	14.3	8	0.320
- Polineuropathy	0	2.7	0	0	4.3	0	1.6	0.471
Treatments (%):								
- Antihypertensive	25.8	34.2	45	20	39.1	42.9	34.7	0.274
- Antidiabetics	9.5	9.7	13.6	10	17.4	0	10.7	0.269
- Hypolipidemic agents	15.9	26	31.7	10	33.3	28.6	25.2	0.750
- Anti- aggregating/coagulants	1.6	16.3	10	10	20.8	28.6	20.8	0.030
- Antidepressant	30.2	34.7	25.8	20	45.8	14.3	31.9	0.362
- Benzodiazepine	28.6	39.7	26.7	20	29.6	28.6	36.2	0.004
- Antipsychotic	4.8	12.2	4.8	20	25	0	10.2	0.032
- Anti-dementia	0	10.2	4.8	0	12.5	0	6.7	0.068
Disease duration (years)	11.9 ± 4.9	14 ± 5.3	10.9 ± 5	10.8 ± 3.9	13.6 ± 3.3	12.7 ± 4.7	12.9 ± 7.4	0.107
Motor phenotype (%):								0.004
- Tremor dominant	27.7	26.1	29.6	33.3	35	100	29.8	
- Indeterminate	40.4	38.1	22.2	44.5	45	0	35.1	
- PIGD	31.9	35.8	48.2	22.2	20	0	35.1	
Previous psychosis (%)	1.6	15.1	3.3	10	21.7	0	10	0.006
Cognitive impairment (%):								0.341
- MCI (%)	20.6	28	21.7	50	34.8	0	24.9	
- Dementia (%)	0	3.4	3.3	0	4.3	0	2.8	
Time with fluctuations (years)	4.7 ± 2.7	5.7 ± 3.8	4.6 ± 2.6	4 ± 2.1	7.1 ± 3.1	6.3 ± 3.9	5.3 ± 3.3	0.015
Daily OFF time (hours)	4.3 ± 2	4.9 ± 2.1	4.7 ± 1.9	5 ± 1.8	7.8 ± 3.3	6 ± 3.7	4.9 ± 2.4	<0.0001
H&Y – OFF	2 [2,3]	3 [2,4]	3 [2,3]	3.5 [3,4]	3 [3,4]	2 [2,3]	3 [2,4]	<0.0001
H&Y – ON	2 [1,2]	2 [2,2]	2 [2,2]	2 [2,2]	2 [2,2]	2 [1,2]	2 [2,2]	0.030
UPDRS – III – OFF	34.4 ± 9.8	37.7 ± 10.9	37.3 ± 11.2	45.9 ± 12.2	44 ± 15.7	46.3 ± 11.8	37.3 ± 11.4	0.015
UPDRS – III – ON	14.7 ± 8	19.1 ± 10.8	21.9 ± 10.6	25.7 ± 10.1	28.1 ± 12.3	26 ± 10.5	19.4 ± 10.9	<0.0001
NMS score[1]	13.6 ± 5.5	19.4 ± 6.7	15.2 ± 7	13 ± 5.7	16.4 ± 4.8	N.A.	17.3 ± 6.8	0.016
Treatment for PD (%):	68.9	64.9	79.7	40	47.8	57.1	66.3	0.036
- MAO-B inhibitor	66.7	47.8	69.5	50	30.4	71.4	55.3	0.003
- Dopamine agonist	61.3	59	54.2	30	47.8	14.3	53.1	0.120
- COMT inhibitor	24.6	32.8	20.3	0	17.4	0	17.4	0.045
- Amantadine	1,115.3 ± 517.4	1,236.3 ± 585.2	1,273.6 ± 500.3	1,092.3 ± 222.9	1,165.4 ± 760.1	701.7 ± 413.6	1,196.8 ± 561.1	0.137
LEDD (mg)	48.3 ± 22.7	62.9 ± 21.7	59.2 ± 24.6	60.4 ± 20.7	68.4 ± 20.6	N.A.	59.7 ± 22.9	0.015
PDQ-39*	25.6 ± 4.3	22.7 ± 5.2	23.2 ± 4.8	22 ± 4.6	21.7 ± 4.2	N.A.	23.3 ± 4.9	0.071
EUROHIS-QOL8**	72 ± 17.8	57 ± 20.4	60.4 ± 22.9	48.9 ± 19	50.6 ± 18.4	N.A.	60.2 ± 21.2	<0.0001
ADLS – OFF	89 ± 12.5	80.8 ± 14.2	84.3 ± 13.8	71.1 ± 17.6	79.3 ± 12.2	N.A.	82.9 ± 14.2	0.001
ADLS – ON								

The results represent percentages, mean ± SD or median [p25, p75]. Chi-squared and ANOVA test were applied. N. A., not available (not collected). [1], information about 20 non motor symptoms (visual hallucinations; psychosis; impulse control disorder; depression; anxiety; apathy; REM behavior disorder; restless legs; falling asleep insomnia; maintenance insomnia; nicturia; other urinary symptoms; diurnal somnolence; symptomatic orthostatic hypotension; constipation; dysphagia; sialorrhea; fatigue; pain; sweating) was collected with a score for each one from 0 to 4 (0, no symptom; 1, slight; 2, moderate; 3, severe; 4, very severe) and a total score from 0 (20 x 0, minimum) to 80 (20 x 4; maximum). The information was not collected for all patients. The lowest sample size was N=97 for the NMS score, N=196 for weight and BMI (62.6%), N=187 for the PDQ-39 (59.7%), and N=158 for the EUROHIS-QOL8 (50.7%). For the rest majority of variables the data was collected in more than 90% of the patients.

ADL, Schwab and England Activities of Daily Living Scale; BMI, body mass index; COMT, catechol-O-methyltransferase; CSAI, continuous subcutaneous apomorphine infusion; DAT, device-aided therapy; DBS, deep brain stimulation; EUROHIS-QOL8, EUROHIS-QOL 8-item index; fLD/fCD, foslevodopa-fosacarbidopa; H&Y, Hoehn & Yahr; LCIG, levodopa-carbidopa intestinal gel infusion; LECIG, levodopa-entacapone-carbidopa intestinal gel infusion; LEDD, levodopa equivalent daily dose; MAO-B, type B monoamine oxidase; MCI, mild cognitive impairment; NMS, nonmotor symtoms; PDQ-39SI, 39-item Parkinson's Disease Quality of Life Questionnaire; PIGD, postural instability gait difficulty; UPDRS, Unified Parkinson's Disease Rating Scale.

Table 1. Sociodemographic and general and clinical PD-related variables of patients treated with a DAT.

Conclusion: Subcutaneous therapies and DBS were the most frequent DATs (86.9%) implemented in Spain in 2024. Patients treated with DBS were younger and had less advanced disease, whereas those who received LECIG were the most affected.

Disclosure: The authors report no conflict of interest.

EPR-153 | Impairment of eye movements in early-stage Parkinson's disease patients

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Background and aims: One of the most prevalent motor symptoms in Parkinson's disease (PD) is eye movement impairment, presenting in 75% of PD patients, which have fragmented and hypometric smooth pursuit movements with prolonged latency, and slow and hypometric saccades with impaired precision. We aimed to investigate differences in smooth pursuit, memory saccades and reading between patients with early-stage PD and healthy controls.

Methods: We conducted a cross-sectional study with idiopathic PD patients in early stage of PD (Hoehn and Yahr stage 0, 1 and

2) and healthy controls. The impairment of smooth pursuit, saccades, antisaccades, and memory-guided saccades was evaluated with eye-tracker analysis using a battery of tests.

Results: Forty two subjects with early-stage idiopathic PD and 50 healthy controls participated in the study. There were no statistically significant differences in age, gender, years of education, or cognition between the groups. Average duration of disease in PD patients was 4 (2-7) years. Early-stage PD patients showed impairment in velocity, phase, and range of motion of smooth pursuit eye movements (Table 1), as well as impaired precision and recollection performing visually-guided memory saccades (Table 2). There is also a reading dysfunction, with slower reading speed and longer duration of eye fixations (Table 3).

TABLE 1 Comparison of smooth pursuit parameters in all observed cycles between patients with early-stage PD and healthy controls.

	Cycle duration	Axis	Early stage PD	Healthy controls	P*
Accuracy of movement (MSE)	1600ms	Horizontal	0.0088	0.0067	0,093
		Vertical	0.0089	0.0065	0,046
	2400ms	Horizontal	0.0042	0.0034	0,421
		Vertical	0.0047	0.0038	0,175
	4800ms	Horizontal	0.0016	0.0009	0,481
		Vertical	0.0019	0.0018	0,395
Velocity of movement (MSE)	1600ms	Horizontal	0.0000160	0.0000006	<0,001
		Vertical	0.0000163	0.0000007	<0,001
	2400ms	Horizontal	0.0000116	0.0000004	<0,001
		Vertical	0.0000119	0.0000005	<0,001
	4800ms	Horizontal	0.0000063	0.0000003	<0,001
		Vertical	0.0000044	0.0000003	<0,001
Phase of movement (MSE)	1600ms	Horizontal	0.0091	0.0063	<0,001
		Vertical	0.0079	0.0053	0,002
	2400ms	Horizontal	0.0036	0.0027	0,002
		Vertical	0.0035	0.0018	0,001
	4800ms	Horizontal	0.0003	0.0002	0,007
		Vertical	0.0009	0.0004	0,046
Number of fixations (N)	1600ms	Horizontal	3	2	0,113
		Vertical	6	5	0,437
	2400ms	Horizontal	3	3	0,891
		Vertical	5	6.5	0,043
	4800ms	Horizontal	5	4	0,038
		Vertical	7.2	7.4	0,896†
Range of movement	1600ms	Horizontal	0.0247	0.0619	0,006
		Vertical	0.0344	0.0830	0,013
	2400ms	Horizontal	0.0098	0.0805	<0,001
		Vertical	0.0449	0.1163	0,001
	4800ms	Horizontal	0.0146	0.0371	0,002
		Vertical	0.0276	0.1360	0,004

* Mann-Whitney U test
† Student T-test
t MSE, mean squared error; ms, miliseconds

TABLE 2 Comparison of visually guided memory saccades parameters between patients with early-stage PD and healthy controls.

Corsi test	Early stage PD	Healthy controls	P*
	Median (interquartile range)		
Difference between correct hits forwards and backwards (N)	0 (-1-0)	0 (-2-0)	0,69
Number of correct hits forwards (N)	0 (0-1,25)	2 (0-5)	0,010
Number of correct hits backwards (N)	0 (0-2)	3 (0-5)	0,002
Highest number of correct hits in one trial (N)	0,5 (0-2,25)	4 (0-6)	0,003
Highest level reached in one trial (N)	1,5 (1-3)	3 (0-4)	0,47
Total number of correct hits (N)	1 (1-3)	6 (0-10)	0,003
Highest level reached (N)	1 (0-4)	4.5 (0-7)	0,031

* Mann-Whitney U test

TABLE 3 Comparison of fake reading test parameters between patients with early-stage PD and healthy controls.

Fake reading test	Early stage PD	Healthy controls	P*
	Mean/Median (SD/IQR)		
Percentage of text read before returning back (%)	20,15 (13,84-41,18)	17,20 (9,76-35,95)	0,13
Standard deviation of eye fixations while reading backwards (ms)	18,38 (15,26-20,24)	16,05 (1,77-19,08)	0,016
Percentage of read text before stopping –reading speed (%)	7,47 (6,89-7,89)	7,96 (6,98-9,17)	0,008
Saccade velocity (m/s)	3,01 (2,71-3,26)	2,90 (2,43-3,33)	0,38
Number of eye fixations in 1s-minimal (N)	2,91 (2,71-3,26)	2,65 (2,43-3,33)	0,08
Number of eye fixations in 1s-maximal (N)	3,12 (2,74-3,44)	3,05 (2,17-3,37)	0,27
Ratio of number of saccades during reading forwards and backwards - minimal	3,16 (0,82)	2,73 (1,01)	0,031†
Ratio of number of saccades during reading forwards and backwards - maximal	3,46 (3-3,99)	3,29 (2,41-4,33)	0,32
Duration of eye fixation (ms)	244,53 (57,41)	202,23 (49,83)	<0,001†
Standard deviation of eye fixations (ms)	144,79 (129,68-185,45)	138,63 (109,06-176,76)	0,29

* Mann-Whitney U test
† Student T-test
t MSE, mean squared error; ms, miliseconds; m/s, meters in second; SD, standard deviation; IQR, interquartile range

Conclusion: Results suggest that impaired smooth pursuit movements, visually-guided reflexive saccades and reading functions are present in early-stage PD, even without other expressed motor symptoms. These findings could potentially contribute to the development of new and non-invasive diagnostic biomarkers in PD.

Disclosure: Nothing to disclose.

EPR-154 | Retinal structural changes in Parkinson's disease (PD): Comparison between GBA1-PD and non-mutated PD

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Background and aims: Retinal thinning has been observed in Parkinson's disease (PD) patients compared to healthy controls, and few studies correlated these changes with disease severity and cognitive impairment although data are still controversial. To date, there are no data about retinal structural changes in GBA1-related PD (GBA1-PD) patients. The aim of the study was to assess differences in retinal thickness between GBA1-PD and non-mutated PD (NM-PD) and to explore correlations between clinical and retinal parameters.
Methods: A consecutive cohort of GBA1-PD patients was matched for age, sex, disease duration, H&Y stage with a cohort of NM-PD patients. All patients underwent a clinical assessment (MDS-UPDRS and MoCA) and optical coherence tomography (OCT) to evaluate retinal nerve fiber layer (RNFL) thickness with three circular scans (diameters: 3.5-,4.1- and 4.7-mm).
Results: A total of 52 PD patients (104 eyes from 26 GBA1-PD and 26 NM-PD) were included. The two groups did not show statistically significant differences in clinical variables. Temporal RNFL thickness was significantly reduced in NM-PD compared to GBA1-PD at 3.5-, 4.1- and 4.7 mm ($p=0.021$, $p=0.006$, $p=0.005$ respectively). In the total PD cohort, the average temporal RNFL thickness (4.1 mm scan) inversely correlated with MDS-UPDRS part I total score ($p=0.04$).
Conclusion: This study highlights a reduced retinal thickness in NM-PD compared to GBA1-PD, showing a greater involvement of papillo-macular bundle in NM-PD than in GBA1-PD. This may suggest differential involvement of retinal cells, potentially related to distinct pathophysiological mechanisms. Interestingly, in the total PD cohort temporal RNFL thickness was inversely correlated with non-motor symptoms burden.
Disclosure: The authors have no conflicts of interest to declare that are relevant to the content of this abstract. Patients included in the study are part of the FIN-RER study.

EPR-155 | Patient-reported outcomes of long-term deutetrabenazine use in the RIM-td open-label extension study European cohort

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Background and aims: Deutetrabenazine is approved by the United States Food and Drug Administration for the treatment of tardive dyskinesia (TD) in adults. This analysis assessed outcomes self-reported by patients treated with deutetrabenazine in a European cohort of the RIM-TD study.
Methods: Patients completing the phase 3 ARM-TD or AIM-TD study could enter RIM-TD, a 3-year, single-arm open-label extension study (NCT02198794), where they received deutetrabenazine for ≤145 weeks. This post hoc subgroup analysis focused on participants from European countries. Assessments included Abnormal Involuntary Movement Scale (AIMS), Patient Global Impression of Change (PGIC), a modified Craniocervical Dystonia Questionnaire (mCDQ-24) scale, and adverse event (AE) and discontinuation rates.
Results: Among the 142 participants enrolled in Europe (Table 1), mean ± SE total deutetrabenazine dose at Week 145 was 39.5 ± 1.13 mg/day. At Week 145, symptom improvement was observed based on reductions in total motor AIMS scores (mean −6.4; items 1–7, total score range 0–28) and on patient-reported awareness of abnormal movements or resulting incapacitation (Table 2). Most patients (56%) scored much/very much improved on the PGIC. At Week 106, improvements in quality of life were observed on the mCDQ-24 scale total score (mean −4.0) and 4 subdomain scores; the largest change was in the stigma subdomain (mean −8.2). AEs and treatment-related AEs were reported for 77.5% and 45.8% of patients, respectively; 66.2% of patients reached Week 145 (Table 3).

Table 1 Baseline characteristics and patient demographics.

	RIM-TD European cohort (N=142)
Patient demographics	
Age, mean (SD) [range], years	58.2 (12.6) [21–81]
Female, n (%)	83 (58)
White, n (%)	142 (100)
Patient clinical characteristics	
Total mCDQ-24 score, mean (SD)	32.1 (19.4)
Total motor AIMS score, mean (SD)	8.3 (3.6)
Disease duration, mean (SD), years	5.1 (4.7)
Dopamine receptor antagonist use, n (%)	100 (70)

Baseline characteristics were recorded at the start of each pivotal study.

Table 2 AIMS, PGIC, and mCDQ-24.

	RIM-TD European cohort (N=142)
AIMS, mean (SE) change from baseline to Week 145	n=94
Total motor AIMS score (items 1–7)	−6.4 (0.54)
Item 9: Incapacitation due to abnormal movements	−1.4 (0.10)
Item 10: Patient's awareness of abnormal movements	−1.5 (0.11)
PGIC at Week 145, n (%)	n=95
Very much improved	21 (22.1)
Much improved	32 (33.7)
Minimally improved	22 (23.2)
Not changed	13 (13.7)
Minimally worse	7 (7.4)
Much worse	0
Very much worse	0
mCDQ-24, mean (SE) change from baseline to Week 106	n=107
Total score (24 items)	−4.0 (1.55)
Stigma (6 items)	−8.2 (2.23)
Emotional (5 items)	0.1 (2.03)
Pain (3 items)	−5.8 (2.21)
Activities of daily living (6 items)	−3.6 (1.84)
Social (4 items)	−2.0 (1.59)

Table 3 AEs and study discontinuation.

	RIM-TD European Cohort (N=142)
Any AE	110 (77.5)
Treatment-related AEs	65 (45.8)
Serious AEs	26 (18.3)
Discontinuation	55 (38.7)
Discontinuation due to	
AE	12 (8.5)
Death	4 (2.8)
Lack of efficacy	3 (2.1)
Lost to follow-up	1 (0.7)
Non-compliance with study drug	2 (1.4)
Withdrawal by subject	32 (22.5)
Study terminated	1 (0.7)

Data are presented as n (%)

Conclusion: Long-term deutetrabenazine treatment was associated with improvements in patient-reported measures of treatment success and was well tolerated in patients with TD treated at European sites.

Disclosure: This study was funded by Teva Branded Pharmaceutical Products R&D, Inc.

EPR-156 | Abstract withdrawn

EPR-157 | Multimodal deep learning approaches to predict motor outcomes in Parkinson's disease patients

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Background and aims: Parkinson's disease (PD) trajectories are highly variable and the identification of prognostic features represents a challenge toward personalized approaches. Multicenter studies collecting data from multiple modalities (imaging, electronic health records – EHRs) allow to investigate the prognostic role of single data types and of their combination. This study investigates the ability of Deep Learning (DL) in predicting motor functions both from single and multimodal information.

Methods: Imaging (DaTSCAN) and EHRs data (including demographic, motor, clinical and pharmacological data) from $n=339$ patients from the Parkinson's Progression Markers Initiative (PPMI) were used to predict motor impairments at three years follow-up assessed through the unified Parkinson's disease rating scale part III (UPDRS <30). Prediction was done using a modified PDNet applied to imaging volumes alone or combined with radiomic features (unimodal), while the multimodal approach combined DaTSCAN with EHRs data. Models' performance was measured through Matthews Correlation Coefficient (MCC) and Balanced Accuracy (Acc) on a 20% holdout PPMI validation set and on an external cohort of $n=64$ PD patients collected for the project NeuroArtP3 (NET-2018-12366666).

Results: DaTSCAN imaging was informative of motor outcomes (Table 1. PPMI Acc=0.67; NeuroArtP3 Acc=0.73). Adding radiomic features improved the accuracy on the PPMI cohort (Acc=0.76) but reduced generalization to the NeuroArtP3 group (Acc=0.59). Multimodal approach increased prediction performance to 0.71 and 0.76 on the PPMI and NeuroArtP3 cohort, respectively.

TABLE 1 Performances of unimodal and multimodal PDNet on the PPMI and NeuroArtP3 validation cohort.

	PPMI		NeuroArtP3	
Model Input	*MCC*	*Balanced Accuracy*	*MCC*	*Balanced Accuracy*
UPDRS	0.201	0.581	0.263	0.672
DaTSCAN	0.334	0.673	0.323	0.727
DaTSCAN + radiomics	**0.459**	**0.76**	0.174	0.59
DaTSCAN + clinical	0.371	0.712	**0.368**	**0.763**

Conclusion: Combining imaging and EHRs with a multimodal approach lead to an improvement in the prognostic accuracy of DL models, which is robust to the generalization to external cohorts.

Disclosure: Nothing to disclose.

EPR-158 | Microstructural MRI and glymphatic flow alterations in patients with isolated REM sleep behavior disorder

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Background and aims: To assess neurological, gait analysis, microstructural MRI, glymphatic flow alterations features in isolated-REM sleep behavior disorder (iRBD) subjects relative to controls; to study the correlations between clinical and MRI features; and to compare sub-groups of iRBD patients.

Methods: Forty-four iRBD subjects and 52 controls underwent motor, non-motor and cognitive assessments, gait analysis and MRI evaluations. Brain microstructural alterations were studied using Tract-Based Spatial Statistic (TBSS) and Gray-matter-Based Spatial Statistics (GBSS). Diffusion-Tensor Image Along the Perivascular Space (DTI-ALPS) index was obtained for the evaluation of glymphatic flow functionality. Cluster analysis was applied to divide iRBD patients in sub-groups. ANOVA models were used to compare clinical, and MRI data. Correlations between clinical and MRI data were assessed.

Results: IRBD subjects showed worse sleep quality, a reduced manual dexterity and spatio-temporal gait parameters alterations relative to controls. iRBD showed microstructural alterations in the gray-matter of frontal and parietal lobes, and in the white-matter of brainstem and frontal lobe. iRBD showed lower DTI-ALPS index relative to controls. Correlation analyses in the iRBD group showed that worse gray matter microstructural alterations correlated with worse performance in the Nine-Hole-Peg-Test, lower peak turning velocity during Timed Up and Go test with a cognitive dual-task and worse sleep quality. Cluster analysis resulted in two clusters, with one showing generally worse clinical, neuropsychological and gait performances together with a worse DTI-ALPS index.

Conclusion: Clinical, gait analysis and MRI data collected longitudinally could be useful in the creation of predictive models for the conversion from iRBD to parkinsonisms.

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EPR-159 | Evaluating beta-sensing for the optimization of deep brain stimulation in Parkinson's disease

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Background and aims: Deep brain stimulation (DBS) is a well-established treatment for advanced Parkinson's disease (PD). We aimed to compare beta-sensing with clinical monopolar review and 3D-radiological reconstructions to optimize DBS parameters in PD patients.

Methods: We included PD patients implanted with beta-band sensing DBS devices. Baseline motor performances were evaluated using the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part III in the OFF-stimulation/OFF-medication state. Non-motor symptoms, motor fluctuations, and quality of life were assessed using MDS-UPDRS parts I, II, and IV, and the Parkinson's Disease Questionnaire (PDQ-39). DBS was activated using parameters pre-established through monopolar review and 3D-reconstructions. Three hours later, patients were clinically examined using MDS-UPDRS-III in an OFF-med state, and new parameters were set based on beta-sensing. At follow-up visits, we reassessed the patients and examined beta-band sensing recording. We also calculated Total Electrical Energy Delivered (TEED) at every timepoint.

Results: Eight PD patients (5 males, 3 females, mean age at onset 53.5 ± 5.5 years) underwent DBS surgery at a mean age of 63.4 ± 4.1 years. Seven received STN-DBS and one GPi-DBS. Baseline mean MDS-UPDRS part III scores were 35.3 ± 7.0 (OFF-med/OFF-stim) and 23.3 ± 5.4 (OFF-med/ON-stim). Scores for parts I, II, IV, and PDQ-39 were 8.0 ± 5.1, 7.3 ± 3.7, 3.9 ± 3.3, and 29.6 ± 27.9, respectively. Beta-sensing suggested new parameters in six patients. Three attended the first

follow-up visit, showing trends toward improved MDS-UPDRS and PDQ-39 scores, though differences were not significant, with reduced TEED.

Conclusion: Beta-sensing appears as effective as traditional methods for short-term DBS optimization. We are collecting long-term follow-up data in a larger cohort to establish long-term efficacy.

Disclosure: Nothing to disclose.

EPR-160 | Development of diagnostic, prognostic biomarkers and rehabilitation strategies in functional motor disorders

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Background and aims: Functional motor disorders (FMD) present delayed diagnoses and inadequate treatments underscoring the need for diagnostic and prognostic biomarkers [2,3].This research, funded by the European Union – Next Generation EU (NRRP M6C2 – Investment 2.1, PNRR-MAD-2022-12376826), aimed to address this gap. To develop diagnostic and prognostic disease-specific biomarker algorithms in motor, exteroceptive, and interoceptive domains through advanced behavioral, neurophysiological, and MRI assessments supported by explainable artificial intelligence.

Methods: FMD patients, healthy controls (HC), and patients with "organic" motor disorders underwent behavioral, neurophysiological, and MRI assessments targeting motor, exteroceptive, interoceptive, and cerebral domains.

Results: Preliminary analyses comparing 115 HC (mean age 39.62 ± 11.5 years) and 41 FMD patients (mean age 45.5 ± 13.3 years) revealed alexithymia, anxiety, depression, fatigue, pain and reduced quality of life in FMD patients ($p < 0.05$). Age-matched subgroup analysis showed significant motor impairment in FMD, including reduced stride length and slower walking speed ($p < 0.001$, for all), with improved gait metrics in dual-task visual conditions. Balance challenges were evident in Romberg index performance under single-task conditions ($p < 0.003$) but not during dual-task conditions (Figure 1). Blink reflex R2 response modulation between baseline and prepulse conditions differed significantly in FMD ($p < 0.021$), partially aligning with HC patterns (Table 1). Exteroceptive assessments showed altered laser-evoked potentials in FMD, with N2P2 amplitude reductions during Diffuse Noxious Inhibitory Controls (DNIC) returning to baseline post-DNIC ($p < 0.05$), mirroring HC patterns (Table 2). Interoceptive and MRI findings remain under analysis.

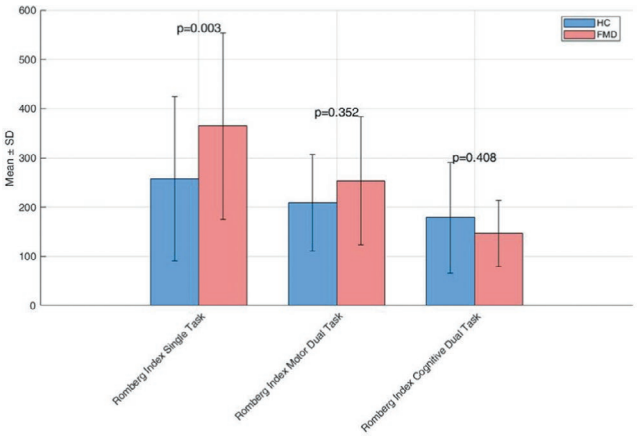

FIGURE 1 Comparison of Romberg Index between Healthy Control (HC) and Functional Movement Disorders (FMD) subjects across single and dual-task. Significant statistical *p*-value set at 0.05.

TABLE 1 Comparison analysis on Blink reflex across Baseline and Prepulse condition both Healthy Control (HC) and Functional Movement Disorders (FMD) subjects. Mean ± SD with corresponding *p*-values. Significant results are shown in bold.

HC	Basaline Mean ± SD	Prepulse Mean ± SD	p-value
Baseline R2 Area contralateral	1.14 ± 0.53	0.99 ± 0.44	**<0,001**
FMD	**Basale**	**Prepulse**	**p-value**
Baseline R2 Area contralateral	0.99 ± 0.44	0.78 ± 0.58	**0.021**

TABLE 2 Comparison analysis on laser-evoked potentials across Baseline (1), during Diffuse Noxious Inhibitory Controls (DNIC) (2), and post-DNIC (3) both Healthy Control (HC) and Functional Movement Disorders (FMD) subjects. Mean ± SD with corresponding.

HC	1.Basaline Mean ± SD	2.DNIC Mean ± SD	3.Post-DNIC Mean ± SD	p-value	Post-hoc p-value
Upper Limb N2P2 Amp	30.12 ± 9.88	25.49 ± 9.70	28.89 ± 14.68	**<0.001**	<0.001 (1-2) <0.001 (2-3)
Lower Limb N2P2 Amp	28.66 ±10.47	23.97±12.28	26.29 8.02	**<0.001**	0.001 (2-3) <0.001 (1-2) 0.073 (1-3)
FMD	**1.Basale**	**2.DNIC**	**3.Post-DNIC**	**p-value**	**Post-hoc p-value**
Upper Limb N2P2 Amp	31.94 ± 14.60	26.06 ± 14.14	29.94 ± 9.49	**0.019**	0.006 (1-2)
Lower Limb N2P2 Amp	28.11±10.17	27.11±12.69	27.32±12.11	**0.047**	0.018 (1-2)

Conclusion: Preliminary results reveal distinct motor and exteroceptive biomarkers in FMD, offering insights into mechanisms and diagnostic tools. Findings support multimodal assessments to improve FMD diagnosis.

Disclosure: This research funded by the European Union – Next Generation EU (NRRP M6C2 – Investment 2.1, PNRR-MAD-2022-12376826; title of scientific research "A window into the mind-brain-body interplay: development of diagnostic, prognostic biomarkers and rehabilitation strategies in functional motor disorders"). Collaborators: S. Mariotto, S. Tamburin, M. Fiorio, C. Vinciguerra, A. Botto, L. Zenere, E. Canu, E. Sibilla, M. Filippi, E. Sarasso, C. Geroin, M. Fasoli, A. Marotta, E. Pizzolla, F. Salaorni, I. Lozzi, F. Bombieri, G.M.Squintani, G. De Biasi,

MS and related disorders 2

EPR-161 | Anti-BCMA CAR T cell therapy in patients with multiple sclerosis

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Background and aims: B cells and neuroinflammation within the central nervous system (CNS) contribute to disease progression in multiple sclerosis (MS) (Correale et al., 2017). Eque-cel is a fully human B-cell maturation antigen (BCMA) targeted chimeric antigen receptor (CAR) T-cell therapy. This study investigates the potential of anti-BCMA CAR T cell therapy in treating three patients with MS.

Methods: Autologous T cells were collected and enriched from patients with MS. Eque-cel was generated by transducing these T cells with a lentiviral vector encoding a fully human anti-BCMA CAR. As of December 31, 2024, three progressive MS patients received a three-day consecutive lymphodepletion regimen and 1.0×10^6 total CAR T cells/kg. All MS related medications were discontinued the day before lymphodepletion therapy.

Results: Baseline patient characteristics are summarized in Table 1. CAR T cells rapidly reached peak expansion by day 10, with flow cytometry showing significant B cell depletion post infusion (Figure 1). All patients experienced transient grade 1 cytokine release syndrome (CRS). No ICANS or other neurologic toxicities. Functional improvement were noted, including better Expanded Disability Status Scale (EDSS) scores, reduced times on the Nine-Hole Peg Test and Timed 25-Foot Walk test, and resolution of oligoclonal bands (OCBs) in cerebrospinal fluid (CSF) (Figure 2).

TABLE 1 Demographic and clinical characteristics. PPMS: primary progressive multiple sclerosis. SPMS: Secondary progressive multiple sclerosis. EDSS: expanded disability status scale. OCBs: Oligoclonal bands.

Characteristics	Patient 1	Patient 2	Patient 3
Sex	Male	Female	Male
Age at baseline; years	53	43	48
Age at onset; years	50	34	39
Diagnosis	PPMS	SPMS	SPMS
EDSS at baseline	7	6	6
OCBs in CSF at baseline	Positive	Positive	Positive
Follow-up; months	3	3	3
Previous treatment	corticosteroid Siponimod Fampridine	corticosteroid Siponimod Ozanimod Teriflunomide Ofatumumab Fampridine	corticosteroid Siponimod Ozanimod Teriflunomide

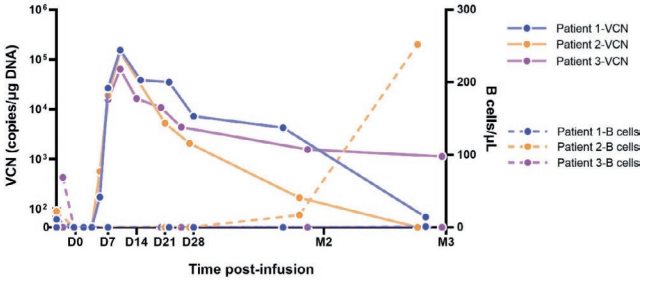

FIGURE 1 Vector copy numbers (VCN) and B cells following CAR-T cell therapy.

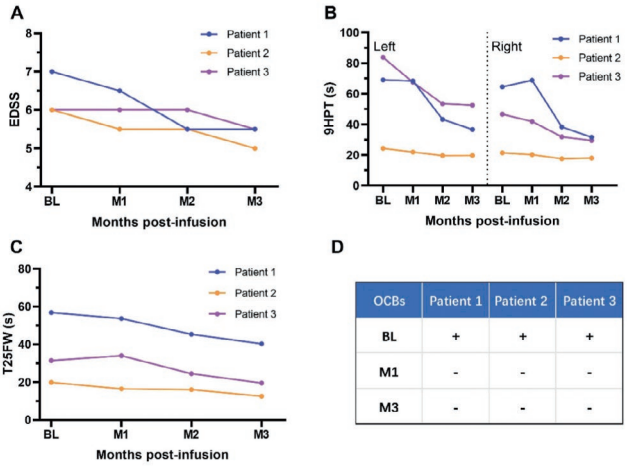

FIGURE 2 Clinical evaluation and Oligoclonal bands. (A) EDSS scores of the patient before and after CAR-T cell therapy. (B) Results of Nine-Hole Peg Test (9HPT) evaluation. (C) Results of Timed 25-Foot Walk (T25FW) evaluation. (D) Oligoclonal bands (OCB).

Conclusion: Anti-BCMA CAR T cells are well tolerated and show high efficacy in treating progressive MS, as demonstrated by improved physical function and resolution of OCBs in CSF.

Disclosure: Huan Ye and Song-Bai Cai are employees of Nanjing IASO Biotechnology Co., Ltd.

EPR-162 | Ocrelizumab subcutaneous: Updated analyses at week 72 and PATIENT PREferences from the OCARINA II study

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Background and aims: OCARINA II (NCT05232825) showed ocrelizumab (OCR) subcutaneous (SC) 920 mg (co-formulated with recombinant human hyaluronidase PH20 [rHuPH20]) has a similar benefit–risk profile to OCR intravenous (IV) 600 mg in people with relapsing and primary progressive multiple sclerosis (PwRMS/PwPPMS). Updated safety and clinical data, and new patient-reported outcomes (PROs) are presented at clinical cut-off date (CCOD: up to September 2024).
Methods: OCR-naive PwRMS/PwPPMS (18–65 years; Expanded Disability Status Scale [EDSS] score: 0–6.5) were randomized 1:1 to OCR IV 600 mg (OCR IV/SC) or OCR SC 920 mg (OCR SC/SC). At Week (W)24, all patients received OCR SC up to W96. Endpoints reported include EDSS, safety and PROs (Multiple Sclerosis Treatment Preference Questionnaire [MSTPQ] and Patient Preference Questionnaire [PPQ]).
Results: Mean (SD) changes in EDSS scores from baseline were −0.14 (0.77) and −0.06 (0.80) in OCR IV/SC and SC/SC, respectively. Safety data from patients who received ≥1 OCR SC dose are shown in Table 1. Injection reactions (IRs) were the most common adverse event. All IRs were non-serious and mild/moderate in intensity; 99.4% resolved. At the CCOD, no treatment-emergent antidrug antibodies to OCR were reported; one patient experienced treatment-emergent anti-rHuPH20 antibodies. At W48, the MSTPQ showed that 98.2% were satisfied/very satisfied with OCR SC; among 139 patients who previously received other disease-modifying therapies, 82.0% preferred OCR. Per the PPQ, 80.4% of patients who received both OCR IV and SC preferred SC administration.
Conclusion: Ocrelizumab SC continues to show similar clinical and safety profiles to ocrelizumab IV. Patients showed stronger preferences for ocrelizumab SC.

Patients with ≥1 event, n (%)	OCR SC 920 mg (N=233)
Adverse event	196 (84.1)
Serious adverse event	10 (4.3)
Injection reactions	134 (57.5)
Local injection reactions	127 (54.5)
Systemic injection reactions	29 (12.4)

[a]Patients who received at least one OCR SC dose.

OCR, ocrelizumab; SC, subcutaneous.

Table 1. Overall safety in the OCR SC all-exposure group[a]

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EPR-163 | Clinico-demographic and radiological features associated with sleep disorders and multiple sclerosis

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Background and aims: People with Multiple Sclerosis (MS) often experience sleep disorders, usually resulting from a combination of physical and psychological factors as well as from cerebral damages. In this study we aimed to analyze the correlation between sleep impairment and clinical, neuropsychological and radiological findings.
Methods: This cross-sectional study included 400 MS patients. Neuropsychological assessments included Brief International Cognitive Assessment for MS (BICAMS), Beck Depression Inventory (BDI-II) and Modified Fatigue Impact Scale (MFIS) and BAI. Sleep Impairment was assessed through the PSQI (score > 5 indicating impairment). A forward stepwise multivariable linear regression model evaluated the association between PSQI scores and clinical features and between PSQI scores and radiological features using age, gender, BDI-II, BAI and MFIS as correcting factors.

Results: Among the study population 181 MS patients showed cognitive impairment, and 90 MS patients showed sleep impairment. Sleep impairment was linked to greater depressive symptoms (OR = 1.10, $p < 0.001$) and higher EDSS (OR = 1.30, $p = 0.02$). Furthermore, PSQI scores correlated with increased bilateral hippocampal and nucleus pallidus volume (corr. coeff. = 2.04, $p < 0.001$ and corr. coeff. = 3.15, $p = 0.02$, respectively), higher T2 Lesion Volume (corr. coeff. = 0.26, $p < 0.001$) and reduced bilateral amygdala and caudate nucleus (corr. coeff. = -2.34, $p = 0.03$; corr. coeff. = -1.49, $p = 0.05$).

Conclusion: Motor and depressive symptoms in MS patients may affect sleep through different manifestations such as muscle spasms, cramps and increased anxiety. At the same time sleep impairment may result from imbalanced structural alterations in subcortical gray matter, suggesting disrupted connectivity between subcortical structures.

Disclosure: A.E. has received honoraria from Novartis. M.M. has received research grants from ECTRIMS-MAGNIMS, the UK MS Society, and Merck, and honoraria from Biogen, BMS Celgene, Ipsen, Janssen, Merck, Novartis, Roche, and Sanofi-Genzyme. M.P. has received research grants from the Italian MS Foundation and Baroni Foundation, honoraria from Health & Life and Biogen, and sponsorship for travel/meeting expenses from Novartis, Roche, and Merck. S.C. received personal fees from Shire and Genzyme, outside the submitted work. R.L. has received honoraria from Biogen, Merck, Novartis, Roche, and Teva. V.B.M. has received research grants from the Italian MS Society and Roche, and honoraria from Bayer, Biogen, Merck, Mylan, Novartis, Roche, Sanofi-Genzyme, and Teva. A.C. has received research grants from Almirall, research grants from ECTRIMS-MAGNIMS, and honoraria from Almirall, Biogen, Roche, Sanofi-Genzyme, Merck, Ipsen, and Novartis. None of the other authors has any conflict of interest to disclose.

EPR-164 | Predicting disability level in multiple sclerosis using MSCopilot®: A real-world post-market surveillance study

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Background and aims: This real-world post-market surveillance study evaluates the ability of MSCopilot®, a clinically validated software-as-a-medical-device, to differentiate disability levels, as measured by the Expanded Disability Status Scale (EDSS), in a French cohort of patients with multiple sclerosis (PwMS).

Methods: Digital biomarkers, self-reported socio-demographic and clinical parameters, were collected using MSCopilot® in a subgroup of adult PwMS who provided informed consent (October 2017 to September 2023). MSCopilot® was used at home without supervision to assess walking capacity, low-contrast visual acuity, cognitive processing, and dexterity. Disability levels were categorized as low to mild (EDSS < 4) or moderate to severe (EDSS ≥4).

Results: Among 590 PwMS included, the majority (71%, n = 421) reported an EDSS < 4. In this group, participants were younger (mean age = 40 ± 11 years) and had shorter disease duration (mean duration since diagnosis = 7 ± 8 years) compared to the EDSS ≥4 group (mean age = 48 ± 12, disease duration = 14 ± 10; $p < 0.001$, for both). Significant differences were observed with decreased performance in walking capacity, cognitive function, and dexterity in the EDSS ≥4 group (all p-values < 0.01). The digital walking test demonstrated strong discriminatory ability between EDSS groups, with an AUC of 0.8 (sensitivity = 0.86, specificity = 0.71) in univariate logistic regression. Multivariate regression improved sensitivity but did not enhance discriminatory power.

Conclusion: This pioneering real-world study demonstrates the feasibility of using MSCopilot® to support clinicians in making informed decisions about their patients' MS-related disability, between in-person routine visits, using reliable real-world data.

Disclosure: L. Carment, P. Drouin, N. Sellami, L-E. Pillet, S. Zinaï are employees of Ad Scientiam, A. Tourbah is a member of Ad Scientiam scientific committee and received honoraria for lectures, travel grants and research support from Biocara, Hikma, Novartis, Roche.

EPR-165 | Clinical integration of brain and cord MRI features improves differential diagnosis of multiple sclerosis

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Background and aims: To explore the role of brain and spinal cord MRI features in differentiating patients with suspected central nervous system (CNS) inflammatory diseases.

Methods: Prospective data from 125 patients undergoing diagnostic evaluation, including 1.5T brain and spinal cord MRI scans from February 2021 and March 2024 were analyzed. The cohort comprised 91 patients with multiple sclerosis (MS), 15 with other inflammatory neurological diseases (OIND), and 19 with non-inflammatory neurological diseases (NIND). Brain and spinal cord lesion topographies and morphological features

were evaluated to identify MRI features discriminating MS from OIND and NIND.

Results: Random forest analysis identified key MRI features supporting MS diagnosis over OIND: absence of longitudinally extensive transverse myelitis (relative importance [RI] = 100%), presence of >=1 Dawson's finger (RI = 55.3%), >=1 cortical lesion (RI = 42.6%), and >=1 brain T2-hyperintense white matter (WM) lesion (RI = 36.4%). After excluding the presence of >=1 brain T2-hyperintense WM lesion, fulfilling >=2 of the 3 selected criteria distinguished MS from OIND patients with a sensitivity of 0.59 and a specificity of 0.80. For distinguishing MS from NIND, relevant MRI features included >=1 T2-hyperintense spinal cord lesion (RI = 100.0%), >=1 Dawson's finger (RI = 84.3%), >=1 cortical lesion (RI = 61.4%), >=1 cerebellar peduncle lesion (RI = 52.2%) and >=3 central vein sign-positive lesions (RI = 27.8%). Fulfilling >=2 of the 5 selected criteria identified MS patients with a sensitivity of 0.64 and a specificity of 0.84.

Conclusion: Integrating novel MRI features in the diagnostic work-up of patients with suspected CNS inflammatory disease improves differentiation between MS, OIND, and NIND, reducing the risk of misdiagnosis.

Disclosure: MAR consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche, and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva. SR, AM, MG,PV, EP, AG, AF, FE nothing. PP speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon, Sanofi. BC travel grants or honoraria for advisory boards, speaker panels, or investigation studies from Novartis, Teva, Eli Lilly, Pfizer, and Lusofarmaco. MF consulting or speaking fees from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; research support from Biogen Idec, Merck-Serono, Novartis, Roche.

EPR-166 | The impact of national policies on reimbursement of DMT for MS on disease outcomes: Slovenia versus Croatia

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Background and aims: The aim of this research was to determine the impact of national policies on reimbursement of disease-modifying therapies (DMT) for multiple sclerosis (MS) on disease outcomes.

Methods: The population included the consecutive Slovenian and Croatian people with MS (pwMS) cohort entered in the MSBase registry database. We calculated the following DMT variables from the above information: time to first ever DMT, total DMT duration, and ever used DMT. We applied 1:1 propensity score matching to match pwMS from Slovenia and Croatia to mitigate baseline differences between the groups.

Results: Out of 894 pwMS from Slovenia and 1363 from Croatia, 565 pwMS from both countries were enrolled after propensity score matching. pwMS living in Croatia had statistically significantly higher levels of disability measured with EDSS compared to pwMS living in Slovenia (2.0 vs. 1.5 respectively, $p = 0.004$) (Table 1). The time to first-ever DMT was longer in the Croatian cohort (2.76; 1.20-6.92) than in the Slovenian cohort (1.29; 0.48-4.60), $p < 0.001$. In a multivariable logistic regression, pwMS who lived in Croatia had an increased probability of EDSS ≥3 by 52.8% (Exp(B) 1.528, 95% C.I. 1.182-1.974, $p = 0.001$). Furthermore, the time to first-ever DMT increased the probability of EDSS ≥3 by 10.6% (Exp(B) 1.106, 95% C.I. 1.083-1.129, $p < 0.001$).

TABLE 1 Baseline characteristics of the matched study population.

	Slovenia	Croatia	p value
Age (Years)	46.0±11.9	45.7±11.7	0.681
Sex (female)	404 (71.5)	394 (69.7)	0.557
Disease duration (Years)	11.0 (5.6-16.2)	10.6 (6.0-16.8)	0.722
EDSS	1.5 (1.0-3.5)	2.0 (1.0-3.5)	0.004
DMT exposure			<0.001
No	112 (19.8)	45 (8.0)	
Yes	453 (80.2)	520 (92.0)	
Number of DMTs			<0.001
1	233 (41.2)	292 (51.7)	
2	127 (22.5)	169 (29.9)	
3	61 (10.8)	48 (8.5)	
4	21 (3.7)	11 (1.9)	
5	9 (1.6)	0	
6	2 (0.4)	0	
DMT category (N, %)			<0.001
1st line injectables	189 (41.7)	281 (54.0)	
1st line orals	144 (31.8)	119 (22.9)	
HET	120 (26.5)	120 (23.1)	
DMT exposure			<0.001
Treatment naïve	112 (19.8)	45 (8.0)	
1st line	333 (58.9)	400 (70.8)	
HET	120 (21.2)	120 (21.2)	
Time from first symptom to first DMT (years*	1.29 (0.48-4.60)	2.76 (1.20-6.92)	<0.001
DMT duration (years)*	6.72 (2.86-11-87)	4.64 (2.29-9.58)	<0.001

TABLE 2 Results of the univariable and multivariable logistic regression analysis.

	Univariable logistic regression			Multivariable logistic regression		
	Exp(B)	95% C.I. for Exp(B)	p value	Exp(B)	95% C.I. for Exp(B)	p value
EDSS ≥3						
Country*	1.553	1.218-1.979	<0.001	1.528	1.182-1.974	0.001
DMT	0.937	0.662-1.324	0.710			
Time to DMT	1.106	1.083-1.129	<0.001	1.106	1.083-1.129	<0.001
DMT duration	1.002	1.000-1.004	0.055	1.002	1.000-1.004	0.114

*Slovenia as a reference country
EDSS expanded disability status scale; DMT disease-modifying therapy

Conclusion: This study provides evidence for the impact of national policies on the reimbursement of DMTs on disability outcomes in pwMS. pwMS living in a country with less stringent reimbursement policies have a higher probability of having lower levels of disability.

Disclosure: GBJ: Clinical investigator and/or received consultation and/or speaker fees from: Amgen, AstraZeneca, Biogen,

Janssen, Lek, Merck, Novartis, Pliva/Teva, Roche, Sanofi Genzyme, Swixx, Viatris. MKS, IA, TG, BB, MH: Clinical investigator and/or received consultation and/or speaker fees from: Biogen, Sanofi Genzyme, Merck, Novartis, Pliva/Teva, Roche, Zentiva, Actelion, Alexion Pharmaceuticals, TG Pharmaceuticals. UR: has received consultation fees/Honoraria from: Bayer, Biogen, Janssen, Lek, Merck, Novartis, Roche, Sanofi-Genzyme, Teva and Grants/Research support from Biogen and Novartis. AHL: Clinical investigator and/or received consultation and/or speaker fees from: AstraZeneca, Biogen, Janssen, Lek, Merck, Novartis, Pliva/Teva, Roche, Sanofi Genzyme. MFT: has received speaker fees from: Biogen, Novartis, Janssen. SG: has received speaker fees from: Merck, Novartis. RB: Nothing to disclose.

EPR-167 | Social determinants of health and multiple sclerosis in Italy: The SocialMS study

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Background and aims: SocialMS is an observational cross-sectional study on social determinants of health (SDoH) in Italian patients with multiple sclerosis (MS). Data were collected based on self-administered surveys and started in March 2024.
Methods: Patients who completed sections on demographics, MS and SDoH by August 17 were included in this interim analysis. The SDoH section covered: sex, gender and sexuality, origin, education, employment, socioeconomic status, abuse, healthcare access, food, air pollution and social support. Disability was assessed by the Patient Determined Disease Steps (PDDS) scale.
Results: 1090 patients were included (37% North, 29% Centre, and 34% South and Islands). Median(interquartile range) PDDS was 1(0-3); PDDS was greater for patients with financial difficulties ($p < 0.001$) and with less education ($p = 0.001$); education was related to economic and employment status ($p < 0.001$). Lower income was associated with longer months between MS symptoms and diagnosis ($p = 0.020$) and diagnostic delay was associated with disability ($p < 0.001$). Long waiting lists was a common issue for care-access; patients who could afford private healthcare (59%) often had greater income, higher education and medical insurance ($p < 0.001$). MS itself had a negative impact on SDoH: educational (40%) and professional (45%) goals; job quit/change due to MS diagnosis (12%) or disability (16%); financial resources (33%); abuse (3%); social life (44%), relationship with partner (31%) and friends (23%). The impact of MS was stronger for more disabled patients.

FIGURE 1 Number of participants by location of the MS center

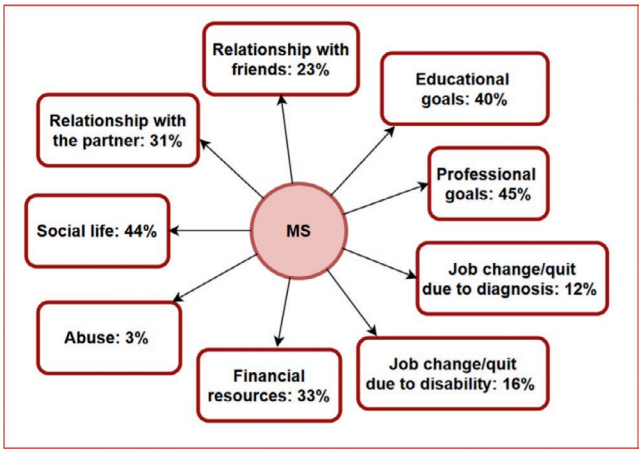

FIGURE 2 Impact of MS

Conclusion: In Italy, more efforts are needed to address SDoH that drive inequities and to support more effectively MS patients.
Disclosure: Nothing to disclose.

EPR-168 | Aerobic and cognitive training effects on insular functional connectivity in progressive multiple sclerosis: CogEx trial

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Background and aims: The anterior insula (AI) is crucial for cognitive attentional processes, while the posterior insula (PI) is related to somatosensory properties. CogEx trial (NCT03679468) investigated the effects of aerobic exercise (EX) and cognitive rehabilitation (CR) on cognitive impairment in progressive multiple sclerosis (MS). The aim of this study was to assess the effects of rehabilitation on resting state functional connectivity (RSFC) of AI and PI exploiting CogEx data.
Methods: CogEx participants were randomized to: 'CR+EX', 'CR+sham EX (EX-S)', 'EX+sham CR (CR-S)' and 'CR-S+EX-S'. We selected all subjects ($n=87$) who underwent the 12-week intervention period and completed baseline and 12-week physical/cognitive and RS-fMRI assessments. RSFC of AI and PI was assessed using a seed-based approach.
Results: At week-12 compared to baseline, groups performing CR were both characterized by increased RSFC between AI and the left temporal pole, while groups performing EX were both characterized by increased RSFC between AI and the left hippocampus. Conversely, 'CR-S+EX-S' patients were characterized by decreased RSFC of AI/PI with cingulate cortex and frontoparietal regions. In the 'EX+CR-S' group, increased RS FC between AI and left hippocampus tended to be associated with concomitant increase in California Verbal Learning Test score ($p=0.063$). In contrast, in 'CR-S+EX-S' group, over time modifications of insular RSFC with cingulate and parieto-temporal regions were associated with concomitant worsening of visuospatial memory performance ($p<0.047$).
Conclusion: EX and CR modulated RSFC of anterior and posterior insular regions in patients with progressive MS. Adaptive compensatory mechanisms occurring in insular RSFC seem to support cognitive mnemonic function.
Disclosure: Funding. Funded by MS Society of Canada (EGID3185). Ancillary funding: CMSC, Danish MS Society, US MS Society.

EPR-169 | Comparison of different age-derived cut-offs for plasma neurofilament light chain in multiple sclerosis

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Background and aims: Clinical use of blood neurofilament light chain (NfL) requires cut-off values that reflect disease status independently of confounding factors, such as age, hemodilution and cardiovascular risk factors. We compared the performance of different previously-suggested cut-offs in separating MS cases and controls, and in identifying different MS clinical features, across age groups.
Methods: In this cross-sectional study, we included people with MS ($n=312$) and age, sex and eGFR-matched controls ($n=236$). For MS cases, we collected descriptors of disease progression (relapsing or progressive), EDSS, and evidence of disease activity in the previous year (including relapses, active MRI, and EDSS progression). Plasma NfL (pNfL) was evaluated using Lumipulse™ fully automated chemiluminescent enzyme immunoassay. We classified MS cases and controls based on three suggested cut-offs derived from pNfl and age.
Results: In individuals aged 18-50 years, pNfL was able to discriminate MS cases and controls (AUC=0.73; 95%CI=0.67, 0.78; $p=0.028$) with high specificity (>85%): In the MS population pNfL was able to discriminate relapsing and progressive cases (AUC=0.70; 95%CI=0.63, 0.77; $p=0.034$), patients with EDSS≥4.0 and EDSS <4.0 (AUC=0.69; 95%CI=0.63, 0.76; $p=0.032$), and patients with EDSS≥6.0 and EDSS <6.0 (AUC=0.70; 95%CI=0.62, 0.78; $p=0.040$), with high sensitivity (>75%). Different cut-offs provided similar sensitivity and specificity, but the accuracy decreased in older age groups.
Conclusion: Previously-validated cut-offs provided similar sensitivity, specificity and accuracy in separating MS cases and

controls and in identifying MS clinical features across different age groups, with the best performance before 50 years.

Disclosure: Valerio Nicolella discloses travel/meeting expenses from Alexion. Antonio Carotenuto has received research grants from Almirall and ECTRIMS- MAGNIMS and honoraria from Almirall, BMS Celgene, Biogen, Roche, Sanofi-Genzyme, Merck, Ipsen and Novartis. Maria Petracca discloses travel/meeting expenses from Novartis, Janssen, Roche, Merck and Alexion; speaking honoraria from HEALTH&LIFE S.r.l., AIM Education S.r.l., Biogen, Novartis and FARECOMUNICAZIONE E20; honoraria for consulting services and advisory board participation from Biogen; research grants from Baroni Foundation and the Italian Ministry of University and Research (PRIN 2022LP5X2E). Vincenzo Brescia Morra and Roberta Lanzillo received research grants from the Italian MS Society, and Roche, and honoraria from Bayer, Biogen, BMS Celgene, Merck, Mylan, Novartis, Roche, Sanofi-Genzyme, and Teva Marcello Moccia is editorial board member of Neurology (AAN, MN, US), and the Multiple Sclerosis Journal (Sage, UK); has received research grants from MUR PNRR Extended Partnership (MNESYS no. PE00000006, DHEAL-COM no. PNC-E3-2022-23683267), ECTRIMS-MAGNIMS, UK MS Society, and Merck; and has received honoraria from Abbvie, Biogen, BMS Celgene, Ipsen, Janssen, Merck, Novartis, Roche, Sanofi-Genzyme.

Muscle and neuromuscular junction disorder 2

EPR-170 | Differential effect of Eculizumab and Efgartigimod on subscores of the MG-ADL and QMG in generalized Myasthenia Gravis

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Background and aims: Eculizumab and Efgartigimod are both approved for the treatment of generalized Myasthenia Gravis. Objective of our study is to describe the differential response of both treatments on subscores of the MG-ADL, and QMG scale in a real-life setting.

Methods: We included patients receiving either ECU or EFGA and retrospectively collected data on the MG-ADL and QMG. We limited the observation of MG-ADL to weekly scores for the first 8 weeks, and of QMG at baseline and every 12 weeks.

Results: We enrolled 38 patients, 22 treated with ECU and 16 with EFGA. We found a higher response to Eculizumab at MG-ADL, with significant difference at week 7 and for QMG with significant difference at week 24, 36 and 48. We then compared the response to both treatments at subscores of MG-ADL and QMG and found no difference for the ocular and limb subscores. We found a significant treatment difference at the bulbar subscores both at the MG-ADL and QMG, with a higher drop for Eculizumab treated patients at MG-ADL at week 6 and 7, and for Eculizumab at QMG at week 12 and 36. Mean QMG score for the forced vital capacity (FVC) decreased more with Eculizumab throughout the entire observation period.

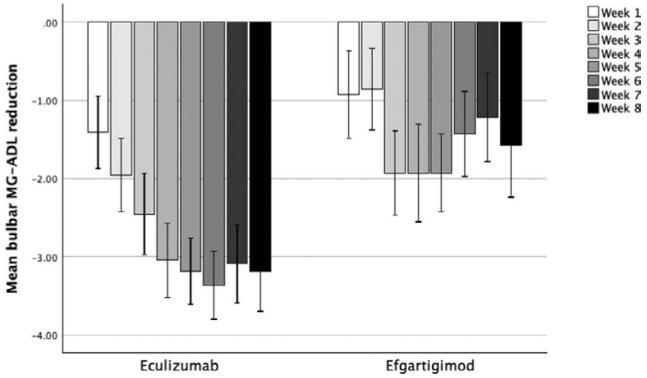

FIGURE 1 MG-ADL bulbar subscore

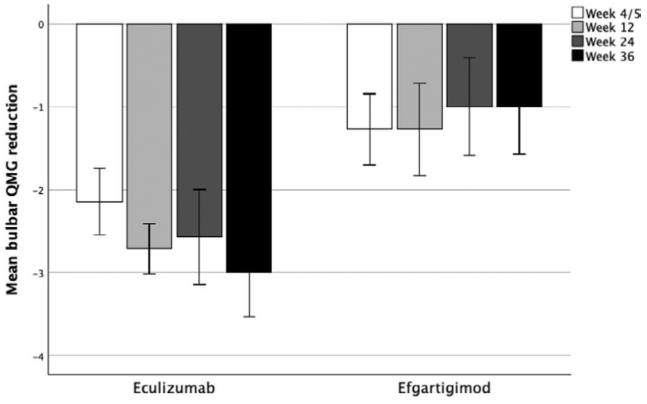

FIGURE 2 QMG bulbar subscore

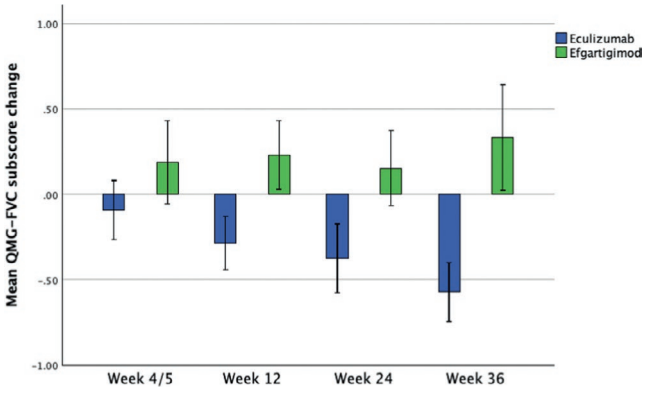

FIGURE 3 FVC comparison

Conclusion: Our study shows a differential effect of Eculizumab and Efgartigimod on the MG-ADL and QMG with a deeper effect of Eculizumab on bulbar scores. This differential effect should be considered when treating patients with high bulbar scores and ventilatory insufficiency as they may benefit more from Eculizumab.

Disclosure: Nothing to disclose.

EPR-171 | Observed efficacy of efgartigimod in generalized myasthenia gravis across patient subgroups in the ADAPT-SC+ study

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Background and aims: Efgartigimod is a human immunoglobulin G1 (IgG1) antibody Fc fragment that reduces total IgG levels (including pathogenic autoantibodies) through neonatal Fc receptor blockade. In the ADAPT-SC study, subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20) showed noninferior total IgG reduction compared with intravenous efgartigimod in participants with generalized myasthenia gravis (gMG). The objective of the current analysis was to assess efficacy of efgartigimod PH20 SC in several subgroups of participants with acetylcholine receptor antibody–positive (AChR-Ab+) gMG ($n=130$) during the first cycle of the open-label extension (OLE), ADAPT-SC+.
Methods: Efgartigimod PH20 SC 1000 mg was administered in cycles of 4 once-weekly injections. Myasthenia Gravis Activities of Daily Living (MG-ADL) scores evaluated clinical efficacy.
Results: The largest improvements in MG-ADL total score (mean change [SE] from OLE baseline) were observed at week 4 of cycle 1, 1 week after last administration, (−4.1 [0.27]). Improvements were observed in multiple subgroups, including: disease duration < 3 years (−3.4 [0.62]), 3- < 6 years (−4.6 [0.48]), and > = 6 years (−4.1 [0.39]); aged 18-64 years (−4.5 [0.32]) and > = 65 years (−2.5 [0.43]); MG-ADL baseline total score 0-4 (−1.3 [0.35]), 5-8 (−3.2 [0.28]), and > = 9 (−6.3 [0.44]); thymectomized (−4.5 [0.40]) and nonthymectomized (−3.8 [0.37]); receiving only concomitant acetylcholinesterase inhibitors (−5.5 [0.77]), any nonsteroidal immunosuppressive treatments (−3.8 [0.38]), or any steroids (−3.8 [0.31]). Efgartigimod PH20 SC was well tolerated; no new safety signals observed.

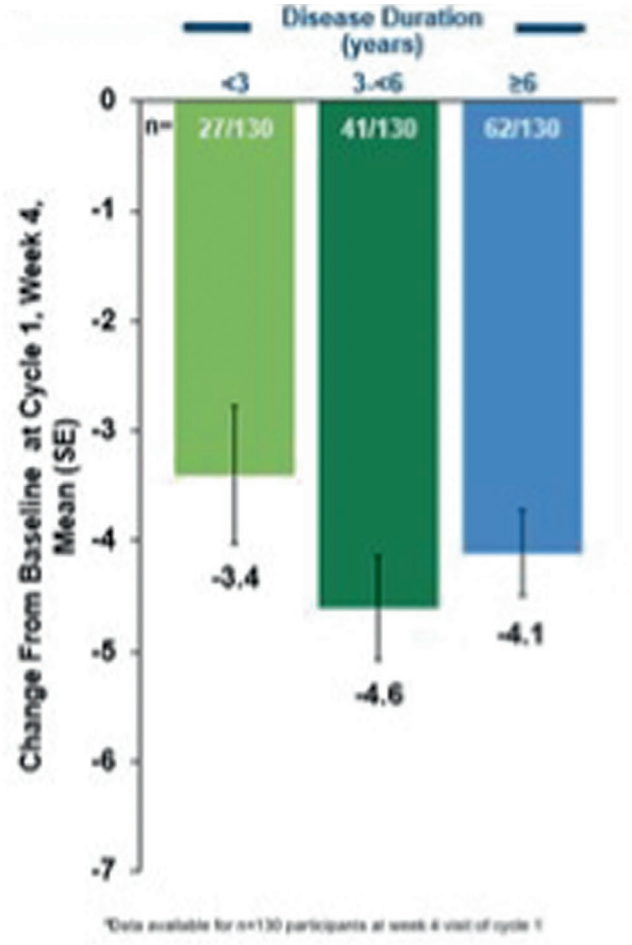

Figure 1. Week 4[a] MG-ADL Score Change from Baseline by Disease Duration
AChR-Ab+ Population

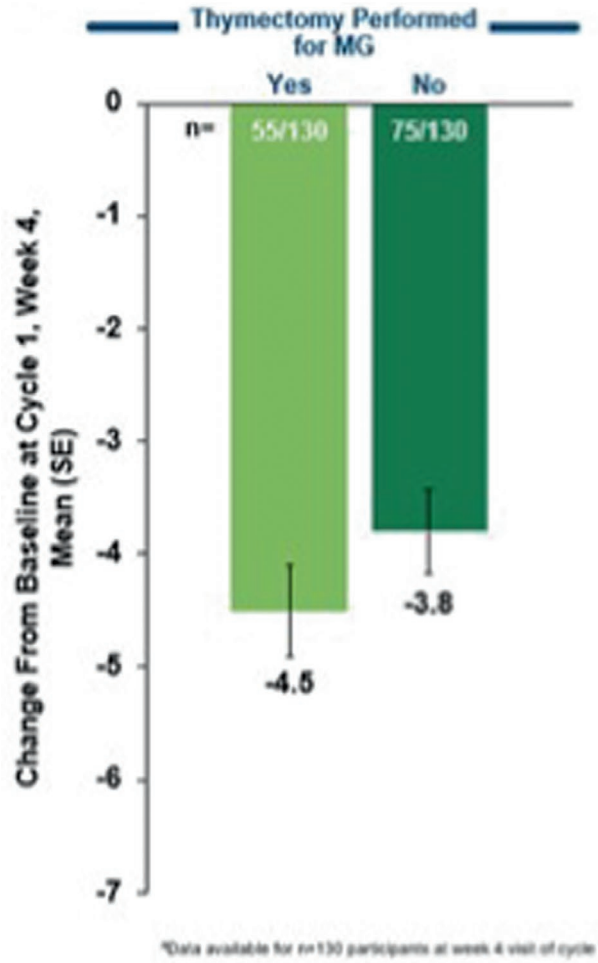

Figure 2. Week 4[a] MG-ADL Score Change from Baseline by Thymectomy Status
AChR-Ab+ Population

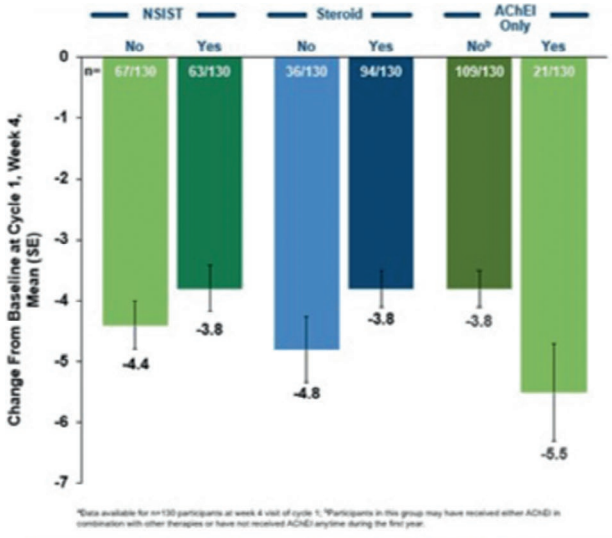

Figure 3. Week 4[a] MG-ADL Score Change from Baseline by Concomitant Therapy
AChR-Ab+ Population

Conclusion: Efgartigimod PH20 SC resulted in consistent clinical improvements in AChR-Ab+ participants across various subgroups, reinforcing the efficacy of efgartigimod PH20 SC across a broad gMG population.
Disclosure: This study was sponsored by argenx; EB and RK are employees of argenx; SM, TV, KU, and AM have reported financial/nonfinancial relationships with argenx at the time of submission.

EPR-172 | Treatment of very-late-onset myasthenia gravis with Efgartigimod: A retrospect cohort study

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Background and aims: Given the potential for very-late-onset myasthenia gravis (VLOMG) patients to manifest with more severe symptoms and poor response to treatment, hence, our evaluation was conducted to ascertain the safety and efficacy of efgartigimod in the VLOMG population.
Methods: This was a retrospective single-center cohort study of 42 patients with VLOMG (onset ≥65 years), MG-ADL score, QMG score, prednisone dose, laboratory data, and adverse events were assessed at each follow-up.
Results: The MG-ADL responder (≥2 MG-ADL scores improvement sustained for ≥4 weeks) exhibited 97.6% (41/42), and 83% demonstrated sustained response for 12 weeks follow-up. As the mean baseline MG-ADL scores was 9.88 ± 3.48, after 1 cycle of efgartigimod, the change of MG-ADL reached 8.23 ± 3.62. With a mean QMG score of 13 ± 4.24 at the time of enrollment, 97% achieved clinical meaningful improvement (CMI, ≥3 decreased QMG scores) and the mean duration was 6.37 ± 5.46 days. Minimal symptom expression (MSE, MG-ADL score of 0 or 1) was achieved in 45% patients at week 4, rising to 60% at week 8 and remaining at up to 45% at 12 weeks follow-up. All patients were able to reduce their daily dose of steroids. None of the patients experienced serious adverse events or worsening of pre-existing comorbidities during the study period.
Conclusion: With significant efficacy and clinical durability, efgartigimod showed a more pronounced response without impact on comorbidities in VLOMG patients in our study. An early escalation of therapy could achieve rapidly control of disease activity and appears to be beneficial for sustained long-term prognosis of VLOMG.
Disclosure: Nothing to disclose.

EPR-173 | Unraveling myasthenia-myositis overlap: Clinical insights into immune checkpoint inhibitor-related autoimmunity

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Background and aims: Myasthenia gravis (MG) and inflammatory myopathies (IM) are autoimmune disorders affecting the neuromuscular junction and skeletal muscle fibers, respectively. The coexistence of MG and IM can pose significant diagnostic and therapeutic challenges, particularly in patients treated with immune checkpoint inhibitors (ICIs). This study aimed to compare clinical, serological, and pathological characteristics, treatment strategies, and outcomes of sporadic MG-IM (s-MG-IM) and ICI-associated MG-IM (ICIs-MG-IM).
Methods: A retrospective, multicenter study was conducted, enrolling patients with s-MG-IM and ICIs-MG-IM. Inclusion criteria required clinical, neurophysiological, and serological confirmation of both MG and IM. Data were collected from medical records across participating centers. Clinical characteristics, laboratory findings, treatment strategies, and outcomes were statistically analyzed.
Results: A total of 28 patients were included: 15 with s-MG-IM and 13 with ICIs-MG-IM. ICIs-MG-IM patients were predominantly older males with more severe clinical manifestations, including higher rates of respiratory involvement (76.9%) and myocarditis (76.9%). Acute-phase mortality was significantly higher in ICIs-MG-IM (30.8%). s-MG-IM patients had longer diagnostic delays and frequent relapses. Treatment outcomes varied, with s-MG-IM requiring prolonged corticosteroids and immunosuppressants, while ICIs-MG-IM patients demonstrated a more stable long-term course after acute management.
Conclusion: The findings highlight distinct clinical and pathological differences between s-MG-IM and ICIs-MG-IM. Early recognition and tailored treatment strategies are critical, particularly in ICIs-MG-IM, where severe complications may arise. Survivors of the acute phase generally achieve stable remission without the need for chronic immunosuppressive therapy.
Disclosure: Nothing to disclose.

EPR-174 | Mortality in Myasthenia Gravis in Denmark from 1985 to 2020: A population-based cohort study

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Background and aims: Myasthenia gravis (MG) is generally associated with a favorable prognosis due to progressive treatment but remains linked to elevated mortality. We determined the short-term (< 1 year) and long-term (1-5 years) MG mortality compared to the general population.
Methods: Through nationwide health registers from 1985 to 2020, we identified MG patients and matched each patient with 10 individuals from the general population by age, sex, and diagnostic index date. We used Cox regression analysis to compute matched hazard ratios (HRs) for short- and long-term mortality, stratified by sex, age, period, and baseline comorbidities. We adjusted for baseline comorbidities to assess their possible impact on MG mortality.
Results: Our cohort included 2,110 MG patients (1,059 females) and 21,100 general population members, with 77.3% under 75 years at index date. The short-term cumulative mortality was 4.8% for MG patients compared to 2.6% in the general population, with an associated HR of 1.8 (95% CI 1.5-2.3). Long-term mortality decreased to a HR of 1.3 (95% CI 1.1-1.5). While short-term mortality declined from 1985 to 2014, it rose again from 2015 until 2020, particularly in patients over 75 years (HR 2.8, 95% CI 1.8-3.6). The comorbidity-adjusted analyses reduced short-term mortality to a HR of 1.6 (95% CI 1.3-2.0) and long-term mortality became comparable to the general population.
Conclusion: MG remains associated with increased mortality, especially in patients over 75 years within the first year of diagnosis. Early intervention and close monitoring are indispensable to improve patient outcomes.
Disclosure: Nothing to disclose.

EPR-175 | A real-world experience with Efgartigimod in AChR+ generalized myasthenia gravis

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Background and aims: Efgartigimod(EFG) was recently approved for the treatment of acetylcholine receptor antibody positive(AChR+) generalized myasthenia gravis(gMG). Real-world evidence is needed to fully evaluate the drug. We aimed to assess efficacy and safety of EFG in a single-center real-world clinical setting.
Methods: This was a retrospective chart review of 21 patients with anti-AChR gMG treated with EFG at the Institute of Clinical Neurophysiology, UMC Ljubljana. The patients were followed-up for a median time of 40 weeks and received a median of 4 cycles of EFG. Efficacy was assessed by MG-activity of daily living(ADL), MG-composite(MG-C) and MG-quality of life 15r(MG-QoL15r) scale change, and steroid dose reduction. Data on adverse events were collected.
Results: EFG was selected mainly for patients who were treatment refractory, had side effects to other treatments, and/or required quick improvement in their symptoms. All patients had been previously treated with at least one medication for MG and had a median baseline MG-ADL score of 6 points. Upon treatment, the patients' MG-ADL, MG-C and MG-QoL15r score improved by a median of 6, 5, and 10 points at 12 weeks ($p < .001$) and 4, 5 and 9 points by 24 weeks ($p < .001$). Forty-five percent of patients achieved minimal symptom expression and 57% of patients were able to reduce the steroid daily dose ≦4mg. Adverse events were reported in 67% of patients on EFG, the most common being mild urinary tract infection.

Conclusion: The present study provides real-world evidence supporting the use of EFG for the treatment of patients with refractory anti-AChR gMG.
Disclosure: Mateja Baruca Grad received public speaking honoraria and consultation fees from Alexion, Astra Zeneca, Argenx and Medison Pharma.

EPR-176 | Quantitative muscle magnetic resonance imaging as a possible biomarker in late onset Pompe disease

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Background and aims: Identifying biomarkers for early muscle changes and monitoring progression is critical in late onset Pompe disease (LOPD).
Methods: This study included 33 LOPD patients (16 asymptomatic or paucisymptomatic, Walton score ≤1; 17 symptomatic, Walton score ≥2) and 34 age and sex matched healthy controls. Thigh magnetic resonance imaging was performed using T1-weighted and STIR sequences. Fat fraction (FF) was calculated by selecting three slices of the 6-point Dixon images from proximal/medial/distal thigh levels to be automatically segmented into eleven regions of interest, then computed using the Fatty Riot algorithm. Clinical assessments included manual muscle testing, six minutes walking test, functional scales (Quick Motor Function Test; Gait, Stairs, Gowers, Chair Test), and patient-reported outcomes.
Results: Symptomatic patients showed significantly higher thigh FF compared to asymptomatic patients and controls, with differences evident in most individual thigh muscles. While asymptomatic patients showed no overall differences in thigh FF compared to controls, the adductor magnus (AM) exhibited significantly higher FF. In fact, even in asymptomatic patients, AM was the first muscle to show fatty replacement. No clinical differences were observed between asymptomatic patients with at least one muscle exceeding 10% FF and those with none. A significant correlation was found between average thigh FF and most clinical scales.
Conclusion: These results highlight quantitative MRI with the Dixon method as a sensitive, objective, and non-invasive biomarker for detecting early fat replacement in LOPD.
Disclosure: This project was funded with the support of the Italian Ministry of Health (RC 22-24).

EPR-177 | Coexisting autoantibodies in idiopathic inflammatory myopathies: Role of antinuclear antibodies and line blot testing

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Background and aims: Idiopathic inflammatory myopathies (IIMs) are autoimmune disorders with diverse presentations, making diagnosis challenging. Line blot assays detect myositis-specific antibodies (MSAs) and myositis-associated antibodies (MAAs) but have limitations, including false results. Antinuclear antibody (ANA) testing complements these assays, improving diagnostic precision.
Methods: We studied 228 patients with suspected IIM, recruited from Gangnam Severance Hospital (2003–2024). Line blot assays tested 16 MSAs, and enzyme-linked immunosorbent assays (ELISA) quantified anti-HMGCR and anti-NT5c1A antibodies. ANA indirect immunofluorescence (ANA-IIF) classified nuclear speckled and cytoplasmic patterns.
Results: Initial diagnoses included polymyositis (169), dermatomyositis (40), and inclusion body myositis (19). Line blot assays identified ≥2 MSAs/MAAs in 59 patients (25.9%), a single MSA/MAA in 103 (45.2%), and no autoantibodies in 66 (28.9%). ANA-IIF confirmed ≥2 MSAs/MAAs in 24 patients; anti-Ro52 was present in 23 (95.8%), coexisting with anti-SRP in 12 (52.2%). Combining ANA with line blot assays improved sensitivity and negative predictive value, reclassifying 80 patients as immune-mediated necrotizing myopathy, 38 as dermatomyositis, 19 as inclusion body myositis, 12 as anti-synthetase syndrome, and 79 as polymyositis.
Conclusion: Combining ANA testing with line blot assays significantly improves diagnostic accuracy in IIM, reducing false results and supporting better patient care.
Disclosure: Nothing to disclose.

EPR-178 | Muscle fiber response to mitochondrial dysfunction in mitochondrial myopathies

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Background and aims: Mitochondrial diseases affect 1 in 8,000 adults in north-east England, often causing disabling weakness, fatigue, and exercise intolerance. The unfolded protein response (UPR) and metabolic remodeling have been associated with mitochondrial dysfunction, but their relationship remain poorly characterized in mitochondrial myopathies. We investigated protein markers across pathways of mitochondrial biology and disease to understand how muscle fibers respond to mitochondrial dysfunction at the cellular level.
Methods: Muscle biopsies from 19 patients with mitochondrial myopathy associated with mitochondrial DNA deletions, were studied using Imaging Mass Cytometry for 25 protein markers of UPR, oxidative phosphorylation (OXPHOS), and mitochondrial metabolism. MT-ND4, MT-CYB, MT-CO1 and MT-ATP8 were used to classify fibers as deficient or normal for OXPHOS complexes I, III-V. Fiber classes were compared for all proteins using Generalized Linear Mixed Models (GLMM).
Results: GLMM analyzed 48,472 fibers, revealing significant protein fold-change increases in OXPHOS-deficient fibers, highest in MT-ATP8-deficient fibers, including TFAM (1.41), DLAT (1.65), HSPD1 (2.10), and HSPA9 (2.16); whereas C1QBP (1.31) was highest in MT-CYB-deficient fibers. MT-ND4, MT-CO1, and MT-ATP8 deficiencies co-occurred in 41.5% of fibers, whereas MT-CYB deficiency was rarer, co-occurring with others in 8%.

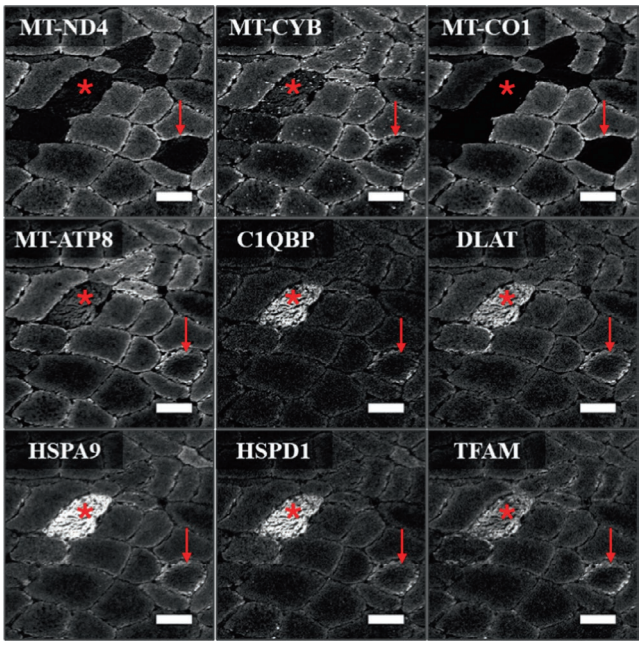

FIGURE 1 Fibers stained for OXPHOS, DLAT, C1QBP, HSPA9, HSPD1, and TFAM. *OXPHOS deficient fiber with increased non-OXPHOS proteins. Arrows show the same but only at fiber's periphery, suggesting peripheral origin of mitochondrial pathology. Scale bar 100 μm.

Conclusion: These results suggest that accumulation of OXPHOS dysfunction is associated with increased markers of mitochondrial biogenesis (TFAM), metabolic remodeling (DLAT), and mitochondrial proteostasis and UPR (C1QBP, HSPA9, and HSPD1). This study represents the most comprehensive analysis of these markers in human tissues at the single-fiber level, helping to address the knowledge gap and informing the development of targeted, disease-specific treatments for mitochondrial myopathy.
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EPR-179 | Upper limb rehabilitation using virtual reality vs. a real-setting training in people with Parkinson's disease

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Background and aims: Bradykinesia affects upper-limb functions in Parkinson's disease (PD). This study assessed the efficacy of physiotherapy on upper-limb motor function and brain activity in patients with PD (pwPD) comparing virtual-reality and real-setting training.
Methods: Forty pwPD and 30 age-/sex-matched healthy controls (HC) were included. We obtained kinematic data on touchscreen gestures and handwriting through customized tests on tablet/smartphone. Subjects performed a fMRI hand-tapping task. PwPD were randomized into two groups performing 8-week rehabilitation program stimulating speed/amplitude of handwriting and tap/swipe/slide movements in a real-setting (RS-training-group) or using technological devices/virtual-reality (VR-training-group).
Results: Relative to HC, pwPD showed reduced manual dexterity and movement speed/amplitude, and reduced fMRI activity of motor-related brain areas. After rehabilitation, VR-training-group showed greater improvement in manual dexterity. Both patient groups showed improved speed/amplitude during handwriting; however, VR-training-group showed greater improvement in handwriting on tablet. Both patient groups improved in tap/swipe tasks on smartphone, particularly RS-training-group. Both patient groups showed reduced sequence effect on amplitude during finger-tapping task, with RS-training-group showing greater improvement. After training, RS-training-group showed increased activity of sensorimotor areas and reduced activity of extra-motor areas; VR-training-group showed increased activity of thalamus and parietal areas and reduced activity of caudate and temporal areas.
Conclusion: Physiotherapy can promote improvements in upper-limb function and brain functional reorganization in pwPD. Real-setting or virtual-reality trainings have some specific effects that might help tailoring the therapeutic approach, but one cannot be considered superior. Imaging results could be interpreted as a pattern of recovery in RS-training-group and of mixed compensatory/recovery mechanisms in VR-training-group.
Disclosure: Funding. Italian Ministry of Health (GR-2018-12366005). Disclosures. AG, LZ, AGr, RB, DE, ES, VC, FF, CT, MM, MAV nothing to disclose. ES, SB, EC, DC grants form the Italian Ministry of Health. MF received compensation for consulting services or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM. FA received speaker honoraria from Biogen Idec, Roche, Eli Lilly and GE Healthcare; and grants from Italian Ministry of Health, Italian Ministry of University and Research, AriSLA, European Research Council, EU Joint Programme—Neurodegenerative Disease Research, and Foundation Research on Alzheimer Disease (France).

EPR-180 | Efficacy on disphagia of swallowing therapy plus neuromuscular electrostimulation vs. tst plus sham-nmes in MS

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Background and aims: Dysphagia is a disabling symptom in MS. The effectiveness of neuromuscular electrical stimulation (NMES) for dysphagia has limited research in pwMS. The aim of the study was to determine whether NMES benefit to a standard rehabilitative therapy (SRT) in dysphagic pwMS.
Methods: This multicenter, double-blind, randomized clinical trial compared SRT-NMES versus SRT with sham NMES (SRT-S). Patients underwent 16 therapy sessions and assessments at baseline (T0), after 16 sessions (T2) and 12 weeks post-treatment (T3). Main outcomes was ASHA scale, Visual VAS, DYMUS, and DOSS scores on FEES.
Results: 101 patients (mean age: 56.2 ± 10.9 years; 55% female). Both interventions led to significant improvements in ASHA, DYMUS, VAS and DOSS. In ASHA scores in the SRT-NMES

improved from 4.3 ± 1.3 at T0 to 5.2 ± 0.8 at T2 ($p < 0.001$), in the SRT-S group from 4.5 ± 1.0 at T0 to 5.0 ± 0.8 at T2 ($p < 0.001$). DYMUS in the SRT-NMES group from 4.3 ± 2.2 at T0 to 2.8 ± 2.2 at T2 ($p < 0.001$) and in the SRT-S group from 5.1 ± 2.8 at T0 to 3.9 ± 2.4 at T2 ($p < 0.001$). DOSS scores improved in SRT-NMES group from 4.4 ± 1.1 at T0 to 5.3 ± 0.8 at T2 ($p < 0.001$) and the SRT-S group from 4.6 ± 1.1 at T0 to 5.1 ± 0.9 at T2 ($p = 0.001$).
Conclusion: Both SRT-NMES and SRT-S therapies significantly improved swallowing function in pwMS. The inter-group analysis showed a trend in favor of SRT-NMES, Future research should explore the long-term benefits of these therapies to enhance rehabilitation strategies.
Disclosure: Nothing to disclose.

EPR-181 | Impact of experimentally induced fatigability on motor and cognitive functions in MS: a cross-sectional study

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Background and aims: Fatigability is a major symptom in People with Multiple Sclerosis (PwMS), affecting walking, balance, and cognitive function, and reducing quality of life. This study aimed to assess the acute effects of induced fatigability on gait, balance, and cognitive functions in PwMS using objective, instrumented assessments before (Pre), immediately after (Post), and after 30-minute (Rest) an overground Fatiguing Walking Test (FWT).
Methods: 96 PwMS (age: 54.1 ± 10.2 EDSS: 3.1 ± 1.2 points, 52% women) and 22 HC were assessed at three Italian MS centers. Participants completed a 30-minute or until exhaustion (Rate of Perceived Exertion; RPE; > 17 points) FWT, followed by balance tests (firm/foam surface, eyes open/closed) with three Inertial Measurement Units and cognitive assessment using the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) at Pre, Post, and Rest.
Results: All HS completed the FWT with a RPE of 10.5 ± 2.6 points, while 49% of PwMS completed the FWT (RPE: 14.5 ± 3.7 points), and 51% walked for 15.6 ± 6.3 minutes (RPE: 19.1 ± 1.1 points, p Time * Group < 0.001). (Figure 1) Static balance tests showed significant Time* Group interactions for trunk Medio-Lateral (ML) sway amplitude ($p = 0.011$) and sample entropy ($p = 0.043$). (Figure 2) Dynamic balance showed increased ML instability in PwMS versus a decrease in HS ($p = 0.007$). No changes were observed in BICAMS ($p > 0.05$
Conclusion: Data show an acute effect of motor fatigability on balance but on cognition. Next step will be to apply an ad-hoc rehabilitation protocol in order to interferee with faticability
Disclosure: This work was supported by the Italian Multiple Sclerosis Foundation [FISM Grant 2022/R-Multi/005] Nothing to disclose.

EPR-182 | Rehabilitation after stroke: The role of educational programs for family members

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Background and aims: Stroke is considered as one of the major causes of permanent disability across the globe contributing to increased functional impairment and reduced quality of life. Rehabilitation is largely dependent on family support, but the role of trained caregivers on recovery outcomes needs to be studied further.
Methods: A randomized controlled trial was conducted with 60 post-stroke patients, with an intervention group ($n = 30$) whose family members were taken through an education program, while the control group ($n = 30$) received the standard care Functional recovery was assessed using the Fugl-Meyer Assessment (FMA) at 1, 3, and 6 months. Preliminary evaluations were done using Modified Rankin Scale (MRS), the National Institutes of Health Stroke Scale (NIHSS) and the Rivermead Mobility Index (RMI). At six months follow up, quality of life was measured using Stroke-Specific Quality of Life Scale (SS-QOL).

	Intervention group (n=30)	Control group (n=30)
Age (yr.), mean±SD	55±10	55±11
Sex (male), n Sex (female), n	14 7	15 6
Stroke type: Ischemic, n	21	21
Comorbid diseases: Hypertension, n Ischemic heart disease, n DM, n	19 10 5	19 11 3
National Institutes of Health Stroke Scale (NIHSS) Score±SD	8,4±1	9±1
Modified Rankin Scale (MRS)	2	2
Rivermead Mobility Index (RMI) Score±SD	7.2±0.7	7±0.7

Table 1. Comparison of the initial data of patients of the two groups

Results: The intervention group proved to have improved functional recovery, with FMA scores increasing from 59 ± 11 at 1 month to 92.7 ± 12 at 6 months, unlike the control group (51 ± 11 to 67 ± 14) with significant improvements ($p < 0.01$). Quality of life was notably good in the intervention group which SS-QOL scored them at 162.2 ± 11 compared to the control group with 106.9 ± 17 with ($p < 0.01$). The program prepared family members to enhance their support in rehabilitation activities leading to better recovery trajectories.

Time intervals	Intervention group	Control group
1st month, mean±SD	59±11	51±11
3rd month, mean±SD	77.4±12	62.2±12
6th month, mean±SD	92.7±12	67±14

Table 2. FMA results (Fugl-Meyer Assessment)

Conclusion: Structured educational programs for relatives significantly improve the functional recovery and quality of life of patients after stroke. Further studies with larger samples are recommended to confirm the findings and optimize educational programs.
Disclosure: Nothing to disclose.

EPR-183 | Functional neural correlates of improvements after aerobic training in people with multiple sclerosis

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Background and aims: Aerobic training (AT) has shown promising results for the improvement of motor and cognitive functions in people with multiple sclerosis (pwMS). The aim of this study was to investigate the neural correlates of such changes using functional magnetic resonance imaging (fMRI).
Methods: Fifty-seven pwMS and 39 healthy controls (HC) were randomized to receive either AT or a control intervention (CT) for 8 weeks. Treatment was performed 3 times/week in 30-minute sessions. AT consisted of treadmill walking at progressively increasing intensities, while CT included mobilization, stretching, and balance exercises. The assessments, performed before and after treatment, evaluated cardiorespiratory fitness (V02peak), gait, mobility, cognitive functions (Brief Repeatable Battery of Neuropsychological tests), and brain activations during the Stroop test, which evaluates the ability to inhibit cognitive interference.
Results: After training, both MS groups improved in mobility ($p <= 0.24$) and verbal learning ($p <= 0.01$). MS-AT improved in V02peak, gait endurance, and cognitive interference inhibition ($p <= 0.02$), while MS-CT improved in verbal memory, visuospatial memory, and semantic fluency ($p <= 0.03$). All MS and HC groups improved in information processing speed ($p <= 0.45$). Stroop fMRI activity increased in the pre/postcentral gyri, thalamus, and cerebellum in MS-AT, while it decreased in the thalamus, insula, and occipital cortex in MS-CT ($p < 0.001$, uncorrected). No fMRI changes were found in HC. There were significant correlations between functional improvements and changes in fMRI activity in both MS groups.
Conclusion: AT is a valid strategy for the management of motor and cognitive dysfunctions in pwMS. Functional neuroplasticity represents one of the possible mechanisms underlying improvements after treatment.
Disclosure: Funding. Partially supported by Italian Ministry of Health (GR-2019-12369599). Disclosures. FR, PV, MA, TM, NT have nothing to disclose. PP received speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon and Sanofi. He received research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). MAR received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche, and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva, she receives research support from the MS Society of Canada, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM. MF received compensation for consulting services or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM.

EPR-184 | Challenges in neurorehabilitation in a war zone

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Background and aims: In war zones, neurorehabilitation faces unique challenges that impact the delivery and effectiveness of care for individuals with neurological diseases. Scarcity of medical supplies, equipment, and trained personnel hampers the ability to provide rehabilitation. Ongoing conflict poses risks to both patients and healthcare providers, making it difficult to access facilities&maintain consistent care. The trauma associated with war exacerbates psychological conditions, complicating rehabilitation efforts. Many individuals are displaced due to conflict, affecting their access to rehabilitation services and continuity of care.
Methods: Mixed-methods approach, combining quantitative data from rehabilitation centers in conflict-affected areas with qualitative interviews from healthcare providers/patients. Surveys assessed resource availability, treatment outcomes, and patient satisfaction, while interviews explored personal challenges faced during rehabilitation.
Results: Critical resource shortages, with 70% of centers reporting inadequate access to essential medical supplies and rehabilitation equipment. Security issues were cited by 85% of healthcare providers as a major barrier, resulting in interrupted services and limited patient access. Psychosocial challenges were prevalent, with 80% of patients exhibiting increased anxiety, depression, which negatively impacted their rehabilitation progress. Coordination issues among healthcare providers led to fragmented care, as reported by 75% of surveyed professionals.
Conclusion: Addressing these challenges requires innovative strategies, collaboration with local communities, and adaptable rehabilitation models that consider the complexities of providing care in a war-torn environment. There's urgent need for targeted interventions to address these challenges. Strategies that enhance resource allocation, ensure safety, integrate mental health support, foster cultural competence are essential for improving rehabilitation outcomes in the war zone environments.
Disclosure: Nothing to disclose.

EPR-185 | Predictors of response to physical exercise in patients with multiple sclerosis: A structural and functional MRI study

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Background and aims: Aerobic exercise is a promising rehabilitation strategy for multiple sclerosis (MS). However, a certain heterogeneity in individual response may be observed. This study aimed to assess how baseline demographic, clinical, and MRI features of MS patients influence their response to aerobic and non-aerobic motor training.
Methods: Eighty-eight MS patients and 70 healthy controls underwent structural and functional MRI acquisition to evaluate lesional, volumetric, cortical thickness, diffusivity, and resting-state functional connectivity measures. Clinical evaluation included expanded disability status scale, modified fatigue impact scale, timed 25-foot walk test, peak oxygen consumption and 6-minute walking test (6MWT). Patients were divided into two groups following aerobic or non-aerobic exercise programs and classified as "responders" or "non-responders" based on a 6MWT post-treatment improvement of at least 21.6 meters. Predictive factors for improvement were assessed among demographic, clinical, and MRI measures using random forest analyses.
Results: Independent predictors of treatment response were corticospinal tract (CST) fractional anisotropy (FA) and middle cerebellar peduncle (MCP) FA in the aerobic group (out-of-bag [OOB]-area under the curve [AUC] = 0.682), superior cerebellar peduncle (SCP) mean diffusivity (MD) in the non-aerobic group (OOB-AUC = 0.713), and SCP MD, MCP MD, CST MD, CST FA, and MCP FA in all MS patients (OOB-AUC = 0.734).
Conclusion: Response to physical exercise in MS patients is associated with specific markers of microstructural damage in key white matter tracts related to motor function for both the treatment strategies proposed. These findings highlight the potential role of neuroimaging in identifying MS patients who most likely benefit from motor rehabilitation.
Disclosure: Funding. Grants from Italian Ministry of Health (GR-2019-12369599) and MS Society of Canada (EGID3185). Disclosures. TM, AM, EP, PV, CA nothing to disclose. PP received speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon and Sanofi. He received research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). MAR received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche, and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva, she receives research support from the MS Society of Canada, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM. MF received compensation for consulting services or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM.

EPR-186 | Bimanual motor skill learning in acute stroke patients: robotic assessment and neural substrates

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Background and aims: Activities of daily life are mostly bimanual, learned, and may be impaired by stroke. While rehabilitation of bimanual coordination and skills is crucial, it is currently unknow whether bimanual motor skill learning (bim-MSkL) is enhanced or impaired during (sub)acute stroke. We aimed to quantify bim-MSkL in acute patients and unveil the neural structures related to impaired and successful bim-MSkL.
Methods: 74 (sub)acute stroke patients and 62 age-matched healthy individuals (HI) trained during three consecutive days with a bim-MSkL cooperation task on the REA2plan® robot (AXINESIS, Belgium). Using the REA2plan's handles, they had to complete as many laps as possible on a complex circuit over 1-minute blocks. One hand controlled the common cursor's lateral displacements, the other its sagittal displacements; which hand controlled which axis was randomized. Bim-MSkL was quantified with a bimanual speed/accuracy trade-off (biSAT) and coordination with a bimanual coordination factor of hands speeds (BCF). The patients underwent a comprehensive evaluation and a multimodal MRI.
Results: Overall, the patients improved bim-MSkL and bimanual coordination over the three days, but less than the HI (log(biSAT): -0.43, $p < 0.001$; BCF: -0.08, $p < 0.001$), likely because more patients (42%) were poor learners (biSAT improvement < 25%) than HI (16%). Clusters of injured voxels associated with reduced motor function at baseline and reduced ability to improve coordination were located along the corticospinal tract and in the corpus callosum.

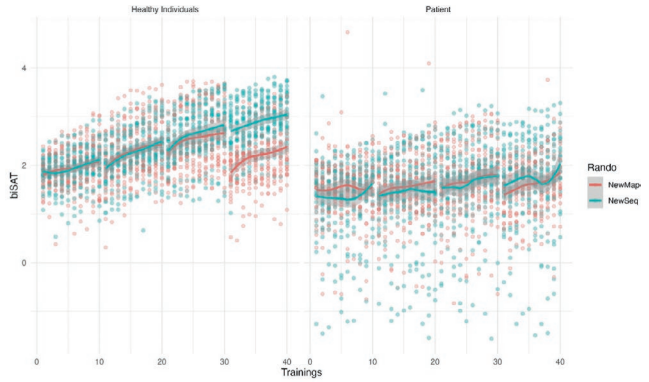

FIGURE 1 log(biSAT) in HI and patients (10 training/day). For generalization on Day 3, either the sequence (CIRCUIT NewSeq) or the hands mapping (NewMap) changed.

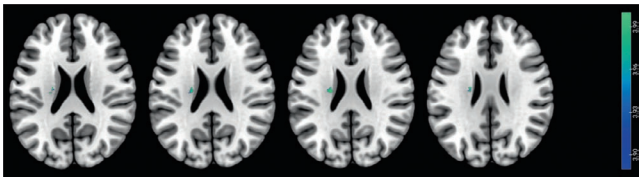

FIGURE 2 Voxel-based Lesion Symptom Mapping ($n = 50$). Acute stroke involving the corticospinal tract impaired the improvement of bimanual coordination over 3 days.

Conclusion: Shortly after the stroke, the patients showed a reduction in bim-MSkL, which correlated with damage to the corticospinal tract and corpus callosum.
Disclosure: Nothing to disclose.

Neuroimmunology 2

EPR-187 | HLA Class I and II alleles in myasthenic patients of Romanian descent: considerations regarding genotype and phenotype

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Background and aims: In Eastern European populations data regarding positive and negative associations between certain Human Leukocyte Antigen (HLA) alleles and myasthenia gravis (MG) subtypes are scarce. The main aim of this study was to analyze the associations of HLA Class I and II alleles with MG in patients of Romanian descent.
Methods: We consecutively enrolled adult Romanian unrelated myasthenic patients. After genotyping them by next-generation sequencing for six primary loci (HLA-A, -B, -C, -DRB1, -DQB1 and -DPB1) we compared their allelic frequencies with the controls'. The latter were represented by three separate groups of random normal subjects, two descent-matched and one of Italian descent, collected from the Allele Frequency Net Database.

TABLE 1 The control lot.

The population correspondent in the control group of the study	C1	C2	C3
Subject pool size	5758 6010 1612 6936 3328	1234	380
Genotyped HLA loci	A B C DRB1 DQB1	A, B, C, DRB1	DPB1
Resolution level of allelic genotyping	Two-digit level	Four-digit level	Four-digit level
Descent	Romanian	Romanian	Italian
Reported by	Constantinescu	Pingel *et al.*	Adorno *et al.*
The population correspondent in the Allele Frequency Net Database	Romaniapop2	GermanyDKMS-Romania minority	ItalyCentral

Results: We included 40 heterogenous patients (women: 80%; early-onset MG: 57.50%; juvenile MG: 7.50%; thymomatous MG: 22.50%; anti-acetylcholine receptor autoantibodies positive MG: 75%) and identified a total of 109 alleles. We obtained four previously acknowledged allelic associations in Western-European and North-American Caucasian subjects: negative for DRB1*13 and positive for HLA-B*08, DRB1*14:54 and DRB1*16:01. Surprisingly, we discovered six potential novel significant positive allelic associations with MG (HLA-A*02:36, B*47, B*73, B*44:27, B*57:02 and HLA- DPB1*51:01). Further, we analyzed the HLA allelic profile of specific MG subtypes and discussed potential immunological mechanisms involved.
Conclusion: Our work pioneers allelic association studies in Romanian myasthenic patients. The results suggest that the geographical and ethnical disparities of the MG-associated HLA alleles are perhaps overrated. Consequently, one can deduce that at least some of the immunopathogenic mechanisms of MG might also be common in patients of different descent.
Disclosure: This research was co-funded by the Romanian Operational Program for Competitiveness 2014–2020, Axis 1, under POC/448/1/1 Research Infrastructure Projects for Public R&D Institu-tions/Universities "Multidisciplinary Medical Research-Development Platform in the NE re-gion "CENEMED", mySMIS code: 127606.

EPR-188 | Immune checkpoint inhibitor-related myositis-myasthenia: A retrospective cohort study in Spain

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Background and aims: The combination myositis-myasthenia with or without myocarditis, is a rare but life-threatening complication of immune checkpoint inhibitors (ICI). Diagnostic and treatment approaches vary across hospitals. We evaluated the clinical spectrum, treatments, and outcomes of patients with this ICI-related complication.

Methods: This retrospective observational multicenter study in Spain collected clinical information on patients diagnosed with ICI-related myositis-myasthenia with/without myocarditis over the past 7 years using a structured questionnaire. Syndromes were classified as definite, probable, or possible based on the 2021 consensus disease definitions.

Results: We included 133 patients from 33 hospitals, with a median age of 72 years [IQR 34-89], 67% male. Symptoms began 30 days [IQR 18-68] after ICI initiation, including limb weakness, ptosis, diplopia, dysphagia, dysphonia, dyspnea, myalgia and axial weakness. Mean time from onset to hospital admission was 11 days [IQR 6-27]. Initial diagnoses were myositis in 88% (isolated 22%, combined with myasthenia 15%); myocarditis in 54% (with myositis 27%), and myasthenia in 9% (with myositis and myocarditis 24%). According to consensus definitions, 74% of myositis cases were definite, 61% of myasthenia cases probable, and 49% of myocarditis cases possible. During the acute phase, 74% had mRS > 2, 26% required intensive care, 96% received steroids, and 60% received immunoglobulins. At 30 days, 16% had died, 9% worsened, 3% stabilized, and 72% improved. At last follow-up (175 days [IQR 47-579]), ICI-related mortality was 23%. Predictors of poor outcomes will be presented.

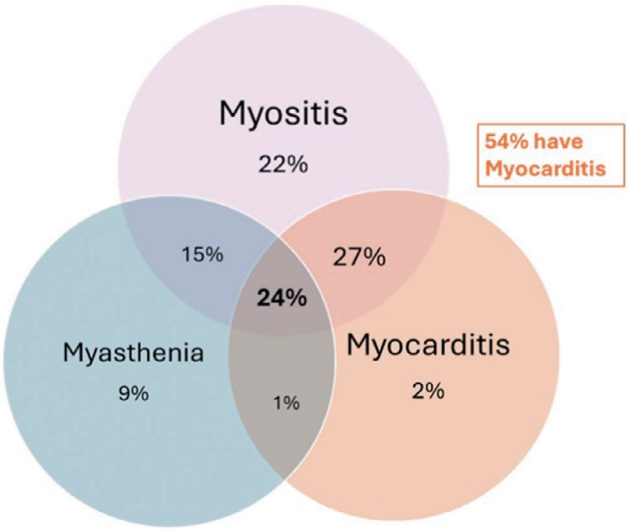

FIGURE 1 Frequncy and combinations of myositis, myasthenia and myocarditis

Conclusion: ICI-related myositis-myasthenia develops early after ICI initiation, progresses with severe symptoms, often includes myocarditis, and has a high first-month mortality rate.

Disclosure: This study is supported, in part, by a grant from the Neuroepidemiology Study Group of the Spanish Society of Neurology.

EPR-189 | The rs10191329 risk allele is associated with retinal layer thinning in multiple sclerosis

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Background and aims: The minor allele of the genetic variant rs10191329 in the DYSF–ZNF638 locus, associated with CNS resilience rather than immune-mediated pathology, has been linked to faster disability progression in MS. Retinal layer thinning measured by OCT is a biomarker of neuroaxonal damage. We aimed to investigate whether rs10191329 is associated with retinal layer thinning in relapsing MS.

Methods: We included relapsing MS patients with ≥2 OCT scans from a prospective observational study, excluding eyes affected by optic neuritis. DNA was genotyped using the Illumina Infinium Global Screening Array-24 and imputed to the Haplotype Reference Consortium panel using Minimac4 (V1.0.2). A multivariate linear regression model evaluated mean annualized rates of retinal layer thinning (%/year) in the peripapillary retinal nerve fiber layer (aLpRNFL) and ganglion cell-inner plexiform layer (aLGCIPL) using rs10191329*A allele count as the independent variable, adjusted for age, sex, and ancestry components.

Results: We included 208 patients (mean age 30.5 years [SD 7.9], 74.1% female, median EDSS 2.0, median follow-up 25 months, median OCT scans 3). The rs10191329 risk allele was associated with faster retinal thinning (estimate 0.119 [SE 0.056], $p < 0.001$). Each rs10191329*A allele increased aLpRNFL thinning by 0.10%/year (95% CI 0.05–0.19) and aLGCIPL thinning by 0.11%/year (95% CI 0.07–0.19), contributing 26.4% and 27.2% of the mean atrophy rates, respectively.

Conclusion: The minor rs10191329 allele may predispose carriers to MS-related neuroaxonal damage. Genotypic stratification in clinical trials may be warranted.

Disclosure: Gabriel Bsteh: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene/BMS, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting Biogen, Celgene/BMS, Novartis, Roche, Sanofi-Genzyme and Teva. He has received unrestricted research grants from Celgene/BMS and Novartis.

EPR-190 | Efgartigimod combined with glucocorticoid in the treatment of severe generalized myasthenia gravis

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Center of Treatment of Myasthenia Gravis, People's Hospital of Shijiazhuang, Shijiazhuang, China

Background and aims: High-dose glucocorticoid pulse (IVMP) is effective in treating generalized myasthenia gravis (gMG), but early treatment may cause transient aggravation, with some patients experiencing MG crisis. This study investigates the safety and efficacy of efgartigimod combined with different doses of IVMP in gMG patients.

Methods: Myasthenia gravis patients treated at Shijiazhuang People's Hospital from December 2023 to May 2024 were retrospectively analyzed. Patients received efgartigimod (D1, D8) combined with IVMP or IVMP alone. Efficacy was assessed using the Quantitative Myasthenia Gravis Score (QMG) at baseline, 2 and 12 weeks.

Results: A total of 57 patients were included: 20 in the 1000 mg IVMP group (A), and 7, 10, and 20 in the 1000 mg (B), 500 mg (C), and 250 mg (D) IVMP combined with efgartigimod groups, respectively. QMG scores for groups A, C, and D gradually decreased over 12 weeks. Group B showed an increase in QMG score at week 12 compared to week 2 but remained below baseline (Figure 1). There was a significant difference between group A and group B at week 2 in QMG score reduction (Figure 2). Group A had a significantly higher incidence of transient exacerbations than groups C and D (Table 1). The incidence of adverse reactions was higher in group A than in the other three groups, especially in the development of osteoporosis and electrolyte disturbances (Table 2).

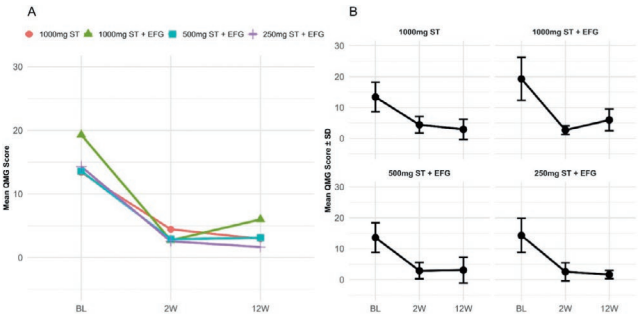

FIGURE 1 Changes in QMG score during the observation period.

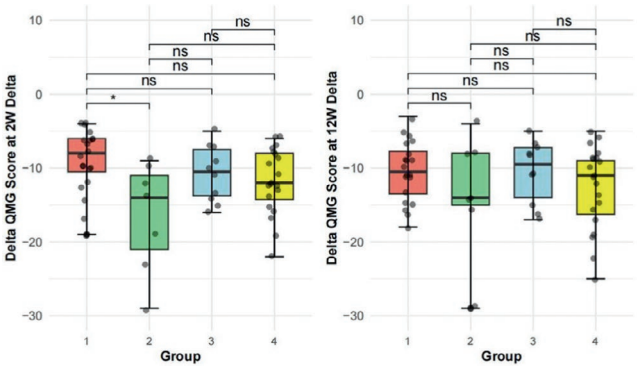

FIGURE 2 QMG score reductions in various groups.

Comparison	p
Group A vs group B	0.6618
Group A vs group C	*0.00159
Group A vs group D	*0.0000451
Group B vs group C	0.05147
Group B vs group D	0.01197
Group C vs group D	1

*P<0.0083

Table 1. Pairwise comparisons of the incidence of transient exacerbations by group (Fisher 's exact test)

Group	A组 (N=20)	B组 (N=7)	C组 (N=10)	D组 (N=20)
AE	17 (85.0%)	3 (42.9%)	5 (50.0%)	5 (25.0%)
Blood glucose increased	7 (35.0%)	2 (28.6%)	1 (10.0%)	1 (5.0%)
Osteoporosis	6 (30.0%)	0 (0.0%)	0 (0.0%)	1 (5.0%)
Electrolyte disturbances	12 (60.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)
Abnormal liver function	7 (35.0%)	2 (28.6%)	3 (30.0%)	4 (20.0%)
Hyperlipidemia	2 (10.0%)	0 (0.0%)	1 (10.0%)	0 (0.0%)

Table 2. Incidence rates of adverse events in various treatment groups

Conclusion: Efgartigimod combined with low-dose IVMP pulse therapy rapidly improved myasthenic symptoms and reduced the transient exacerbations and adverse reactions in severe gMG patients.

Disclosure: This work was supported by the National Natural Science Foundation of China (No. 82274582), Central guidance for local scientific and technological development funding projects (No. 246Z7706G), Key Laboratory Construction Subsidy Fund Project (No. 236790017H) S&T Program of Hebei (231201013D).

EPR-191 | Do people with Multiple Sclerosis age differently? Reference values for natural killer cell aging and study outline

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Background and aims: Chronological age is the most consistent factor influencing the observed disease course of people with Multiple Sclerosis (pwMS). We aim to explore differences in biological aging and identify covariates linked to accelerated aging in pwMS. The expression of the marker CD57 on CD56dim natural killer (NK) cells and its proportion of the whole NK population is a well-established indicator for matured NK cells and may therefore serve as a surrogate marker for biological age.
Methods: Peripheral blood mononuclear cells (PBMCs) from healthy blood donors in Switzerland, Austria, and Germany were analyzed using flow cytometry, gating for CD3, CD56, and CD57. Age-adjusted z-scores for CD57+CD56dim NK-cell proportions were estimated. In this ongoing study, PBMCs from 100 pwMS will be collected for comparisons of NK-cell aging. Potential covariates, including disease duration, treatment duration, and disease-modifying treatment type, will be evaluated in 80 pwMS across 16 subgroups.
Results: Data from 10,437 HCs aged 18-70 years (mean age: 45.9 years [SD 13.3], 33.6% female) were analyzed. The mean proportion of CD57+CD56dim cells was 38.4% [SD 15.4], and it increased fourfold from individuals younger than 21 to those older than 64 years. On average, the proportion of CD57+CD56dim NK cells increased by 3.9% per year. Adding sex as a covariate did not improve the model fit.
Conclusion: CD57+CD56dim NK cells are a robust marker of NK-cell aging and may indicate biological age, regardless of sex. Based on these findings, age-adjusted z-scores can be predicted for pwMS to assess whether biological and chronological age differ.
Disclosure: Nothing to disclose.

EPR-192 | Regression of pre-existing white matter hyperintensities after CD19 CAR T-cell induced ICANS: A case series.

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Background and aims: Chimeric antigen receptor (CAR T-cell) therapy has revolutionized the treatment of hematological malignancies, but its use is often limited by toxicity, such as in immune effector cell-associated neurotoxicity syndrome (ICANS). The mechanisms behind ICANS are still poorly understood, but evidence suggests that cytokines increase blood-brain barrier (BBB) permeability and a potential off-target effect of CD19 CAR T-cells on pericytes. White matter hyperintensities (WMHs) are part of the spectrum of small vessel disease and are often considered irreversible. We present the regression of pre-existing WMHs in three patients treated with CAR T-cell therapy who experienced ICANS.
Methods: All patients who receive CAR T therapy in our center undergo a baseline brain magnetic resonance imaging (MRI) before infusion as part of our CAR T interdisciplinary protocol. We included three patients with diffuse large B-cell lymphoma (DLBCL), treated with anti-CD19 CAR T-cell therapy, that developed ICANS and in which longitudinal MRI scans were available.
Results: We report the regression of WMHs present in the baseline MRI in three patients upon ICANS resolution. The severity of ICANS was heterogeneous: speech impairment appeared in the three patients and encephalopathy in two of them. All patients received levetiracetam and thiamine, two received corticosteroids and one received anakinra. All patients progressed favorably.

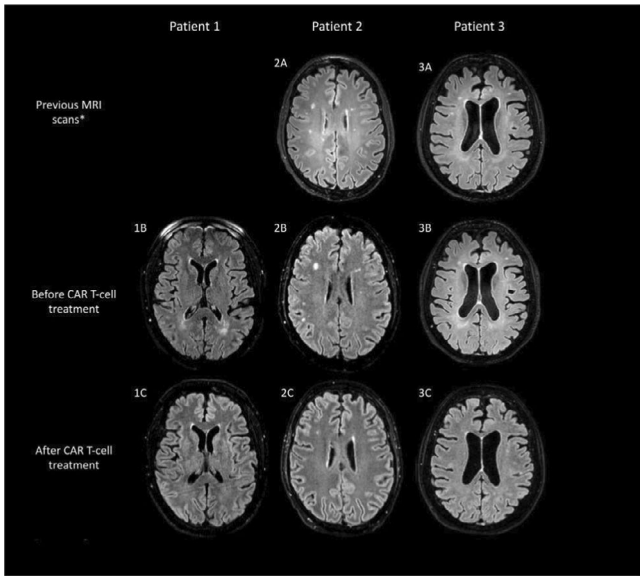

FIGURE 1 Axial MRI FLAIR of patients 1 to 3. "A" and "B" show subcortical white matter hyperintensities (WMH) in scans prior to CAR T-cell treatment. "C" shows the disappeareance or decrease in size of the same WMHs, after CAR T-cell infusion.

TABLE 1 Main characteristics of the three patients. CAR, Chimeric Antigen Receptor; CRS, Cytokine Release Syndrome; ICANS, Immune effector Cell Associated Neurotoxicity Syndrome; LEV, levetiracetam.

	Patient 1	Patient 2	Patient 3
CAR T-cell therapy	anti-CD19 (Axicabtagen ciloleucel - Yescarta)	anti-CD19 (Axicabtagen ciloleucel - Yescarta)	anti-CD19 (Axicabtagen ciloleucel - Yescarta)
Pre-conditioning	Fludarabine - Cyclophosphamide	Fludarabine - Cyclophosphamide	Fludarabine - Cyclophosphamide
CNS infiltration	No suspicion	Suspected, not confirmed. Received rescue intrathecal treatment previous to CAR T.	No suspicion
CRS severity	Grade 2	Grade 1	Grade 2
ICANS severity	Grade 1	Grade 3	Grade 2
ICANS symptoms	Mild speech impairment	Moderate encephalopathy with speech disturbance	Mild encephalopathy with speech disturbance
ICANS treatment	Thiamin, LEV. No steroids.	Thiamin, LEV, dexamethasone (up to 10mg/6h), Anakinra.	Thiamin, LEV, dexamethasone (up to 10mg/12h).
Other complications	Hematologic toxicity grade 4	Hematologic toxicity grade 4 Septic shock (E. faecium)	Hematologic toxicity grade 4
EEG	Posterior dominant alpha rhythm, no epileptiform activity.	Frontal Intermittent Rhythmic Delta Activity (FIRDA).	Moderate slowing of background activity with diffuse theta rhythms. Occasional bursts of anterior polymorph delta waves. Findings correspond to moderate encephalopathy.
CSF study during ICANS	Not practiced.	Normal glucose. Protein 0.89 g/L. 12 cells/mm3 (100% lymphocytes expressing T phenotype). Basic microbiology negative.	Not practiced.
Day of target MRI in relation to CAR T	+11	+10	+8
Time between first and target MRI	21 days	2 months	1 year

Conclusion: To our knowledge, this is the first report of WMHs disappearance in DLBCL patients after CAR T-cell therapy. Further research is needed to understand the nature of WMHs in patients with DLBCL and to gain more insight into the mechanisms underlying CAR T-cell neurotoxicity.
Disclosure: Nothing to disclose.

EPR-193 | Immunological signature to guide treatment in anti-NMDAR encephalitis

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Background and aims: Anti-N-methyl-D-aspartate receptor (NMDAR) encephalitis is a severe autoimmune disorder with a broad spectrum of clinical manifestations and disease severity. Although many patients significantly improve after first line immunotherapy, others experience refractory disease, highlighting variability in treatment response. This heterogeneity underscores the need to better understand the underlying pathophysiology, and to identify reliable biomarkers to guide therapeutic response.
Methods: Using the SOMAscan proteome platform, we identified potential relevant proteins from the CSF of 29 untreated anti-NMDARE patients and compared these to 15 healthy controls. The results were confirmed using Luminex, initially for two cytokines. Obtaining promising pilot data, STRING database was used to create a 21-cytokine pane, linked by immunological pathways to the initial two. The 21-cytokine panel is tested in 75 untreated CSF samples from Dutch and South Korean anti-NMDAR encephalitis patients.
Results: TNFsR-ll and sL-Selectin were upregulated in anti-NMDARE using SOMAscan (median 57,032 vs. 17,487RFU and 107,862 vs. 46,636RFU, respectively, both $p < 0.0001$)), and TNFsR-II more so in patients with poor prognosis (median 96,913 poor vs. 46,303 good). These results were confirmed by Luminex (median concentration 1,037 vs. 135pg/ml and 11,600 vs. 4,113pg/ml, respectively, $p < 0.0001$), TNFsR-ll was more outspoken in poor prognosis patients (1,438pg/ml poor vs. 546 good). Full cohort data are currently being analyzed ($n = 75$ anti-NMDARE patients [54 good, 21 poor outcome], 22 controls)
Conclusion: Preliminary data suggest that distinct immune pathways contribute to outcomes in anti-NMDAR encephalitis. Measuring these signatures in CSF from untreated anti-NMDAR encephalitis patients might provide the opportunity to apply targeted therapeutic strategies.
Disclosure: Nothing to disclose.

EPR-194 | Genetic insights into multiple sclerosis, myasthenia gravis and immune-mediated disorders

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Background and aims: Immune-mediated diseases can be classified as a continuum from pure autoimmune to autoinflammatory with mixed diseases in between [McGonagle, 2006, 2021]. Here we investigate the polygenic continuum of immune-linked disorders using statistical genetics methods and define genetic architecture focusing on the place of multiple sclerosis (MS) and myasthenia gravis (MG) in the continuum.
Methods: We analyzed genome-wide association studies for MS (*n* cases 14802), MG (*n* cases 1873) and 13 immune-linked disorders (SLE, SS, SjS, PSC, PBC, AITD, UC, CD, CeD, PS, RA, JIA, T1D) using statistical genetics methods (LDSC, MiXeR, LAVA and genomicSEM) for characterization of overlap and genetic architecture. FUMA and MAGMA were used for functional annotation.
Results: GenomicSEM suggested a continuum structure with four underlying factors from autoimmune diseases at one end to inflammatory on the opposite end (Fig. 1). Genetically MG was located between cluster 2 (together with coeliac disease) and cluster 3 disorders. MS shows high correlation and overlap with UC, CD, PSC and PBC (Fig. 2), and these findings show that genetically MS has common genetic background not only with autoimmune but also with inflammatory diseases. We observed a balanced mixture of negative and positive local correlations within the MHC region, while outside this region they were predominantly positive. MAGMA analysis shows genes associated with monogenic immune diseases in diseases with prominent autoimmune and inflammatory components.

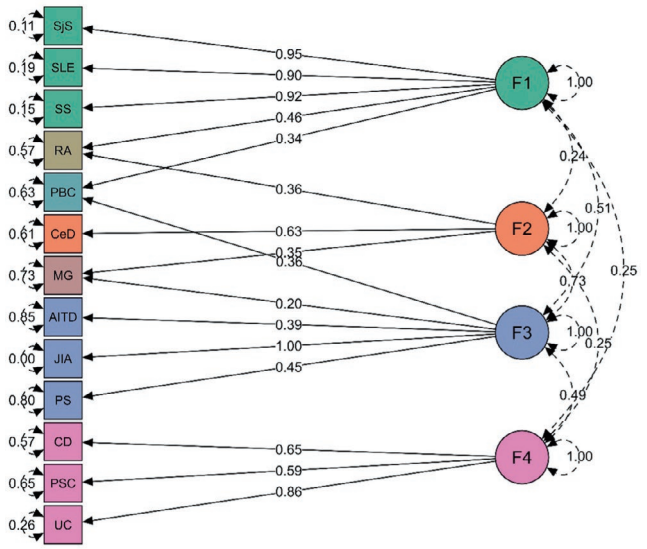

FIGURE 1 Four groups of immune-mediated diseases identified in genomic SEM analysis.

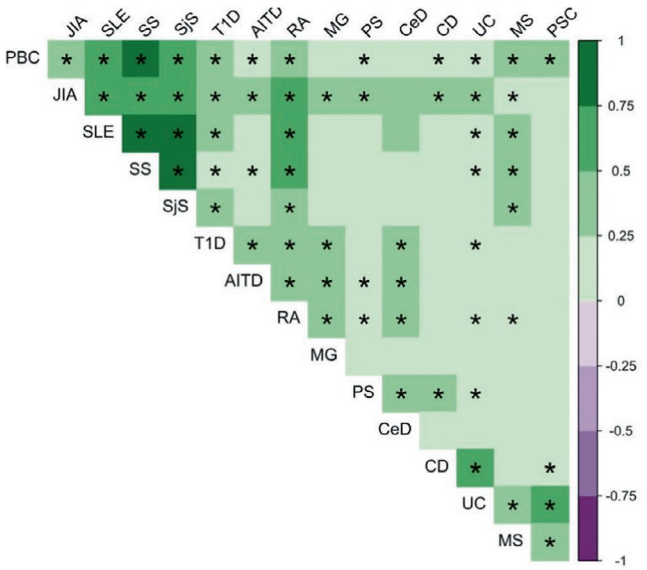

FIGURE 2 Heatmap of genome-wide genetic correlations across 15 immune-mediated diseases.

Conclusion: This study explores the genetic aspects of the autoimmune-autoinflammatory continuum, highlighting the position of MS and MG. The findings provide insights that can inform future research in this field.

Disclosure: Disclosures: No special disclosures. This work was supported by an RCN grant 324252.

EPR-195 | Efficacy of prokinetics in preventing pneumonia in post-stroke patients with nasogastric tubes: A meta-analysis

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Background and aims: Post-stroke patients using nasogastric tubes are at increased risk of developing aspiration pneumonia. Prokinetics may help prevent pneumonia by enhancing gastric emptying and reducing gastroesophageal reflux, both of which are risk factors for aspiration. However, studies are controversy regarding the prevention of pneumonia in such patients. Our aim was to evaluate the efficacy of prokinetics in preventing pneumonia in post-stroke patients using nasogastric tubes.

Methods: We systematically searched the literature for randomized controlled trials on Cochrane, PubMed, Embase, Web of Science and Scopus databases from inception to November 2024. The primary efficacy outcome assessed was incidence of pneumonia. Risk of bias was assessed using the RoB 2 and the ROBINS-1 tools.

Results: Of 326 articles screened, 3 randomized controlled trials were included, with a total of 600 patients. The intervention group comprised 291 patients, and the control group comprised 309 patients. The overall risk ratio (RR) for pneumonia in the intervention group compared to the control group was 0.80 (95% CI: 0.50–1.27, $p > 0.05$), indicating no statistically significant reduction in pneumonia risk with the intervention. High heterogeneity was observed among studies ($I^2 = 87\%$, $p < 0.001$), reflecting substantial variability in outcomes.

Conclusion: Current data does not indicate any correlation between the use of prokinetics and the incidence of pneumonia in patients in use of nasogastric tubes. More trials would help with more robust evidence. Currently, there are no formal guidelines or standardized recommendations for their use in this context.

Disclosure: All authors report no relationships that could be construed as a conflict of interest. All authors take responsibility for all aspects of the reliability and freedom from bias of the data presented and their discussed interpretation.

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Background and aims: Mild traumatic brain injury (mTBI) often leads to cognitive dysfunction, yet effective treatments remain scarce. Ferroptosis, a form of regulated cell death, plays a key role in mTBI. This study explores the potential of MSC-Exos to inhibit ferroptosis and improve cognitive function.
Methods: mTBI was induced in rats using a weight-drop model. MSC-Exos (50 μg, 100 μg, 200 μg) were administered. Cognitive function was assessed using NOR and MWM tests. Lipid peroxidation (MDA, 4-HNE) and Gpx4 expression were measured to evaluate ferroptosis.
Results: MSC-Exos improved cognitive function in mTBI rats, with the 200 μg group showing the best results. MSC-Exos reduced lipid peroxidation (MDA, 4-HNE) and restored Gpx4 expression, inhibiting ferroptosis and enhancing cognitive performance.
Conclusion: MSC-Exos inhibit ferroptosis and improve cognitive function in mTBI by activating the PI3K/AKT/mTOR pathway, offering a promising therapeutic approach for mTBI.

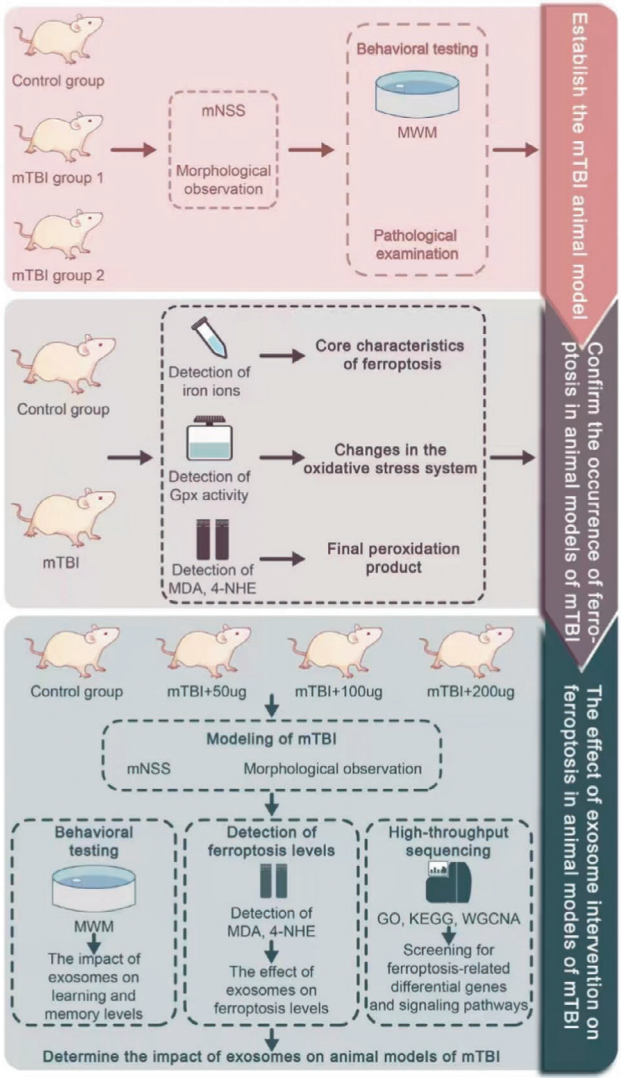

FIGURE 1 Behavior test

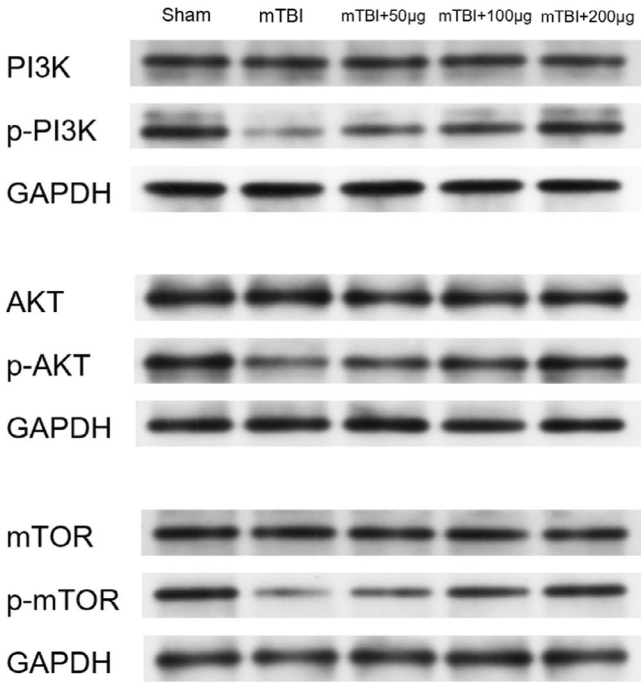

FIGURE 2 Western Blot Test

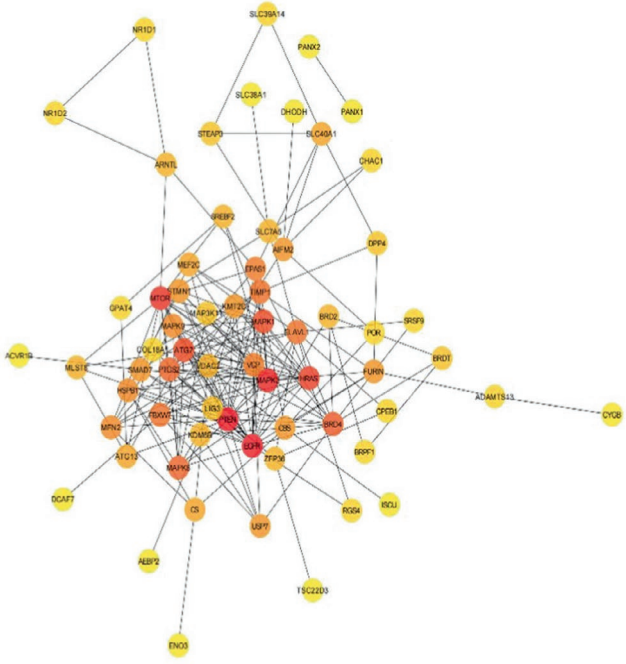

FIGURE 3 PPI network

Disclosure: The authors declare no conflict of interest.

EPR-197 | Safety and efficacy of ALMB-0166 in patients with acute spine cord injury (SCI): A randomized, phase I/II study

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Background and aims: ALMB-0166 is a first-in-class humanized monoclonal antibody that block connexin-43 hemichannels in spinal cord astrocytes, which have the potential to prevent further injuries following SCI and promote neurological recovery.

Methods: Eligible patients had an acute SCI with American Spinal Injury Association (ASIA) levels at C3 and below and ASIA impairment scale (AIS) B or C, and were within 72 hours after injury. Patients were randomized to receive a single intravenous infusion of ALMB-0166 200, 600 (2:1) and 1200, 2400, 4800 mg (3:1) or placebo with best supportive care. Primary outcome was safety.

Results: 24 patients with C3-C7 SCI received treatment (17 with ALMB-0166, 7 with placebo). Treatment emergent adverse events (TEAEs) occurred in 94.1% (16/17) and 100% (7/7) of ALMB-0166 and placebo treated patients. ≥Grade 3 TEAEs were 17.6% (3/17) with ALMB-0166 and 42.9% (3/7) with placebo, commonest being hypokalemia, pulmonary inflammation, respiratory failure, and deep venous thrombosis ($n=1$) with ALMB-0166 and hypokalemia ($n=2$), hyponatremia ($n=1$) with placebo. At day 56, patients treated with ALMB-0166 had improvement compared with those given placebo in motor function (scores increased from baseline by 66.0 for 2400 mg and 45.6 for placebo), sensatory function (scores increased by 77.5, 62.7 for 600, 1200 mg and 52.3 for placebo), AIS (2 patients recovered to grade E for ALMB-0166 and 0 patient for placebo), and pain (VAS scores decreased by 44.3, 23.7 for 1200, 2400 mg and 20.9 for placebo).

Conclusion: ALMB-0166 demonstrated great safety profile and improved neurologic recovery in patients with acute SCI.

Disclosure: Chao Li, Miao Jin, Shaonan Ni, Yumei Yang, and Qingxi Wang are employees of CSPC Pharmaceutical Group, Ltd. Yanfeng Zhang is an employee of AlaMab Therapeutics Inc. Other authors have nothing to disclose.

EPR-198 | Liberal vs. restrictive transfusion strategy in patients with acute brain injury: A systematic review and meta-analysis

A. Menegaz de Almeida[1]; F. Alves de Paiva[2]; F. Alves Kelly[3]; J. Martinez-Lemus[4]; C. Rocha Dantas[5]; A. Boris de Mesquita[5]; L. Violeta Rodrigues de Matos[6]; K. Violeta Rodrigues de Matos[7]; A. Machado Silva[8]; H. Roberto Moreira de Oliveira Carriço[9]; J. Patino[10]; V. Vyas[10]; L. Fernandes Torres[11]; M. Carolina Chaves do Vale[12]

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Background and aims: Brain injury is the leading cause of death and disability worldwide. Anemia is common among brain injury patients, with transfusion of red blood cells (RBC) often being required. Evidence is lacking to determine the preferred hemoglobin (Hb) threshold for transfusion, whether a restrictive (< 7 g/dL) strategy or a liberal approach (< 10 g/dL).

Methods: MEDLINE, Web of Science, SCOPUS, and Cochrane databases were searched for randomized clinical trials (RCTs) comparing the restrictive transfusion method with a liberal threshold. RCTs published up to December 9, 2024 were eligible. Differences between groups were estimated using the Mantel-Haenszel method; heterogeneity was assessed using I2 statistics.

Results: 6 RCTs with data from 2599 patients were included. Statistically significantly better rates of neurological recovery were found in the liberal transfusion group [GOS-5; 21.1% vs. 16.3%; OR, 1.39; 95% CI, 1.13–1.72; $p=0.001$; $I^2=0\%$]. The restrictive group was found to have higher rates of remaining in a vegetative state [GOS-2; 1.7% vs. 3.2%; RR, 0.54; 95% CI, 0.29–1.00; $p=.050$; $I^2=0\%$] and higher rates of sepsis/septic shock [6.4% vs. 9%; RR, 0.73; 95% CI, 0.56–0.95; $p=.020$; $I^2=0\%$]. Higher Hb levels at enrollment and more units of RBC units used per patient were associated with a lower rate of GOS-3.

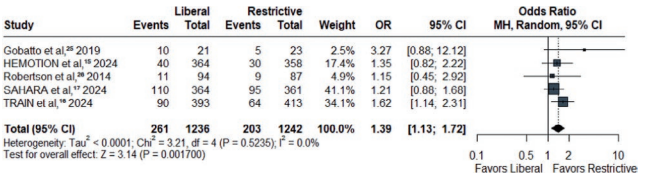

FIGURE 1 Glasgow Outcome Scale 5 (GOS), reporting good neurologic recovery in six months

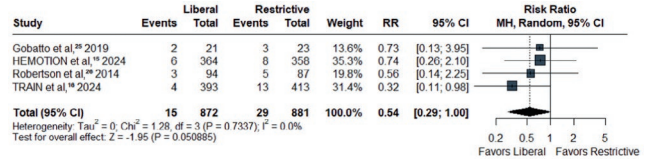

FIGURE 2 Glasgow Outcome Scale 2 (GOS), reporting patients remaining in a vegetative state in six months

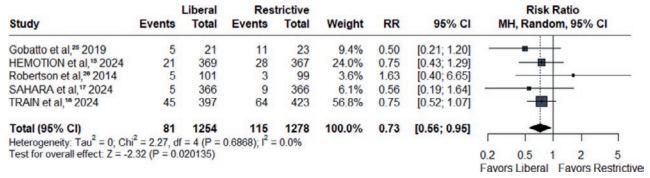

FIGURE 3 Sepsis or septic shock occurrence

Conclusion: This meta-analysis establishes the liberal strategy as having a better rate of neurological recovery and safety compared to a restrictive approach for managing acute brain injury patients.
Disclosure: Nothing to disclose.

EPR-201 | Evaluating stroke recognition and time metrics in Emergency Dispatch: Comparing mimics versus true strokes/TIA

N. Leto[1]; E. Farbu[2]; P. Barach[3]; C. Bjørshol[1]; M. Kurz[3]; A. Fromm[4]; C. Bjerkvig[5]; T. Lindner[1]
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Background and aims: Recognition of acute stroke by the Emergency Medical Dispatch Centre (EMDC) can lead to efficient management, yet many alerts are false due to stroke mimics. We aimed to quantify EMDC over-triage by comparing stroke mimics and confirmed stroke cases.
Methods: This retrospective study included patients with a suspected stroke admitted via the EMDC in Western Norway from January 1, 2021, to December 31, 2022. Data on EMDC dispatch criteria, prehospital time metrics, and discharge diagnoses were collected. The EMDC used the Norwegian Medical Priority Dispatch System (MPDS) algorithm with eight stroke suspicion criteria.
Results: Of 8259 patients, 7080 (86%) were stroke mimics and 1181 (14%) were confirmed stroke cases: 15 (1%) transient ischemic attack (TIA), 998 (85%) acute ischemic stroke (AIS), and 168 (14%) intracerebral hemorrhage (ICH). Five EMDC criteria had stroke mimic rates > 90%, including breathing problems (96%), acute dizziness (94%), acute hemianopsia (91%), acute ataxia/confusion (94%), and acute headache (95%). The Face-Arm-Speech (FAST) criteria had higher confirmed stroke rates compared to the five other EMDC criteria (OR 2.82, 95% CI 1.69-4.67). Median EMS response times were similar for mimics and confirmed strokes (10 vs. 9 min; $p = 0.47$), but on-scene times were longer for mimics (16 vs. 10 min; $p < 0.001$).
Conclusion: EMDC stroke dispatch criteria have low positive predictive value. EMDC FAST dispatch criteria were associated with higher specificity in stroke recognition. Confirmed stroke diagnoses correlate with shorter EMS on-scene times. Our findings indicate the need for new EMDC stroke assessment tools, although requiring validation in prospective studies.
Disclosure: Nothing to disclose.

EPR-202 | Laboratory diagnostics of rhinoliquorrhea – Re-evaluation of cut-off values of beta-trace protein

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Background and aims: Cerebrospinal fluid rhinorrhea (CSFR) occurs when cerebrospinal fluid (CSF) leaks through a bony defect into the nasal cavity. This condition poses a significant risk of bacterial meningitis, necessitating timely and accurate diagnosis. Beta-trace protein (BTP) is the most widely used biomarker for detecting CSF contamination in nasal mucus, but diagnostic reliability is hindered by inconsistent cut-off values, ranging from 0.24 to 6.00 mg/L in the literature. This study re-evaluates these cut-offs to improve diagnostic precision.
Methods: We analyzed BTP levels using nephelometry in pure ventricular and lumbar CSF, serum, and nasal mucus samples from 265 patients with clinically suspected CSFR. Data were further assessed through experimental setups, including pure sample measurement, laboratory modeling of CSF contamination, and retrospective analysis of clinical cases. Receiver operating characteristic (ROC) analyses were performed to determine optimal cut-off values.
Results: BTP concentrations were significantly higher in lumbar CSF (25.10 mg/L) than ventricular CSF (6.70 mg/L, $p < 0.001$), and higher in serum (0.46 mg/L) compared to nasal mucus (0.29 mg/L, $p < 0.001$). ROC analysis identified 1.40 mg/L as the most feasible cut-off for nasal mucus BTP, achieving 100% sensitivity and 94% specificity. Incorporating serum BTP levels did not enhance diagnostic accuracy.
Conclusion: A cut-off of 1.40 mg/L for nasal mucus BTP provides high diagnostic reliability. However, multi-center studies are needed to validate these findings across various laboratory systems. Interim recommendations include tailoring cut-offs to specific laboratory protocols to optimize diagnostic validity.
Disclosure: The study was approved by the ethics commission of the Medical University of Graz (EK 32-149 ex 19/20). MTH declares no conflict of interest. VV declares no conflict of interest. AFR declares no conflict of interest. JJA declares no conflict of interest. TK declares no conflict of interest. CE declares no conflict of interest. SW declares no conflict of interest. MG declares no conflict of interest. SH declares no conflict of interest. MK

has received travel funding and speaker honoraria from Bayer, Biogen, Novartis, Merck, Sanofi and Teva and serves on scientific advisory boards for Biogen, Bristol-Myers Squibb, Gilead, Merck, Neuraxpharm, Novartis, Alexion, Amgen and Roche. He received research grants from Biogen, Novartis and Teva.

Movement disorders 3

EPR-203 | Post-hoc analysis of the GUT-PARFECT trial for fecal microbiota transplantation in Parkinson's disease

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Background and aims: Dysregulation of the gut microbiome has been implicated in Parkinson's disease (PD). The recently published GUT-PARFECT trial evaluated the clinical effects and safety of a single fecal microbiota transplantation (FMT) in patients with early- stage PD. Mild, but long-lasting beneficial effects on motor symptoms and colon transit time were reported. This exploratory post hoc analysis aimed to investigate which factors might predict the magnitude of response to FMT.
Methods: Univariate and multivariate analyses were conducted to determine possible predictors of motor response to FMT. Responders were defined by an improvement of more than 3.25 on the Movement Disorders Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) part 3 motor score, which is considered a clinically relevant difference. Potential treatment by subgroup interactions for changes in the major outcomes were evaluated among post hoc subgroups defined by age, age at diagnosis, disease duration, sex, motor phenotype, and presence of certain non-motor symptoms (e.g., constipation, REM sleep behavior disorder). Gut microbiota analysis was performed through 16S rRNA sequencing.
Results: FMT responders were more likely to have shorter colon transit time, less REM sleep behavior disorder, less motor fluctuations, and less severe non-motor symptoms at baseline. Greater alpha diversity of gut microbiota (measured by the Shannon index) at baseline was associated to a more beneficial response to FMT. Individual healthy donors that provided the stool samples for treatment could not predict response in their respective acceptors.
Conclusion: The results of this exploratory post hoc analysis can guide future planned clinical trials of FMT in PD.
Disclosure: Nothing to disclose.

EPR-204 | Patient-reported outcomes, psychosocial health and healthcare utilization in patients with friedreich ataxia

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Background and aims: Friedreich's ataxia (FA) is a rare neurodegenerative disorder characterized by worsening movement and speech impairments. This study aimed to assess FAs impact on patient-reported, psychosocial, and health service outcomes.
Methods: Within the PROFA study, we assessed 102 FA patients in France, Germany, and Austria, including a baseline study center and remote mobile assessment, capturing disease severity (SARA), daily living deficits (FARS-ADL), cognitive and affective impairments (CCAS), health-related quality of life (HRQoL: PROM-ATAX, EQ-5D-5L), mental well-being (WEMWEBS), hearing (HearWHO) and communication disabilities (COMATAX) and healthcare service and informal care utilization. Spearman correlations and multivariate regressions were used to evaluate associations between outcomes and between outcomes and disease severity, respectively.
Results: 33% of patients received formal and 61% informal care (on average, 12.6 hours/week). 32%, especially females and younger patients with higher daily living deficits and lower disease severity, Omaveloxolone, the first approved FA treatment. Daily living deficits (rs = 0.707), communication disabilities (rs = 0.630), HRQoL (rs = 0.569) correlated strongly, and cognitive impairment (rs = -0.317), informal care provision (rs = 347), and hearing problems (rs = 0.346) moderately with disease severity. Further associations were found for daily living deficits with HRQoL (rs = 0.6518) and communication disabilities (rs = 0.567). Regression analyses showed a significant worsening of communication (b = 0.58), HRQOL (b = 0.57), mental well-being (b = -0.30), daily living activities (b = 0.75), cognitive abilities (b = -0.41), informal care dependency (b = 0.38), and hearing (b = 0.16) with increasing disease severity.
Conclusion: Results emphasize FA's multidimensional burden and the need for comprehensive care addressing physical and mental health. The reliance on informal care underscores FA's societal and economic burden.
Disclosure: Ksenija Schirduan is an employee and may hold stock in Biogen.

EPR-205 | Global approaches to device-aided therapies in Parkinson's disease

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[1]Clinical Ageing Research Unit, Newcastle University, Campus for Ageing and Vitality, Newcastle Upon Tyne, UK; [2]Translational and Clinical Research Institute, The Medical School, Newcastle University, Newcastle Upon Tyne, UK

Background and aims: Patients with Parkinson's Disease (PwPD) who develop medication-refractory motor complications and/or tremor may undergo treatment with Device-Aided Therapies (DAT). These therapies include surgical options such as Deep Brain Stimulation (DBS), MRI-guided Focused Ultrasound (MRgFUS), and infusion therapies. There is limited information on the factors influencing the timing and global preference for these treatments during the disease course.
Methods: We analyzed clinical, demographic, and genetic data from a large cohort of PwPD in the Parkinson's Progression Markers Initiative (PPMI) study.
Results: At the time of analysis, a total of 1291 PwPD had participated in the PPMI study. PwPD had been followed up for up to 14 years. During follow-up, 8.1% of PwPD underwent treatment with DAT, with the majority using DBS. This cohort includes patients from 52 different sites internationally. Genetics, dominant clinical symptoms, and site preference appear to influence the selection timing for DAT.
Conclusion: DBS was the most common form of DAT used in this cohort of patients. Understanding the current global use of DAT and the factors that influence the selection for early DAT has important health-economic significance and can help optimize treatment strategies for PwPD.
Disclosure: Nothing to disclose.

EPR-206 | Long-term effectiveness of foslevodopa/foscarbidopa vs. real-world standard of care in advanced Parkinson's disease

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Background and aims: People with advancing Parkinson's disease(PwaP) experience motor fluctuations despite optimized oral therapies(standard of care;SoC). Foslevodopa/foscarbidopa(LDp/CDp) showed greater motor symptom improvements than oral immediate-release levodopa/carbidopa in a 3month(M) randomized controlled trial. This study evaluated long-term comparative effectiveness of LDp/CDp versus real-world SoC in PwaP over 24M.
Methods: PwaP receiving LDp/CDp in a 12M open-label study(NCT03781167) plus open-label extension (NCT04379050) were indirectly compared to PwaP receiving SoC in a 24M prospective observational study(PROSPECT). Analyses included completers and discontinuers to maximize statistical power and reduce selection bias. Imputed and non-imputed analyses were conducted. Change from baseline and achievement of minimum clinically important differences(MCID) between treatment cohorts were evaluated for motor symptoms(PD diary), QoL(PDQ-39,EQ-5D-5L), daily living(MDS-UPDRS II), and sleep disturbances(PDSS-2) at 6M intervals. Comparative measures were adjusted for baseline characteristics and outcomes.
Results: Analyses included 129 LDp/CDp- and 185 SoC-treated patients (Table 1). LDp/CDp showed significantly greater improvements for OFF and good ON time over 24M and PDSS-2 over 12M, compared with SoC (Table 2). At all points, ≥66% of LDp/CDp and ≤49% of SoC achieved MCID for these outcomes (Table 3). LDp/CDp showed greater improvements in MDS-UPDRS II, PDQ-39, and EQ-5D-5L than SoC; effects decreased over time in both cohorts, with SoC worsening (Table 2). Overall, 42%-61% of LDp/CDp versus 13%-22% of SoC achieved MCID for these outcomes (Table 3). Results were similar between imputed and non-imputed analyses.

TABLE 1 Baseline demographics and clinical characteristics.

	SoC (N=185)	LDp/CDp (N=129)	p-value
Demographics			
Age, mean (SD)	68.3 (9.7)	63.1 (9.2)	<.001
Gender, n (%)			0.009
Female	95 (51.4%)	47 (36.4%)	
Male	90 (48.6%)	82 (63.6%)	
Race, n (%)			<.001
Asian	53 (28.6%)	16 (12.4%)	
Black	1 (0.5%)	0	
Other	1 (0.5%)	1 (0.8%)	
White	130 (70.3%)	112 (86.8%)	
Country, n (%)			<.001
Australia	24 (13.0%)	17 (13.2%)	
Canada	16 (8.6%)	4 (3.1%)	
Europe[a]	30 (16.2%)	44 (34.1%)	
Japan	50 (27.0%)	12 (9.3%)	
United Kingdom	7 (3.8%)	7 (5.4%)	
United States	58 (31.4%)	45 (34.9%)	
Clinical Characteristics			
PD Duration, years, mean (SD)	8.8 (5.5)	10.2 (5.0)	0.023
Motor Fluctuations, years, mean (SD)	6.4 (5.4)	6.4 (4.4)	0.973
Hoehn & Yahr stage, n (%)			<.001
0	8 (4.4%)	0	
1	13 (7.1%)	9 (7.0%)	
2	91 (49.7%)	96 (74.4%)	
3	57 (31.2%)	18 (14.0%)	
4	14 (7.6%)	6 (4.6%)	
OFF time[b], hours, mean (SD)	5.1 (2.5)	5.9 (2.2)	0.002
Good ON time[b,c], hours, mean (SD)	0.5 (1.2)	0.8 (1.5)	0.0495

PD, Parkinson's disease.
[a]Included Belgium, Denmark, Germany, Italy, The Netherlands, and Spain
[b]Normalized to a 16-hour waking day
[c]Good ON time is the sum of ON time with non-troublesome dyskinesia and ON time without dyskinesia

TABLE 2 Mean change from baseline in clinical outcomes.

	SoC (N=185)	LDp/CDp (N=129)	p-value[a]
OFF time, hours[b]			
6M	-0.9	-3.0	<.001
12M	-0.9	-3.2	<.001
18M	-1.2	-2.4	.004
24M	-1.1	-2.4	.004
Good ON time, hours[b,c]			
6M	0.8	3.4	<.001
12M	0.8	3.4	<.001
18M	0.9	2.8	<.001
24M	0.9	2.8	<.001
MDS-UPDRS Part II			
6M	-0.9	-3.0	.012
12M	-1.1	-2.3	.217
18M	0.3	-1.5	.067
24M	0.4	-1.1	.167
PDSS-2[d]			
6M	-0.7	-7.6	<.001
12M	-0.3	-6.6	<.001
PDQ-39 SI			
6M	0.1	-7.4	<.001
12M	-0.3	-6.4	<.001
18M	1.4	-3.9	.003
24M	2.0	-2.3	.023
EQ-5D-5L			
6M	0.01	0.16	<.001
12M	0.02	0.12	.005
18M	0.02	0.08	.107
24M	0.03	0.04	.799

EQ-5D-5L, European Quality of Life-Five Dimension-Five Levels; LDp/CDp, foslevodopa/foscarbidopa; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; PDQ-39 SI, Parkinson's Disease Questionnaire Summary Index; PDSS-2, Parkinson's Disease Sleep Scale-2; SoC, Standard of Care.
Data in table are from non-imputed analyses. Sample sizes varied at each time point. All values represent group means. Regression models were adjusted for age, gender, race, country, Hoehn & Yahr, PD duration, motor fluctuation, OFF time, ON time with troublesome dyskinesia, and baseline outcome.
[a]P-values represent comparisons of the changes from baseline between groups
[b]Normalized to a 16-hour waking day
[c]Good ON time is the sum of ON time with non-troublesome dyskinesia and ON time without dyskinesia
[d]PDSS-2 was not captured in the open-label extension (18M and 24M)

TABLE 3 Proportion of Responders Achieving MCID for Clinical Outcomes

% of patients	SoC(N=185)	LDp/CDp (N=129)	p-value[a]
OFF time[b]			
6M	42%	79%	<.001
12M	44%	79%	<.001
18M	44%	68%	<.001
24M	49%	72%	<.001
Good ON time[b,c]			
6M	39%	80%	<.001
12M	42%	81%	<.001
18M	39%	75%	<.001
24M	44%	78%	<.001
MDS-UPDRS Part II			
6M	18%	50%	<.001
12M	22%	50%	<.001
18M	16%	47%	<.001
24M	13%	42%	<.001
PDSS-2			
6M	25%	69%	<.001
12M	31%	66%	<.001
PDQ-39 SI			
6M	19%	61%	<.001
12M	22%	57%	<.001
18M	20%	49%	<.001
24M	16%	47%	<.001
EQ-5D-5L			
6M	17%	55%	<.001
12M	19%	56%	<.001
18M	21%	51%	<.001
24M	18%	51%	<.001

EQ-5D-5L, European Quality of Life-Five Dimension-Five Levels; LDp/CDp, foslevodopa/foscarbidopa; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; PDQ-39 SI, Parkinson's Disease Questionnaire Summary Index; PDSS-2, Parkinson's Disease Sleep Scale-2; SoC, Standard of Care.
Responders were defined based on unadjusted outcomes using the following MCID thresholds: OFF time = -1.0h; Good ON time = 1.0h; MDS-UPDRS Part II = -3.05; PDSS-2 = -3.44; PDQ-39 SI = -4.72; EQ-5D-5L = 0.11
[a]P-values represent comparisons of responder proportions between groups
[b]Normalized to a 16-hour waking day
[c]Good ON time is the sum of ON time with non-troublesome dyskinesia and ON time without dyskinesia
[d]PDSS-2 was not captured in the open label extension (18M and 24M)

Conclusion: LDp/CDp showed greater and sustained improvements in motor symptoms, sleep, and QoL than SoC in PwaP. Results suggest meaningful advantages of LDp/CDp as PD advances where SoC impact is diminished.

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EPR-207 | Deep brain stimulation in neurological features of Lesch-Nyhan syndrome: A critical review of literature

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Background and aims: Lesch-Nyhan syndrome (LNS) is a rare X-linked metabolic disorder characterized by hyperuricemia, motor dysfunction (primarily dystonia), and self-injurious behavior (SIB), often resistant to medical treatment. Deep brain stimulation (DBS) has emerged as an alternative for managing refractory dystonia and SIB in LNS patients.
Methods: A comprehensive analysis of reported LNS cases treated with DBS was conducted, focusing on demographics, motor and behavioral outcomes, adverse events, and follow-up durations.
Results: Twenty-eight cases of DBS targeting the Globus Pallidus Internus (GPi) were identified 53.6% with 2 electrodes, and 46.4% with 4 electrodes). Patients (all male) had a mean age of 12 years (SD 6, range 5–28) at surgery, with a median follow-up of 3.75 years (range 0.5–12). Dystonia was the most common motor feature, and all but one patient exhibited SIB. DBS led to motor improvements in 64% of cases, with reductions in dystonia ranging from 16% to 75%, based on the Burke-Fahn Marsden Dystonia Rating Scale or caregiver assessment, especially with posterolateral GPi targeting. Behavioral outcomes included reduced SIB, improved impulsivity, and better caregiver-reported comfort. Complications occurred in 57% of cases, including infections, hardware failures, and electrode displacement, but behavioral improvements often persisted.
Conclusion: DBS targeting GPi shows promise in treating severe motor and behavioral symptoms in LNS. Long-term

follow-up and standardized assessments are critical to optimize patient outcomes while mitigating adverse events.
Disclosure: Nothing to disclose.

EPR-208 | Sleep-related complaints and early morning dystonia in Parkinson's patients receiving opicapone: Results from OASIS

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Background and aims: Sleep disturbances are common and challenging to manage in Parkinson's disease (PD). By optimizing levodopa, the catechol-O-methyl transferase inhibitor opicapone (OPC) may alleviate specific PD-related sleep issues in patients with motor fluctuations. This study assessed the effect of OPC on different sleep issues in PD patients with sleep disturbances.
Methods: The 6-week, open-label, single-arm OpicApone in Sleep dISorder (OASIS) study evaluated the efficacy of OPC 50 mg in treating sleep disturbances as levodopa add-on therapy. The primary endpoint was changes from baseline to Week 6 in PD Sleep Scale-2 (PDSS-2) total score. This post-hoc analysis evaluated changes in specific PDSS-2 items and in the number of patients reporting early morning dystonia at Week 6.
Results: Of the 16 patients included in the OASIS, 15 completed treatment. At Week 6, patients experienced improvements in several sleep issues as indicated by the mean (standard error) reductions in the scores for poor sleep quality in the previous week (-1.1 [0.3]; -42%), sleep latency (-0.9 [0.4]; -50%), sleep fragmentation (-1.3 [0.4]; -39%), and restorative sleep (-1 [0.3]; -41%) (Figure 1A). Patients also reported significantly less difficulty moving or turning in bed (-0.9 [0.3]; -35%) and significantly less tremor upon waking (-0.7 [0.3], -39%) (Figure 1A). Among patients reporting early morning dystonia at baseline (25%), half transitioned to no dystonia (Figure 1B).

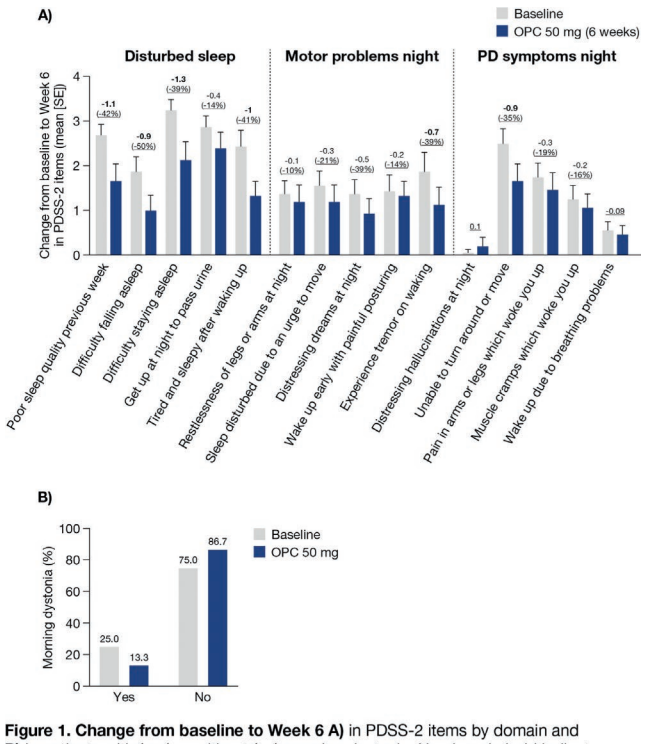

Figure 1. Change from baseline to Week 6 A) in PDSS-2 items by domain and **B)** in patients with (yes) or without (no) morning dystonia. Numbers in bold indicate a significant p-value (<0.05), according to paired t-test analysis.
OPC, opicapone; PD, Parkinson's disease; PDSS-2, Parkinson's Disease Sleep Scale-2; SE, standard error.

Conclusion: OPC adjunct to levodopa therapy improved sleep-related symptoms by > 30%, including insomnia and restorative sleep and also nighttime and morning motor symptoms, offering dual benefit for PD patients with wearing-off and sleep-related disturbances.
Disclosure: JJF has received grants from GlaxoSmithKline, Grunenthal, Fundação MSD (Portugal), TEVA, MSD, Allergan, Novartis and Medtronic. JFF also received consultancy and speaker fees, and participated in advisory boards for GlaxoSmithKline, Novartis, TEVA, Lundbeck, Solvay, BIAL, Merck-Serono, Merz, Ipsen, Biogen, Acadia, Allergan, Abbvie, Sunovion Pharmaceuticals, Zambon, Affiris and Angelini. MFG has received payment/honoraria for lectures from Zambon, Bial Portugal, Takeda and Amicus Therapeutics, and payment/honoraria for advisory boards from Abbvie and Bial Portugal. MMF, RC, HB and JH are employees of Bial. CT has received consulting/independent contractor fees from AbbVie, UCB, Roche, Bial, Ono, Boehringer and Convatec, and speakers honoraria from AbbVie, STADA, Bial and Esteve. CT also receives royalties from Thieme Publisher, License fee: PDSS-2; and grant and contracted research support from The Michale J. Fox Foundation, EU: Era-Net program, BRAVA Project; and is an employee (full or part-time) of Paracelsus-Elena Hospital, Kassel. Study supported by Bial.

EPR-209 | Long-term effect of opicapone in Parkinson's patients without motor complications: 1.5-Year EPSILON study findings

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Background and aims: The EPSILON study assessed the clinical efficacy of adjunctive opicapone (OPC) in levodopa-treated Parkinson's Disease (PD) patients without motor complications. Long-term effects of OPC exposure are reported.

Methods: EPSILON consisted of a double-blind (DB) and a 1-year open-label-extension (OLE) phase. In the DB phase, levodopa-treated PD patients without motor complications received OPC 50 mg or placebo: primary endpoint was change in Movement Disorder Society-Unified PD Rating Scale-Part III (MDS-UPDRS-III) score from baseline to Week 24. In the OLE, patients completing the DB phase received OPC 50 mg; key endpoint was mean change from OLE baseline to Week 52 in MDS-UPDRS-IV scores. Other endpoints included: safety/tolerability, Clinician's and Patient's Global Impression of Improvement (CGI-I, PGI-I), non-motor symptoms and quality of life (QoL).

Results: At Week 24, significantly greater improvements in MDS-UPDRS-III score and lower proportions of patients with motor complications were reported for OPC versus placebo (Figure 1). At study end, patients treated with OPC in both phases (N = 151) maintained reductions in MDS-UPDRS-III scores (mean [standard error] change of -7.2 ± 0.8 from DB baseline), with minimal changes in daily levodopa dosage and lower rates of patients with motor complications than those who received placebo in the DB (Figure 1). After 1.5 years, minimal changes in MDS-UPDRS-IV scores, improvements on PGI-C and CGI-I, and no changes in non-motor symptoms and QoL were reported (Table 1). Opicapone was well-tolerated.

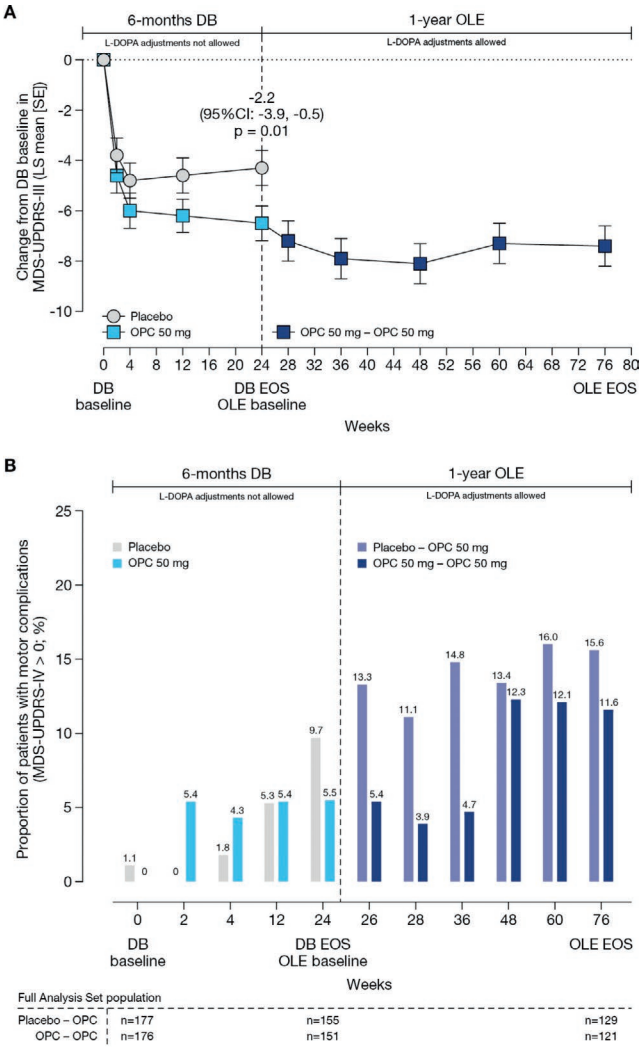

Figure 1. Efficacy outcomes at the end of the DB and OLE phase: A) LS mean (SE) change in MDS-UPDRS-III motor scores and B) proportion of patients who developed motor complications (MDS-UPDRS-IV score >0) from DB baseline until the end of the OLE phase (1.5 years).

SE, standard error; DB, double-blind; EOS, end of study; L-dopa, levodopa; LS, least squares; MDS-UPDRS-III, Movement Disorder Society-Unified PD Rating Scale-Part III; MDS-UPDRS-IV, Movement Disorder Society-Unified PD Rating Scale-Part IV; OLE, open-label extension; OPC, opicapone.

Efficacy outcomes	Patients treated with OPC in the DB phase who entered the OLE (N=151)
MDS-UPDRS-IV score	
Change from DB baseline, LS mean (SE)	0.6 (0.14)
PDSS-2 total score	
Change from DB baseline, LS mean (SE)	-0.4 (0.65)
NMSS total score	
Change from DB baseline, LS mean (SE)	-0.9 (1.17)
PDQ-39 total score	
Change from DB baseline, LS mean (SE)	-0.37 (0.733)
CGI-I scores	
Improvement on CGI-I, n/N (%)	94/121 (77.7)
Odds in favour of a response	2.74
PGI-I scores	
Improvement on PGI-I, n/N (%)	87/121 (71.9)
Odds in favour of a response	2.22

Table 1. Efficacy outcomes: change from baseline to the end of the OLE phase (1.5 years exposure to OPC) in the key efficacy outcomes. CGI-I, Clinical Global Impression of Improvement; DB, double-blind; LS, least squares; MDS-UPDRS-IV, Movement Disorder Society-Unified PD Rating Scale-Part IV; NMSS, Non-Motor Symptoms Scale; OPC, opicapone; PGI-I, Patient's Global Impression of Improvement; PDQ-39, Parkinson's Disease Questionnaire; PDSS-2, Parkinson's Disease Sleep Scale-2; SE, standard error; N, Number of patients in the analysis set.

Conclusion: OPC provided sustained motor benefits over 1.5 years with few patients developing motor complications, supporting its long-term use in PD patients without motor fluctuations.

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EPR-210 | Phenotypic and genotypic spectrum of late-onset dystonia

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Background and aims: Dystonia is a dyskinetic movement disorder with significant phenotypic and genotypic variability. Recent advances in genetic testing have shown that genetically determined dystonic syndromes are typically associated with early onset, generalized forms, and/or complex neurological symptoms. Although genetically determined late-onset dystonia (LOD) has also been described, its genotypic and phenotypic characteristics remain systematically unexplored. This study aimed to analyze the phenotypic and genotypic spectrum of LOD (onset > = 21 years).

Methods: All 728 patients with dystonia included in a whole-exome sequencing project were categorized by age of onset, phenotype, and genotype, that is, pathogenic or likely pathogenic variants, variants of uncertain significance (VUS), and no identified mutations.

Results: A total of 160 patients with LOD were identified. Pathogenic or likely pathogenic variants were detected in 21 patients, and VUS in 13, together representing 21.2% of identified variants. Complex neurological symptoms were observed in 71% of patients with pathogenic or likely pathogenic mutations, compared to 17% in the mutation-negative group. Among those with complex symptoms and pathogenic or likely pathogenic mutations, cerebellar phenotype occurred in 67%, compared to 32% in the mutation-negative group. Similarly, cognitive impairment was observed in 60% of patients with pathogenic or likely pathogenic mutations versus 36% in the mutation-negative group.

Conclusion: In conclusion, our findings suggest that patients with LOD, particularly those with complex dystonia involving cognitive and/or cerebellar impairments, may have a substantial genetic background. These symptoms could serve as markers, increasing the likelihood of mutation identification and highlighting the need for a tailored approach to genetic testing.

Disclosure: The study was supported by the grant: AZV Czech Republic: NW24-04-00067 and EU program EXCELES: LX22NPO5107.

EPR-211 | Outcomes of MVD surgery in hemifacial spasm: A single-center experience

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Background and aims: Hemifacial spasm (HFS) is characterized by involuntary tonic and clonic contractions of the facial muscles, commonly caused by vascular compression at the root entry/exit zone of the facial nerve (CN VII). This study aimed to evaluate the clinical outcomes of microvascular decompression (MVD) for HFS in our patient series.
Methods: We conducted a retrospective analysis of 58 patients who underwent MVD for HFS at our institution between January 2014 and December 2023. Data collected included demographics, symptom duration, intraoperative findings, and postoperative outcomes. Follow-up ranged from 12 months to 10 years.
Results: Among 58 patients, 28 (48.3%) were women (mean age: 47.8 years) and 30 (51.7%) were men (mean age: 46.6 years). Immediate postoperative outcomes were excellent or good in 93.1% of cases. Long-term success was achieved in 84.5%, with a mean follow-up of 4.1 years. Recurrence occurred in 10.3% at a mean of 8.5 months post-surgery. Transient complications included facial paralysis (37.9%) and hearing loss (27.6%), while permanent complications included hearing loss (13.8%) and facial paralysis (5.2%). No mortality was reported. In 98.3% of cases, the vascular culprit was identified, with the most common offender being the anterior inferior cerebellar artery (48.3%).
Conclusion: MVD is highly effective for the treatment of HFS, with excellent immediate and long-term outcomes. Early surgical intervention is recommended to enhance prognosis, as delayed treatment may increase the risk of complications and recurrence.
Disclosure: Nothing to disclose.

Monday, June 23 2025

Clinical neurophysiology

EPR-212 | Temporal interference stimulation of the hippocampus suppresses epileptic biomarkers in patients with epilepsy

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Background and aims: Medication-refractory focal epilepsy presents a significant clinical challenge, with approximately 30% of patients ineligible for surgery due to the involvement of eloquent cortex in the epileptogenic network. For such patients with limited surgical options, electrical neuromodulation represents a promising alternative therapy. In this study, we assess the potential of non-invasive temporal interference (TI) electrical stimulation to reduce epileptic biomarkers in patients with epilepsy by comparing intracerebral recordings obtained before, during, and after TI stimulation to those recorded during low and high kHz frequency (HF) sham stimulation (ClinicalTrials.gov: NCT06716866).

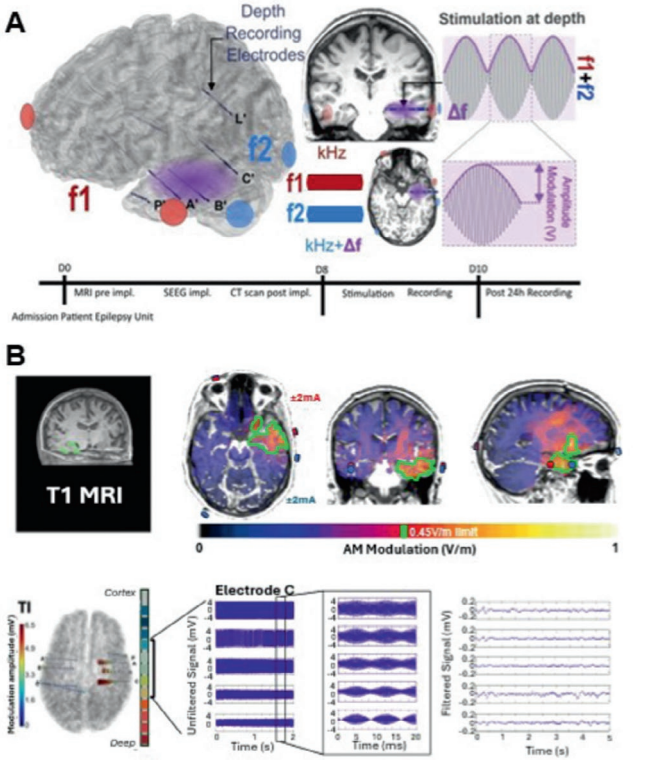

FIGURE 1 Temporal interference protocol in sEEG-implanted patients with epilepsy.

Methods: Thirteen patients diagnosed with mesiotemporal epilepsy (MTLE) and implanted with stereoelectroencephalography (sEEG) depth electrodes received TI stimulation with an amplitude modulation (AM) frequency of 130Hz (Δf). AM was applied using low-frequency carriers (1kHz + 1.13kHz) or high-frequency carriers (9kHz + 9.13kHz), targeting the hippocampus. Epileptic biomarkers, including interictal epileptiform discharges (IEDs) and pathological high-frequency oscillations (HFOs), were evaluated across conditions.
Results: TI stimulation significantly reduced IEDs and fast-ripple (FR) HFOs in the hippocampal focus, with suppression propagating brain-wide. HF sham stimulation at 1kHz impacted IEDs in the cortex but failed to reach the hippocampus, and its effects diminished with increasing frequency. Unlike HF sham, TI demonstrated a frequency-independent effect and exhibited a strong carry-over suppression post-stimulation.

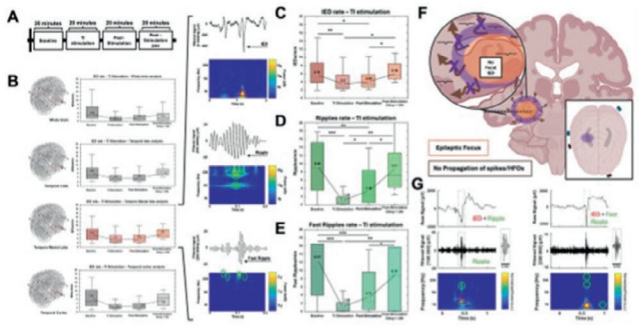

FIGURE 2 Epileptic biomarkers are suppressed during TI stimulation, and a post-stimulation carrier-over effect is observed.

Conclusion: These findings support TI as a promising non-invasive neuromodulation approach for epilepsy, providing a potential pre-screening tool before deep brain stimulation (DBS) or responsive neurostimulation (RNS). TI's distinct biophysical properties highlight its advantages over HF conduction block.
Disclosure: Nothing to disclose.

EPR-213 | Prediction of abnormal responses to single-pulse electrical stimulation in drug-resistant epilepsy using adaptive AI

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Background and aims: Delayed responses (DRs) to Single pulse electrical stimulation (SPES) during intracranial EEG (iEEG) recordings observed 100ms-1s after the stimulation, are associated with epileptogenicity and are useful for identifying the seizure onset zone (SOZ). We employed discriminative underlying features of iEEG signals in a custom adaptive attention-based deep neural network to predict the DRs to SPES.
Methods: We analyzed iEEG data from 60 patients. DRs were annotated and the iEEG was fed to a peak-detection algorithm to identify SPES artifact and select 1.5-second segments prior to this. The segments were labeled as normal (no visible DRs) and abnormal (with visible DRs) and fed to a features-extraction algorithm. A sequential floating forward selection (SFFS) algorithm was used to identify the most discriminative subset of features between normal and abnormal channels for each case in an iterative fashion. We input these features to a custom adaptive deep-neural network pipeline that employs the attention-layer mechanism in its architecture to prioritize the features based on importance.

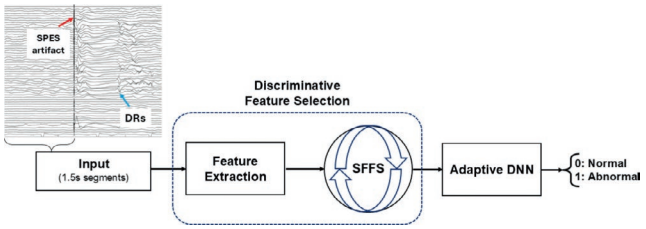

FIGURE 1 The overall pipeline used in this study for prediction of SPES DRs. The red arrow points to the SPES artifact and the blue array shows examples of annotated visible DRs.

Results: The most discriminative subset of features identified by the SFFS algorithm were spectral centroid, wavelet entropy, peak frequency, spectral flatness, and beta band power. The adaptive attention-based deep neural network achieved an area under the ROC curve (AUC) of 0.87, indicating strong predictive capability. Sensitivity and specificity were above 80%.
Conclusion: The findings demonstrate a direct relationship between pre-stimulation iEEG patterns and the SPES response, suggesting that pre-stimulation iEEG features can serve as predictive factors for SPES DRs, and abnormal areas can be better identified by analyzing the background activity.
Disclosure: Part of this work was supported by a European Union's Horizon 2020 grant, the Multidisciplinary Expert System for the Assessment and Management of Complex Brain Disorders (MES-CoBraD) [grant agreement No 965422].

EPR-214 | Decremental response in patients with amyotrophic lateral sclerosis

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Background and aims: Neuromuscular junction (NMJ) denervation plays a critical role in amyotrophic lateral sclerosis (ALS). Lately, repetitive nerve stimulation (RNS) has been applied to assess the efficacy of drugs targeting the NMJ. However, the sensitivity and stability of parameters during RNS, and factors contributing to the decremental response, have yet to be fully elucidated.
Methods: A total of 626 patients who were diagnosed with ALS and underwent 3Hz RNS test from June 2016 to August 2023 were enrolled. Data on their clinical, biochemical and electrophysiological indicators were divided into a training set and a test set. Stepwise regression was used in model building.
Results: Forty-two percent of patients had a decrement larger than 10% and 24% had a decrement larger than 15%. Area decrement had a higher rate of abnormal result and a lower coefficient of variation than amplitude decrement. No significant difference in the rate of abnormal decrement was found when the first compound muscle action potential was compared with either the fourth or fifth one. High-density lipoprotein cholesterol, serum uric acid, forced vital capacity, onset site, sex, and motor unit potential duration were independent factors contributing to the decremental response.

Conclusion: In patients with ALS, NMJ safety factor is reduced during re-innervation. During RNS test, assessing area decrement significantly enhances our ability to detect the impairment of neuromuscular transmission in patients with ALS. Independent factors contributing to decremental response need to be considered in clinical trials targeting NMJ in patients with ALS.
Disclosure: Nothing to disclose.

EPR-215 | Unraveling Guillain-Barré Syndrome: Predictors, patterns and outcomes from a decade of care

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Background and aims: We aimed to analyze Guillain-Barré Syndrome (GBS) patients over the last 10 years, correlating clinical, analytical, and electrophysiological findings with outcomes.
Methods: Retrospective analysis of clinical and additional diagnostic data of all patients admitted to a tertiary center between January 2013-December 2023.
Results: Ninety-nine patients (52.5% women), with a mean age at presentation of 45.5 ± 26.3 years, were included. Fifty-nine (59.6%) presented with the acute inflammatory demyelinating polyneuropathy subtype, with a median of 4 days (IQR 5) to first evaluation. Among 27 pediatric patients, limb muscle pain was more common at presentation compared to adults (37%, $p < 0.001$). Upper airway infections(44.4%) was the most frequent trigger, followed by gastroenteritis (19.2%), which was associated with the acute motor axonal neuropathy subtype (52.9%,$p = 0.013$). Decreased motor amplitude on electromyography (EMG) correlated with higher disability at discharge (median modified Ranking score (mRS)≥3, IQR 2, $p = 0.001$), though not at 1-year. Spontaneous activity on EMG (27.8%,p 0.048), cranial nerve involvement (27%, $p < 0.001$), and respiratory failure (41.2%, $p < 0.001$) were linked to need of rescue treatment. A GBS disability score≥4 was associated with a lower MRC sum score (28 vs. 63, $p < 0.001$) and invasive ventilation (30.8%, $p < 0.001$). Hyponatremia at admission predicted worse 1-year outcomes (mRS≥3, 40%, $p = 0.004$).
Conclusion: EMG findings (decreased motor amplitude and spontaneous activity) and hyponatremia at admission were predictors of higher initial disability and worse long-term outcomes, respectively. Despite the severity of cases requiring ventilation, long-term outcomes were unaffected. This study highlights key features of GBS in a diverse cohort and the need of tailored management of risk factors.
Disclosure: Nothing to disclose.

EPR-216 | Personalized acoustic-based music neuromodulation in epilepsy

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Background and aims: Music-based neuromodulation has emerged as a promising therapeutic approach for drug-resistant epilepsy. This study builds on previous research by investigating how distinct musical features affect interictal epileptiform discharges (IEDs) in intracerebral EEG (iEEG).
Methods: Twenty-five patients with drug-resistant epilepsy undergoing presurgical iEEG evaluation participated in a two-day study. Patients listened to a variety of musical compositions with defined acoustic properties. EEG recordings were taken before and after each listening session to assess changes in IEDs.
Results: The study revealed individualized patterns of IED reduction, with certain acoustic properties showing consistent effects across musical genres. Mozart's Piano Concerto No. 27 (K 595c) reduced IEDs by 28% during music listening ($p = 0.0191$) and by 19% in the post-music resting state ($p = 0.0111$). In contrast, relaxation music increased IEDs by 55% ($p = 0.0197$). Individualized acoustic analyses identified compositions that significantly reduced IEDs, with reductions ranging from 32% to 44% ($p = 0.0001$). Compositions with contrasting acoustic properties did not show significant effects, highlighting the influence of acoustic features rather than musical genre.
Conclusion: Specific acoustic properties can reproducibly modulate brain activity at the individual level, reducing IEDs based on personalized testing and selection across musical genres. These findings support the potential of music-based neuromodulation as a tailored therapeutic approach for epilepsy management. Further research is needed to explore individual variability in music-based interventions for epilepsy treatment.
Disclosure: Nothing to disclose.

EPR-217 | Synkineses as a marker for neuroplasticity in nerve transfer surgeries

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Background and aims: Synkineses occure after neurotization operations on peripheral nerves, when an anatomically close nerve or its fascicle is used to reconstruct an destroyed, unreconstructible nerve (impossibility of suture or grafts use). This study explores its clinical implications in patients with brachial plexus injuries treated with nerve transfers.
Methods: A total of 34 nerve transfers in 21 patients were evaluated at a minimum of three years post-surgery. Synkineses were verified by a two-channel needle EMG in the muscle originally innervated by the donor nerve and in the target muscle (recipient). We monitor the voluntary activity in both muscles during the voluntary contraction of the original and target muscles. The follow-up period is set to 3 years.
Results: Synkineses were observed in 70.6% (24/34) of cases. Patients without synkineses achieved significantly higher voluntary activation scores ($p < 0.05$). Early reinnervation correlated positively with reduced synkineses and improved outcomes (Rs = 0.528). Time from injury to surgery inversely impacted neuroplastic adaptation (Rs = -0.500), highlighting the importance of early intervention.
Conclusion: Synkinesis reflects both adaptive and maladaptive neuroplasticity in nerve transfer patients. Monitoring the dynamics of synkinesis donor - recipient serves as an indirect evidence of reorganization of the motor cortex. Future research should focus on optimizing protocols to leverage neuroplasticity while minimizing synkinetic interference.
Disclosure: Nothing to disclose.

EPR-218 | Treatment of the spastic hemiparesis with selective dorsal rhizotomy in adults

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Background and aims: Spasticity is a common cause of disability. Selective dorsal rhizotomy (SDR) successfully reduces lower limb spasticity (LLS) in children but its efficacy in adult spasticity is being investigated. Aim: evaluate the efficacy of SDR for LLS in adults with spastic hemiparesis (SH).
Methods: Five male patients with SH were included (aged 18-45 years): 2 - traumatic brain injury, 1 had cerebral hemorrhage, 2 had cerebral palsy. The GMFCS, modified Ashworth score (MAS), EMG, range of motion (ROM) of the involved joints were controlled. In all patients single-level SDR with intraoperative triggered EMG were done.
Results: Preoperatively, 4 patients had GMFCS II, one had I. The target of SDR was the key muscles (KM) with MAS 2-3. Intraoperative ipsilateral L3-S1 sensory nerve roots were divided into 3-5 portions that were EMG tested. Portions with pathological KM pattern were dissected up to 75%. The spastic EMG pattern was different from the normal KM innervation. One week after surgery, EMG analysis showed that KM spasticity was significantly reduced. The H-reflex, foot clonus completely disappeared in all patients. 3 patients with GMFCS II improved to I. There were statistically significant differences in the KM MAS, the ROM of the ankle and knee, 25-Foot Walk Test between preoperatively and postoperatively ($p < 0.05$). All patients had ipsilateral L5-S1 hypesthesia which significantly decreased after 1 month. No urinary/bowel dysfunction was observed. After a month, all patients considered that they had benefited from SDR.
Conclusion: SDR is effective in SH for adults. Intraoperative EMG monitoring is necessary for the SDR.
Disclosure: Nothing to disclose.

Epilepsy

EPR-219 | Genetic variability in inflammatory genes and susceptibility to mesial temporal lobe epilepsy and drug resistance

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Background and aims: Genetic Variability in Inflammatory Genes and Susceptibility to Mesial Temporal Lobe Epilepsy and Drug Resistance
Methods: A total of 218 MTLE-HS patients (101 males, 116 with febrile seizure antecedents, and 173 with drug-resistant epilepsy [DRE]) and 177 healthy controls (82 males) were genotyped for the selected SNPs using TaqMan Real-Time PCR.
Results: The rs4612666 TT genotype, which enhances NLRP3 activity, was more frequent in MTLE-HS patients compared to controls, but this difference was not statistically significant (6.7% vs. 3.4%; OR [95% CI] = 2.18 [0.79–6.04]; $p = 0.13$). The rs3751143 AC genotype was more frequent in DRE patients compared to non-DRE patients (33.8% vs. 16.2%; OR [95% CI] = 2.56 [0.99–6.62]; $p = 0.05$). No other significant associations were observed.
Conclusion: The rs3751143 polymorphism impairs the function of the purinergic receptor P2X7, affecting the inflammatory

response and seizure-induced damage repair. This could potentially contribute to a poor anti-seizure treatment response. Although no direct association between the studied polymorphisms and MTLE-HS susceptibility was found, our results highlight the possible role of inflammatory genes, especially P2X7R, in the clinical presentation of MTLE-HS, emphasizing the need for further research.

Disclosure: Work partially funded by a Tecnifar Grant.

EPR-220 | Effects of NMDAR and LGI1 antibodies on absence seizures: Insights from genetic and pentylenetetrazol-induced models

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Background and aims: Leucine-rich glioma-inactivated protein 1 (LGI1) and N-methyl-D-aspartate receptor (NMDAR) are key proteins involved in regulating neuronal excitability within the central nervous system. In conditions like anti-LGI1 encephalitis and anti-NMDAR encephalitis, autoantibodies target and disrupt these proteins, leading to epileptic seizures. However, the roles of LGI1 and NMDAR dysfunction in the pathophysiology of absence seizures remain unclear.

Methods: IgG purified from the peripheral blood of patients with anti-NMDAR ($n=3$) encephalitis, anti-LGI1 encephalitis ($n=4$) and healthy controls (HC) ($n=4$) was administered chronically every other day for 11 days via stereotaxic injection into the lateral ventricle of genetic absence epilepsy rat model (GAERS) and Wistar rats. Before and after antibody administration, electroencephalography (EEG) recordings were taken for 2 hours to analyze the duration and number of spontaneous spike-and-wave discharges (SWDs) in GAERS rats and 120 minutes after 35 mg/kg pentylenetetrazol (PTZ)-administration in Wistar rats.

Results: In GAERS rats, NMDAR IgG infusion significantly increased the duration and number of SWDs compared to the healthy control group, highlighting its acute effect on SWD activity. In contrast, LGI-1 IgG did not cause significant changes in SWD parameters. Similarly, NMDAR- but not LGI1-IgG-infused Wistar rats exhibited increased susceptibility to PTZ-induced absence seizures compared to healthy control group.

Conclusion: Our findings demonstrate differential roles of NMDAR and LGI-1 antibodies in modulating absence seizure activity. NMDAR IgG infusion significantly enhances SWD duration and number in GAERS rats and PTZ-induced absence seizures in Wistar rats, highlighting the role of NMDAR in absence seizure induction.

Disclosure: Nothing to disclose.

EPR-221 | Describing patients with prolonged seizures: European subgroup results from a global real-world point-in-time study

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Background and aims: People with epilepsy (PwE) can experience prolonged seizures (PS), which may progress to Status epilepticus (SE; seizure(s) lasting ≥5min). However, the definition, prevalence, and patient population of PS are not well characterized.

Methods: European data were drawn from Adelphi PS Disease Specific Programme™ (real-world, point-in-time survey) conducted in France/Germany/Italy/Spain/United Kingdom/United States/Japan/China, from March/2023-February/2024. Neurologists/epileptologists/internal medicine specialists (IMs) completed record forms for PwE on stable antiseizure medication (including rescue medications [RM]) regimen who had experienced ≥1 PS (≥2min and/or longer than "normal"/"non-PS") in prior 12-months. Outcomes of PS and non-PS are presented.

Results: 132/28/9 neurologists/epileptologists/IMs completed records for 1,411 PwE experiencing PS. Median [Q1-Q3] patient age 34.0 [22.0-50.0] years, 58% male, 41% required caregiver(s). 49% of sample had had SE, 27% seizure clusters (SC). During prior 12-months, proportion of sample experiencing events (related to PS vs. non-PS): SE (34%), SC (PS: 15%; non-PS: 11%), aura (PS: 45%; non-PS 38%), injuries (PS: 27%; non-PS 23%), required emergency services (PS: 27%; non-PS: 22%) – necessitating emergency-room (ER) admission (PS: 78%; non-PS: 41%), intensive-care unit (ICU) (PS: 14%; non-PS: 5%) – and hospitalization (PS: 25%; non-PS: 14%). 64% of sample were prescribed RM (often including oral benzodiazepines), 57% had seizure action plans. PwE self-reported seizure worry via 0-10 scale where 10 = "worry all the time": PS (median [Q1-Q3]) 5.0/10 [2.0-7.0]; non-PS 4.0/10 [1.3-6.0].

Conclusion: PwE experiencing PS regularly encounter progression to SE and/or SC, leading to emergency care, and hospital/ER/ICU admissions, despite best practice. Rapid and early seizure termination is essential to avoid harmful outcomes. UCB-sponsored

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has received personal fees from Arvelle Therapeutics, Inc., Argenx, Alexion, Bial, Biogen, Biocodex, Böhringer Ingelheim, Eisai, Epilog, Everpharma, GlaxoSmithKline, GW Pharma, Jazz Pharmaceuticals, LivaNova PLC, Marinus Pharmaceuticals, Inc., Medtronic, NewBridge Pharmaceuticals, Novartis, Sandoz, Sanofi, Sunovion Pharmaceuticals, Inc., Takeda, UCB, Xenon; grants from Austrian Science Fund (FWF), Bayer, Biogen, Eisai, European Union, GlaxoSmithKline, Novartis, Österreichische Nationalbank, Red Bull, UCB; he is CEO of NeuroConsult GmbH. MCW has received honoraria/consulting fees from Bioquest, Eisai, UCB, Angelini, Seer, EpilepsyGtx; has shares in EpilpesyGtx, an epilepsy gene therapy company. SH is a consultant for UCB, Neurelis, Ventus; and a DSMB member for AbbVie. JS is an advisor for Ceribell, Jazz, Neurelis, SK Life Science, UCB, Xenon; holds stocks in Ceribell; is a speaker for Ceribell, Jazz, LivaNova, Neurelis, SK life Science, UCB; has royalties for Cambridge University Press, MedScape, Springer, Wolters Kluwer. LH declares consultation fees for advising from Accure, Ceribell, Gilead, Marinus, Natus, Neurelis, Neuropace, Rapport Therapeutics, UCB; royalties from Wolters-Kluwer for authoring chapters for UpToDate-Neurology, from Wiley for co-authoring the book "Atlas of EEG in Critical Care", 1st/2nd editions; honoraria for speaking from Neuropace, Natus, UCB. AG, LL, and ES are employees of Adelphi Real World. UCB contracted Adelphi Real World to perform this secondary analysis. CL, OR, and JCW are salaried employees of UCB and receive stocks or stock options from their employment.

EPR-222 | First in human study in drug resistant epilepsy: Safety and performance of a novel optoelectronic vagus nerve stimulator

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Background and aims: Drug-resistant epilepsy (DRE) affects nearly 30% of patients. For those ineligible for resective surgery, Vagus Nerve Stimulation (VNS) is an alternative treatment. However, current VNS systems face limitations, particularly regarding MRI safety and device longevity. A novel optoelectronic VNS system was developed to address these challenges, providing unconditional MRI access and extended device lifespan. This first-in-human study evaluates its safety, performance, and usability in DRE patients.
Methods: Patients were recruited from three clinical sites: Cliniques Universitaires Saint-Luc (CUSL), Ghent University Hospital (UZ Gent), and Universitätsklinikum Freiburg. Eligible participants were adults with DRE and candidates for VNS therapy. The primary endpoint assessed procedure- and device-related adverse events within three months. Secondary endpoints included long-term safety, seizure outcomes, quality of life, and mood over 24 months.
Results: The first five patients were successfully implanted at CUSL and UZ Gent. Postoperative recovery was smooth, and stimulation therapy began 2 weeks post-implantation. Over the next 10 weeks, the step by step increase of the stimulation delivered was well tolerated. Laryngeal Muscle-Evoked Potential (LMEP) were successfully recorded in all patients, providing indirect confirmation of vagus nerve activation. By 3 months, the primary safety endpoint was met, with no serious adverse events and other safety events within expected VNS response ranges. No failures were reported with the implanted device, as confirmed by device self-checks. Initial therapy efficacy was observed.
Conclusion: Initial results demonstrate the system's safety and reliability, and the potential for the optoelectronic VNS system to transform the treatment landscape for DRE.
Disclosure: Study is supported by Synergia Medical.

EPR-223 | Graph neural networks for enhanced epileptogenic zone localization in epilepsy surgery: An innovative method

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Background and aims: Epilepsy surgery often fails due to inaccurate localization of the epileptogenic zone (EZ). This study introduces a new method using Graph Neural Networks (GNNs) to analyze interictal biomarkers like epileptiform discharges (IED) and high-frequency oscillations (HFO). By mapping these features onto a graph that reflects each patient's unique electrode implantation topology, the method aimed to more accurately depict the dynamics of epileptic networks.
Methods: A GNN model was developed to pinpoint the EZ, identified as contacts removed during effective epilepsy surgery. The model underwent training and validation through leave-one-patient-out cross-validation involving 31 seizure-free patients. Interictal biomarkers were detected across 30 minutes of NREM sleep SEEG, then encoded into a graph structure for each patient as node features. In the graph structure, electrode contacts within 8 mm were connected by edges weighted by the Euclidean distance. Benchmark models, LR (Logictic Regression) and SVM (Support Vector Machines), analyzed the same features without considering implantation topology.
Results: The GNN model outperformed LR and SVM in terms of median Area Under the Receiver Operating Characteristic (AUROC) and Area Under the Precision-Recall Curve (AUPRC). Specifically, GNN achieved an AUROC of 0.93 and an AUPRC of 0.69, whereas LR and SVM posted lower scores, nevertheless there were no statistically significant differences between GNN and LR.
Conclusion: The GNN model outperformed traditional methods like SVM in modeling SEEG data as graphs, incorporating electrode implantation topology. This approach suggests that acknowledging spatial relationships between electrode contacts,

typically overlooked by conventional methods, can significantly enhance localization precision.

Disclosure: This work was supported by the Czech Science Foundation, project number 22-28784S, and by project nr. LX22NPO5107 (MEYS): Financed by European Union – Next Generation EU.

EPR-224 | Effect of cenobamate on sudden unexpected death in epilepsy (SUDEP) risk in a Spanish cohort of a phase 3 clinical trial

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Background and aims: SUDEP accounts for 2-17% of deaths in patients with epilepsy (Ficker 2000, Epilepsia 41 Suppl 2:S7-S12). SUDEP-3 (score 0-4) and SUDEP-7 (score 0-10) scales assess the potential risk of SUDEP. For each point reduction in SUDEP-3, SUDEP odds decrease by 64%; for SUDEP-7, per-point odds decrease is 29% (Rasekhi 2021, Epilepsia 62(7):1536-1545).

Methods: NCT02535091 (C021, $N=1340$) was a global, multicenter, phase 3, open-label safety study of cenobamate as adjunctive treatment in adults with uncontrolled focal-onset seizures (FOS). Efficacy data pre- and post-cenobamate treatment were collected in in a multicenter retrospective observational study of the C021 Spanish cohort ($n=127$). SUDEP-3 and SUDEP-7 risk scores (RS) were calculated for patients in that cohort before and after cenobamate treatment.

Results: At baseline, 76% and 24% patients had SUDEP-3 RS of 2 and 3. After 2 years of cenobamate treatment, 6% had a RS point reduction of 3, 11% of 2, and 14% of 1 point; 69% remained stable (Figure 1). Using the SUDEP-7 inventory, at baseline, 51% of patients had a RS of 1-3 and 49% had a RS of 4-8. After 2 years of cenobamate treatment, 1% had a RS point reduction of 4, 9% of 3, 9% of 2, and 30% of 1 point. 44% remained stable, and 7.5% increased SUDEP risk (Figure 2).

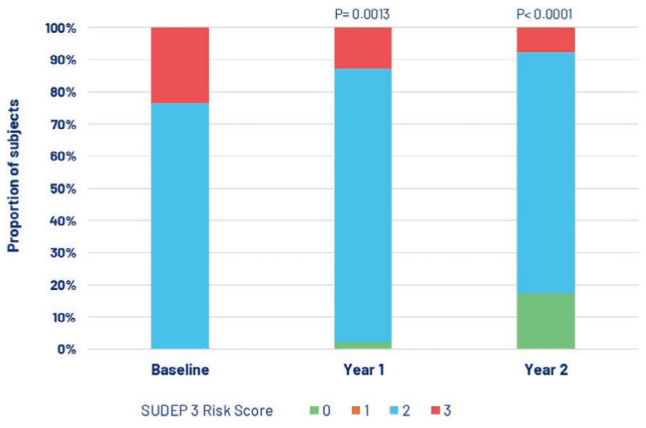

Figure 1. Study subjects stratified by SUDEP 3 Risk Score

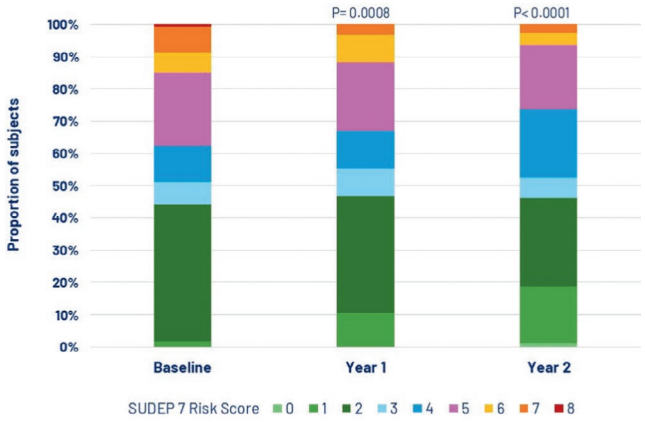

Figure 2. Study subjects stratified by SUDEP 7 Risk Score

Conclusion: Cenobamate treatment significantly reduced SUDEP risk in some Spanish cohort patients as measured by two SUDEP risk scales. The potential for reducing SUDEP risk should be considered when initiating/changing treatment in patients with uncontrolled FOS.

Disclosure: The original study C021 (NCT02535091) was supported by SK Life Science, Inc (Paramus, NJ, USA), the Spanish cohort study was supported by Angelini Pharma Spain, and these analyses were supported by Angelini Pharma S.p.A. (Rome, Italy). VV: Consultant/advisor: Angelini Pharma, BIAL, Eisai, Esteve, GlaxoSmithKline, Jazz, Novartis, Sandoz, Takeda, UCB Pharma, Xenon; Speaker: Angelini Pharma, BIAL, Cevomed, Eisai, Esteve, Jazz, Newbridge, Paladin, UCB Pharma; Research support: Angelini Pharma, BIAL, Eisai, Jazz, UCB Pharma. JPL, PPD, EAB: Employees, Angelini Pharma. KT: Consultant: Angelini Pharma.

EPR-225 | Peri-ictal MRI abnormalities in status epilepticus, seizure clusters, and single seizures: A prospective study

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Background and aims: Brain MRI frequently identifies peri-ictal abnormalities (PMA) during or after seizures, especially in status epilepticus (SE), but also in single seizures (SiS) and seizure clusters (CS). The prevalence, features, and natural course of PMA remain poorly understood. This study prospectively

evaluated PMA prevalence, clinical correlations, and progression in SE, CS, and SiS.

Methods: Patients with SE, CS, and SiS were prospectively enrolled and underwent brain MRI within 120 hours of the ictal event. Demographic, clinical, EEG, and MRI data were collected. For patients with PMA, follow-up MRI was conducted until resolution. The study assessed the incidence, clinical associations, and progression of PMA across the three groups.

Results: Among 76 patients (30 with SE, 22 with CS, and 24 with SiS), PMA were identified in 31 individuals (41%), with significant differences between groups ($p=0.011$). PMA were less frequent in SiS (17%) compared to SE (57%) and CS (45%). Acute symptomatic SE or seizures were linked to a higher likelihood of PMA ($p=0.045$), while a history of epilepsy was associated with a lower incidence ($p=0.011$). The temporal cortex and hippocampus were most frequently affected. Follow-up MRI in 16 patients showed PMA resolution in 75% of cases, with a median recovery time of 24 days (IQR: 8–39).

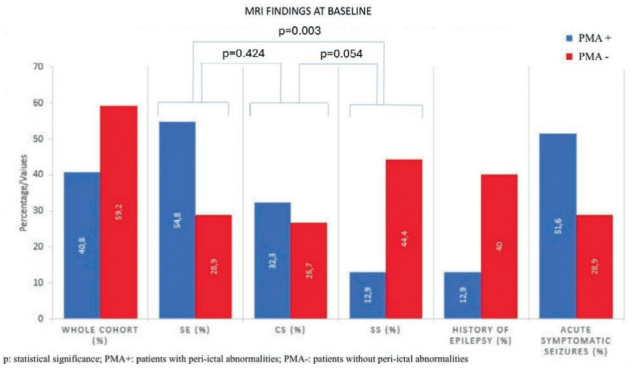

FIGURE 1 *p*: statistical significance: PMA+: patients with peri-ictal abnormalities: PMA-: patients without peri-ictal abnormalities.

Conclusion: PMAs were more common in SE and CS than in SiS, with acute pathology as a key predictor. While ictal duration may contribute to PMA development, it was not the main factor. Most PMAs resolved spontaneously, especially in SiS. Further studies are required to understand their significance.

Disclosure: Nothing to disclose.

Cerebrovascular diseases 3

EPR-226 | Intra-arterial thrombolysis after mechanical thrombectomy in acute ischemic stroke: A meta-analysis

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Background and aims: Mechanical thrombectomy (MT) is the standard treatment for acute ischemic stroke (AIS) caused by large vessel occlusions. The potential role of adjunctive intra-arterial thrombolysis (IAT) in improving outcomes following MT remains unclear. This meta-analysis evaluates the efficacy and safety of IAT after MT compared to MT alone in AIS patients.

Methods: A systematic search was conducted across PubMed, Cochrane Library, and EMBASE to identify RCTs comparing IAT following MT versus MT alone in patients with acute ischemic stroke. Statistical analysis was performed using a random-effects model in R.

Results: Four RCTs encompassing 1,392 patients (MT and IAT: 700; MT alone: 692) met the inclusion criteria. The pooled analysis demonstrated significantly improved excellent functional outcome (mRS 0-1 at 90d: OR = 1.31, 95% CI = 1.06 to 1.63) in patients receiving IAT after MT compared to MT alone. No statistically significant difference was observed for good functional outcome (mRS 0-2 at 90d: OR = 1.07, 95% CI = 0.86 to 1.32), symptomatic intracranial hemorrhage (OR = 1.31, 95% CI = 0.74 to 2.34), any intracranial hemorrhage (OR 1.30, 95% CI 0.96 to 1.96) and all-cause death (OR 0.92, 95% CI 0.70 to 1.21).

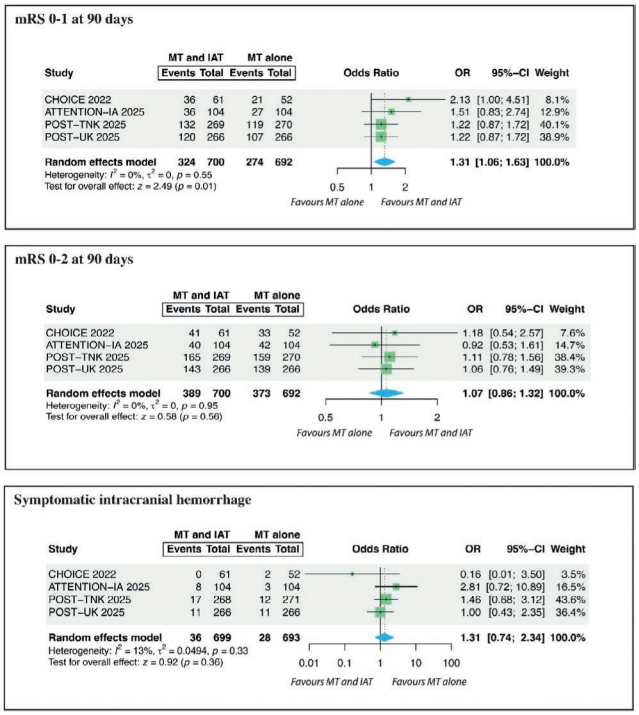

FIGURE 1 Forest plots for (A) Excellent functional outcome, (B) Good functional outcome, and (C) Symptomatic intracranial hemorrhage.

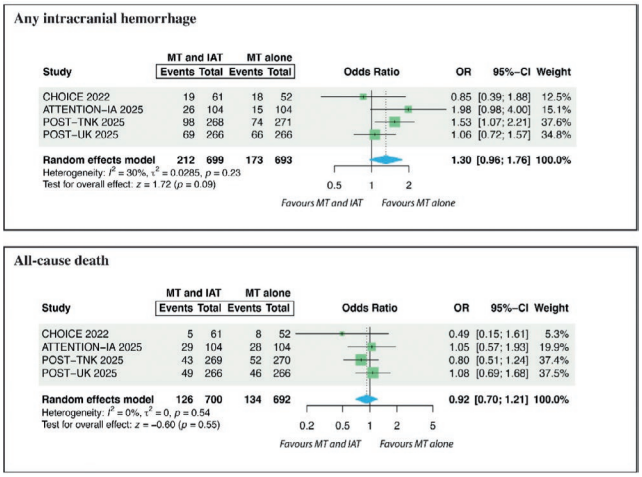

FIGURE 2 Forest plots for (A) Any intracranial hemorrhage, and (B) All-cause death.

Conclusion: Intra-arterial thrombolysis after mechanical thrombectomy improves excellent functional outcomes at 90 days in acute ischemic stroke patients, with similar safety profiles to mechanical thrombectomy alone.
Disclosure: NA

EPR-227 | Association between cardiac morphological changes and cerebrovascular lesion load in patients with atrial fibrillation

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Background and aims: Neurological complications of atrial fibrillation(AF) extended beyond cardioembolic stroke and neuroimaging examination of patients with AF have revealed unexpected cerebrovascular features. However, the link between AF and neurological and neuroimaging manifestations remains unclear. To elucidate this relation, we aimed to evaluate the association between cardiac structural changes and cerebrovascular load (either microangiopathic or non-microangiopathic) in patients with AF.
Methods: This is a preliminary cross-sectional analysis of data derived from the observational, prospective, single center Strat-AF2study (Stratification of cerebral bleeding risk in AF), enrolling older AF-patients on oral anticoagulants. All patients underwent a comprehensive clinical assessment, including neuroimaging (CT or MRI) and cardiological evaluations (echocardiography).
Results: Among 179 patients (mean age:78.6 years) high prevalence of cerebral small vessels disease markers (cSVD-m) (Figure 1) and left atria (LA) cardiomyopathy were found. Structural changes in left cardiac chambers, particularly LA-dilatation and ventricle hypertrophy, were significantly associated with higher burden of cSVD-m (mainly cerebral atrophy and lacunes), even after adjusting for major cardiovascular risk factors (CRFs). However, in multivariate logistic regression analysis, LA-dimension was not a key predictor of non-microangiopathic lesions, whereas CRFs and AF duration remains significant determinants. Main results are presented in Figure 2.

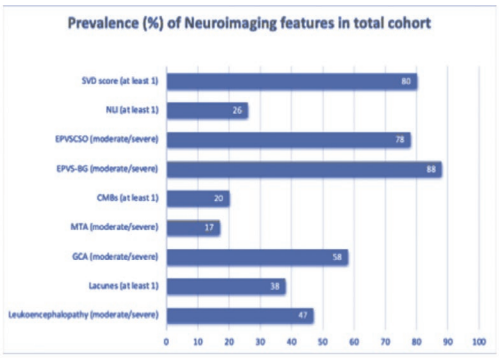

Figure.1 CMBs: Cerebral Microbleeds; EPSV-BG: Enlarged perivascular spaces-basal ganglia; EPSV-CSO: Enlarged perivascular spaces-Centro Semiovale, GCA: Global cortical atrophy; MTA: Medial temporal atrophy (MTA); NLI: Non-lacunar infarcts; SVD: small vessels disease

FIGURE 1 Prevalence of neuroimaging features in the total cohort.

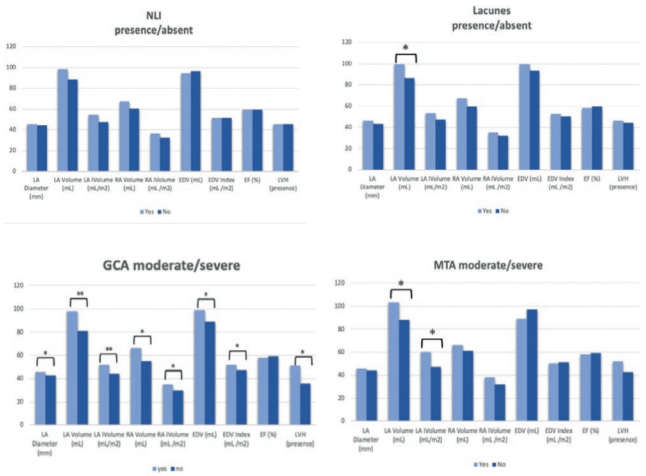

*Figure.2 LA: Left Atrium; RA: Right Atrium; EDV:end Diastolic Volume; EF: Ejection Fraction; LVH: Left Ventricle Hypertrophy Independent samples t tests , Chi-squared tests. (*p<.05, **p>.005)*

FIGURE 2 Association between cardiac structural changes and neuroimaging features.

Conclusion: This is the first study to examine the link between cardiac parameters and the overall burden of cerebrovascular lesions in AF-patients. According to our results, we speculate that cSVD-m may be associated with chronic and systemic effects of left heart changes in AF-patients. Despite limitations, our findings provide preliminary insight into complex association between cardiac morphological changes and cSVD in AF-patients.
Disclosure: Nothing to disclose.

EPR-228 | c-Jun N-terminal kinase 3 serum levels in ischemic stroke: Preliminary findings for a potential biomarker

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Background and aims: Reliable biomarkers for stroke are essential for identifying therapeutic targets. Brain-specific JNK3, implicated to synaptic dysfunction in experimental stroke models, has yet to be explored in clinical settings. This observational prospective study aimed to investigate serum JNK3 concentrations in stroke patients and their correlation with neuronal damage marker Neurofilament-Light-Chain (NfL).
Methods: We included 18-80-year-old patients with stroke at neuroimaging, onset <24h, NIHSS >1, pre-stroke mRS <2, without: previous stroke/TBI/other neurological disease, chronic immunosuppression, pregnancy, eGFR <30mL/min. As comparison, subjects hospitalized for acute neurologic symptoms meeting enrollment criteria except for ischemic lesion at neuroimaging (NL) were considered. Sera were collected within 24h (T0) from patients and NL, after 3-5d (T1) and 7 ± 2d (T2) in patients. JNK3 levels were measured by commercial ELISA kit, NfL by Ella Automated-Immunoassay-System.
Results: At present, 96 patients have been enrolled (49M, mean age $64.5y\pm1.3$). At onset, 51% had minor (NIHSS:1-4), 40.6% moderate (NIHSS:5-15), 8.3% severe stroke (NIHSS >16). NL are 12 (8M, mean age $63.2y\pm4.5$). At T0, JNK3 was higher in patients (2.84[IQR 0.28]) vs. NL (2.48[IQR 0.19]; $p<0.001$). Across the considered time-points, JNK3 was not different, while NfL was lower at T0 vs. T1, and T0 vs. T2 ($p<0.001$) (Fig. 1). No correlations were found between JNK3 and NfL concentrations.

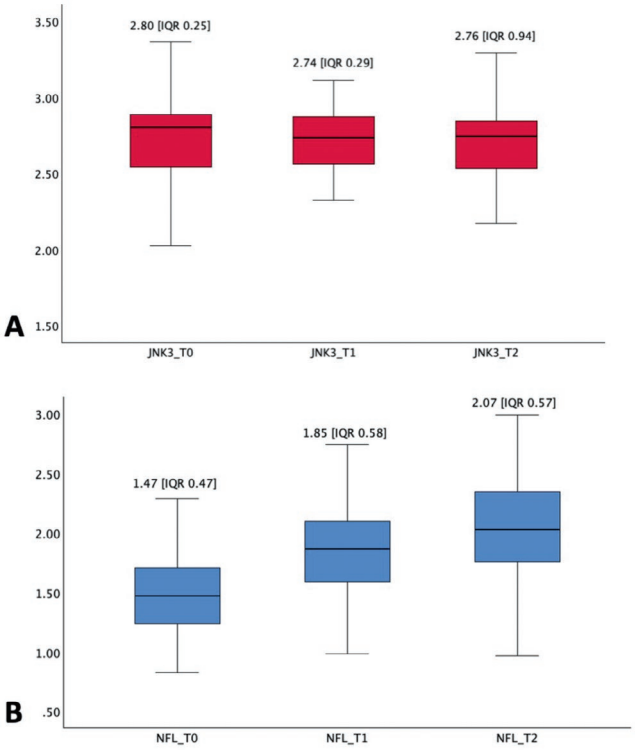

FIGURE 1 JNK3 (A) and NfL (B) serum concentrations in stroke patients at T0 (24h), T1(3-5d), T2(7 ± 2d), expressed as Log10(pg/mL). Indicated are median values with interquartile range (IQR).

Conclusion: Serum JNK3 levels were measurable in humans and were elevated when an ischemic lesion was present, indicating JNK3 release after stroke. No significant temporal differences were observed at the considered time-points, suggesting slower kinetics or distinct release mechanisms versus NfL, with which no correlations were documented. Further research to explore JNK3 in stroke is needed.
Disclosure: Funding: "Ricerca Corrente 2022-2024" granted by Italian "Ministero della Salute" (IRCCS Mondino Foundation); SEED for Innovation Patent 2.0 (SEED4IP 2.0) granted by Italian "Ministero dello Sviluppo Economico", now renamed "Ministero delle imprese e del Made in Italy -MIMIT". Double affiliations: FF: Cerebrovascular Disease & Stroke Unit, IRCCS Neurological Institute Foundation Mondino, Pavia, Italy; TB, AG, ST, NP: Mario Negri Institute for Pharmacolgical Research-IRCCS, Department of Neuroscience, Via Mario Negri 2, 20156 Milano, Italy.

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Background and aims: Acute ischemic stroke (AIS) is a leading cause of morbidity and mortality worldwide. While alteplase has been widely used for acute management, recent clinical trials suggest that tenecteplase (TNK) may offer improved clinical outcomes. This study aimed to compare the efficacy and safety of TNK compared with alteplase.

Methods: A comprehensive literature search was conducted using PubMed, Embase and Cochrane Library from inception to October 2024 to identify randomized controlled trials that compared TNK at 0.25 mg/kg dosage with alteplase. Data about clinical outcomes was extracted from both groups and assessed by generating forest plots using the random-effects model and pooling odds ratios (ORs).

Results: A total of 11 RCTs with 7,546 patients were included in the analysis. TNK showed statistically significant improvement in excellent functional outcome (mRS 0-1) compared with alteplase (OR = 1.14, 95% CI = 1.03-1.25). No statistically significant difference was observed for good functional outcome (mRS 0-2) (OR = 1.11, 95% CI = 0.9-1.25), early neurological improvement (OR = 1.08, 95% CI = 0.93-1.26), all-cause death (OR = 0.99, 95% CI = 0.08-1.22), symptomatic intracranial hemorrhage (OR = 1.16, 95% CI = 0.84-1.59) and poor functional outcome (mRS = 4-6) (OR = 0.95, 95% CI = 0.79-1.14).

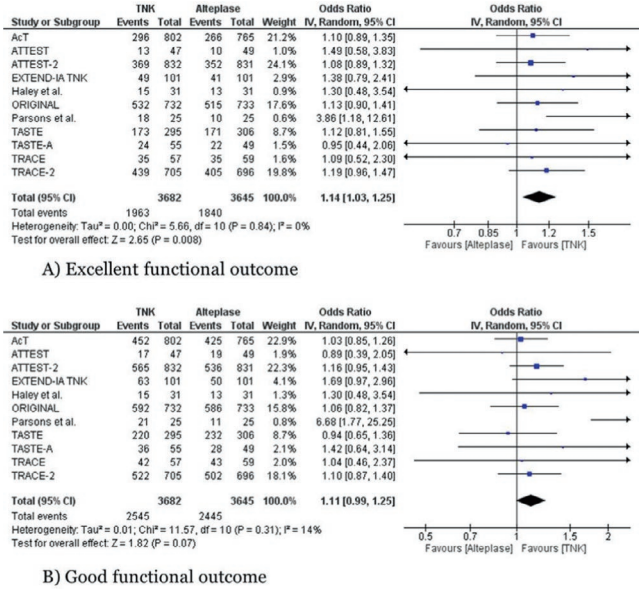


FIGURE 1 Forest plots for (A) Excellent functional outcome (B) Good functional outcome.

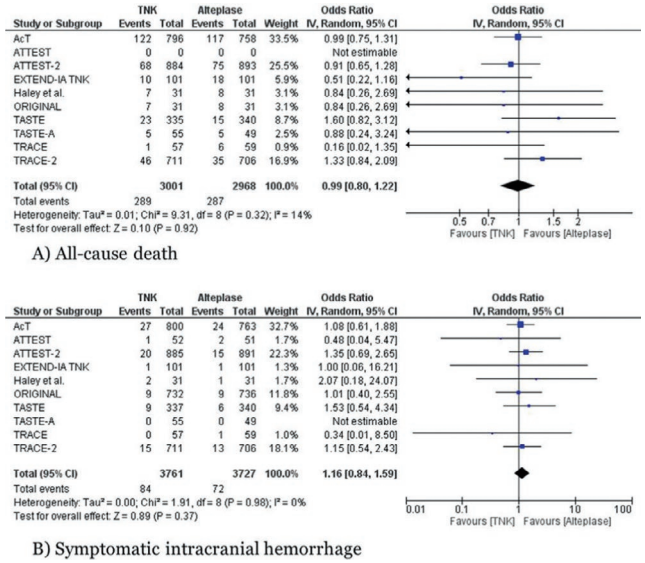
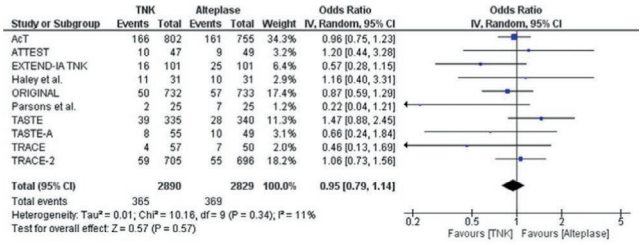
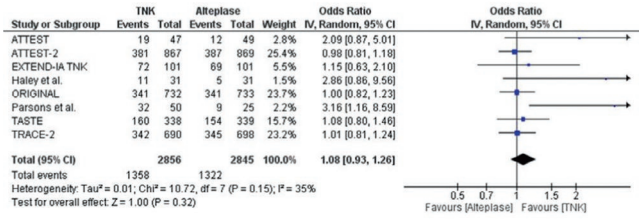


FIGURE 2 Forest plots for (A) All-cause death (B) symptomatic intracranial hemorrhage.



A) Poor functional outcome



B) Early neurological improvement

FIGURE 3 Forest plots for (A) Poor functional outcome (B) Early neurological improvement.

Conclusion: In patients with acute ischemic stroke, TNK demonstrated a significant advantage over alteplase in achieving excellent functional outcomes. The incidence of early neurological improvement, symptomatic intracranial hemorrhage, all-cause death, and poor functional outcome remained comparable across the two groups.
Disclosure: NA

EPR-230 | Patent foramen ovale closure in patients older than 60 years. 6-year experience of a comprehensive stroke center

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Background and aims: Patent foramen ovale (PFO) is a well-known cause of stroke in the young, but the benefit of PFO closure in older patients remains unclear. We aimed to evaluate the differences in outcomes of patients with PFO-attributed stroke according to age.
Methods: Retrospective observational study of patients with PFO-attributed stroke from 2018 to 2024. We compared clinical characteristics, procedural complications, atrial fibrillation (AF) and stroke recurrence between younger (≤60 years) and older (> 60 years) groups.
Results: We included 102 patients. Thirty (29%) were > 60 year old. Older patients had higher rates of hypertension (50% vs. 4%, $p < .001$) and cortical infarction (63% vs. 38%, $p = .017$), higher NIHSS score on admission (median [IQR] 3 [0-12] vs. 2 [0-5], $p = 0.006$), lower RoPE scores (median [IQR] 4 [2-6] vs. 7 [4-10]), and underwent percutaneous closure less frequently (77% vs. 97%, $p = .001$) than younger patients. There were no differences in PFO size or frequency of procedural complications (7/70 in the younger and 2/23 in the older group, all minor complications). Patients with minor complications had longer PFO tunnels (median [IQR] 21 mm [11-31] vs. 10 mm [8-13], $p = .032$). AF was observed in three (4.3%) treated patients from the younger cohort (all in the first two months after procedure), and in none of the older cohort. No stroke recurrence was observed in either group over a median follow-up of 3 [1-4] years.

TABLE 1 Demographic data.

	Total (N=102)	< 60 years (N=72)	> 60 years (N=30)	P- value
Age (years), median (IQR)	53 [42-61]	47 [30-64]	65 [58-72]	**<0,001**
Female, n (%)	45 (44,1%)	32 (44,4%)	13 (43,3%)	0,918
HTA, n (%)	25 (24,5%)	10 (13,9%)	15 (50,0%)	**<0,001**
Diabetes Mellitus, n (%)	5 (4,9%)	2 (2,8%)	3 (10,0%)	0,150
Active smoking, n (%)	17 (16,8%)	13 (18,3%)	4 (13,3%)	0,541
Previous Stroke / TIA, n (%)	27 (26,5%)	16 (22,2%)	11 (36,7%)	0,132
Cortical infarction, n (%)	46 (45,1%)	27 (37,5%)	19 (63,3%)	**0,017**
ROPE >7, n (%)	42 (41,2%)	42 (58,3%)	0	**<0,001**
ROPE Scale, median (IQR)	6 [5-7]	7 [4-10]	4 [2-6]	**<0,001**

	< 60 years (N=72)	> 60 years (N=30)	P- value
Percutaneus clossure, n(%)	70 (97,2%)	23 (76,7%)	**0,001**
Medical treatment, n (%)	2 (2,8%)	7 (23,3%)	

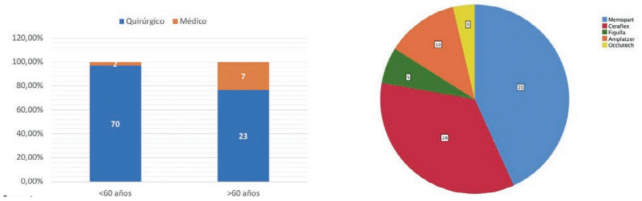

FIGURE 1 Treatment of PFO

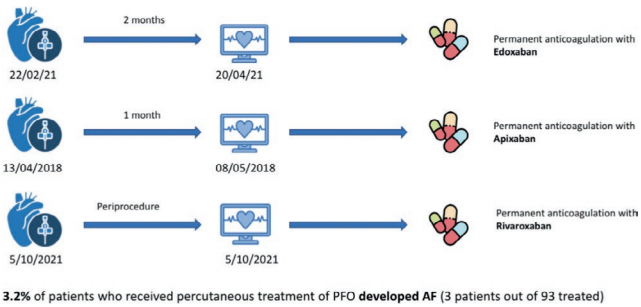

FIGURE 2 AF after closure

Conclusion: Procedural complications and early recurrences of percutaneous PFO closure seem as uncommon in > 60 years as in younger patients with PFO-attributed stroke.
Disclosure: Nothing to disclose.

EPR-231 | Carotid strain predicts 3-year stroke and coronary risk in metabolic syndrome: A new diagnostic insight

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Background and aims: This study aimed to determine if carotid strain and strain rate might predict major cardiovascular events (MACE) in individuals with metabolic syndrome (MS) during a three-year period.
Methods: This prospective observational study included 220 adult MS patients (60.7 ± 7.5 years old, 53% male). CS and CSR were measured using bilateral 2D common carotid artery (CCA) speckle-tracking ultrasonography. Clinical outcomes were monitored for three years.
Results: After a 3-year follow-up, 14 (7%) had MACE: Four (2%) experienced acute coronary syndrome, eight (4%) had atherothrombotic ischemic stroke, and two (1%) were hospitalized for heart failure. Univariate regression analysis of MS patients' clinical and echocardiographic parameters indicated that age, systemic hypertension, diabetes, and CCA circumferential strain and strain rate were substantially linked with MACE risk. Using multivariate logistic regression, two independent predictors of MACE in MS patients were identified: CCA-related CS (%) and CSR (1/s), $p < 0.01$. The ROC curve assessments of these independent MACE predictors showed suitable sensitivities and specificities. CS: AUC = 0.806 (sensitivity = 82.6%, specificity = 79.2%, $p < 0.0001$); CSR: AUC = 0.779 (sensitivity = 82.6%, specificity = 72.4%, $p < 0.0001$). The cut-off values were ≤2.9% for carotid CS and ≤0.35 s–1 for CSR. According to Kaplan-Meier survival curves, MS patients with lower carotid CS and CSR had significantly decreased MACE, ischemic stroke, and ACS-free survival ($p < 0.0001$).

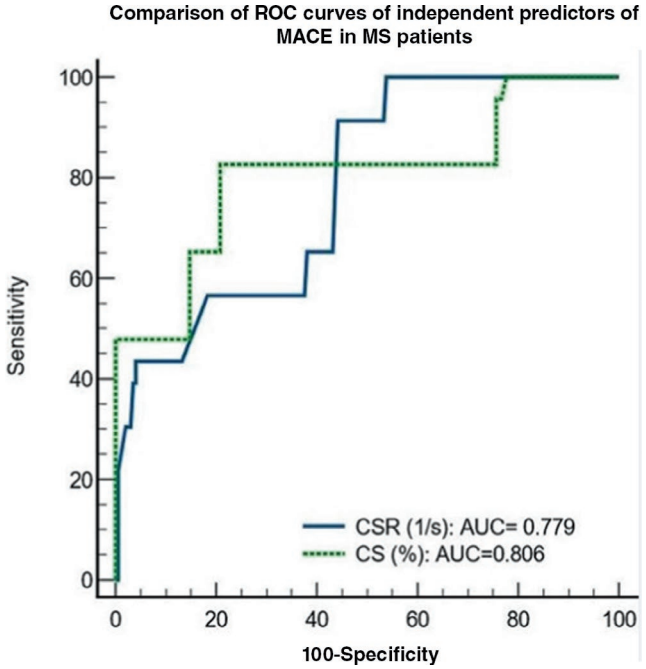

FIGURE 1 Comparison of ROC curves

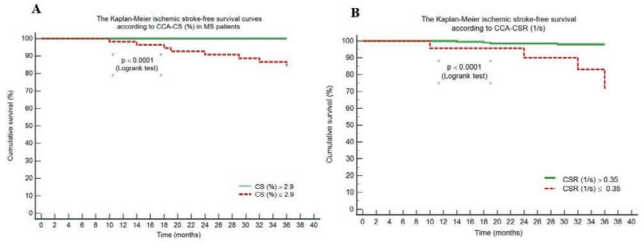

FIGURE 2 The Kaplan-Meier MACE-free survival curves in metabolic syndrome patients according to common carotid artery circumferential strain and strain rate rate.

Conclusion: Carotid CS and CSR independently predicted major cardiovascular and cerebrovascular events in prospectively studied MS patients without cardiovascular disease. In this demographic, carotid distortion may indicate cardiovascular risk early on.
Disclosure: Nothing to disclose.

EPR-232 | Safety and efficacy outcomes of LAAO in patients with prior ICH or cerebral amyloid angiopathy: A meta-analysis.

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Background and aims: Patients under oral anticoagulation for atrial fibrillation (AF) with a history of intracerebral hemorrhage (ICH) or cerebral amyloid angiopathy (CAA), have and increased risk of recurrent ICH. In those high-bleeding risk patients, left atrial appendage occlusion (LAAO) provided a promising alternative. Limited data from observational studies have shown that LAAO is safe and feasible with antiplatelet therapy or short-term OAC post-procedure. This meta-analysis aimed to provide data regarding the safety and efficacy of LAAO in patients with prior ICH or CAA.
Methods: PubMed/MEDLINE and EMBASE were systematically reviewed for randomized control trials, observational studies, and case series reporting stroke (ischemic and hemorrhagic) events in patients with AF undergoing LAAO who had a history of previous ICH and/or CAA. Pooled incidence rates (IRs) with corresponding 95% confidence intervals (CIs) were calculated for primary (post-procedural stroke and recurrent ICH) and secondary outcomes.

Results: Fourteen studies were included in the final analysis including 1,235. The pooled IRs for recurrent ICH, ischemic stroke, and all-cause mortality were 0.02% (95%CI: 0.004%–0.03%), 0.02% (95%CI: 0.01%–0.03%), and 0.04% (95%CI: 0.01%–0.08%), respectively (Figures 1-3). Subgroup analyses of patients with intraparenchymal hemorrhage and/or CAA reported pooled IRs of 0.04% (95% CI: 0.004–0.1%) for recurrent ICH, 0.04% (95% CI: 0.01–0.08%) for ischemic stroke, and 0.09% (95% CI: 0.01–0.22%) for all-cause mortality (Figures 1-3).

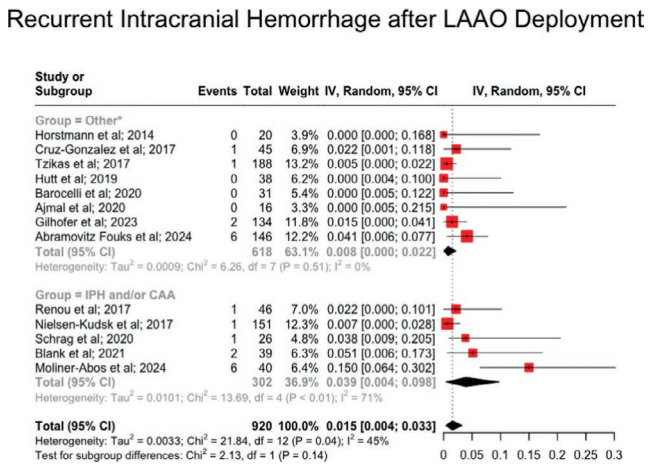

FIGURE 1

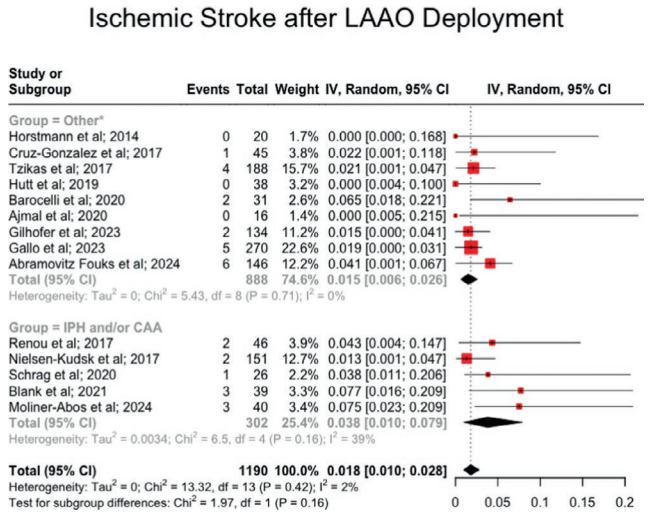

FIGURE 2

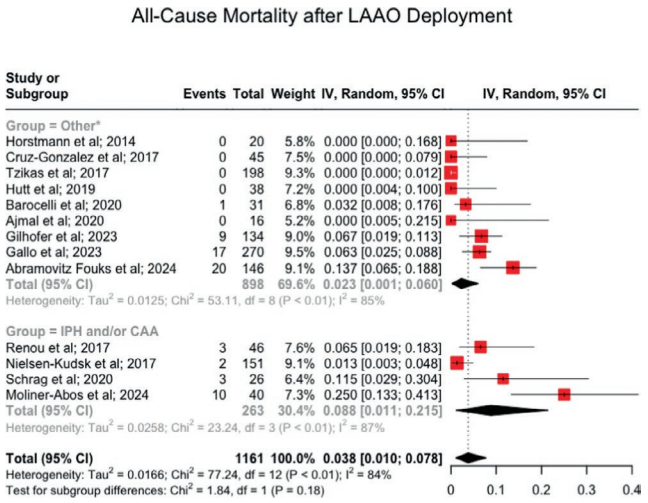

FIGURE 3

Conclusion: For selected AF patients with a history of ICH and/or CAA, LAAO is considered safe and effective, exhibiting low rates of major cerebrovascular events.
Disclosure: Nothing to disclose.

EPR-234 | Protective effects of bavachin in a rat middle cerebral artery occlusion stroke model

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Background and aims: Bavachin is a flavonoid isolated from the seeds of Psoralea corylifolia. Recent studies have shown that bavachin inhibits neuroinflammation and protects against lipopolysaccharide-induced oxidative stress in mice. However, its protective effects in ischemic stroke remain unclear. In this study, we investigated the therapeutic potentials of bavachin and its underlying mechanisms in a rat middle cerebral artery occlusion (MCAO) stroke model.
Methods: Adult male Sprague Dawley (SD) rats underwent right-sided MCAO for 90 minutes with intraperitoneal injection of with bavachin at 40 mg/kg or its vehicle for 3 consecutive days. The first dose was given 3 hours before MCAO onset, and the remaining doses were given on days 1 and 2 after MCAO. Body weight and a modified Neurological Severity Score (mNSS) were assessed daily before and after MCAO until sacrifice on day 3 when infarct volume, cerebral edema index, brain weight, spleen, and thymus index were determined.

Results: Compared with the sham group, the thymus index was significantly decreased after MCAO; this was reversed by bavachin treatment. Bavachin also significantly reduced the infarct volume and mNSS but not the spleen index on day 3. Furthermore, the cerebral edema index was significantly increased after MCAO; this was not affected by bavachin treatment. Finally, bavachin did not affect the body weight.
Conclusion: The present results indicate that bavachin has some neuroprotective effects in a rat MCAO stroke model. Bavachin may be a potential treatment for ischemic stroke. However, the underlying mechanisms need to be further investigated.
Disclosure: Nothing to disclose.

Motor neurone diseases

EPR-235 | Connecting SBMA international registries/databases: A retrospective study

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Background and aims: Over the years, several groups have collected retrospective data on different national series of Spinal-Bulbar Muscular Atrophy (SBMA) subjects in national databases/registries. We propose a retrospective study collating together data across different populations into a large international database, in order to better understand clinical/laboratory features, compare disease across different countries, and detect disease evolution on a global scale.
Methods: Centers from following countries accepted the invitation to join Italy in this project and already shared data: USA, Germany, South Korea, Finland, Greece, Denmark, Turkey. Data are due to be sent by UK, France, Japan. In Canada, the majority of patients have Indigenous ancestry, and participation is pending a community engagement process. We collected data with greatest overlap across the different databases, including symptoms at onset, symptoms progression, medications, comorbidities, MRC of 6 muscle pairs, bulbar involvement, cardiologic/respiratory parameters (ECG, spirometry), outcome measures/scales (SBMA-FRS/ALS-FRS, AMAT, IPSS, IIEF scales, and two/six minutes walking test), extensive lab tests, follow-up visits, and outcome.
Results: To date, we have collected data on 335 patients: 139 from Italy, 87 from Finland, 29 from Denmark, 25 from USA, 21 from Greece, 20 from South Korea, 8 from Turkey, 6 from Germany. We estimate that data from ~320 more patients will be integrated from UK, Canada, France, Japan.
Conclusion: Through an international joint effort, we created an international SBMA dataset that potentially encompasses up to ~650 subjects, with the aim of better characterize disease course, and explore regional differences within the disease.
Funded by KDA-Kennedy Disease Association
Disclosure: AB acknowledges support of EAN fellowship.

EPR-236 | Iron metabolism in als patients: A cohort study

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Background and aims: Given the evidence for altered iron metabolism in ALS, we aimed to investigate the relationship between iron homeostasis, genetic background and clinical variables in a larger cohort.
Methods: 77 ALS patients were tested for ferritin, iron and transferrin. A subset of 46 patients were also tested for common variants in iron-related genes, including ERFE, HFE, IL6, IL6R, SLC11A1. ANCOVA, adjusted correlation analysis and multiple linear regression were performed to test significant associations with clinical variables. Ferritin levels were normalized to the mean values in the men and female groups.
Results: Ferritin levels were abnormally elevated in 50% of men and 59.3% of women and correlated positively with the neutrophil to lymphocytes ratio (NLR) ($p=0.021$) and negatively with the ALSFRS-R ($p=0.001$). Iron levels were lower than normal in 7.8% of the patients and correlated negatively with the NLR ($p=0.012$) and positively with the ALSFRS-R ($p=0.006$). Transferrin levels were lower than normal in 44.7% and correlated negatively with the NLR ($p=0.049$). The ALSFRS-R was lower in SLC11A1 carriers ($p=0.047$), whereas the disease progression rate (DPR) and the NLR were both higher in ERFE carriers ($p=0.003$ and $p=0.020$, respectively). IL6R carriers had lower ferritin levels than non-carriers ($p=0.003$). IL6R status was the only predictor of ferritin levels ($p=0.003$) among sex, site of onset, disease duration and DPR.
Conclusion: Altered iron homeostasis in ALS is associated with systemic inflammation and high disease burden. This study also suggests a possible protective role of the IL6R D358A variant against higher ferritin levels, highlighting the importance of genetic characterization for disease prognosis.
Disclosure: Nothing to disclose.

EPR-237 | The CCL2-CCR2 axis drives neuromuscular denervation in ALS

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Background and aims: Systemic immune changes have been implicated in the pathogenesis of amyotrophic lateral sclerosis (ALS), but the precise mechanisms and cellular targets remain unknown. Here we aimed to characterize the inflammatory response around neuromuscular junctions (NMJs) in skeletal muscle and evaluate the potential therapeutic effects of modulating these immune pathways.
Methods: Confocal microscopy and proteomic analysis were used to characterize the immune alterations in skeletal muscle of ALS patients and the hTDP-43 mouse model of ALS. Local antibody-based treatment was administered to examine the effects of CCL2 suppression in hTDP-43 mice. Treatment efficiency was evaluated via immune cell quantification and NMJ analysis.
Results: We observed a marked leukocyte infiltration in the skeletal muscle of ALS patients. Major leukocyte and macrophage infiltration was recapitulated in hTDP-43 mice, most notably in close proximity to NMJs and in muscles severely affected by denervation, such as gastrocnemius. Proteomic analysis revealed elevated levels of chemokines CCL2, 3, 4 and 5 in gastrocnemius, but not in less affected muscles. Increased numbers of CCL2+ cells were located near NMJs in hTDP-43 mice, alongside CCR2 receptor-expressing immune cells, present from pre-symptomatic stages of disease. Increased numbers of CCR2+ cells were also observed in skeletal muscle from ALS patients. Local immunomodulatory treatment with either CCL2-neutralising antibodies or normal IgG antibodies in hTDP-43 mice reduced leukocyte infiltration and robustly ameliorated NMJ denervation.
Conclusion: These results demonstrate that the CCL2-CCR2 axis drives immune cell infiltration targeting NMJs in ALS and suggest that these immune pathways can be therapeutically modulated to protect NMJs from denervation.
Disclosure: THG has provided advisory services for Roche and Novartis. SA-M is a named inventor on a patent related to neurological disorders. SA-M also have ownership in Miaker Developments S.L., a startup related with a pipeline on Neurodegenerative and Neuromuscular Diseases.

EPR-238 | Safety and efficacy data from the phase 2 ARDA study of empasiprubart in multifocal motor neuropathy

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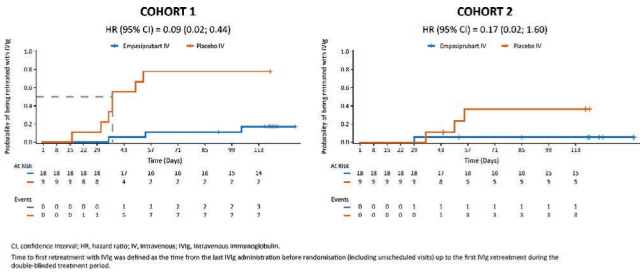
Background and aims: Multifocal motor neuropathy (MMN) is a rare, immune-mediated, chronic neuropathy leading to axonal degeneration and progressive, disabling, asymmetric limb weakness. Empasiprubart binds C2, blocking classical and lectin complement pathways involved in MMN pathophysiology. In a neuropathy ex vivo mouse model, blocking C2 prevented neurofilament light protein (NfL) loss, maintaining axonal integrity. The phase 2 ARDA (NCT05225675) study assessed the safety and efficacy of empasiprubart in adults with MMN.

Methods: Enrolled participants had probable/definite MMN (2010 EFNS/PNS guidelines) and proven intravenous immunoglobulin (IVIg) dependency and were on a stable IVIg regimen before randomization. Participants were assigned to 1 of 2 dosing cohorts, each randomized 2:1 to empasiprubart or placebo. Efficacy endpoints included IVIg retreatment rate, Patient Global Impression of Change scale score, change from baseline in grip strength (most affected hand), and serum NfL concentration in the double-blind treatment period.

Results: 27 participants (empasiprubart, $n=18$; placebo, $n=9$) were randomized per cohort. Cohort 2 participants were older, with longer duration of disease and time since first IVIg treatment. Empasiprubart was well tolerated overall. Most adverse events were mild/moderate. Empasiprubart was associated with reduced IVIg retreatment risk versus placebo in both cohorts (Figure). Improvements in patients' self-assessment (Table 1) and grip strength (Table 2) were greater with empasiprubart versus placebo in both cohorts. NfL levels were low and decreased with empasiprubart treatment.



CI, confidence interval; HR, hazard ratio; IV, intravenous; IVIg, intravenous immunoglobulin.
Time to first retreatment with IVIg was defined as the time from the last IVIg administration before randomisation (including unscheduled visits) up to the first IVIg retreatment during the double-blinded treatment period.

FIGURE 1 Time to first retreatment with IVIg in cohorts 1 and 2

TABLE 1 Summary of PGIC at last assessment during DBTP.

	Cohort 1		Cohort 2	
Change in condition since baseline, n (%)	**Empasiprubart (n=18)**	**Placebo (n=9)**	**Empasiprubart (n=18)**	**Placebo (n=9)**
Very much improved	7 (38.9)	0	4 (22.2)	0
Much improved	3 (16.7)	1 (11.1)	8 (44.4)	2 (22.2)
Minimally improved	7 (38.9)	0	3 (16.7)	2 (22.2)
No change	0	3 (33.3)	2 (11.1)	2 (22.2)
Minimally worse	1 (5.6)	2 (22.2)	0	2 (22.2)
Much worse	0	1 (11.1)	1 (5.6)	1 (11.1)
Very much worse	0	2 (22.2)	0	0

DBTP, double-blinded treatment period; PGIC, Patient Global Impression of Change.

TABLE 2 Change from baseline* in grip strength by treatment group at last assessment during DBTP.

	Cohort 1		Cohort 2	
	Empasiprubart (n=18)	**Placebo (n=9)**	**Empasiprubart (n=18)**	**Placebo (n=9)**
Grip strength – 3-day moving average, kPa, median (Q1, Q3)	11.28 (0.00, 28.78)	0.89 (−0.67, 9.00)	19.89 (3.33, 38.89)	0.78 (−2.22, 7.89)

DBTP, double-blinded treatment period; Q, quartile.
*Baseline values were established following IVIg monitoring period and prior to initiation of the DBTP.

Conclusion: Efficacy and safety results from the ARDA trial support proof of concept of empasiprubart in MMN and pave the way for a phase 3 trial.

Disclosure: LQ: Annexon, Alnylam, argenx, Avilar, Biogen, CIBERER, Fundació La Marató, CSL Behring, Dianthus, Grifols, Janssen, LFB, Lundbeck, Merck, Novartis, Octapharma, Roche, Sanofi, UCB TH: Annexon, argenx, Dianthus, Immunovant, Janssen, Nuvig, Sanofi, Takeda SP: ADOC, argenx, Berlin-Chemie Menarini, Kedrion, Mylan, Octapharma, Pfizer, Roche, Salveo, Sanofi Genzyme, Teva Actavis, Wörwag YMH: Nothing to disclose SC: PPD, part of Thermo Fisher Scientific, argenx IVdW, EKP, MV, OVdS: employees of argenx JAA: Akcea, Alexion, Alnylam, Annexon, argenx, CSL Behring, Grifols, Immunovant, ImmuPharma, Johnson & Johnson, Pfizer, Takeda EN-O: argenx, CSL Behring, Kedrion, LFB, Roche, Sanofi, Takeda SA: Alexion, argenx, Biogen, Janssen, LFB, Pfizer, Sanofi, UCB CK: Alexion, Alnylam, Alpine, Annexon, argenx, AstraZeneca, Biogen, Corino, CSL Behring, Genentech, Ionis, Neuroderm, Novo Nordisk, Pfizer, Sanofi, UCB, Takeda, Zai Lab HK: Alexion, argenx, CSL Behring, Grifols, Octapharma, Takeda, UCB MS: argenx, Bayer, Biogen Idec, Biotest, CSL Behring, Genzyme, Grifols, Immunovant, Kedrion, Merck, Novartis, Octapharma, PPTA, Roche, Sanofi-Aventis, Teva, UCB SR: Annexon, argenx, CSL Behring, Dianthus, EXCEMED, Fresenius, Hansa Biopharma, Takeda, UCB WLvdP: argenx, Biogen, Biohaven, NMD Pharma, Novartis, Roche, Scholar Rock, Takeda.

EPR-239 | Pridopidine for the treatment of ALS: Benefits in definite, probable and early subjects in the Healey ALS platform trial

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Background and aims: Pridopidine, a S1R agonist, demonstrates neuroprotective effects by improving cellular pathways impaired in ALS including ER stress. Pridopidine (1μM) reduced parameters of ER stress including expression of BiP (72% reduction, $p < 0.0001$) and CHOP (50% reduction, $p < 0.0001$) and increased cell viability by 69% ($p < 0.0001$). Rare mutations in S1R cause ALS. Pridopidine 45mg (bid) was evaluated in the Ph2 HEALEY ALS Platform Trial.
Methods: A post hoc analysis of El Escorial definite+probable ALS and early (symptom onset < 18mo) subjects in the Ph2 HEALEY ALS Platform Trial was performed. Endpoints include change from baseline to 24 weeks in ALSFRS-R, and measures of respiration, bulbar, speech, and quality-of-life (QoL).
Results: Pridopidine was well tolerated, consistent with its prior safety profile. Pridopidine ($n = 37$) shows 32% slowing of decline versus placebo ($n = 35$) in ALSFRS-R (wk24 Δ2.9, $p = 0.03$). Benefits are observed in ALSFRS-R respiratory (wk24 Δ1.20, $p = 0.03$), and bulbar (wk24 Δ0.93, $p = 0.06$) domains. Pridopidine shows no worsening in dyspnea (wk24 Δ0.62, $p = 0.04$). Benefits in speaking rate (Δ0.39, $p = 0.005$) and articulation rate (Δ0.40, $p = 0.002$) are observed. A Kaplan-Meier survival analysis shows a prolongation of median survival time (~300 to 600 days) compared to the delayed-start (168 days) placebo-to-pridopidine participants ($n = 12$)(log rank $p = 0.069$). The Cox Proportional Hazard Ratio (HR), adjusted for baseline characteristics is 0.429 ($p = 0.052$).
Conclusion: Pridopidine demonstrated beneficial effects across multiple clinical measures of ALS, including survival benefits in definite+probable ALS and early participants. These encouraging observations support and inform planning for a Ph3 study.
Disclosure: Prilenia Therapeutics supported this study.

EPR-240 | Managing multifocal motor neuropathy: A survey of neurologists from Japan, Canada, and six European countries

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Background and aims: Multifocal motor neuropathy (MMN) is a rare, immune-mediated, chronic neuropathy characterized by progressive, disabling, asymmetric limb weakness without sensory loss. We report results from a survey of neurologists treating MMN, aimed at understanding diagnostic and treatment patterns, perceived patient illness burden, and future treatment directions.
Methods: Neurologists in Japan, Canada, Denmark, Germany, Italy, the Netherlands, Spain, and the UK ≥2 years since residency who consult/treat ≥2 patients with MMN per year completed a 47-item online survey.
Results: 150 neurologists completed the survey: 53% reported practicing at an academic/referral center, 24% in the community/outpatient setting, and 23% in both settings. Neurologists considered 23% of the patients they treat to have severe MMN, 43% to have moderate MMN, and 33% to have mild MMN. Use of established diagnostic guidelines was variable (Table). 82% of neurologists reported using intravenous immunoglobulin as first-line therapy. In the previous year, neurologists switched 20% of patients to second-line therapies, primarily due to a lack of significant improvement (39%) or disease progression (36%). The most commonly used second-line therapies were rituximab (35%) and plasmapheresis (27%). Corticosteroids were used second-line by 17%, despite not being recommended by guidelines. 57% of neurologists were satisfied with current treatments' ability to improve symptoms. 45% of neurologists considered "better efficacy that improves daily functioning to perform tasks" an important attribute of potential new treatments.

TABLE. Treatment guidelines and the percentage of neurologists who consider them the most useful.

Treatment guidelines	%
European Federation of Neurological Societies	54
American Academy of Neurology	48
American Association of Neuromuscular & Electrodiagnostic Medicine	31
Other	8
Do not use a specific guideline	9

Respondents could select more than one answer; therefore, the total percentage may exceed 100.

Conclusion: This survey highlights the unmet need for greater awareness of diagnostic and treatment guidelines in MMN.

Disclosure: LQ: Alnylam Pharmaceuticals, Annexon Biosciences, argenx, Avilar Therapeutics, Biogen, CIBERER, CSL Behring, Dianthus Therapeutics, Fundació La Marató, GBS/CIDP Foundation International, Grifols, Instituto de Salud Carlos III – Ministry of Economy and Innovation (Spain), Janssen, LFB, Lundbeck, Merck, Novartis, Octapharma, Roche, Sanofi, UCB RAL: Alexion, Annexon Biosciences, argenx, Avilar Therapeutics, BioCryst, Boehringer Ingelheim, CSL Behring, Dianthus Therapeutics, Grifols, GBS/CIDP Foundation International, Immunovant, Intellia Therapeutics, Johnson & Johnson, Medscape, MGFA, Novartis, Nervosave Therapeutics, Nuvig Therapeutics, Sanofi, Seismic Therapeutic, Takeda, TGTX, UpToDate CS: AKIGAI, Algiax Pharmaceuticals, Alnylam Pharmaceuticals, Annexon Biosciences, argenx, CSL Behring, Grifols, GBS/CIDP Foundation International, Kedrion, Nevro, Novartis, Pfizer, Takeda, Teva Pharmaceuticals MBB: Accordant Health Care, argenx, Cambridge University Press, Oxford University Press, Takeda, UpToDate PN has nothing to disclose SB-S, CA-B, DG, JTG, JW are employees of argenx

EPR-241 | Low-intensity pulsed ultrasound modulates disease progression in a mouse model of amyotrophic lateral sclerosis

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Background and aims: Amyotrophic lateral sclerosis (ALS) is a devastating neurodegenerative disease characterized by the progressive loss of motor neurons in the brain and spinal cord, and there are no effective drug treatments. Low-intensity pulsed ultrasound (LIPUS) has garnered attention as a promising non-invasive neuromodulation method. In this study, we investigate its effects on the motor cortex and underlying mechanisms using the SOD1G93A mouse model of ALS.

Methods: The Rotarod test and CatWalk test were used to assess the disease onset and measure gait function in different groups of mice. 9.4T MRI was used to detect cerebral blood flow in the motor cortex. In vivo multiphoton images were used to measure microvascular density in the motor cortex of mice. The change in mRNA expression after LIPUS treatment was detected by transcriptome sequencing analysis.

Results: Our results show that LIPUS treatment delays disease onset and prolongs lifespan in ALS mice. LIPUS significantly increases cerebral blood flow in the motor cortex by preserving vascular endothelial cell integrity and increasing microvascular density, which may be mediated via the ion channel TRPV4. RNA sequencing analysis reveals that LIPUS substantially reduces the expression of genes associated with neuroinflammation.

Conclusion: We demonstrate that LIPUS on the motor cortex leads to delayed disease progression in a mouse model of ALS. Enhanced cerebral blood flow, which is achieved by maintaining vascular endothelial cell integrity and increasing microvascular density, is crucial for the protective effects of LIPUS in ALS.

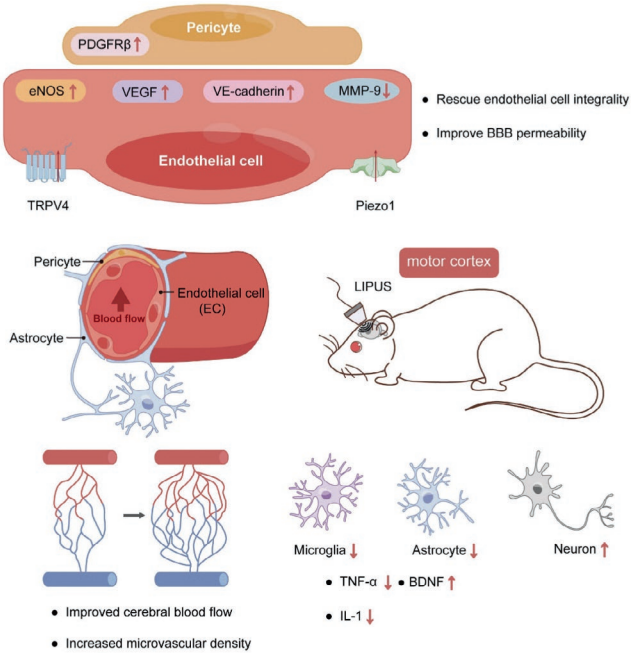

FIGURE 1 Graphical abstract

Disclosure: The authors declare no competing interests.

EPR-242 | Lower creatinine-to-cystatin C ratio associated with increased risk of incident ALS in the UK Biobank Cohort

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Background and aims: Reduced muscle mass has been associated with the progression and prognosis of amyotrophic lateral sclerosis (ALS). However, it remains unclear whether decreased muscle mass is a risk factor for ALS or a consequence of motor neuron degeneration. Recently, serum creatinine-to-cystatin C ratio (CCR) have emerged as promising biomarkers for assessing muscle mass. We aimed to explore the association between CCR and the incidence of ALS using data from the UK Biobank.

Methods: Between 2006 and 2010, 446,945 participants were included in the baseline. CCR was calculated as the ratio of serum creatinine to cystatin C. Cox regression models were used to analyze the relationship between CCR and ALS incidence. Furthermore, subgroup analyses were conducted to investigate potential covariates in these relationships.

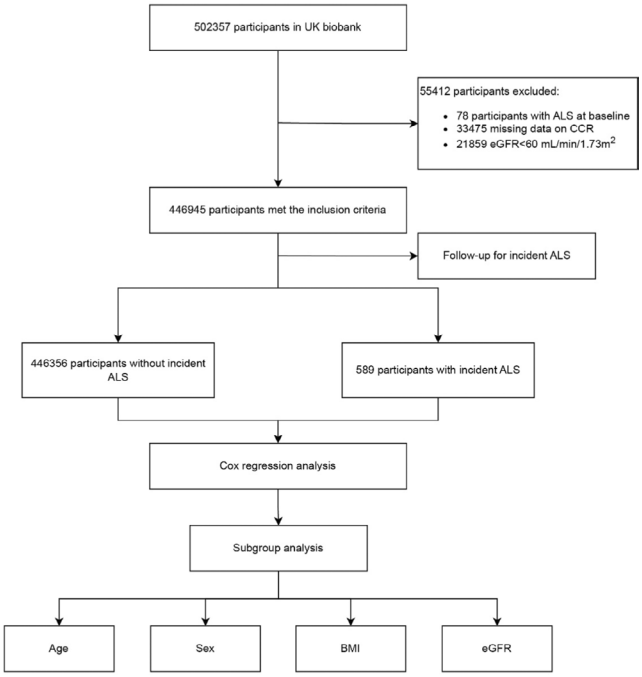

FIGURE 1 Flowchart of the study.

Results: After adjusting for all covariates, the multivariate Cox regression analysis revealed a significant association between decreased CCR and an increased risk of ALS (hazard ratio (HR) = 0.990, 95% confidence interval (CI): 0.982-0.999, $p = 0.026$). Participants were stratified into groups based on CCR tertiles. Compared with participants in the highest tertiles of CCR, those in the lowest (HR = 1.388, 95% CI: 1.032-1.866, $p = 0.030$) and medium tertiles (HR = 1.348, 95% CI: 1.045-1.739, $p = 0.021$) had an increased risk of ALS incidence. Subgroup analysis showed that the relationship between CCR and ALS incidence was particularly significant among participants aged < 65 years.

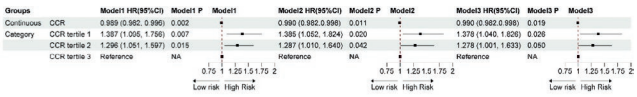

FIGURE 2 Forest plot of the CCR on ALS incidence.

Conclusion: The present results demonstrate that lower CCR is significantly associated with a higher risk of ALS.
Disclosure: Nothing to disclose.

EPR-243 | Handwriting, touchscreen dexterity and bradykinesia measures in Parkinson's disease: A feature selection study

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Background and aims: Bradykinesia affects handwriting and smartphone usage in Parkinson's disease patients (pwPD). This study aimed at assessing handwriting, hand dexterity, smartphone usage and bradykinesia in pwPD, and at identifying the features that best describe upper-limb alterations in pwPD.
Methods: Forty pwPD and 30 age/sex-matched healthy controls were included. We used standard handwriting/dexterity tests: Manual-Ability-Measure-36, Purdue-Pegboard-Test (PPT) and copy of a text on paper. Spatiotemporal handwriting parameters were assessed using tests on a tablet: copy of text and prewriting tasks. To obtain objective data on movement speed and amplitude on the smartphone, we developed tests involving the most commonly used gestures (tap, swipe, slide). Bradykinesia during a finger tapping task was evaluated using electromagnetic sensors. Sequential feature selection models were used to identify the parameters best distinguishing pwPD and healthy controls.
Results: PwPD relative to healthy controls showed reduced manual ability and dexterity. They showed reduced movement amplitude and speed in smartphone tests and signs of micrographia during handwriting tests. Moreover, kinematic parameters correlated with both PPT and Movement Disorder Society Unified Parkinson's Disease Rating Scale III. Each feature selection model demonstrated a good accuracy, particularly when including standard handwriting/dexterity tests (R2 = 0.90), tests on smartphone (R2 = 0.94) and all the features together (R2 = 0.97). The best features were self-reported manual abilities, PPT, tap and swipe speed/amplitude on smartphone.
Conclusion: This study showed that technological devices with customized software can provide quantitative measures of

handwriting, dexterity and bradykinesia that will be useful to assess PD progression and the effects of interventions in pwPD.
Disclosure: Funding: Italian Ministry of Health, grant number GR-2018-12366005. Disclosures. A.G. L.Z., D.E., A.Gr., V.C., E.S., M.M., R.B. and M.A.V. Nothing to disclose. E.S., S.B., D.C., and E.C. grants form the Italian Ministry of Health. MF received compensation for consulting services or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM. F.A. is Associate Editor of NeuroImage: Clinical, has received speaker honoraria from Biogen Idec, Italfarmaco, Roche, Zambon and Eli Lilly, and receives or has received research supports from the Italian Ministry of Health, the Italian Ministry of University and Research, AriSLA (Fondazione Italiana di Ricerca per la SLA), the European Research Council, the EU Joint Programme—Neurodegenerative Disease Research (JPND) and Foundation Research on Alzheimer Disease (France).

EPR-244 | Diabetes impact on nigrostriatal vulnerability in Parkinson's Disease

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Background and aims: Less is known about mechanisms underlying the role of diabetes mellitus (DM) as modulator of clinical severity in Parkinson's Disease (PD).
Methods: Patients with and without diabetes were first contrasted and secondarily matched for age, sex, MDS-UPDRS-I and III. Regional differences in 123I-FP-CIT binding within nigrostriatal pathways in PD with and without diabetes were addressed via ROI-based and voxel-wise univariate analyses. Alterations in molecular connectivity between the groups were assessed via correlation analysis.
Results: 269 drug-naïve PD patients were enrolled ($n=174$ patients from PPMI; $n=95$ patients from DNA). In both cohorts, patients with diabetes (PD-DM) were older, exhibited a higher male prevalence, and exhibited worse non-motor and cognitive symptoms than PD without (PD-n). After the severity-matching procedure, PD-DM exhibited higher dopamine binding in left putamen compared to PD in both independent cohorts. PD-DM showed significant dopaminergic connectivity alterations within nigrostriatal nodes (20%), primarily due to a loss of connectivity (98%). PD-n showed a higher percentage of connectivity alterations within nigrostriatal nodes (33%), characterized by both loss (84%) and gained connections (16%).
Conclusion: This is the first study demonstrating the impact of diabetes on striatal dopaminergic motor reserve, amplifying the effect of dopaminergic loss on motor symptoms.
Disclosure: none

EPR-245 | ADL impairments in prodromal Parkinson's: Impact of RBD, hyposmia, and combined phenotypes

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Background and aims: Activities of daily living (ADL) impairments are important markers of Parkinson's disease (PD) progression. However, limited research exists on ADL impairments in individuals with prodromal symptoms, such as rapid eye movement sleep behavior disorder (RBD) and hyposmia, who have not been diagnosed with PD. This study aimed to evaluate ADL impairments in prodromal subgroups—RBD, hyposmia, and combined RBD and hyposmia (RBD+H) to assess whether these phenotypes are associated with worse ADL function.
Methods: Data from 245 healthy controls (HC), 74 RBD, 491 hyposmia, and 476 RBD+H participants in the Parkinson's Progression Markers Initiative (PPMI) were analyzed. RBD was confirmed via polysomnography, while hyposmia was defined as an UPSIT score $<=$ 15th percentile without RBD symptoms. ADL impairments were assessed using the MDS-UPDRS Parts I and II and Schwab and England scales. Statistical tests included Kruskal-Wallis and generalized linear modeling (GLM), adjusted for age and sex, with Bonferroni-corrected post-hoc analyses.
Results: Subgroup membership significantly predicted ADL impairments (Chi-square $=240.519$, $p<0.001$). Estimated means indicated higher ADL impairments in pure RBD (10.38) and RBD+H (7.88), compared to hyposmia (4.87) and HCs (3.04). RBD participants reported higher impairments due to anxiety ($p<0.001$), and RBD+H participants had more impairments related to constipation compared to hyposmia ($p=0.002$).
Conclusion: Subgroup membership is a strong predictor of ADL impairments, emphasizing the need to address these challenges in prodromal PD, for early intervention and improved disease staging. Furthermore, this research highlights the importance of further investigating prodromal phenotypes to better understand PD progression.
Disclosure: No specific funding was received for this study. All authors are involved in the recruitment and/or conduct of the PPMI study at the Newcastle UK study site.

EPR-246 | Treatment stability comparison among different ADD-ON therapies in fluctuating Parkinson's disease patients

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Background and aims: Motor fluctuations are a major challenge in advanced Parkinson's disease (PD), often managed using add-on therapies such as catechol-O-methyl transferase (COMT) or monoamine oxidase-B (MAO-B) inhibitors. However, real-life comparisons between these therapies are limited. This study investigates the efficacy and tolerability of selegiline (SL), rasagiline (RS), safinamide (SF), and opicapone (OP) in fluctuating PD patients, focusing on treatment stability and demographic influences.

Methods: This retrospective longitudinal study included 160 fluctuating PD patients treated at two Italian tertiary centers (2012–2023). Inclusion criteria required motor fluctuations (WOQ-19 ≥2) and at least 12 months of follow-up. Patients were grouped by add-on therapy (SL, RS, SF, OP). The primary outcome was the stability of antiparkinsonian therapy, defined as months without significant modifications in treatment or adverse events (AEs). Demographic and clinical factors were analyzed using Cox regression.

Results: The OP group had the longest disease duration (9.8 ± 4.6 years, $p = 0.003$) and the highest baseline LEDD ($p = 0.022$). Stability did not differ significantly between groups ($p = 0.167$). However, females exhibited higher therapy modification rates ($p = 0.013$). AEs occurred in 15% of patients, predominantly dyskinesia (6.9%) and hallucinations (5%). OP was more frequently prescribed to younger patients (64.3 ± 7 years).

		Overall (N = 160)	SL (N =11)	RS (N =26)	SF (N =78)	OP (N =45)	P value
Sex	M	97 (60.6%)	7 (63.6%)	15 (57.7%)	47 (60.3%)	28 (62.2%)	.980[a]
	F	63 (39.4%)	4 (36.4%)	11 (42.3%)	31 (39.7%)	17 (37.8%)	
Age at ADD-ON start (years)		67.36 ± 9.08	68.45 ± 9.38	70.96 ±9.54	67.82 ±9.30	64.33 ±7	**0.029** (RS vs. OP 0.023)[c]
H&Y at ADD-ON start		2.11 ± 0.36	2.18 ± 0.98	2.07 ± 0.37	2.26 ± 0.76	2.08± 0.28	0.544
Disease duration at ADD-ON start (years)		7.94 ± 4.70	9.63 ± 7.57	6.67 ± 3.74	7.14 ± 4.27	9.77± 4.60	**0.003** (OP vs. RS 0.014; OP vs. SF 0.012)[c]
Total LEDD at ADD-ON start (mg)		766.93 ± 429.79	684.09 ± 393.74	562.60 ± 252.09	804.77 ±440.35	846.38 ±485.04	**0.022** (SF vs RS 0.038; OP vs. RS 0.028)[c]

Results are reported as average ± standard deviation *(range)* or absolute values (percentage), as appropriate.
Bold indicates the significant value of p-value: statistical significance.
H&Y: Hoehn and Yahr stage; LEDD: Levodopa Equivalent Daily Dose.
[a]Fisher exact test
[b]Kruskal-Wallis test
[c]Bonferroni pairwise post hoc comparisons

Table 1. Baseline demographic and clinical features of included patients

		Overall (N = 160)	SL (N =11)	RS (N =26)	SF (N =78)	OP (N =45)	P value
Follow up-duration (months) (mean ± SD)		34.23 ± 24.14	24.81 ± 16.56	43.00 ± 26.80	37.96 ± 25.63	25.22 ± 17.76	0.003
Stability of therapy (months) (mean ± SD)		22.07 ± 17.28	24.63 ± 15.90	25.50 ±17.07	22.87 ±19.64	18.08 ± 12.46	NS (0.167)[a]
Levodopa change (n, %)	Increase	65 (40.6)	2 (18.2)	11 (42.3)	37 (47.4)	15 (33.3)	NS (0.186)[a]
	Reduction	16 (10.0)	2 (18.2)	0 (0)	6 (7.7)	8 (17.8)	NS (0.066)[a]
Start of new antiparkinsonan therapy (n, %)		31 (19.4)	3 (27.3)	5 (19.2)	20 (25.6)	3 (6.7)	NS (0.70)[a]
ADD-ON interruption (n, %)		36 (22.5)	2 (18.2)	9 (34.6)	13 (16.7)	12 (26.7)	NS (0.233)[a]
AEs (n, %)		24 (15.0)	2 (18.2)	3 (11.5)	13 (16.7)	6 (13.3)	NS (0.877)[a]
Dyskinesia (n, %)		11 (6.9)	0 (0)	1 (3.8)	9 (11.5)	1 (2.2)	-
Hallucination/Behavioural (n, %)		8 (5)	1 (9.1)	1 (3.8)	3 (3.8)	3 (6.7)	-
Gastrointestinal (n, %)		2 (1.2)	1 (9.1)	0 (0)	1 (1.3)	0 (0)	-
Miscellaneous (n, %)		3 (1.9)	0 (0)	1 (3.8)	0 (0)	2 (4.4)	-

Results are reported as average ± standard deviation *(range)* or absolute values (percentage), as appropriate.
Bold indicates the significant value of p-value: statistical significance.
Miscellaneous include orthostatic hypotension, confusion, pain, global worsening, weight change, or not specified reason.
[a]One-way ANOVA

Table 2. Comparisons of ADD-ON therapy stability, treatment modification and AEs among groups

	B	SE	Wald	df	P Value	Exp(B) (95% CI)
Gender	-.064	.193	.111	1	**.739**	.938 (.640 – 1.369)
Age	-.004	0.11	.127	1	.722	.996 (.957 – 1.018)
Disease duration	-.008	.022	.142	1	.707	.992 (.949 – 1.036)
LEDD	.000	.000	3.357	1	.067	1.000 (1.000 – 1.001)
Tremor dominant phenotype			.303	2	.859	
Akinetic-rigid phenotype	-.092	.265	.120	1	.729	.912 (.543 – 1.533)
Mixed phenotype	-.129	.235	.302	1	.583	.879 (.554 – 1.394)
Safinamide			.428	3	.934	
Selegiline	.035	.412	.007	1	.932	1.036 (.462 – 2.323)
Rasagiline	-.074	.258	.082	1	.774	.929 (.560 – 1.540)
Opicapone	.126	.249	.257	1	.613	1.134 (.696 – 1.848)

B: Beta; SE: standard error; df: degrees of freedom; Exp(B): Hazard ratio; CI: Confidence interval.
Bold indicates the significant value of p-value: statistical significance.
LEDD: Levodopa Equivalent Daily Dose.

Table 3. Cox regression analysis: stability predictors of therapy in PD patients

Conclusion: No single add-on therapy demonstrated superior stability, highlighting comparable efficacy across options. Sex significantly influenced therapy adjustments, with females requiring more frequent modifications. These findings underscore the importance of personalized treatment strategies in fluctuating PD management.

Disclosure: Nothing to declare.

EPR-247 | Theta-gamma frequency subthalamic stimulation for verbal fluency in Parkinson's Disease: A randomized, crossover trial

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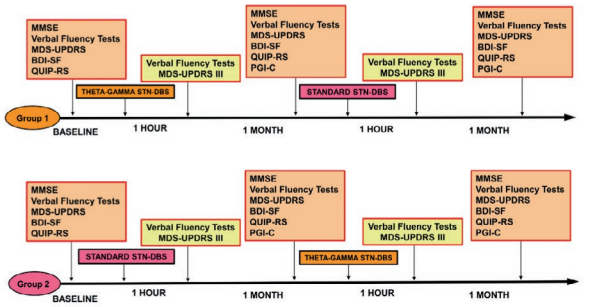
Background and aims: High-frequency Deep Brain Stimulation (DBS) of the subthalamic nucleus (STN) improves motor symptoms in Parkinson's disease (PD), but may affect cognition, especially verbal fluency (VF). Low-frequency stimulation (theta, 4-10 Hz) showed potential cognitive benefits but can worsen motor symptoms in PD. This randomized, double-blind, cross-over study evaluated the safety and efficacy of combined theta-gamma frequency stimulation on VF in PD patients with STN-DBS.

Methods: Patients were randomly assigned 1:1 to start with either standard or theta-gamma STN stimulation, followed by the reverse. VF was assessed at baseline, one hour, and one month after each stimulation change. Secondary endpoints included adverse events (AEs), motor and non-motor symptoms (including mood and impulsivity) and their complications. Data were analyzed using a linear mixed-effects model, considering fixed effects for visit time, stimulation setting, and their interaction.



Legend: BDI-SF: Beck Depression Inventory-Short Form; STN-DBS: Subthalamic Nucleus - Deep Brain Stimulation; MDS-UPDRS: Movement Disorder Society – Unified Parkinson Disease Rating Scale; MMSE: Mini Mental State Examination; PGI-C: Patient Global Impression of Change; QUIP-RS: Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale.

Figure 1. Timeline of the clinical assessments

Results: Twelve patients completed the study. No significant effects of the stimulation settings were observed one hour after stimulation change. After one month, theta-gamma stimulation significantly improved non-episodic category VF ($p=0.037$) and episodic category VF ($p=0.034$) over standard stimulation. No significant differences were found in phonemic fluency or category switching. Motor and non-motor outcomes were not significantly affected by the stimulation setting. AEs were mild and evenly distributed between conditions.

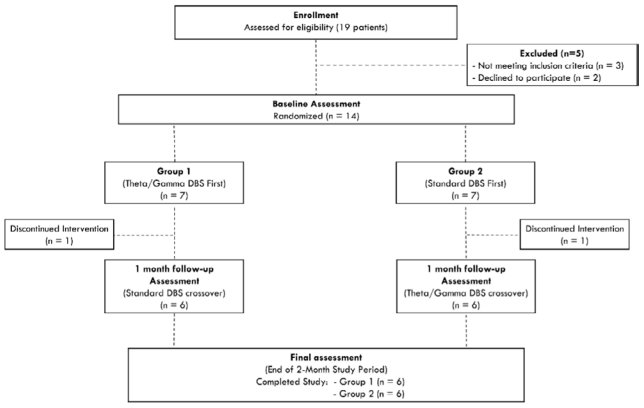


Figure 2. Flow diagram of study design

Patient ID	Stimulation settings	Phonemic VF	Episodic Category VF	Non-episodic Category VF	Switching VF	MDS-UPDRS – part III	MDS-UPDRS – Total score	BDI-SF – Total score	QUIP-RS – Total score
001	S	43	11	5	18	10	52	7	2
	T-G	50	17	9	22	15	52	7	2
002	S	59	12	7	15	12	19	0	0
	T-G	63	14	11	20	14	20	0	2
003	S	24	9	5	12	44	83	3	0
	T-G	27	5	4	14	34	69	3	17
004	S	21	5	6	7	9	57	2	3
	T-G	12	6	3	9	23	60	1	18
005	S	74	12	9	31	6	20	5	11
	T-G	67	18	9	22	18	38	3	9
006	S	65	11	3	12	21	67	6	14
	T-G	61	15	8	14	12	54	3	22
007	S	25	7	5	15	32	78	14	26
	T-G	24	10	8	14	20	62	14	12
008	S	44	12	7	16	29	85	8	24
	T-G	40	14	11	16	26	76	8	16
010	S	31	7	1	15	19	60	8	30
	T-G	29	6	4	16	18	55	5	13
011	S	37	7	9	16	39	87	16	62
	T-G	30	11	6	14	30	72	16	55
013	S	39	11	2	17	34	90	20	16
	T-G	42	16	7	17	26	80	16	31
014	S	54	10	6	19	27	74	3	10
	T-G	41	15	9	18	40	90	4	10

Legend: BDI-SF: Beck Depression Inventory Short Form; MDS-UPDRS: Movement Disorder Society – Unified Parkinson Disease Rating Scale; QUIP-RS: Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease-Rating Scale; S: Standard; T-G: Theta-Gamma; VF: Verbal Fluency.
Data for ID 009 and 012 are not presented due to their premature withdrawal from the study.

Figure 3. Principal raw scores at one-month mark of the patients which completed the trial.

Conclusion: Combined theta-gamma frequency stimulation may improve VF in PD patients treated with STN-DBS safely and without worsening motor symptoms. This approach could be integrated into existing stimulation paradigms, though further studies are needed to confirm these findings and explore broader clinical implications.

Disclosure: Nothing to disclose.

EPR-248 | GLP-1 receptor agonist: a new disease-modifying therapy in Parkinson's disease? A systematic review and meta-analysis

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Background and aims: Glucagon-like peptide-1 receptor (GLP-1R) agonists, primarily used for treating diabetes, have recently demonstrated neuroprotective properties in a mouse model for Parkinson's disease (PD). Despite this, their efficacy as a potential disease-modifying therapy for PD remains controversial. Therefore, we conducted a meta-analysis to evaluate the impact of GLP-1R agonists on slowing the progression of motor and non-motor symptoms in PD patients.

Methods: We performed a systematic review and meta-analysis of randomized clinical trials (RCTs) comparing GLP-1R agonists to placebo or best medical therapy (BMT) in patients with mild to moderate PD. We searched in Scopus, Cochraine and PubMed. The primary goal was to assess the efficacy of GLP-1R agonists in reducing motor disability progression valuing the change in MDS-UPDRS part III scores after a washout period from PD therapy

Results: Four RCTs with a total of 515 patients were included. Among these, 300 (58%) received GLP-1R agonists, and 215 (42%) received a placebo or BMT. GLP-1R agonists were associated with significantly slower progression of motor symptoms, as indicated by changes from baseline in the MDS-UPDRS part III score (MD -2.08, 95% CI -3,87 to -0,28, $p=0.02$, I^2 = 30%

Study	Design	Patients	Female	Age[1], y	Age at diagn[1], y	Follow-up[1], mo	UPDRS part III [1]	Levodopa [1]	PDQ39 index [1]	GLP1R- ago
Athauda, D et al	RCT	31/29	9/7	62/58	56/53	15	32,8/27,1	773/825	19.9/21	Exenatide
AvilesOlmos et al	RCT	21/24	5/4	61/59	52/48	12	31/34	973/977	19,2/24,5	Exenendin-4
McGarr et al	RCT	170/84	56/32	62/62	NA	9	22,7/22,3	0/0	NA	NLY01
Meissner et al	RCT	78/78	34/30	60/60	NA	14	14,8/15,5	317/355	NA	Lixisenatide

[1]Mean or median; GLP1R-ago: GLP1R-agonist; Levodopa: Levodopa starting dose; § weight in kg.

Table 1: Baseline characteristics of included studies

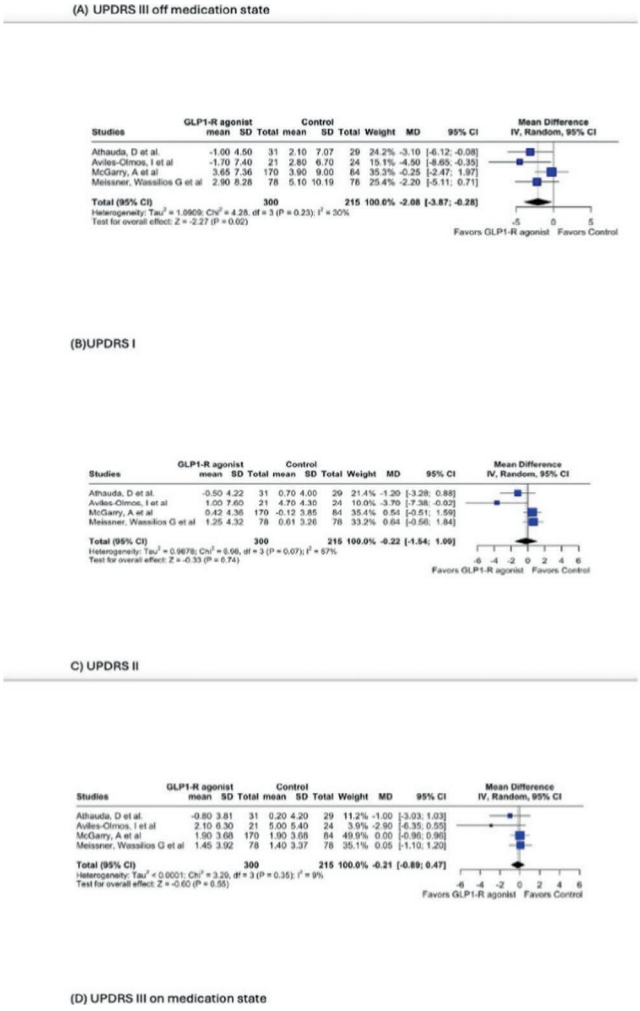

FIGURE 1 Meta-analysis (A) UPDRS III off medication state (B) UPDRS I on medication state (C) UPDRS II

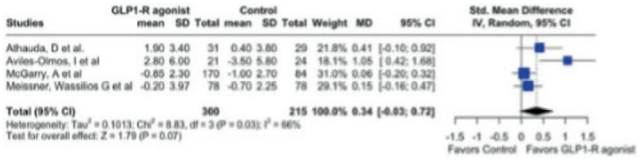

FIGURE 2 Cognitive functions assessed by standardized mean difference of Moca and MDRS-2 from baseline

Conclusion: This meta-analysis, encompassing 515 patients from four RCTs, demonstrated that GLP-1R agonists are associated with a slower deterioration of motor symptoms and cognitive functions in patients with mild to moderate Parkinson's disease.

Disclosure: Nothing to disclose.

EPR-249 | Advancing Deep Brain Stimulation programming in Parkinson's disease: Automated algorithms for electrode selection

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Background and aims: The programming of stimulation settings is a critical aspect in the postoperative management of individuals with Parkinson's disease undergoing deep brain stimulation [1]. However, the process of identifying effective stimulation contacts and optimizing stimulation parameters is not standardized yet, resulting in a time-consuming and resource-intensive task. This study aimed to i) evaluate state-of-the-art methods for electrode selection and ii) to validate a novel automated

Methods: This retrospective analysis includes 16 individuals who were consecutively entered in the One Hospital ClinicalService Brain Modulation Project and underwent implantation of a PerceptTM PC (Medtronic) neurostimulator. A comparative analysis was conducted on three methods for beta peak selection and stimulation electrode suggestion. The methods differ in their definition of the beta band, the cut-offs considered for peak amplitude, and the criteria chosen for electrode selection. Two Medtronic algorithms (the device algorithm and a novel one) and an existing method [2] were analyzed. The electrode detected by the algorithms was then compared with the final programming decision made by clinicians.

Results: Data from both hemispheres were available in 29 out of 36 recording sessions (81%). The device current and novel algorithm match the final programming decision on the stimulation electrode in 63.2% and 67.9% of cases, respectively. In contrast, the algorithm developed by Strelow et al. [2] matches in only 2 cases (7.1%).

Conclusion: This study highlights the potential of automated algorithms in supporting the selection of stimulation electrodes, thereby reducing the complexity of DBS programming and enhancing clinical efficiency, while ensuring concordance with clinician-guided programming decisions.

Disclosure: Nothing to disclose.

EPR-250 | CSF tau protein levels as a predictor of motor fluctuation risk in de novo Parkinson's disease patients

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Background and aims: Motor fluctuations (MF) are a disabling complication of Parkinson's disease (PD). While multiple factors contribute to MF onset, the role of brain co-pathology, including tauopathy and amyloidopathy, remains unclear. The objective of this study was, therefore, to explore the association between CSF co-pathology profiles and MF development in a longitudinal de novo (DN) PD cohort.
Methods: We conducted a single-center retrospective study with 108 DN PD patients, assessed by the MDS-UPDRS and MoCA scores, and the measurement of CSF total alpha-synuclein (alpha-syn), total and phosphorylated-181 tau (t-tau, p-tau), amyloid-beta42 and amyloid-beta40 (ABeta42, ABeta40) levels, p-tau/t-tau, ABeta42/ABeta40, and p-tau/ABeta42 ratios. Patients were classified as "fluctuator" (FLUCT) or "no-fluctuator" (NoFLUCT) based on MF development (MDS-UPDRS part IV >=1) during follow-up. Baseline variables were compared; ROC and Cox regression analyses were run to estimate their predictive values.
Results: The DN PD cohort was followed for 5 (±1.45) years, with 32 (29.6%) patients developing MF. At baseline, patients showed lower CSF alpha-syn and t-tau levels than controls, while FLUCT had higher p-tau, p-tau/t-tau, and p-tau/ABeta42 ratios. The p-tau/t-tau ratio best predicted MF development; above the cutoff of 0.135, MF were 5 times more likely with 87.1% sensitivity and 63.5% specificity (AUC=0.81).
Conclusion: Elevated CSF p-tau/t-tau ratios in DN PD patients indicate a higher risk of MF. These findings suggest that tau and, to a lesser extent, amyloid-beta, co-pathology might be involved in the mechanisms leading to MF onset, supporting lines of evidence that show their contribution to the degeneration of motor circuits in PD.
Disclosure: The research leading to these results has received funding from the European Union (NextGenerationEU) through the Italian Ministry of University and Research under PNRR–M4C2-I1.3 Project PE_00000019 "Heal Italia" to T.S. (CUP E83C22004670001). The views and opinions expressed are those of the authors only and do not necessarily reflect those of the European Union or the European Commission. The authors have no conflicts of interest to declare.

EPR-251 | Mobility in people with Parkinson's disease with and without nocturnal hypokinesia: A propensity score-matched study

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Background and aims: Mobility impairment and nocturnal hypokinesia (NH) are common in people with Parkinson's disease (PwPD) and significantly impact quality of life. Reduced hip muscle strength/torque could contribute to NH and link it to mobility problems. However, no studies investigated the relationship between these two aspects in PwPD.
Methods: Data from 30 PwPD with NH [females: 11 (37%); age: 69.8±7.8; disease duration: 6.4±3.3] and 60 without NH, propensity score-matched for age, sex and disease duration were included. NH was defined as MDS-UPDRS-II-2.9 ≥1. Participants performed three supervised mobility tasks with a lower-back-mounted inertial sensor (BTS G-WALK): a 25-meter forward walking at self-selected speed (FW), a Timed-Up-and-Go (TUG) and 3-meter backward walking test (3MBWT). Spatiotemporal gait parameters, TUG duration, mean (MAV) and peak angular velocity (PAV) of TUG 180° turning and 3MBWT speed were measured. Participants wore a Garmin Vivosmart 4 smartwatch for 5 consecutive days on the least affected wrist and average daily steps (avDS) were calculated.
Results: PwPD with NH showed a lower gait speed ($p=0.024$), normalized stride length ($p=0.036$), TUG duration ($p=0.033$), MAV ($p=0.011$), PAV ($p=0.009$), 3MBWT speed ($p=0.022$) and avDS ($p=0.011$). Moreover, PwPD with NH showed a higher prevalence of falls ($p=0.001$)
Conclusion: NH was associated with worse supervised and real-world mobility as well as a higher prevalence of falls. This could suggest a shared mechanism between NH and mobility impairments as part of a more severe disease phenotype. Our results highlight the need to investigate NH and develop therapeutical strategies for this symptom.
Disclosure: Nothing to disclose.

EPR-252 | Plasma pTau217 detection for Alzheimer's Disease co-pathology in Parkinson's Disease and Parkinsonism

E. Fiorenzato[1]; G. Musso[3]; F. Vianello[1]; S. Cauzzo[1]; R. Biundo[4]; V. Misenti[1]; G. Bonato[1]; M. Campagnolo[1]; M. Carecchio[1]; A. Guerra[1]; V. D'Onofrio[1]; A. Cagnin[2]; M. Montagnana[3]; A. Antonini[1]

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Background and aims: Alzheimer's disease (AD) co-pathology is common in Parkinson's spectrum disorders and independently contributes to dementia. Plasma pTau217 has emerged as a promising blood-based biomarker for detecting AD pathology, correlating with amyloid and tau PET, and may help to identify AD co-pathology in movement disorders. We evaluated plasma pTau217 for detecting AD co-pathology in PD and parkinsonism and its association with cognitive impairment.

Methods: We included 170 participants from PADUA-CESNE cohort: 57 PD, 4 dementia with Lewy bodies (DLB), 28 Progressive Supranuclear Palsy (PSP), 4 corticobasal syndrome (CBS), 51 healthy aged controls (HC), 26 mild cognitive impairment (MCI). All participants underwent an extensive cognitive assessment, including MoCA and MMSE, and were classified accordingly (PD-cognitive spectrum: PD-NC normal cognition, PD-MCI, PDD dementia). Plasma pTau217 was measured through Lumipulse G1200; amyloid positivity was defined as pTau217 > 0.22 ng/L

Results: Among PD spectrum, PD-NC showed lower levels of pTau217 than PD-MCI ($p = 0.042$), PDD/DLB ($p = 0.049$), and PSP/CBS ($p = 0.002$). No pTau217-positive cases were observed in PD-NC. Amyloid positivity was highest in the MCI group (32.14%), followed by CBS/PSP (28.13%), PDD/DLB (27.27%), and PD-MCI (15.63%), with the lowest in HC (7.84%). Negative correlations were found between pTau217 and MoCA ($r^2 = -0.38$, $p = 0.004$) and MMSE ($r^2 = -0.37$, $p = 0.006$).

Conclusion: pTau217 is elevated in PD patients with cognitive impairment, particularly PDD/DLB, and in patients with atypical parkinsonism such as PSP and CBS, but not in cognitively normal PD. It may serve as a reliable marker of AD co-pathology and cognitive involvement, warranting further validation with PET imaging.

Disclosure: Nothing to disclose.

EPR-253 | Nocturnal heart rate variability in iRBD

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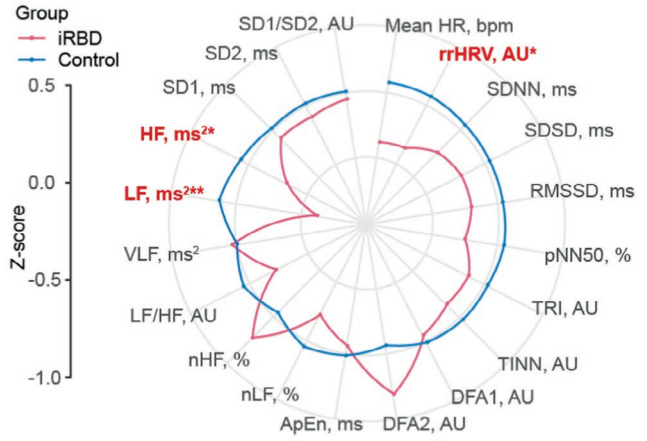
Background and aims: Idiopathic REM sleep behavior disorder (iRBD) is a prodromal marker of neurodegenerative diseases, often preceding their clinical diagnosis by years. Autonomic dysfunction, a hallmark of early neurodegeneration, is a clinical feature of iRBD. We investigated the autonomic function during sleep in iRBD by analyzing nocturnal heart rate variability (HRV).

Methods: In this case-control study, patients with iRBD were matched 1:6 for age, sex, and apnea-hypopnea index with non-iRBD controls without known brain damage (e.g., stroke) from the Bern Sleep-Wake Registry ($n \approx 11000$). All participants underwent clinical polysomnography. iRBD patients were followed for the development of an overt alpha-synucleinopathy such as Parkinson's Disease (PD). Twenty nocturnal HRV parameters, including time-domain, frequency-domain, and nonlinear measures, were derived from routine clinical polysomnography. Group differences in nocturnal HRV were analyzed using the Wilcoxon rank-sum test.

Results: Seventeen patients with iRBD and 102 controls were included in the analysis. Patients with iRBD showed low HRV, with low absolute power in both low- and high-frequency components, indicating impaired autonomic modulation during sleep. Three out of seventeen iRBD patients subsequently developed PD (follow-up: 132 person-years). In an exploratory analysis, the patients, who progressed to PD, had higher nocturnal heart rate, lower HRV, and higher sympathetic dominance compared to those, who did not.

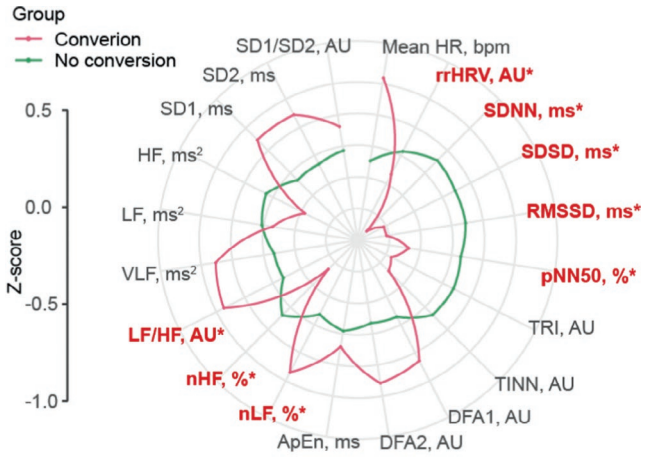
TABLE 1 Study population: iRBD versus control group.

Parameter	iRBD (n=17)	Control group (n=102)	P-value
Demographics			
Age, years	66.33 [63.81, 70.09]	66.82 [63.71, 71.82]	0.861
Male gender, %	14 (82.4)	84 (82.4)	1.000
Basic sleep parameters			
Total Sleep Time (TST), min	346.00 [292.50, 356.50]	303.50 [259.00, 343.38]	0.029*
NREM1, %TST	22.42 [15.46, 31.30]	19.65 [14.72, 25.98]	0.554
NREM2, %TST	38.76 [34.71, 47.40]	48.10 [42.28, 55.28]	0.012*
NREM3, %TST	23.66 [8.46, 27.45]	15.20 [6.27, 22.28]	0.084
REM, %TST	17.52 [16.53, 23.43]	15.50 [12.00, 18.45]	0.027*
Apnea-hypopnea index, /h	6.08 [4.32, 13.02]	6.00 [4.05, 12.38]	0.627



* p<0.05, ** p<0.010, ***p<0.001; Wilcoxon rank sum test: iRBD vs. control
ApEn - approximate entropy, DFA1 or DFA2 - detrended fluctuation analysis component α1 or α2, LF - absolute low-frequency power, LF/HF - low to high frequency power (normalized), nHF - normalized high-frequency power, nLF - normalized low-frequency power, pNN50 - percentage of adjacent NN intervals that differ from each other by more than 50 ms, RMSSD - root mean square of successive RR interval differences, SD1 - standard deviation of the first Poincaré plot axis, SD2 - standard deviation of the second Poincaré plot axis, SDNN - standard deviation of NN intervals, SDSD - standard deviation of successive RR interval differences, TINN - triangular interpolation of NN intervals, TRI - triangular index, VLF - very low frequency power.

FIGURE 1 Circular plot of the differences in nocturnal HRV between iRBD patients and the control group.



* p<0.05, ** p<0.010, ***p<0.001; Wilcoxon rank sum test: conversion vs. no conversion
ApEn - approximate entropy, DFA1 or DFA2 - detrended fluctuation analysis component α1 or α2, LF - absolute low-frequency power, LF/HF - low to high frequency power (normalized), nHF - normalized high-frequency power, nLF - normalized low-frequency power, pNN50 - percentage of adjacent NN intervals that differ from each other by more than 50 ms, RMSSD - root mean square of successive RR interval differences, SD1 - standard deviation of the first Poincaré plot axis, SD2 - standard deviation of the second Poincaré plot axis, SDNN - standard deviation of NN intervals, SDSD - standard deviation of successive RR interval differences, TINN - triangular interpolation of NN intervals, TRI - triangular index, VLF - very low frequency power.

FIGURE 2 Circular plot of the differences in nocturnal HRV between iRBD patients depending on the conversion to Parkinson's disease.

Conclusion: Low nocturnal HRV is a potential marker of autonomic dysfunction in iRBD. Sympathetic hyperactivation may signal the approaching conversion of iRBD to PD and might serve as a marker for neurodegenerative progression in iRBD.
Disclosure: Nothing to disclose.

EPR-254 | Biomarkers in early-stage Huntington's disease

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Background and aims: Huntington's disease (HD) is a neurodegenerative disorder characterized by motor, cognitive, and behavioral abnormalities. Optical Coherence Tomography (OCT) and olfactory testing offers a non-invasive method to measure retinal changes and olfactory dysfunction, respectively, that reflect neurodegenerative processes.
Methods: This cross-sectional study compared spectral domain OCT data, and olfactory testing using the Sniffin' Sticks battery for identification and discrimination in HD patients and healthy controls (HC). HD patients were classified into Stage1 and Stage2 based on motor symptoms and functional capacity.
Results: We recruited a total of 68 participants including 39HD patients (22 stage1, 17 stage2) and 29 age-matched HC. There were no significant differences in age and gender between the groups. Stage2 HD patients showed worse motor function (UHDRS-TMS 28.44±18.13 vs. 13.74±8.78, $p=0.002$), functional capacity (UHDRS-TFC 8.13±2.03 vs. 12.44±0.99, $p<0.001$), and lower scores on MMSE (27.36±1.64 vs. 28.73±1.74, $p=0.005$ vs. 29.45±0.91, $p<0.001$) compared to stage1 HD patients and HC, respectively. Both stage1 and stage2 HD groups displayed significantly reduced macular retinal nerve fiber layer thickness (mRNFL) (33.45±4.70, 31.90±3.47 vs. 38.45±5.00; $p<0.01$) and ganglion cell-inner plexiform layer thickness (GCIPL) (71.63±6.38, 60.42±4.67 vs. 77.03±8.40; $p<0.01$) as compared to HC. Odor identification and discrimination were significantly reduced in both stage1(10.87±3.11, 9.62±2.99 respectively; $p<0.001$) and stage2(9.88±2.90, 7.38±3.89 respectively; $p<0.001$) HD patients as compared to HC.
Conclusion: In this study, HD patients showed significantly thinner GCIPL and mRNFL, and olfactory dysfunction compared to healthy controls, even in early disease stages. These findings suggest that OCT and olfactory testing may serve as a valuable biomarker especially in the early stages of HD.
Disclosure: Nothing to disclose.

EPR-255 | Region-specific treatment preferences in advanced Parkinson's disease: A discrete choice experiment

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Background and aims: Understanding preferences for advanced Parkinson's Disease (aPD) treatments is essential, particularly in the context of varying cultural, healthcare system, and economic factors that shape individual priorities across regions. This study explores treatment preferences and benefit/risk trade-offs among people with aPD (PwaP) in two regions.

Methods: A discrete-choice experiment was conducted with 304 PwaP and care partners based on 7 attributes (Table 1). Random-parameter logit estimates were used to determine Attribute Relative importance (RI) and benefit/risk trade-offs, comparing the United States (US; $n=148$), with the United Kingdom (UK; $n=46$) and Germany combined (DE; $n=110$).

Treatment Attributes	Attribute Levels
ON Time without troublesome dyskinesia **(ONwoTD)**	• 3 hours • 6 hours • 10 hours • 13 hours
Early morning OFF Time **(EMO)**	• Occasionally: once a week • Sometimes: 3 times a week • Very often: 7 times a week
Risk of mild to moderate skin reactions **(Skin reactions)**	• 5 out of 100 • 30 out of 100 • 60 out of 100 • 90 out of 100 patients
Risk of severe side effects requiring hospitalization **(Severe side effects)**	• 1 out of 100 patients • 10 out of 100 patients • 20 out of 100 patients
Route of Administration **(ROA)**	• Only oral pills • Device for infusion under the skin (subcutaneous); No surgery required • Device for infusion in the intestine; Stomach surgery required, • Device for electro stimulation of the brain; Brain surgery required
Frequency of pill regimen **(Pill burden)**	• No need to take pills, • Pills 4 times in a day • Pills 8 times in a day
Device maintenance	• None • Once every 3 days • Once per day

Table 1. Attributes and levels.

Results: For US and UK/DE participants, average age was 66.2 (SD = 8.6) and 56.3 (SD = 9.3), PD duration was 9.8 years (SD = 4.3) and 10.5 (SD = 4.7), and self-reported OFF time was 4.0 hours/day (SD = 2.6) and 4.4 (SD = 1.9), respectively. The most important attributes were ON time without troublesome dyskinesia (ONwoTD) and route of administration (ROA); ONwoTD was statistically more important in the UK/DE group than in US (RI = 31.4 vs. 19.9). In US, ROA was viewed as twice as important as ONwoTD (RI = 37.2 vs. 19.9). US respondents also valued the risk of skin reactions more than their UK/DE counterparts (RI = 15.5 vs. 8.5). Both subsamples showed willingness to accept any risks of skin reactions for switching to a less invasive ROA. Both groups would consider switching from oral pills to subcutaneous ROA for a gain of 2 additional ONwoTD hours.

Conclusion: This study highlights regional differences in aPD treatment preferences, emphasizing need for tailored approaches across geographic locations to enhance personalized care.

Disclosure: JD represents Parkinson's Europe. FDR is employed by Parkinson's Europe. KRC has received fees, honoraria, and/or educational funds from AbbVie, Bial, Britannia, Britannia Bial, US Worldmeds, Otsuka, Medtronic, Zambon, Sunovion, Scion, and UCB. RP has received fees, honoraria, and/or grants from AbbVie, ACADIA, Avid, Acorda, Adamas, Biotie, Civitas, Cynapses, Global Kinetics, Kyowa, Lundbeck, National Parkinson Foundation, Neurocrine, NIH/NINDS, Parkinson Study Group, Pfizer, Sage, Sunovion, Teva Neuroscience, and US World Meds. AA has received fees, honoraria, and/or grants from AbbVie, Bayer, Biopharma, Bial, Britannia, Ever Pharma, Horizon 2020, Italian Ministry of University and Research, Italian Ministry of Health, Jazz, Medscape, Next Generation EU - National Center for Gene Therapy and Drugs, and Investment PE8 – Project Age-It: "Ageing Well in an Ageing Society", Roche, Theravance, UCB, and Zambon. IM has received fees, honoraria, royalties, and/or grants from the Parkinson Foundation, Dystonia Coalition, AbbVie, Emalex, Medscape, Neuroderm, Praxis, Revance, Sage, Tourette Association of America, and Robert Rose Publishers. PA, MB, and HP are employees of OPEN Health. OPEN Health received funding from AbbVie for the conduct of this study. CHY, ES, MS, PK, and JCP are employees of AbbVie and may own stocks/shares in the company. MH was employed by OPEN Health at the time of study conduct. OPEN Health received funding from AbbVie for the conduct of this study.

EPR-256 | Identification of a Novel KIF5A mutation in a Romani family with autosomal-dominant dystonia

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Background and aims: Mutations in the KIF5A gene have been linked to several neurological disorders, including amyotrophic lateral sclerosis, hereditary spastic paraplegia type 10, Charcot–Marie–Tooth disease type 2, and neonatal intractable myoclonus. To date, no association between KIF5A mutations and dystonia has been reported. This study reports the first

family with autosomal-dominant dystonia exhibiting incomplete penetrance, associated with a newly identified KIF5A mutation.

Methods: Between 2017 and 2024, seven members of the same Roma family underwent clinical evaluations, including detailed medical histories and neurological assessments. Genetic testing included Sanger sequencing, MLPA screening of SGCE, PCR-RFLP/BseRI testing for the common TOR1A (c.907-909del) dystonia mutation, and whole-exome sequencing of the proband and one affected family member. The remaining individuals were screened using Sanger sequencing.

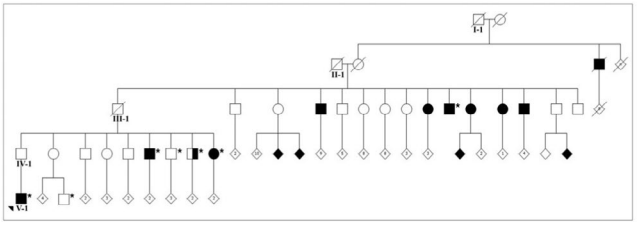

FIGURE 1 Family pedigree

Results: A missense mutation in the KIF5A (c.118G > A, p.Val-40Ile) was found in four individuals with dystonia and one asymptomatic carrier, while it was absent in two unaffected relatives. This mutation is rare in the general population (frequency of 0.00001 in gnomAD 4.0) and affects a conserved amino acid residue. Computational models (M-CAP) predicted its pathogenicity, and it was classified as likely pathogenic based on the ACMG criteria (PM1, PM2, PP2, PP3).

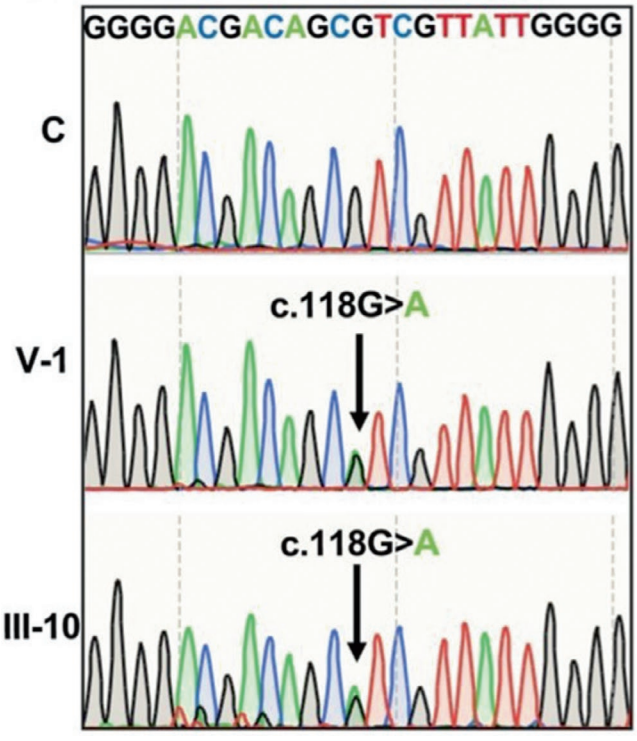

FIGURE 2 Sanger sequencing confirmed KIF5A c.118G > A variant in both the proband (V-1) and his relative (III-10), while it was absent in the control (C).

Conclusion: This study identifies KIF5A as a potential dystonia-related gene and underscores the importance of its inclusion in genetic screening. Integrating historically underrepresented populations into genetic research is essential, as it not only benefits these groups directly but also enhances our understanding of disorders across diverse populations, driving progress in precision medicine and targeted therapies.

Disclosure: J.Dulski: grants from Polish Minister of Science (Scholarship for Outstanding Young Scientists), Haworth Family Professorship in Neurodegenerative Diseases fund; editorial boards: Neurologia i Neurochirurgia Polska; speakers' bureau: VM Media Ltd., Radosław Lipiński 90 Consulting, Ipsen; intellectual property rights: "Application of Hydrogen Peroxide and 17β -Estradiol and its Metabolites as Biomarkers in a Method of Diagnosing Neurodegenerative Diseases In Vitro". D.C. Pant: grants from MDA DG and LLLF CDA; J. Slawek: co-editor-in-chief of Neurologia i Neurochirurgia Polska; consultancies: Allergan, Abbvie, Ipsen, Everpharma, Merz, Novartis, Biogen, Roche, TEVA; speakers' bureau: Allergan, Abbvie, Ipsen, Everpharma, Merz, Novartis, Biogen, Roche, TEVA; intellectual property rights: "Application of Hydrogen Peroxide and 17β -Estradiol and its Metabolites as Biomarkers in a Method of Diagnosing Neurodegenerative Diseases In Vitro"; Z. Wszolek: grants from NIH/NIA, NIH/NINDS, Haworth Family Professorship in Neurodegenerative Diseases fund, Albertson Parkinson's Research Foundation, PPND Family Foundation, Wilchek Family; PI or Co-PI: Biohaven Pharmaceuticals, Vigil Neuroscience, ONO-2808-03, and Amylyx AMX0035-009, Mayo Clinic APDA Center for Advanced Research; external advisory boards: Vigil Neuroscience, Inc.; consultant: Eli Lilli & Company, NovoGlia.

EPR-257 | Differential effect of dopaminergic treatment on bradykinesia features and limb-kinetic apraxia in Parkinson's disease

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Background and aims: Bradykinesia is a primary motor symptom in Parkinson's disease (PD), but other cognitive-motor disorders, such as limb-kinetic apraxia, can also contribute to motor dysfunction and influence treatment responses. This study aimed to investigate the differential effects of dopaminergic therapy on bradykinesia and limb-kinetic apraxia in PD patients using kinematic analysis. Additionally, transcranial magnetic stimulation (TMS) was utilized to examine the neural pathways involved.

Methods: Twenty-five PD patients and 24 age- and gender-matched healthy controls (HC) were assessed in both OFF- and ON-medication states. Kinematic analysis evaluated bradykinesia using a finger-tapping task and limb-kinetic apraxia using a 10-second coin rotation task. Corticospinal excitability was assessed through TMS, measuring resting motor thresholds, motor-evoked potential input/output curves, short-interval intracortical inhibition, and interhemispheric inhibition.

Results: In the OFF-medication state, PD patients showed slower velocity, reduced amplitude (sequence effect), and

decreased regularity in finger-tapping movements compared to healthy controls (HC). Similar findings were observed in the coin rotation task. Dopaminergic therapy improved finger-tapping velocity but had no significant effect on other parameters or the coin rotation task, indicating a differential impact on the two motor tasks. Increased M1 excitability was associated with impaired motor performance in both tasks, but no such correlations were observed in the ON state. Additionally, no correlations were found between changes in kinematic parameters and TMS measures from the OFF to the ON state.
Conclusion: The differential treatment effects on bradykinesia and limb-kinetic apraxia in PD suggest distinct pathophysiological mechanisms, potentially involving cortical and subcortical systems with different sensitivities to dopaminergic therapy.
Disclosure: Nothing to disclose.

EPR-258 | The allosteric activator of glucocerebrosidase VQ-101 shows sustained activation of lysosomal GCase in humans

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Background and aims: People with Parkinson's disease (PD) who carry a heterozygous GBA1 mutation (GBA-PD) have approximately a 30% reduction in glucocerebrosidase (GCase) activity, resulting in lysosome dysfunction and accumulation of misfolded alpha synuclein (aSyn). In GBA-PD-derived dopaminergic neurons, VQ-101 shows a concentration-dependent increase in GCase activity, with 50% activation leading to significant blockage of insoluble aSyn accumulation. Safety/tolerability, pharmacokinetics, food effect, and pharmacodynamics of VQ-101 are assessed in healthy volunteers (HVs) and PD patients with and without GBA1 mutations.
Methods: Phase 1a evaluated single and multiple ascending doses of VQ-101 for up to 14 days in HVs. Target engagement was assessed by measuring lysosomal GCase activity using a validated live cell assay in fresh blood samples.
Results: 88 HVs were randomized to receive VQ-101 or placebo in a double-blind fashion. No serious adverse events or discontinuations due to adverse events were reported. VQ-101 showed full CNS penetrance. Exposures increased with escalating doses and were not influenced by food intake. VQ-101 showed dose-dependent and sustained (> 50% activation observed at Ctrough) lysosomal GCase activation following multiple doses.
Conclusion: VQ-101 is safe and well tolerated at all tested dose levels. VQ-101 has a favorable CSF and plasma PK profile, supporting once daily oral dosing and demonstrates dose-dependent target engagement in HVs. These results, together with preclinical data, support the potential for VQ-101 to slow or stop the progression of PD by increasing GCase activity and blocking the accumulation of misfolded aSyn. Enrolment of PD patients in phase 1b, evaluating multiple doses of VQ-101, is ongoing.
Disclosure: MFF, DY, MH, JS, KH and OS are employees of Vanqua Bio and may own equity in the company. JMC is a clinical consultant for Vanqua Bio and may own equity in the company. JPVDV, ET, LP, GV, and PHCK have nothing to disclose.

EPR-259 | Age at onset of depression/anxiety for people with Friedreich ataxia: Real-world data from medical claims

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Background and aims: Friedreich ataxia (FA) is a rare, genetic, multisystem disorder presenting mainly with ataxia, but features a complex phenotype of non-motor symptoms with variable onset. Because limited data are available on the onset of non-motor manifestations in patients with FA, this study aimed to determine the age at onset of depression/anxiety relative to key progression milestones (i.e., cardiomyopathy; loss of ambulation) based on real-world data from US medical claims.
Methods: We conducted a retrospective study based on de-identified medical claims linked to mortality data covering October 2015 to March 2024. We stratified the cohort by age at FA diagnosis: 0-7, 8-14, 15-24, and 25-39 years. Key endpoints were age at FA diagnosis, as well as age at onset for depression/anxiety, cardiomyopathy, and loss of ambulation.
Results: The cohort included 927 patients with FA. For patients aged 0-7, 8-14, 15-24, and 25-39 years, the median age at FA diagnosis was 4.0 ($n=129$), 11.0 ($n=225$), 19.0 ($n=261$), and 32.0 years ($n=312$), respectively. Depression/anxiety were observed in 6% ($n=8$; median age, not reached), 36.9% ($n=83$; 17.1 years), 44.1% ($n=115$; 23.7 years), and 43.3% ($n=135$; 37.1 years) for patients aged 0-7, 8-14, 15-24, and 25-39, respectively (Figure). In patients diagnosed between age 8-39 years, depression/anxiety were observed in temporal proximity to loss of ambulation (Table).

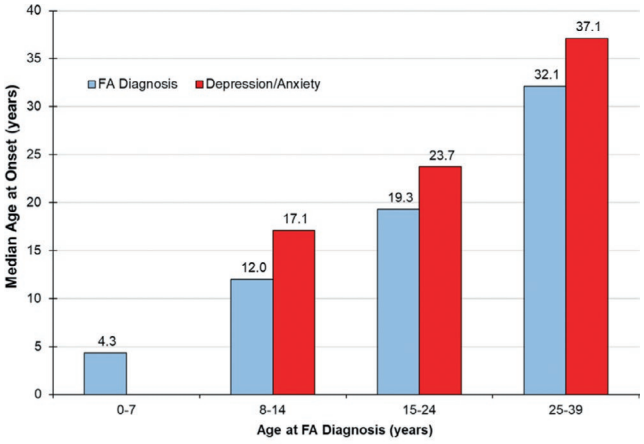

Figure: Age at Onset of Depression/Anxiety and FA Progression Milestones by Age at FA Diagnosis

Age at milestone onset by age at FA diagnosis, median (95% CI)	Early onset (0-7 years)	Typical onset (8-14 years)	Intermediate onset (15-24 years)	Late onset (25-39 years)
Progression milestone	**n=130**	**n=225**	**n=261**	**n=312**
FA diagnosis	4.3 (3.8-4.9)	12.0 (11.5-12.3)	19.3 (18.5-20.1)	32.1 (31.3-33.2)
Depression/anxiety	NR (12.1-NR)	17.1 (16.1-NR)	23.7 (22.4-24.9)	37.1 (35.6-39.2)
Cardiomyopathy composite (CM/HF/death)	9.8 (9.6-NR)	15.4 (13.7-NR)	26.4 (24.2-29.0)	44.8 (41.8-NR)
LoA composite (LoA/death)	12.3 (8.2-NR)	16.8 (13.4-NR)	27.2 (22.0-NR)	37.7 (33.0-43.6)

CM, cardiomyopathy; FA, Friedreich ataxia; HF, heart failure; LoA, loss of ambulation; NR, not reached.

Table: Age at Onset of Depression/Anxiety

Conclusion: The real-world data reveal depression and anxiety are common in FA, reinforcing the importance of comprehensive care for patients, particularly in partnering with trained mental health professionals to counsel patients on the non-motor symptoms.

Disclosure: This study was funded by Biogen. BB, SME, JM, RLA are employees of Biogen and may hold stock/stock options.

EPR-260 | Impact of the LRRK2-G2019S mutation on neuropsychiatric features in Parkinson's disease patients

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Background and aims: Parkinson's disease (PD) is a complex neurodegenerative disorder characterized by both motor and non-motor symptoms, including neuropsychiatric symptoms (NPSs). Among the genetic factors, the LRRK2-G2019S mutation is the most prevalent in certain populations. This study aimed to investigate the prevalence of the correlation of LRRK2-G2019S with NPSs.

Methods: This longitudinal retrospective study was conducted in the Department of Neurology, Razi University Hospital. We included PD patients based on the Movement Disorders Society criteria. Medical records were reviewed for clinical, treatment, and neuropsychological assessments. All patients were screened for the LRRK2-G2019S mutation using Sanger sequencing. Correlations between the mutation and NPSs were analyzed, adjusting for sex, disease duration, and Levodopa equivalent dose.

Results: We included 393 PD patients. The prevalence of the LRRK2-G2019S mutation was 41.5%. Mutation carriers showed significantly fewer sleep disturbances, hallucinations, depression, appetite and eating disorders, delirium, apathy, euphoria, disinhibition, and aberrant motor behaviors (adjusted p-values < 0.05).

Conclusion: This study highlights a distinct neuropsychiatric profile among LRRK2-G2019S mutation carriers, characterized by a lower prevalence of NPSs. These findings could guide personalized management strategies and enhance understanding of genotype-phenotype correlations in PD. Further research is needed to explore the underlying mechanisms and potential therapeutic implications.

Disclosure: Nothing to disclose.

EPR-261 | Nutritional status and Mediterranean diet adherence in pediatric multiple sclerosis, clinical-radiological correlations

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Background and aims: Recent studies have established a relationship between dietary patterns and Multiple Sclerosis (MS), with dietary habits influencing disease onset and progression. The Mediterranean Diet (MD) has been shown to have a protective role in inflammation and neurodegenerative processes in MS, but data on pediatric onset MS (POMS) is limited.

Methods: This multicenter observational study included POMS or Clinically Isolated Syndrome (CIS) patients, aged 24 years or less. Adherence to MD was assessed using the KIDMED questionnaire. Collected data included clinical and radiological features, age at onset/diagnosis, Expanded Disability Status Scale (EDSS), disease duration, MRI lesion load, and Annualized Relapse Rate (ARR). Height, weight, and BMI were also recorded.

Results: The study included 100 POMS and 81 HCs. The mean KIDMED score was 5.1 ± 2.9 in MS patients and 5.0 ± 2.4 in HCs, with no significant difference between the two groups ($p = 0.82$). Linear regression analyses revealed no significant correlation between KIDMED scores and weight, height, or BMI. However, a direct correlation was observed between KIDMED scores and age at diagnosis ($r = 0.24$, $p = 0.03$), an inverse correlation with disease duration at diagnosis ($r = -0.24$, $p = 0.03$) and no significant correlations between KIDMED scores and EDSS at diagnosis, ARR, or the number of relapses pre- and post-diagnosis. Moreover, an higher BMI was associated with increased EDSS ($r = 0.29$, $p = 0.01$) and a higher probability of switching from the first-line therapy ($r = 0.43$, $p = 0.001$).

Conclusion: MD appears related to age of onset in POMS, and BMI influences prognosis. Nutrition and lifestyle interventions, especially in at-risk individuals, could help prevent MS progression.

Disclosure: A.E. has received honoraria from Novartis. M.M. has received research grants from ECTRIMS-MAGNIMS, the UK MS Society, and Merck, and honoraria from Biogen, BMS Celgene, Ipsen, Janssen, Merck, Novartis, Roche, and Sanofi-Genzyme. M.P. has received research grants from the Italian MS Foundation and Baroni Foundation, honoraria from Health & Life and Biogen, and sponsorship for travel/meeting expenses from Novartis, Roche, and Merck. R.L. has received honoraria from Biogen, Merck, Novartis, Roche, and Teva. V.B.M. has received research grants from the Italian MS Society and Roche, and honoraria from Bayer, Biogen, Merck, Mylan, Novartis, Roche, Sanofi-Genzyme, and Teva. A.C. has received research grants from Almirall, research grants from ECTRIMS-MAGNIMS, and honoraria from Almirall, Biogen, Roche, Sanofi-Genzyme, Merck, Ipsen, and Novartis.CP has served on scientific advisory boards for Actelion, Biogen, Genzyme, Hoffmann-La Roche Ltd, Merck, Novartis, Sanofi, Teva, and has received consulting and/or speaking fees, research support and travel grants from Allergan, Almirall, Biogen, Genzyme, Hoffmann-La Roche Ltd, Merck, Novartis, Sanofi and Teva; None of the other authors has any conflict of interest to disclose.

EPR-262 | Choroid plexus volume and serum neurofilament light levels in relation to brain atrophy and lesion load in MS

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Background and aims: The choroid plexus (CP), responsible for cerebrospinal fluid (CSF) production and the blood-CSF barrier, plays a key role in central nervous system inflammation. Increased CP volume (CPV) in multiple sclerosis (pwMS) links to clinical and MRI indicators of disease progression, suggesting CPV's potential as an imaging biomarker. However, the predictive value of CPV, alongside serum neurofilament light (sNfL), a blood-based marker for neuro-axonal damage, for lesion load (LL) and brain atrophy (BA) remains unclear. This study aimed to determine how well CPV and sNfL indicate lesion burden and brain volume changes over a median follow-up of 5.3 years (IQR: 4.6-5.5).
Methods: Ninety-six pwMS (17 with clinically isolated syndrome, 70 with relapsing-remitting MS, and 9 with progressive MS) and 49 age- and sex-matched healthy controls (HC) participated. Participants underwent 3T MRI to evaluate normalized brain volume and lesion load using FreeSurfer and SIENA. sNfL was measured with Simoa HD-X analyzer. Longitudinal data were available for 60 pwMS. We used adjusted partial correlations and multiple linear regression to identify predictors of LL and brain volume.
Results: CPV ($p=0.002$) and sNfL ($p<0.001$) were significantly higher in pwMS compared to HC. Cross-sectional regression showed CPV was independently linked to reduced brain volume and higher LL ($\beta=-0.02$; $p<0.001$ and $\beta=1.55$; $p<0.001$). In longitudinal regression, only sNfL remained a significant predictor of BA ($\beta=1.33$; $p=0.003$), not CPV.
Conclusion: Although both CPV and sNfL correlate with MRI signs of brain damage in pwMS, longitudinal analysis identified sNfL as the sole marker linked to more pronounced BA.
Disclosure: C.T: travel funding (TF) and speaker honoraria (SH) from Merck. M.M, A.B, P.O, A.D, S.W, B.H, P.B: Nothing to disclose R.D: TF from from Janssen, Novartis and Sanofi S.H: SH from Roche and Bristol-Myers Squibb B.H: SH from Roche, Sanofi, and Bristol-Myers Squibb, and TF from Janssen. D.P: a member of the advisory board for "Cognition and MS" for Novartis and has received SH from Biogen, Novartis, MedAhead and Bristol-Myers Squibb D.L: was Chief Medical Officer of GeNeuro until end of 2023 J.K: SH, research support (RS), TF, and/or advisory boards by Swiss MS Society, Swiss National Research Foundation (320030_212534/1), University of Basel, Progressive MS Alliance, Alnylam, Bayer, Biogen, Bristol Myers Squibb, Celgene, Immunic, Merck, Neurogenesis, Novartis, Octave Bioscience, Quanterix, Roche, Sanofi, Stata DX C.E: received TF and SH from Biogen Idec, Bayer Schering Pharma, Merck Serono, Novartis, Genzyme and Teva Pharmaceutical Industries Ltd./Sanofi-Aventis, Shire; received RS from Merck Serono, Biogen Idec, and Teva Pharmaceutical Industries Ltd./Sanofi-Aventis; and scientific advisory boards for Bayer Schering Pharma, Biogen Idec, Merck Serono, Novartis, Genzyme, Roche, and Teva Pharmaceutical Industries Ltd./Sanofi- Aventis M.K: TF and SH from Bayer, Biogen, Novartis, Merck, Sanofi and Teva and scientific advisory boards for Biogen, Bristol-Myers Squibb, Gilead, Merck, Novartis, and Roche. He received RS from Biogen, Novartis and Teva.

EPR-263 | Childhood infections affect timing of multiple sclerosis onset in adults: EnvIMS study

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Background and aims: Since early-life challenge of the immune system can affect the risk of later development of autoimmune diseases, childhood infections have been suggested as risk factors/triggers for multiple sclerosis (MS). Except for Epstein Barr Virus, the role of other infectious agents in the pathogenesis of MS remains poorly understood. We aimed at investigating the association between MS and exposure to childhood infections and its role on timing of disease onset.

Methods: We analyzed data collected within the EnvIMS study, a multinational case-control population-based study, including information on measles, rubella, mumps, and chickenpox of Italian and Norwegian populations. Crude and adjusted odds ratio for index age, smoking habit, infectious mononucleosis, and low sun exposure are presented with 95% confidence intervals. An ANCOVA was performed to investigate the association between infections and age at MS onset, with smoking habit and infectious mononucleosis as covariates. Stratification by sex is presented.

Results: 2,040 Italians, and 2,674 Norwegians were included. MS was not associated with any of the infections considered. Measles was significantly associated with delayed MS onset in all populations, as were rubella and mumps in Norwegians, especially in women. An earlier MS onset was instead associated with chickenpox in Italians and Norwegians and with rubella in Italian men.

TABLE 1

Mean age at onset of MS by infectious diseases, sex and EnvIMS study population.

	ITALY		NORWAY	
	Age at MS onset (marginal mean, 95%IC) years	p	Age at MS onset (marginal mean, 95%IC) years	p
Measles				
Not exposed	26.2 (24.2, 28.1)	*<0.0000001*	31.2 (29.8, 32.7)	*<0.0000001*
Exposed	33.0 (31.9, 34.0)		39.3 (38.4, 40.2)	
Men				
Not exposed	28.6 (25.0, 32.2)	*0.036*	35.3 (32.2, 38.5)	*0.021*
Exposed	33.1 (31.1, 35.0)		39.6 (37.9, 41.3)	
Women				
Not exposed	24.8 (22.4, 27.1)	*<0.0000001*	29.9 (28.3, 31.5)	*<0.0000001*
Exposed	32.9 (31.7, 34.1)		39.2 (38.1, 40.3)	
Rubella				
Not exposed	31.1 (29.7, 35.59	*0.963*	33.8 (32.4, 35.2)	*<0.0000001*
Exposed	31.1 (29.8, 32.4)		38.7 (37.7, 39.7)	
Men				
Not exposed	33.3 (30.9, 35.7)	*0.003*	35.8 (32.8, 38.8)	*0.084*
Exposed	28.1 (25.6, 30.5)		38.9 (37.1, 40.6)	
Women				
Not exposed	30.0 (28.3, 31.7)	*0.053*	33.1 (31.5, 34.7)	*<0.000001*
Exposed	32.3 (30.7, 33.8)		38.6 (37.4, 39.9)	
Mumps				
Not exposed	30.4 (29.0, 31.8)	*0.130*	33.7 (32.5, 34.8)	*<0.0000001*
Exposed	31.8 (30.6, 33.0)		38.9 (37.9, 39.9)	
Men				
Not exposed	30.8 (28.1, 33.6)	*0.415*	35.5 (33.2, 37.8)	*0.005*
Exposed	32.3 (30.1, 34.5)		39.7 (38.0, 41.5)	
Women				
Not exposed	30.2 (28.6, 31.8)	*0.222*	33.0 (31.6, 34.3)	*<0.0000001*
Exposed	31.5 (30.1, 33.0)		38.5 (37.3, 39.6)	
Chickenpox				
Not exposed	35.4 (33.2, 37.7)	*0.0001*	41.0 (38.4, 43.7)	*0.001*
Exposed	30.5 (29.5, 31.5)		36.4 (35.6, 37.3)	
Men				
Not exposed	36.2 (32.1, 40.2)	*0.012*	42.3 (38.1, 46.5)	*0.028*
Exposed	30.4 (28.5, 32.3)		37.3 (35.7, 38.9)	
Women				
Not exposed	35.2 (32.4, 37.9)	*0.003*	40.3 (36.8, 43.7)	*0.023*
Exposed	30.5 (29.3, 31.8)		36.1 (35.1, 37.1)	

Analysis of covariance (ANCOVA) with age at MS onset as dependent variable, infectious diseases as independent variable, and participants' smoking habit and history of infectious mononucleosis as covariates.

Conclusion: Childhood infections are not associated with MS status. Measles consistently delays the MS onset, while chickenpox anticipates it. Mumps and rubella show different effects depending on the population considered. These findings suggest an influence of childhood infections, especially measles and chickenpox, on MS course.

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EPR-264 | Environmental risk factors and risk of MS in subjects with radiologically isolated syndrome: A case-control study

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Background and aims: Radiologically Isolated Syndrome (RIS) is the incidental finding of demyelinating lesions at MRI without history of symptoms of Multiple Sclerosis (MS). Environmental factors play an important role in the development of MS. We investigated the impact of environmental factors and their association with conversion to MS in RIS patients.

Methods: Subjects with a RIS diagnosis (cases) and patients with a Clinically Isolated Syndrome (CIS)/Relapsing-Remitting MS (RRMS) onset (controls) were included. Patients were administered an environmental questionnaire, asking for exposure to environmental factors prior to onset. The distribution of clinical, demographic characteristics and environmental factors between the two groups and their impact on the risk of conversion to MS were analyzed.

Results: Forty-two RIS subjects and 216 controls were included. RIS patients had more frequently a clinical onset with supratentorial symptoms (28.2% vs. 9.8%), while controls with the involvement of the visual pathway (5.1% vs. 24.7%). A higher proportion of controls reported outdoor activity during childhood (44.3% vs. 23.7%). RIS patients that converted within 5 years since onset had more frequently an onset with supratentorial symptoms (33.3% vs. 10.0%), were more likely to be underweight during adolescence (14.3% vs. 0.0%), to have had pregnancy losses before RIS diagnosis (18.2% vs. 0.0%) and to have used Assisted Reproduction Technology (ART) before RIS diagnosis (9.1% vs. 0.0%).

Conclusion: Being underweight during adolescence, the use of ART and a history of pregnancy losses were associated to a higher risk of conversion from RIS to MS. Outdoor activity during childhood was more frequent in patients with CIS/RRMS.

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EPR-265 | Vidofludimus calcium shows potential neuroprotective effects in an in vivo multiple sclerosis model by Nurr1 modulation

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Background and aims: The transcription factor nuclear receptor-related 1 (Nurr1) regulates genes that enhance neuronal development, function and survival. Vidofludimus calcium (VidoCa), currently in phase 2 and 3 clinical trials for progressive and relapsing MS, respectively, exhibited potent Nurr1 activation in vitro. In this study, the potential neuroprotective effects of VidoCa through activating Nurr1 were further elucidated in vivo.
Methods: Mice were immunized with myelin oligodendrocyte glycoprotein (MOG) 35-55 to induce experimental autoimmune encephalomyelitis (EAE) followed by daily scoring for disease progression and treatment with VidoCa or vehicle. At end of study, gene expression in the central nervous system (CNS) was evaluated by qRT-PCR and plasma brain-derived neurotrophic factor (BDNF) and neurofilament light chain (NfL) levels were determined by ELISA. Expression of amyloid precursor protein (APP), ionized calcium-binding adaptor molecule-1 (Iba-1) and myelin basic protein (MBP) was assessed by immunohistochemical staining.
Results: Next to attenuating disease severity, VidoCa induced Nurr1-regulated gene expression in the CNS, including tyrosine hydroxylase (Th), glycosylphosphatidylinositol-specific phospholipase D1 (Gpld1) and delta-like non-canonical Notch ligand-1 (Dlk1), is elevated in the CNS of EAE mice treated with VidoCa. Interestingly, in VidoCa-treated mice a potential peripheral Nurr1 activation biomarker, BDNF, is augmented, while plasma NfL levels as well as APP expression in spinal cord are reduced indicating diminished axonal/neuronal damage. Also, expression of the microglial activation marker Iba-1 was reduced while an increase in MBP as myelin marker was observed.
Conclusion: These data indicate that VidoCa potentially enhances neuroprotection in vivo by activating Nurr1.
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EPR-266 | Wearable-derived data could unveil subtle disability changes in multiple sclerosis

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Background and aims: Multiple Sclerosis (MS) is a disabling disorder affecting young adults. Conventional clinical assessment through the widely used Expanded Disability Status Scale (EDSS) often misses subtle changes occurring along the disease course. Wearable technology provides real-world data, hence enabling a more subtle evaluation of disability in a longer timeframe. This study aimed to validate the correlation between wearable-generated metrics and EDSS.
Methods: We enrolled 70 MS patients (aged 18-60 years old; EDSS < 5 and absence of smartwatch use). Patients underwent EDSS, Timed 25-Foot Walk (T25FW), and Nine-Hole Peg Test (9HPT). Phone device data, including step count, gait asymmetry, and walking speed, were collected via smartphone applications (for iOS and Android). Cross-sectional correlations between wearable metrics, EDSS, T25FW and 9HPT were assessed using pairwise correlations, while longitudinal trends in wearable data and EDSS were analyzed to detect changes over 12 months before enrollment.
Results: Lower walking speed and higher gait asymmetry correlated with higher EDSS (corr.coeff = -0.62, $p < 0.001$ and corr.coeff. = 0.63, $p < 0.001$, respectively). and higher T25FW (corr.coeff. = -0.63, $p < 0.001$ and corr. Coeff. = -0.88, $p < 0.001$, respectively). Moreover, while there were no significant changes for the EDSS over one year before enrollment, we reported a step count decrease (mean: 4536 vs. 4063 steps, $p = 0.04$) during the same period.

Conclusion: Wearable devices offer the potential to remodel disability assessment in MS by detecting subtle progression earlier, allowing a timely diagnosis ultimately resulting in proper pharmacological strategies.

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EPR-267 | Impact of pain, spasticity and bladder dysfunction in MOGAD and NMOSD: Preliminary results of a RIREMS group study

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Background and aims: The impact of pain, fatigue, depression, spasticity and bladder dysfunction in patients with myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) and aquaporin-4-IgG-seropositive neuromyelitis optica spectrum disorder (NMOSD-AQP4+) is still unclear. This ongoing multicenter longitudinal study aimed to compare the frequency of these symptoms in an Italian cohort of adult MOGAD and NMOSD-AQP4+ patients.

Methods: As of January 15 2025, 15 MOGAD (5 F) and 23 NMOSD-AQP4+ (21 F) have been enrolled. Pain is assessed through the Numerical Rating Scale (NRS) and Douleur Neuropathique en 4 Questions (DN4) questionnaire to discriminate neuropathic from non-neuropathic pain. Spasticity is investigated through Ashworth scale. Fatigue Scale - Motor and Cognitive (FSMC) and Beck's Depression Index-2 (BDI-II) are administered to assess fatigue and depression; urinary urgency/incontinence is assessed through International Consultation on Incontinence Questionnaire (ICIQ-UI). Questionnaires and tests are performed at baseline and after 18+/-6 months.

Results: Median ICIQ-UI score was significantly higher in NMOSD-AQP4+ (8, range 0-21) compared to MOGAD patients (0, range 0-7, $p < 0.001$). Median NRS score was 1 (0-9) in MOGAD and 5 (0-9) in NMOSD-AQP4+ ($p = 0.011$); moderate-to-severe pain was less frequent in MOGAD cases (2, 13.3%) compared to NMOSD-AQP4+ (14, 60.9%; $p = 0.006$). Spasticity was observed in 2 MOGAD (13.3%) and 12 NMOSD (57.1%) patients ($p = 0.008$). Neuropathic pain occurrence, FSMC and BDI-II scores did not differ significantly between groups.

Conclusion: Impact of urinary urgency/incontinence, pain and spasticity appears to be lower in MOGAD compared to NMOSD-AQP4+ patients. This data confirms that MOGAD is relatively less disabling compared to NMOSD-AQP4+.

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EPR-268 | Reduced duration of breastfeeding is associated with an increased risk of pediatric MS: The PEDIGREE study

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Background and aims: Investigating the influence of early-life environmental exposures on adult-onset multiple sclerosis (MS) is challenging due to the long interval between the timing of exposures and disease onset, as well as the potential for recall biases. We studied the association between breastfeeding and pediatric MS (pedMS) in an Italian cohort.

Methods: The PEDIGREE (Pediatric Italian Genetic and Environment Exposure) study is a multicenter case-control study assessing genetic and environmental interactions influencing MS risk before the age of 18. The study utilizes the PEQ-IT questionnaire (Pilotto et al., MSJ-ETC. 2021) was used to record environmental and perinatal exposures. Breastfeeding was classified as reference (≥4 months) or absent/reduced (0–3 months).

Results: PEDIGREE data on breastfeeding were available for 96 pedMS cases and 96 controls, of whom, 75 (78.1%) and 55 (57.3%) were females, respectively. The mean (SD) age at study time was 16.8 (2.87) years for cases and 13.6 (5.01) years for controls. Clinical onset occurred at a mean age of 14.1 (2.66) years, with a disease duration of 29.0 (23.33) months. A significant association between pedMS and reduced/absent breastfeeding was observed (OR = 2.04; 95%CI 1.13–3.68;$p = 0.018$). This association was even stronger when exclusively breastfed children were considered (OR = 2.54; 95%CI 1.36–4.75;$p = 0.003$), particularly among females (OR = 2.35; 95%CI 1.10–5.01;$p = 0.027$). These associations remained significant after adjusting for age at study time, preterm birth, and birth order.

TABLE 1 Crude and adjusted odds ratios (95 %CIs) for the association between MS and duration of breastfeeding.

	Cases N (%)	Controls N (%)	Crude OR (95%CI)	*p-value*	Adjusted OR (95%CI)	*p-value*[a]
Breastfeeding						
≥ 4 months	51 (53.1)	67 (69.7)	1.0		1.0	
0-3 months	45 (46.9)	29 (30.3)	**2.04 (1.13, 3.68)**	***0.018***	**2.11 (1.02, 4.39)**	***0.044***
Men	21 (21.9)	41 (42.7)				
≥ 4 months	13 (61.9)	30 (73.2)	1.0		1.0	
0-3 months	8 (38.1)	11 (26.8)	1.68 (0.55, 5.14)	*0.365*	1.58 (0.41, 6.06)	*0.501*
Women	75 (78.1)	55 (57.3)				
≥ 4 months	38 (50.7)	37 (67.3)	1.0			
0-3 months	37 (49.3)	18 (32.7)	2.00 (0.97, 4.12)	*0.060*	2.40 (0.93, 6.24)	*0.071*
Exclusive breastfeeding						
≥ 4 months	36 (44.4)	59 (67.0)	1.0		1.0	
0-3 months	45 (55.6)	29 (33.0)	**2.54 (1.36, 4.75)**	***0.003***	**2.58 (1.19, 5.58)**	***0.016***
Men	16 (19.8)	38 (43.2)				
≥ 4 months	8 (50.0)	27 (71.0)	1.0		1.0	
0-3 months	8 (50.0)	11 (29.0)	2.45 (0.73, 8.19)	*0.144*	2.35 (0.56, 9.91)	0.241
Women	65 (80.2)	50 (56.8)				
≥ 4 months	28 (43.0)	32 (64.0)	1.0		1.0	
0-3 months	37 (57.0)	18 (36.0)	**2.35 (1.10, 5.01)**	***0.027***	**2.84 (1.04, 7.75)**	***0.041***

[a]Adjusted for preterm birth (yes, no), order of birth (firstborn vs not firstborn), age at study time.

TABLE 2 Crude and adjusted odds ratios (95 %CIs) for the association between MS and duration of breastfeeding duration and type.

	Cases N (%)	Controls N (%)	Crude OR (95%CI)	*p-value*	Adjusted OR (95%CI)	*p-value*[a]
Breastfeeding						
Prolonged exclusive (≥ 4 months)	**36 (37.5)**	**59 (61.5)**	1.0		1.0	
Prolonged not exclusive (≥ 4 months)	15 (15.6)	8 (8.3)	**3.07 (1.18, 7.97)**	***0.021***	2.34 (0.83, 6.59)	*0.106*
1-3 months (reduced)	28 (29.2)	20 (20.8)	**2.29 (1.13, 4.66)**	***0.021***	2.01 (0.85, 4.79)	*0.113*
0 months (absent)	17 (17.7)	9 (9.4)	**3.10 (1.25, 7.68)**	***0.015***	**4.14 (1.34, 12.81)**	***0.014***
Men	21 (21.9)	41 (42.7)				
Prolonged exclusive (≥ 4 months)	8 (38.1)	27 (65.9)	1.0		1.0	
Prolonged not exclusive (≥ 4 months)	5 (23.8)	3 (7.3)	**5.62 (1.10, 28.84)**	***0.038***	4.26 (0.72, 25.37)	*0.111*
1-3 months (reduced)	5 (23.8)	8 (19.5)	2.11 (0.54, 8.28)	*0.285*	1.69 (0.33, 8.69)	*0.527*
0 months (absent)	3 (14.3)	3 (7.3)	3.37 (0.57, 20.10)	*0.181*	4.78 (0.53, 43.27)	*0.164*
Women	75 (78.1)	55 (57.3)				
Prolonged exclusive (≥ 4 months)	28 (37.3)	32 (58.2)	1.0		1.0	
Prolonged not exclusive (≥ 4 months)	10 (13.3)	5 (9.1)	2.29 (0.70, 7.49)	*0.172*	2.07 (0.55, 7.75)	*0.281*
1-3 months (reduced)	23 (30.7)	12 (21.8)	2.19 (0.92, 5.19)	*0.075*	2.06 (0.67, 6.34)	*0.207*
0 months (absent)	14 (18.7)	6 (10.9)	2.67 (0.90, 7.87)	*0.076*	**5.40 (1.14, 25.57)**	***0.033***

[a]Adjusted for preterm birth (yes, no), order of birth (firstborn vs not firstborn), age at study time.

Conclusion: Reduced/absent exposure to breastfeeding is associated to a over 2-fold increased risk for pedMS, particularly in females, suggesting immunological effect of breast milk and sex-specific immune response to early-life exposures.

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EPR-269 | Paramagnetic rim lesions as a prognostic and predictive biomarker in Tolebrutinib Phase 3 trials for disability outcomes

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Background and aims: Tolebrutinib, a brain-penetrant Bruton's tyrosine kinase inhibitor that, in phase-3 trials, reduced disability accumulation by 31% and 29% relative to placebo and teriflunomide in non-relapsing secondary progressive multiple sclerosis (MS) and relapsing MS, respectively. This post-hoc analysis evaluated paramagnetic rim lesions (PRLs) at baseline, as prognostic and predictive biomarkers for disability accumulation and treatment response.
Methods: HERCULES (NCT04411641), GEMINI 1 (NCT04410978), and GEMINI 2 (NCT04410991) were phase-3, double-blind trials of 60mg tolebrutinib once-daily. HERCULES randomized participants 2:1 (tolebrutinib:placebo); and GEMINI, 1:1 (tolebrutinib:teriflunomide [14mg once-daily]) with matching placebos. PRLs were evaluated in 39% (437/1131) of HERCULES, and 34% (631/1873) of GEMINI participants from imaging-capable sites. Effect of tolebrutinib on time to onset of 6-month confirmed disability worsening (6-mo-CDW) was analyzed in participants with PRLs (0, 1–3, ≥4) at baseline, manually identified by susceptibility weighted imaging generated from three-dimensional gradient echoes (6-echoes ranging from 4.9-41ms, 0.8-mm isotropic resolution).
Results: Across both trials, 653 participants (61%) had PRLs, and the proportion of participants with 0, 1-3, or ≥4-PRLs at baseline was 40%, 36%, and 24%, respectively. In both trials, the risk of 6-mo-CDW increased as a function of baseline PRLs in placebo and teriflunomide comparator groups. Tolebrutinib mitigated 6-mo-CDW risk by 54% in participants with ≥4-PRLs in HERCULES, and 46% and 49% in participants with 1-3 and ≥4-PRLs, respectively, in GEMINI. In tolebrutinib-treated participants with and without PRLs in both trials, the risk of 6-mo-CDW was numerically similar.
Conclusion: This post-hoc analysis suggests greater impact of tolebrutinib in those with higher number of PRLs.
Disclosure: JO: Consulting and/or speaking (Amgen, Biogen, Eli Lilly and Company, EMD Serono, Novartis, Roche, Sanofi); research (Biogen, Roche). RJF: Consulting (AB Science, Biogen, Bristol Myers Squibb, EMD Serono, Genentech, Greenwich Biosciences, Immunic, INmune Bio, Eli Lilly and Company, Janssen, Novartis, Sanofi, Siemens, TG Therapeutics) and research support (Biogen, Novartis, Sanofi). DLA: Personal compensation for serving as a consultant (Alexion, Biogen, Celgene, Eli Lilly and Company, EMD Serono, Frequency Therapeutics, Genentech, Merck, Novartis, Roche, Sanofi, Shionogi); equity interest (NeuroRx). SS, WSV, YL and TJT: Employees of Sanofi (may hold shares and/or stock options in the company). DSR: Supported by the Intramural Research Program of NINDS, NIH; and additional grant/research support (Abata, Sanofi).

MS and related disorders 4

EPR-270 | Role of free Kappa light chains in CSF as a biomarker in multiple sclerosis

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Background and aims: Free Kappa Light Chains (FKLC) in cerebrospinal fluid (CSF) are biomarkers of intrathecal IgG synthesis, similarly to oligoclonal bands (OCBs). Their potential in the diagnosis of Multiple Sclerosis (MS) has been a matter of research. This study aimed to ascertain the diagnostic accuracy of FKLC in CSF for MS and to evaluate potential clinical, imaging, and laboratory correlations.
Methods: All patients with a definitive diagnosis who underwent FKLC quantification in CSF from November 2019 to November 2024 were selected. Clinical, demographic, laboratory, and imaging variables were evaluated. Sensitivity, specificity, positive predictive value, and negative predictive value of FKLC and OCBs were calculated, and correlations with clinical, imaging and laboratory variables were tested.
Results: Of the 434 patients eligible for analysis, 122 had a definitive diagnosis of MS, 11 had Clinically Isolated Syndrome, 301 had other diagnoses. Using the cut-off point proposed in the literature of 1 mg/L, FKLC in CSF demonstrated similar sensitivity compared to OCBs (72.93% vs. 72.18%, respectively), while both maintained high specificity (82.33% vs. 92.00%). CSF FKLC levels positively correlated with OCB positivity ($p < 0.001$), with the presence of active MRI lesions ($p = 0.044$), of infratentorial lesions ($p = 0.001$), of spinal cord lesions ($p = 0.017$) and with high lesion load ($p < 0.001$).
Conclusion: This study confirms the role of FKLC in CSF as a biomarker for the diagnosis of MS and suggests a possible relationship between FKLC levels and MRI features associated with poor prognosis.
Disclosure: The authors have nothing to declare.

EPR-271 | Steroid-refractory tumefactive multiple sclerosis with favorable outcome following natalizumab

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Background and aims: Tumefactive demyelinating lesions of the central nervous system (CNS) are an aggressive type of

multiple sclerosis (MS) that can resemble tumors or brain abscesses on magnetic resonance imaging (MRI). We report a case of tumefactive MS with inadequate response to intravenous (IV) methylprednisolone and plasma exchange (PLEX), which showed a favorable outcome following natalizumab initiation.
Methods: We reviewed the medical history of a 23-year-old man who presented with right hemiplegia and global aphasia.
Results: Initial MRI revealed a T2-FLAIR hyperintense tumefactive lesion in the left frontal white-matter, and a smaller left posterior-thalamus lesion. MRI spectroscopy suggested a demyelinating etiology (Fig. 1). Cerebrospinal fluid (CSF) analysis showed oligoclonal bands. Blood tests and immunophenotyping of the lymphocytes from the CSF ruled out CNS lymphoma, autoimmune encephalitis, neuromyelitis optica, vasculitis, and sarcoidosis. The patient was started on IV methylprednisolone without a satisfactory response, prompting a 7-day course of PLEX. This resulted in slow recovery of symptoms. After two months, the patient developed left optic neuritis, with partial recovery following another course of IV methylprednisolone. Subsequent MRI (Fig. 2) showed progression of the frontoparietal lesion with perilesional oedema and a new necrotic area in the postcentral parietal gyrus. The patient received the first IV natalizumab infusion, which was well-tolerated. Follow-up MRIs revealed a reduction of the lesions (Fig. 3). The patient demonstrated significant clinical improvement.

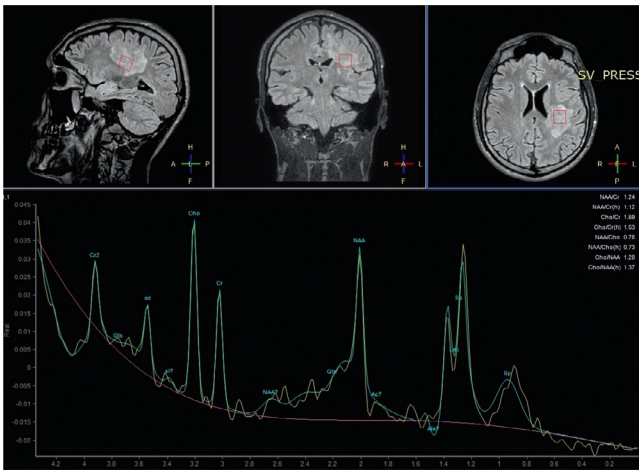

FIGURE 1 Brain MRI spectroscopy showing white matter lesion measuring 56 x 37 x 32.5 mm, suggesting a demyelinating tumefactive lesion according to metabolites measurings

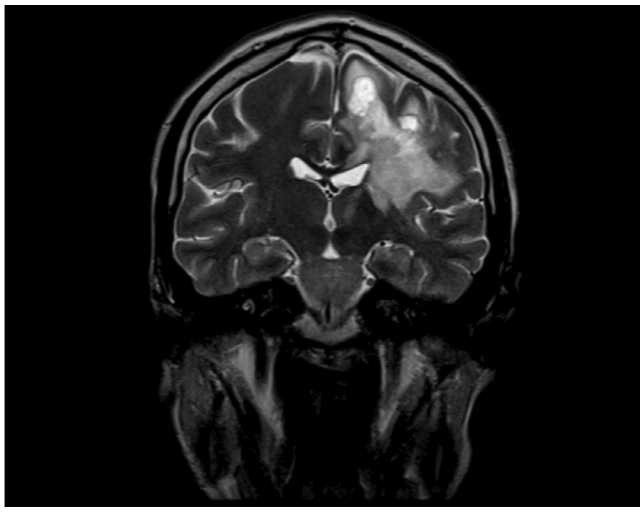

FIGURE 2 T2 weighted image of the lesion in coronal section before natalizumab initiation, measuring 69 × 42 × 59 mm, with perilesional oedema and necrosis

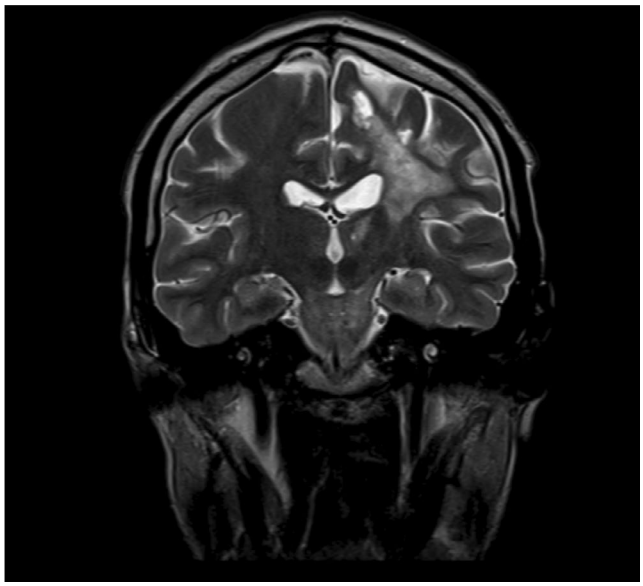

FIGURE 3 The reduced size of the lesion 58 × 37 × 54 mm after two natalizumab iv infusions

Conclusion: The limited case reports regarding the management of tumefactive MS can delay diagnosis and treatment. Further publications and case studies are essential to streamline the diagnostic and therapeutic approach for these patients.
Disclosure: Nothing to disclose.

EPR-272 | Blood-based biomarkers of type IV collagen are upregulated in patients with multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is characterized as an inflammatory neurodegenerative disease in the central nervous system. The pathological hallmarks of active MS

lesions are blood brain barrier disruption, inflammation, and demyelination with axonal damage. Type IV collagen is located in the basement membrane and remodeled in MS lesions. Blood-based biomarkers reflecting type IV collagen changes may reflect MS pathology.

Methods: Biomarkers of type IV collagen reflecting matrix metalloproteinase-degraded of type IV α1 collagen (nordicC4M), NC1 domain of type IV α2 collagen (nordicCAN), NC1 domain of type IV α3 collagen (nordicTUM), and type IV collagen 7S domain (nordicPRO-C4), were developed, validated and measured in 23 serum samples from patients with MS (9 RRMS, 14 PPMS) and 11 healthy donors. Differences between MS groups and healthy donors were assessed with a Mann-Whitney test, and diagnostic accuracy by AUROC. A clinically useful AUROC was set as 0.85.

Results: Mean age of the MS patients was 35.7 years (34.8% male), while healthy donors were 41.9 years (55% male). Patients with MS had significantly higher levels of CAN, TUM, and PRO-C4 compared to healthy donors ($p=0.0045$, $p<0.0001$, and $p=0.0067$, respectively). There were no differences between RRMS and PPMS detected. TUM had an AUROC of 0.996, while C4M, CAN, and PRO-C4 has AUROC of 0.697-0.796.

Conclusion: We developed and evaluated serum biomarkers reflecting type IV collagen in patients with MS. These may be used to assess patients' eligibility for targeted treatments and potentially fill a part of the gap for biomarkers in clinical management and trials.

Disclosure: Authors are full-time employees of Nordic Bioscience.

EPR-273 | The cause but not the clinical course of early multiple sclerosis runs in the family

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Background and aims: Familial aggregation in multiple sclerosis (MS) can partially be explained by shared genetic and environmental determinants. The effect of familial MS on the disease course after a clinically isolated syndrome (CIS) is uncertain, but could reflect impact of known and unknown factors. We determined the association of familial MS with clinical presentation and early disease course after CIS and explored the mediating role of genetic and environmental risk factors.

Methods: CIS participants were included in a prospective cohort study within six months after symptom onset. Family history was assessed at baseline. We evaluated common genetic variants related to vitamin D and body mass index, determined HLA-DRB1*15:01 carriership and weighted genetic risk scores (wGRS) for MS susceptibility and severity and measured Epstein-Barr virus Nuclear Antigen-1 (anti-EBNA1) Immunoglobulin-G (IgG) antibodies. Associations with disease course were estimated using Cox regression.

Results: Family members with MS were reported for 81/415 (19.5%) of CIS participants. More participants with first-degree relatives were HLA-DRB1*15:01 carriers (first 66.7% vs. other-degree 27.9% vs. no 38.0%, $p<0.01$). MS susceptibility wGRS were higher in participants with familial MS (7.19($\pm$1.22) vs. 7.54($\pm$1.17), $p=0.03$). After controlling for HLA-status, anti-EBNA1 IgG titres were higher in familial MS. Baseline characteristics and early disease course were similar between participants with and without familial MS.

Conclusion: Our results confirm that familial MS is associated with common genetic and environmental MS risk factors, but does not reflect distinct clinical phenotype or disease course. These data support that MS risk and disease course are mediated by different pathophysiological processes.

Disclosure: C.C., A.M. Y.v.H. R.F.N. and B.W. report no competing interests. I.S. has received lecture fees from Merck, Biogen Idec and Sanofi. M.v.L. received research support from EMD Serono, Merck, Novartis, GSK and Idorsia Pharmaceutical Ltd. J.S. received lecture and/or consultancy fee from Biogen, Merck, Novartis, Roche and Sanofi Genzyme.

EPR-274 | Ocrelizumab stabilizes fatigue levels in relapsing MS: Key findings from the MoOzaRt study's second interim analysis

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Background and aims: Fatigue is considered the most common and one of the most debilitating symptoms in multiple sclerosis (MS). MoOzaRt aimed to assess the impact of ocrelizumab on patient-reported long term (trait) and transient (state) fatigue in patients with relapsing forms of MS (RMS) on therapy with ocrelizumab.

Methods: The ongoing non-interventional MoOzaRt study (ISRCTN55332718) recruited 272 RMS patients initiating ocrelizumab therapy. The primary combined endpoint is a clinically meaningful reduction in trait fatigue (≥9 points) or stabilization from baseline (range $\pm$8 points), measured by the Fatigue Scale for Motor and Cognitive Functions (FSMC) total score over 24 months. Secondary endpoints include state fatigue (Visual Analogue Scale), Expanded Disability Status Scale (EDSS), Patient Reported Outcomes and safety.

Results: The second interim analysis (data cut-off Dec 16, 2024) included a total of 193 patients (69.9% female, mean age 38.3, SD 10.8 years with a mean EDSS score of 2.43, SD 1.50; table 1), among them 186 patients in the analysis set with a follow-up of at least 12 months. FSMC total scores remained stable or were reduced in 91.4% of patients over 24 months-follow-up. Of those, 28% displayed a clinically meaningful improvement. Patient numbers in FSMC categories over time are presented in table 2.

TABLE 1

Baseline characteristics	Total (N=193)
Sex, female, N (%)	135 (69.6)
Age at baseline [years], mean (SD)	38.3 (10.8)
Any medication history, N (%)	125 (64.8)
EDSS score, mean (SD)	2.43 (1.50)
Time since first MS symptoms [years], mean (SD)	8.73 (9.05)
Time since first MS diagnosis [years], mean (SD)	7.03 (8.15)
Previous treatments and therapies, N (%)	136 (70.5)

TABLE 2

FSMC	Baseline (N=186)	Month 6 (N=164)	Month 12 (N=167)	Month 18 (N=95)	Month 24 (N=60)
FSMC total score, mean (SD), [95% CI]	56.3 (22.8), [[53.0; 59.6]]	54.7 (22.5), [51.2; 58.1]	55.1 (23.2), [51.5; 58.6]	52.1 (22.7), [47.4; 56.7]	52.2 (24.1), [46.0; 58.4]
FSMC total score category, N (%)					
Normal	58 (31.2)	54 (32.9)	54 (32.3)	35 (36.8)	23 (38.3)
Mild	27 (14.5)	19 (11.6)	22 (13.2)	12 (12.6)	6 (10.0)
Moderate	17 (9.1)	30 (18.3)	26 (15.6)	13 (13.7)	5 (8.3)
Severe	84 (45.2)	61 (37.2)	65 (38.9)	35 (36.8)	26 (43.3)

Conclusion: The second interim analysis of the MoOzaRt study showed stable FSMC total scores in a very high proportion of patients after 24 months, with a trend toward more patients without fatigue. Further analyses will specify long-term impact of ocrelizumab on fatigue in RMS patients and factors influencing it.

Disclosure: IKP: Almirall, Biogen, BMS, Celgene, Genzyme, Janssen, Merck, Novartis, Roche, Teva // speakers bureau or advisory board, consulting fees; The German MS Society, Celgene, Novartis, Roche, Teva // research grants. JL: Roche // employee TM: Roche // employee EW: Roche // employee HS: Almirall, Biogen, BMS, Genzyme, Janssen, Merck, Novartis, Roche, Teva // speakers bureau or advisory board, consulting fees, travel reimbursement; Biogen, Novartis, Teva // research grants; Biogen, Novartis, Roche // data monitoring or steering committees.

EPR-275 | Relationship between SDMT and brain volume following short course cladribine tablets: Results from MAGNIFY-MS

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Background and aims: Excessive brain atrophy and cognitive decline can predict disease progression in multiple sclerosis (MS). We explored the relationship between total and regional brain volume (BV) and Symbol Digit Modalities Test (SDMT) scores in MAGNIFY-MS (NCT03364036) participants treated with cladribine tablets (CladT).

Methods: BV and SDMT were assessed at regular intervals over 2 years. The relationship between total and regional (gray matter [GM], deep GM [dGM], and white matter [WM]) BV with SDMT was analyzed using a generalized linear mixed-effects model. SDMT scores (absolute) and 4-point improvement, worsening, or stable status were compared between baseline and months (M)12 and 24. Participants were categorized into low (< 53.5) or high (≥53.5) baseline SDMT groups.

Results: MAGNIFY-MS included 270 participants (66.7% female; 43.7% aged > 40 years). Following CladT initiation, annualized brain atrophy rates were similar to those reported for the normal aging population. The median (quartile [Q]1;Q3)

annualized BV percentage change compared with baseline was -0.452 (-0.880;-0.165) at M12 and -0.420 (-0.719;-0.157) at M24. SDMT changes are shown in Table 1. Significant relationships were observed between total BV, GM, and SDMT (Table 2). dGM volume had the strongest association with SDMT (35.5%, $p = < 0.0001$). In the low baseline SDMT group, GM and dGM were significantly linked to SDMT (Table 2).

Mean (SD) SDMT score	
BL	52.4 ±12.04
M12	54.8 ±12.99
M24	56.3 ±13.29
Kaplan-Meier Estimate of 4-Point Confirmed SDMT Score Changes at M24 [95% CI]	
Improvement	0.43 [0.37; 0.49]
Stable	0.45 [0.37; 0.52]
Worsening	0.12 [0.09; 0.17]

N=270
Improvement defined as SDMT score changes from BL ≥4 at M24. Stable defined as -4< change from MAGNIFY-MS baseline in SDMT at M24 visit <4. Worsening defined as SDMT score changes from BL ≤-4 at M24.
BL, baseline; CI, confidence interval; M, month; SD, standard deviation; SDMT, Symbol Digit Modalities Test

Table 1. SDMT summary statistics

Region	Model estimates [95%CI]	p-value
Relationship between BV and SDMT (all participants, N=268)		
Total BV	0.022 [0.009, 0.036]	0.0012
GM	0.039 [0.018, 0.060]	0.0030
dGM	0.355 [0.229, 0.480]	<0.0001
WM	0.015 [-0.004, 0.034]	0.1227
Relationship between BV and SDMT in baseline SDMT score subgroups		
Low baseline SDMT score (n=133)		
Total BV	0.019 [0.004, 0.035]	0.0133
GM	0.043 [0.019, 0.067]	0.0005
dGM	0.424 [0.277, 0.570]	<0.0001
WM	0.006 [-0.016, 0.028]	0.5702
High baseline SDMT score (n=134)		
Total BV	0.013 [-0.003, 0.029]	0.1214
GM	-0.002 [-0.028, 0.023]	0.8447
dGM	0.103 [-0.047, 0.253]	0.1775
WM	0.028 [0.005, 0.050]	0.0158

BV, brain volume; CI, confidence interval; dGM, deep grey matter; GM, grey matter; SDMT, Symbol Digit Modalities Test; WM, white matter

Table 2. Longitudinal relationships between BV and SDMT scores in all participants and by baseline SDMT score

Conclusion: As expected, total or regional brain atrophy coincided with lower SDMT scores. Participants with low brain atrophy also showed no cognitive decline. This highlights the potential of CladT in supporting cognitive health in MS patients.

Disclosure: NDS has received honoraria from Biogen, Celgene (Bristol Myers Squibb), EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Genzyme, Immunic, Novartis, Roche, and Teva for consulting services, speaking, and travel support. He serves on advisory boards for Biogen, Genzyme, Immunic, Merck, Novartis, and Roche, and has received research grant support from the Italian MS Society. HW is member of scientific advisory boards/steering committees for Bayer, Biogen, Merck, Novartis, Roche, Sanofi, and Teva. He received speaker honoraria and travel support from Bayer, Biogen, CSL Behring, EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Fresenius Medical Care, Merck, Omniamed, Novartis, Sanofi, and Teva. He received compensation as a consultant from Biogen, Merck, Novartis, Omniamed, Roche, and Sanofi. He has received research support from Bayer, Biogen, Merck, Novartis, Sanofi, and Teva, as well as the German Ministry for Education and Research (BMBF), German Research Foundation (DFG), Else Kröner Fresenius Foundation, Fresenius Foundation, Hertie Foundation, NRW Ministry of Education and Research, Interdisciplinary Center for Clinical Studies (IZKF) Münster, and RE Children's Foundation. PV has received honoraria or consulting fees from AB Science, Ad Scientiam, Biogen, Celgene (Bristol Myers Squibb), Imcyse, Janssen (J&J), Merck, Novartis, Roche, Sanofi, and Teva; and research support from Novartis, Roche, and Sanofi. TD serves on scientific advisory boards for Actelion (Janssen/J&J), Bayer, Biogen, Celgene (Bristol Myers Squibb), GeNeuro, MedDay, Merck, Mitsubishi Pharma, Novartis, Roche, and Sanofi; has received funding for travel and/or speaker honoraria from Bayer, Biogen, Merck, Novartis, Roche, and Sanofi; and receives research support from Actelion, the European Union, Novartis, Roche, the Swiss MS Society, and the Swiss National Foundation. XM has received compensation for lecture honoraria and travel expenses, participation in scientific meetings, clinical trial steering committee membership, or clinical advisory board participation in recent years from Abbvie, Actelion, Alexion, Bial PD, Biogen, Bristol-Myers Squibb/Celgene, EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Genzyme, Hoffmann-La Roche, Immunic Therapeutics, Janssen Pharmaceuticals, Medday, Medscape, Merck, Mylan, Nervgen, Neuraxpharm, Novartis, Peervoice, Samsung-Biosys, Sandoz, Sanofi-Genzyme, Teva Pharmaceutical, TG Therapeutics, Excemed, ECTRIMS, MSIF, and NMSS or any of their affiliates. AA has received over the last 5 years honoraria or consulting fees for participating in advisory boards related to clinical trial design, trial steering committees, and data and safety monitoring committees from Biogen, Bristol Myers Squibb, Merck, Novartis, Roche, and Sanofi; and research support for investigator-initiated trials and MS patients' benefits activities from Biogen, Bristol Myers Squibb, Merck, Novartis, Roche, and Sanofi. SH serves on advisory boards for Bayer, Biogen, Merck, Novartis, Roche, and Sanofi. She has received money for travel and speaker honoraria from Bayer, Biogen, Merck, Novartis, Roche, and Sanofi. AC has received speakers'/board honoraria from Actelion (Janssen/J&J), Almirall, Bayer, Biogen, Celgene (Bristol Myers Squibb), Merck, Novartis, Roche, Sanofi, and Teva, all for hospital research funds. He received research support from Biogen, Sanofi, and UCB, the European Union, and the Swiss National Foundation. He serves as associate editor of the European Journal of Neurology, on the editorial board for Clinical and Translational Neuroscience, and as topic editor for the Journal of International Medical Research. AP has received speaking honoraria and travel expenses for participation in scientific meetings, has been a steering committee member of clinical trials or participated in advisory boards of clinical trials in the past years, and/or received operating grants from Alexion, Bayer, Biogen, Celgene (Bristol Myers Squibb), EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Novartis, Roche, Sanofi, and Teva. LL has received honoraria for consulting services or speaking activities from Biogen, Bristol Myers Squibb, Janssen-Cilag, Merck, Novartis, and Roche; and research support from Biogen, Merck, and Novartis. KS has received research support, through Queen Mary University of London, from Biogen, Merck, Novartis, and Sandoz; speaking honoraria from, and/or served in an advisory role for, Biogen, EMD Serono Research & Development Institute, Inc., Billerica, MA, USA, an affiliate of Merck KGaA, Merck, Neuraxpharm, Novartis, Roche, Sanofi, and Teva; and remuneration for teaching activities from AcadeMe and Medscape. FS has served on scientific advisory boards, been on the steering committees of clinical trials, served as a consultant, received support

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EPR-276 | Plasma neurofilament light chain associates with cognitive but not with patient-reported outcomes in multiple sclerosis

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Background and aims: To explore associations between plasma neurofilament light chain (pNfL) and cognition and patient-reported outcome measures (PROMs) in multiple sclerosis (MS)
Methods: In this cross-sectional study, we included 211 people with MS (PwMS) and collected EDSS, education, cognition (SDMT, CVLT and BVMT), Modified Fatigue Impact Scale (MFIS), Beck Depression Inventory (BDI-II), Beck Anxiety Inventory (BAI), and Pittsburgh Sleep Quality Index (PSQI). pNfL was evaluated using fully automated chemiluminescent enzyme immunoassay.
Results: On linear regression models, higher educational attainments were associated with lower pNfL (high school: Coeff = -0.22; 95%CI = -0.41, -0.04; $p = 0.019$; university: Coeff = -0.22; 95%CI = -0.42, -0.02; $p = 0.030$). On logistic regression models, each EDSS step was associated with 56% higher probability of pNfL above normality values (OR = 1.56; 95%CI = 1.23, 1.98; $p < 0.001$), and impaired SDMT with 2.5 higher probability of pNfL above normality values (OR = 2.50; 95%CI = 2.20, 5.21; $p = 0.014$). No associations were found for BDI-II, MFIS, BDI-II, BAI, PSQI
Conclusion: Neuro-axonal injury can express clinically into worse disability and worse attention and processing speed in PwMS, and could be mitigated by increased resilience, as reflected by higher educational attainment. Included PROMs were not associated with pNfL, and could possibly not be sufficiently sensitive to neuro-axonal injury or simply reflect other MS pathophysiologies.
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EPR-277 | Immunoglobulin dynamics in multiple sclerosis patients switching from ocrelizumab or rituximab to ofatumumab

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Background and aims: Immunoglobulin (Ig) M levels fall over time in multiple sclerosis (MS) patients treated with both ocrelizumab and ofatumumab, whereas falling IgG levels have only been reported with ocrelizumab. We wanted to investigate immunoglobulin dynamics in patients switching from high-dose, pulsed anti-CD20 therapies to ofatumumab in a large, real-world cohort.
Methods: We identified consecutive patients with MS switching from ocrelizumab or rituximab to ofatumumab at our center between 2022 and 2024. Serum immunoglobulins were measured every 6 months and mixed effects models used to estimate the rate of change in IgG and IgM levels over time, adjusting for age and sex.
Results: We studied 116 patients (mean age 40.6 years, 73% female) switching to ofatumumab from ocrelizumab ($n = 112$) or rituximab ($n = 4$). The most common reason for treatment switch was convenience. At the time of ofatumumab initiation, 19 (16%) patients had IgG levels less than the lower limit of normal (< LLN, < 7.0g) and 34 (29%) patients had IgM < LLN (< 0.4g/L). Over a mean follow-up of 1.62 years, IgG levels were stable (mean change -0.006g/L/month, p = NS), whereas IgM levels fell (mean change -0.005g/L/month, $p < 0.01$). The findings were similar in patients with and without hypogammaglobulinemia at the time of ofatumumab initiation.

Conclusion: In patients switching from pulsed, high-dose antiCD20 therapies to ofatumumab, IgG levels remain stable over the short-term while IgM levels decline. Longer follow-up is needed to determine whether switching to ofatumumab is an effective strategy for managing low IgG levels in MS patients treated with ocrelizumab or rituximab.
Disclosure: Ms Mertes has nothing to disclose. Ms Woitschach has nothing to disclose. Dr Brownlee has acted as a consultant and/or received speaker honoraria for educational activities for Astra-Zeneca, Biogen, Juvise, Merck, Novartis, Roche, Sandoz and Sanofi.

EPR-278 | Measuring spasticity and treatment in MS: a prospective register pseudo-trial

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Background and aims: Spasticity, characteriszed by muscle stiffness and spasms, is common in people with MS impacting mobility and quality of life. UKMS Register participants have completed the Multiple Sclerosis Impact Scale (MSIS-29) since 2011. There are 2 sub-items related to severity of stiffness and spasms. Typically MSIS-29 is scored by total/psychological/physical components. We developed an MSIS-29 based metric to measure spasticity change (MSIS-spast).
Methods: We created a pseudo-trial of those answering MSIS-29 ≥3 times consecutively ('streaks'), follow-up within 270 days without omission. First visit within 180 days of starting treatment: Baclofen or Sativex. Time to (Kaplan-Meier estimator) MSIS29-physical (6-point) and MSIS-spast sum (1-point) changes (+/-) were used to gauge treatment effect. Using propensity score matching we created controls for treatment groups. Matching: visit number, age, gender, MS-Type, and MSIS-spast, MSIS-physical, and MSIS-psychological scores. Cox proportional hazards modeling was used to control for confounders.
Results: 283 receiving Baclofen were 1:1 matched to 267 controls; Sativex was 1:3 matched ($n = 48{:}172$) Lack of complete streaks affected ratios. In both treatments there was no significant MSIS-physical effect. Baclofen ($p = 0.079$) and Sativex ($p = 0.055$) showed a trend toward spasticity improvement. Controlling for confounders Baclofen had a hazard ratio for spasticity improvement of 1.29 (95% CI: 1.04–1.61; $p = 0.021$). There was no significant treatment effect for Sativex.
Conclusion: Using MSIS-spast components proved more useful than MSIS-physical in determining spasticity change in a treated population. Baclofen showed significant treatment effect, Sativex less so. This may be due to lack of study power or treatment resistance.
Disclosure: JR RM and RN are supported by the UK Multiple Sclerosis Society RN is supported by Multiple Sclerosis Trials Collaboration (MSTC) and the Berkeley Foundation.

Neuro-oncology and palliative care

EPR-279 | Progressive supranuclear palsy – Are we planning for the future? A North-East UK perspective

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Background and aims: Progressive supranuclear palsy (PSP) is a rare neurodegenerative disorder, with an average life expectancy from symptom onset of around seven years (Testa et al., 2001). The intention of this work was to look at the advanced care planning that occurred for patients admitted to hospital with a diagnosis of PSP.
Methods: Data was collected for patients admitted through James Cook Hospital's Accident and Emergency department with a coded diagnosis of PSP on the discharge summary from 2018 to 2022. 91 admissions, and 56 individual patients were identified. Non-PSP patients were removed. Data was recorded for reason for admission, length of stay, advanced care planning completed, and survival at 12 months.
Results: Half of all admissions were related to infection or mobility. 66% of admissions had the patient return to their own home on discharge, with 24% discharged to a care home, and 10% dying. 26% had a do not attempt resuscitation order in place before admission rising to 44% following admission. 15% had an emergency healthcare plan on admission, rising to 16% on discharge. For any single admission, there was a 50% chance the patient died within 12 months.
Conclusion: The primary conditions that lead to hospital admission are falls and infections, with a high chance of death in the following 12 months after admission. There is a lack of advanced care planning done, and hospital admissions can be used to identify at risk, frail patients, enabling them to have more agency and input into their future care.
Disclosure: Nothing to disclose.

EPR-280 | Neurology training and palliative care: Insights from Iberian Peninsula Residents

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Background and aims: Palliative care (PC) is essential in managing severe chronic and progressive neurological diseases. Its importance is increasingly recognized by neurologists and medical educators worldwide. This study evaluates neurology residents' perceptions of PC's relevance in their training and assesses their self-reported competencies in this field.
Methods: An online questionnaire, developed via Google Forms and based on Mehta et al. (2018), was distributed to neurology residents in Portugal and Spain. It comprised 11 questions, including two with 10 Likert-scale items each and nine multiple-choice questions. Residents evaluated the importance of various palliative care topics in postgraduate training and self-assessed their competencies in these areas. Each Likert item offered five response options, scored from 1 to 5. For each participant, two scores were calculated by summing the responses to the 10 Likert items in each question. These scores were analyzed using descriptive and comparative statistical methods.
Results: A total of 127 responses were collected (71% from Portugal), representing neurology residents at various training stages and regions across Portugal and Spain. Approximately 28% referred patients to palliative care at least monthly, while only 15% had access to PC education during residency. "Communication" was rated the most important training topic (mean = 4,65), while "ethical and legal issues" received the lowest self-assessed competency score (mean = 2,22). Around 95% supported integrating palliative care into the residency curriculum, and the mean score reflecting the perceived importance of PC was significantly higher in this subgroup ($p = 0{,}008$).
Conclusion: These findings highlight residents' recognition of palliative care's relevance and training benefits.
Disclosure: Nothing to disclose.

EPR-281 | Advanced care planning of patients with neurologic diseases. First year of experience at a specialized outpatient clinic

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Background and aims: Advanced Care Planning (ACP) involves setting objectives and having discussions with patients and family members/caregivers about care preferences especially -but not only- at the end of life in the context of chronic diseases. Managing patients with neurologic diseases in this setting impose specific challenges that require skilled care. The aim of this study was to describe data gathered in a specialized neurology ACP outpatient clinic.
Methods: We reviewed the medical records of patients seen during the first year of our neurology ACP clinic. We described demographic data, diagnoses, cognitive, functional, and motor severity scales, indicators of palliative care needs, mortality, end-of-life preferences and care outcomes.
Results: We attended 86 patients with a mean age of 78 years. The most common diagnoses were dementia, stroke, and multiple sclerosis. 68% had severe cognitive impairment, and 88% presented moderate-to-severe dependency. The most prevalent indicator of advanced palliative care needs was dysphagia (58%). After our consultation, visits to the emergency department were reduced from 48% to 18%, and hospital admissions from 33% to 13%. Out of the 23 patients who died, the majority (75%) passed away in their preferred place.
Conclusion: Most of our patients presented degenerative diseases involving cognitive, language and decision-making impairment, which highlights the importance of addressing preferences, needs, and strategies from an early stage and with the support of caregivers. Our clinic helped neurologic patients achieve their care preferences and reduced futile interventions.
Disclosure: Nothing to disclose.

EPR-282 | End-of-life and palliative sedation in the neurology inpatient unit of a tertiary hospital

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Background and aims: Neurology departments report higher in-hospital mortality rates compared with other units. Given the complexity of neurological diseases, addressing palliative sedation (PS) at the end of life (EoL) is critical, yet understudied. This study aimed to describe the use of PS at the EoL in patients who died in a Neurology Inpatient Unit (NIU).
Methods: An observational, retrospective clinical audit was conducted in the NIU of a tertiary hospital in Spain. Demographic, medical history, and therapeutic data were reviewed for patients who died in 2024. Descriptive and univariable analyses were performed.
Results: Among 45 patients (mean age 79.7 ± 11.9 years; 46.7% women) who died in 2024, 40(88.9%) deaths were related to stroke. PS was administered to 43 (95.6%; 40 via continuous infusion) with a median duration of 1day (IQR 1–2) from initiation to death. Only 3 (6.7%) had advance directives, while 14 (31.1%) had documented some form of EoL conversation with relatives. Dyspnoea was the most frequently registered refractory symptom (39.5%), although 15 patients (34.9%) lacked documented symptoms. The principal sedatives used were midazolam (97.7%, median dose 45mg/24h, IQR 26-60) and morphine (97.7%, median dose 40mg/24h, IQR 30-50); while anticholinergics were used in 40(93.0%). 10 patients (23.8%) had concurrent active treatments at the moment of PS.
Conclusion: Nearly all patients who died in the NIU received PS, yet only 31.1% had documented EoL conversations with proxies, indicating a need for better communication and documentation. Additionally, the frequent use of opioids despite guideline recommendations underscores the necessity for more standardized PS protocols in neurology settings.
Disclosure: Nothing to disclose.

EPR-283 | Identification of a new travelling oncoprotein associated with poor prognosis in high grade gliomas

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Background and aims: Considering the various roles of Homeodomain proteins (HPs) in cellular migration, proliferation and differentiation, their implication in cancers is attracting increasing interest. Homeobox A2 (HOXA2) was recently found to be overexpressed and an independent prognostic marker in high grade gliomas.1–3 Interestingly, some HPs have the astonishing property to travel between cell.4 More strikingly, these travelling HPs are able to enter target cell nucleus and thereby modify transcriptional activity, potentially spreading oncogenic dysregulation in the healthy neighboring cells.5–7 In this work, we investigated if HOXA2 is a travelling HP.
Methods: To investigate HOXA2 intercellular travel, Human embryonic kidney (HEK) 293 cells were transfected with plasmids containing Flag-HOXA2 and Enhanced Green Fluorescent Protein (EGFP) coding sequences. EGFP was used as positive control for transfection and as negative control of intercellular transfer. ONECUT1, a known travelling HP, was used as positive control for intercellular travel. Anti-Flag and anti-ONECUT immunofluorescence labelings were performed 48 hours after cell transfection.
Results: Intercellular travel was assessed by immunofluorescence. Since cells were either cotransfected or untransfected, HOXA2-positive and EGFP-negative cells were considered homeoprotein recipient cells. Recipient cells were indeed observed in the neighboring of producing EGFP- and HOXA2-positive cells. The ratio between the receiving cells were the Flag-HOXA2 homeoprotein was detected and the transfected producing cells was 0.87. This ratio is comparable with the 0.81 ratio obtained for the travelling HP ONECUT1, and significantly superior to negative control EGFP (0.09).
Conclusion: These results underscore the potential capacities of HOXA2 oncoprotein to travel to, and penetrate surroundings cells in vivo.
Disclosure: Nothing to disclose.

EPR-284 | Clinical, molecular, and transcriptomic features associated with seizures at onset in patients with glioblastoma

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Background and aims: Seizures occur in up to 60% of patients with glioblastoma (GBM), revealing the tumor in 25-30% of cases. The understanding of the tumor biology associated with epilepsy as the presenting symptom remains limited. Moreover, despite growing preclinical evidence of a link between epileptogenesis and tumorigenesis, the prognostic role of seizures at onset remains debated, partly due to study heterogeneity.
Methods: We leveraged a homogeneous cohort of WHO 2021 GBM patients from our Institution with available clinical, molecular, and transcriptomic data. We retrospectively queried clinical records to identify the presence and characteristic of seizures at disease onset.

Results: in our cohort of 231 GBM patients, 36% presented with seizures: of them, 47% were focal, 11% focal with impaired awareness, and 42.2% generalized. We did not observe significant differences in terms of age, sex, type of surgery, and tumor localization between the two groups. Patients presenting with seizures had a higher Karnofsky Performance Status score (median KPS: 90 vs. 80, $p < 0.01$) and tended to have a less frequently mutated TERT promoter (86% vs. 94%, $p = 0.07$). Seizures at onset were not associated with overall survival neither in univariate (HR 1.10, C.I. 0.83 - 1.46, $p = 0.50$) nor in multivariate Cox regression analysis (HR 1.16, C.I. 0.86 - 1.57, $p = 0.33$). Differences in terms of gene expression will be assessed on 3′ RNA sequencing data.
Conclusion: Despite the presence of seizures at diagnosis was associated with higher performance status and a distinct molecular profile, it does not predict survival
Disclosure: Nothing to disclose.

EPR-285 | Exploratory analyses from Phase 3 INDIGO study show lower seizure rates in patients treated with vorasidenib vs. placebo

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Background and aims: Grade 2 isocitrate dehydrogenase 1 or 2 mutant (mIDH1/2) gliomas are slowly progressive, malignant, incurable brain tumors with poor long-term prognosis. Patients may experience tumor-related symptoms (e.g., seizures) that impact their daily lives. Vorasidenib, an oral, brain-penetrant, dual inhibitor of mIDH1/2, has shown significant clinical benefits and a manageable safety profile in the Phase 3 INDIGO study (NCT04164901). Herein, we investigate the potential relationship between vorasidenib and seizure rate, and between tumor volume and seizure activity in patients with mIDH1/2 glioma.
Methods: Patients aged ≥12 years with grade 2 mIDH1/2 oligodendroglioma or astrocytoma, with no prior treatment for glioma other than surgery, and no uncontrolled seizures, were randomized 1:1 to receive vorasidenib 40 mg or placebo daily. Exploratory analyses for the number of on-treatment seizures were conducted in patients with >=1 seizure during the study using a negative binomial regression model. The potential association between seizure activity and tumor volume was assessed using the mixed effect model with repeated measurements.
Results: Patients treated with vorasidenib had lower on-treatment rates of seizures than those treated with placebo; these differences were more pronounced in patients with oligodendroglioma than with astrocytoma (Table 1). There was a highly positive correlation between tumor volume and seizure number (log tumor size estimate of coefficient: 0.7; standard error: 0.26; $p = 0.007$; Table 2).

TABLE 1 Exploratory subgroup analyses of vorasidenib treatment and seizure rate among patients with mIDH1/2 glioma who reported >=1 on-treatment seizure.

	Overall population		Oligodendrogliomas		Astrocytomas	
	Vorasidenib (n=167)	Placebo (n=163)	Vorasidenib (n=88)	Placebo (n=84)	Vorasidenib (n=80)	Placebo (n=79)
Patients with at least one seizure	53	55	28	28	25	27
Total number of on-treatment seizure events	1541	5124	1023	3751	518	1373
Rate of on-treatment seizures per person-year* (95% CI)	18.2 (8.4, 39.5)	51.2 (22.9, 114.8)	9.9 (2.9, 33.2)	71.1 (25.8, 196.3)	18.7 (9.6, 36.3)	20.5 (9.7, 43.1)
Ratio of rates: vorasidenib vs placebo (95% CI)	0.36 (0.14, 0.89)		0.14 (0.05, 0.42)		0.91 (0.39, 2.11)	
P value†	0.0263		0.0005		0.8266	

*The rate was estimated using a negative binomial regression model adjusted by the number of seizures at baseline and the tumour size at baseline; †This *P* value was not prespecified and has not been adjusted for multiplicity; therefore, it should be interpreted with caution. Data cut-off: 7 March 2023.
CI, confidence interval; mIDH1/2, mutant isocitrate dehydrogenase 1 or 2.

TABLE 2 Exploratory analysis of the potential association between seizure activity and tumor volume in patients with mIDH1/2 glioma.

	Overall population (N=331)*
n	308
Intercept	
Estimate of coefficient (SE)	–6.0 (2.38)
P value†	0.012
Log tumour size‡	
Estimate of coefficient (SE)	0.7 (0.26)
P value†	0.007
Number of seizures at baseline	
Estimate of coefficient (SE)	0.5 (0.03)
P value†	<0.001
Chromosome 1p19q co-deleted	
Estimate of coefficient (SE)	0.9 (0.53)
P value†	0.076

*One patient was randomized to vorasidenib but was never treated; †This *P* value was not prespecified and has not been adjusted for multiplicity; therefore, it should be interpreted with caution. Data cut-off: 7 March 2023; ‡Tumour volume assessments were conducted every 12 weeks up until Cycle 36 (with a 28-day cycle), every 6 months for the next 2 years, and annually thereafter.
mIDH1/2, mutant isocitrate dehydrogenase 1 or 2; SE, standard error.

Conclusion: Treatment with vorasidenib was associated with lower seizure activity than with placebo in patients with mIDH1/2 glioma, particularly in those with oligodendroglioma. Smaller tumor volume was associated with a lower seizure rate.

TABLE 3 Author disclosures.

Author	Disclosures
Mehdi Touat	Reports grant/research support from Sanofi Pasteur, Inc and consultant fees from, Novocure Inc, Ono, Servier Pharmaceuticals LLC and NH TherAguix
Ingo K. Mellinghoff	Servier Pharmaceuticals
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Jennifer Clarke	Reports consulting fees for Agios Pharmaceuticals, Inc. and Servier Pharmaceuticals LLC and participation as a site-PI for Merck
Joe Mendez	Reports serving on an advisory board for Servier Pharmaceuticals LLC
Liam Welsh	No disclosures to report
Warren P. Mason	Reports consulting for Merck, Novocure Inc. and Servier Affaires Medicales, and serving on a data and safety monitoring board for Ono Pharmaceutical
Andreas F. Hottinger	Reports grant/research support from Novocure Israel Ltd and consultant fees from Bayer and Novocure Israel Ltd
Juan M. Sepulveda	Reports grant/research support from CANTEX Pharma and Pfizer Pharmaceuticals LLC, consultant fees from Bristol Myers Squibb Company, CeCaVa, Merck Sharp and Dohme, Novocure Israel Ltd, and speaker fees from GlaxoSmithKline
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Riccardo Soffietti	Reports consulting fees from AbbVie, AstraZeneca, Celldex Therapeutics and Merck
Dan Zhao, Denise Yi, Daniel Weidl, Lori Steelman	Are current employees of Servier Pharmaceuticals LLC
Islam Hassan	Is a current employee of Servier Pharmaceuticals LLC and holds stocks in Agios Pharmaceuticals Inc.
Patrick Y. Wen	Reports grant/research support from AstraZeneca, Black Diamond Therapeutics, Bristol Myers Squibb Company; Chimerix, Erasca, Kazia, MediciNova, NuvationBio, Quadriga Biosciences, Servier Pharmaceuticals LLC and VBI Vaccines, consultant fees from AstraZeneca, Bayer, Beigene, Boston Pharmaceuticals, CNS Pharmaceuticals, Curaleq, Dampoon Sumitomo Pharma, Genenta, Genentech/Roche, Insightec, Inc, Karyopharm Therapeutics, Kazia, MediciNova, Merck, Novartis, Novocure Inc., Nuvation Bio, QED Therapeutics, Radiopharm Theranostics, Sagimet, Sapience, Servier Pharmaceuticals LLC, Telix, Vascular Biogenics, VBI vaccines and served on a data and safety monitoring board for Day One Therapeutics
Timothy F. Cloughesy	Reports being a cofounder, major stock holder, consultant, and board member of Katmai Pharmaceuticals; membership of the board and paid consultancy for the 501c3 Global Coalition for Adaptive Research; holding stock in Chimerix and receiving milestone payments and possible future royalties; holding stock in Erasca; membership of the scientific advisory boards for Break Through Cancer and Cure Brain Cancer Foundation; providing paid consulting services to Sagimet, Clinical Care Options, Ideology Health, Servier Pharmaceuticals LLC, Jubilant, Immvira, Gan & Lee, BrainStorm, Katmai, Sapience, Inovio, Vigeo Therapeutics, DNATrix, Tyme, SDP, Novartis, Roche, Kintara, Bayer, Merck, Boehringer Ingelheim, VBL, Amgen, Kiyatec, Odonate Therapeutics QED, Medefield, Pascal Biosciences, Bayer, Tocagen, Karyopharm, GW Pharma, AbbVie, VBI, Deciphera, VBL, Agios, Genoscia, Celgene, Puma, Lilly, BMS, Cortice, Wellcome Trust, Novocure, Novogen, Boston Biomedical, Sunovion, Human Longevity, Insys, ProNai, Pfizer, Notable Labs, Medgia Trizel, and Medscape; contracts with UCLA for the Brain Tumour Program with Oncovir, Merck, Oncoceutics, Novartis, Amgen, AbbVie, DNAtrix, Beigene, BMS, AstraZeneca, Kazia, Agios, Boston Biomedical, Deciphera, Tocagen, Orbus, and Karyopharm, and that the reagents of the University of California (UC's employer) have licensed intellectual property co-invented by UC to Katmai Pharmaceuticals

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EPR-286 | Abstract withdrawn

Neuroimmunology 3

EPR-287 | Predictors and phenotypic features of the wearing-off effect in anti-CD20 therapy for multiple sclerosis: Insights from patient-reported outcomes

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Background and aims: Wearing-off phenomenon may be experienced by people with Multiple Sclerosis (pwMS) under anti-CD20 monoclonal antibodies, which may negatively impact disease control perception and functionality.
Methods: A cross-sectional cohort study of pwMS treated with anti-CD20 drugs and followed at a tertiary care center. A questionnaire was administered to assess symptoms consistent with the wearing-off phenomenon.
Results: A total of 139 pwMS were included of whom 94 (67.6%) had the relapsing-remitting form and 45 (32.4%) had progressive forms. 72 patients (51.8%) were under ocrelizumab, 47 (33.8%) under ofatumumab and 20 (14.4%) patients under rituximab. Wearing-off phenomenon was reported by 43 patients (30.9%), with the majority (72.1%) experiencing at least two concomitant symptoms, most commonly fatigue ($n=37$) and balance disturbances ($n=16$). The majority (67.4%) reported symptom onset more than one week before infusion, with complete symptom resolution occurring after the infusion, Most patients (76.7%) classified their symptoms as moderate to severe, with 26 patients (60.5%) reporting a moderate to severe functional impact. In 28 patients (65.1%), wearing-off was associated with altered perception of disease control. No statistically significant differences were observed in the prevalence of wearing-off among the different anti-CD20 therapies. Wearing-off was more frequent in females ($p=0.046$). A positive correlation was found between body weight and the occurrence of wearing-off, but only in males ($p=0.041$). No statistically significant associations were found with body mass index, drug exposure time, EDSS score, or age.
Conclusion: The wearing-off phenomenon seems to be frequently reported and transversal to different anti-CD20 therapies.
Disclosure: All authors: Nothing to disclose.

EPR-288 | Clinical spectrum of anti-IgLON5 disease: A case series with three distinct movement disorder phenotypes

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Background and aims: Anti-IgLON5 antibody-mediated disease is a neurodegenerative disorder associated with antibodies targeting neuronal cell adhesion proteins. This study describes three clinical cases with distinct movement disorder phenotypes within the spectrum of the disease.
Methods: We reviewed three female patients (75, 75, and 77 years old) with confirmed diagnoses of anti-IgLON5 encephalitis. Data included age, symptom onset duration, clinical phenotypes, diagnostic delay, serological and CSF findings, video-polysomnography (V-PSG), and treatment responses. The IgLON5 Composite Score was calculated to assess clinical severity.

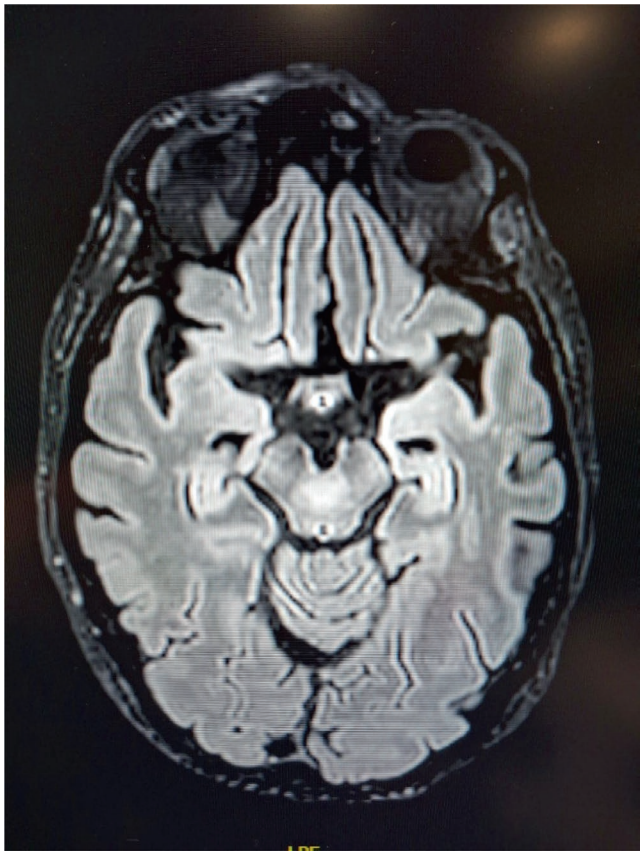

FIGURE 1 Brain MRI of the first patient showed mutiple white matter hyperintensities in T2 and FLAIR in midbrain, pons, both thalami, compatible with IgLON5 encephalitis.

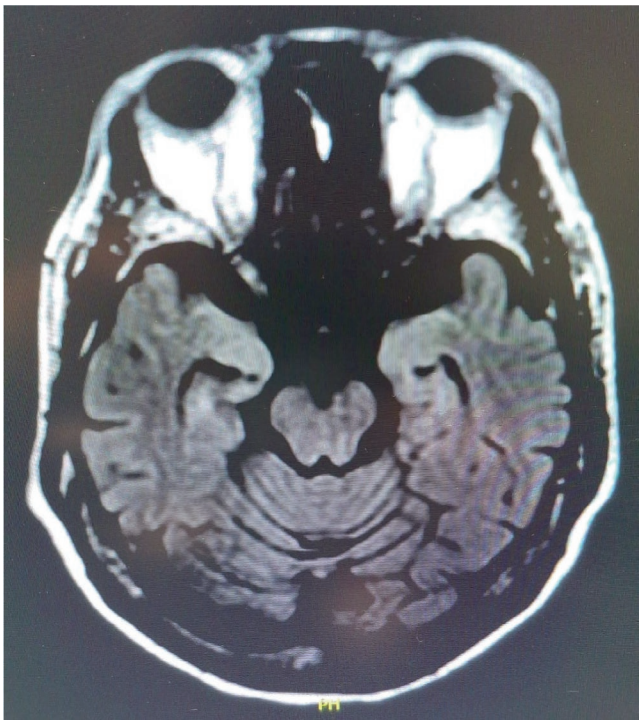

FIGURE 2 Brain MRI of the second patient showed bilateral hippocampus hyperintensity associated with mild volume loss, compatible with subacute autoimmune encephalitis.

Results: The observed phenotypes were: 1. Atypical PSP-like parkinsonism with midbrain involvement and rigid-akinetic features (diagnostic delay: 12 months; composite score: 8). Treated with corticosteroids and intravenous immunoglobulins (IgIV) without optimal response, currently receiving rituximab, awaiting the second dose. 2. Chorea with cognitive decline, basal ganglia involvement, and nocturnal behavioral disturbances (diagnostic delay: 6 months; composite score: 9). Treated with IgIV, rituximab, and cyclophosphamide, pending a rituximab booster dose due to clinical worsening. 3. Ataxia and severe bulbar syndrome with bilateral vocal cord paresis and lower brainstem involvement (diagnostic delay: 1 month; composite score: 10). Treated with corticosteroids and five sessions of plasmapheresis, currently on rituximab with good response.

Conclusion: Anti-IgLON5 disease presents heterogeneous phenotypes, complicating early diagnosis. It should be included in the differential diagnosis of movement disorders and specific testing must be conducted to avoid diagnostic delays, as an early therapeutic intervention is essential to improve patient outcomes. This study underscores the importance of a multidisciplinary approach in managing these cases.

Disclosure: Nothing to disclose.

EPR-289 | Suicidality and depression in pediatric multiple sclerosis

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Background and aims: Pediatric multiple sclerosis (PedMS) is immune-mediated, rare, demyelinating and neurodegenerative diseases of the central nervous system. Studies have shown that depression is being observed in MS patients in approximately 60%, while the prevalence in PedMS patients reaches almost 30% according to studies. So far, only one pilot study has examined rates of suicidal ideation in PedMS. The aim of this study was to examine the presence of depressive symptoms and suicidality in PedMS.

Methods: The assessment of suicidal ideation and depressive symptoms was performed using the C-SSRS and SMFQ, SCARED questionnaires. We used the Extended Neurological Disability Scale (EDSS) to assess neurological disability. Patients with high scores were referred to a child psychiatrist for further evaluation and diagnostic assessment.

Results: In total, 27 patients aged up to 18 years with PedMS were analyzed. The mean age of patients was 15.9 ± 1.9 years, with the male to female ratio of 11 (40.7%): 16 (59.3%). All patients had a relapsing-remitting form of PedMS. The median EDSS is 1.0 (0-3.0). The average SMFQ was 3.67 (0-19), while the average SCARED was 11 (0-54). Depressive symptoms were present in 6 (22.2%) patients, while 1 (3.7%) patient had suicidality. The diagnosis of depression was confirmed in 4 (14.8%).

TABLE 1 Pediatric Multiple Sclerosis – clinical characteristics, depression, suicidality, treatment.

		Percent (%)
Number of patients	27	100
Sex	Male	40.7
	Female	50.3
Age ± SD	15.9 ± 1.9	
Age at PedMS onset	14.6 ± 2.1	
Types of PedMS	Relapsing-remitting PedMS	100
EDSS	Mean	1.33
	Median	1
	Mode	1.0
SMFQ (range)	3.67 (0-19)	
SCARED (range)	11 (0-54)	
C-SSRS	Positive answers	3.7
	Negative answers	88.9
	Refuse to answer	7.4
Child psychiatrist	Confirmed diagnosis	14.8
Treatment	Moderate or low-efficacy	55.6
	High-efficacy	25.9
	Patients expected DMT	11.1
	Refused DMT	7.4

Abbreviations: DMT- disease modifying therapy; EDSS - The Expanded Disability Status Scale; PedMS - Paediatric Multiple Sclerosis; SCARED- Screen for Child Anxiety Related Disorders; SD – standard deviation; SMFQ - Short Mood and Feelings Questionnaire; C-SSRS - Columbia Suicide Severity Rating Scale

Conclusion: In our cohort a significant number of children with PedMS had subclinical depressive symptoms or fully blown depression. Additional research is needed to identify the rates of suicidality in PedMS.
Disclosure: Nothing to disclose.

EPR-290 | Rapidly progressive cerebellar syndrome caused by anti-ITPR1 antibodies in a patient with follicular lymphoma

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Background and aims: Rapidly progressive cerebellar syndrome (RPCS) is a high-risk neurological paraneoplastic phenotype. It is associated with cancers such as small cell lung carcinoma and gynecological cancers. It typically begins with dizziness, nausea, and vomiting, followed by dysarthria, diplopia, nystagmus and ataxia.
Methods: We report a 92-year-old woman with a history of follicular non-Hodgkin lymphoma (NHL) who presented with a 3-week history of dizziness, nausea, and vomiting. On examination, she exhibited mild dysarthria, bilateral gaze-evoked and downbeat nystagmus, truncal ataxia and dysmetria in all limbs.
Results: Blood tests showed mild hyponatremia. Cranial magnetic resonance showed a small acute left occipital infarct and multiple cerebellar hyperintense foci. Cerebrospinal fluid analysis showed mild pleocytosis and positive oligoclonal bands. Immunohistochemistry using indirect immunofluorescence on rodent cerebellar tissue revealed a pattern suggestive of the presence of anti-inositol 1,4,5-trisphosphate receptor type 1 (ITPR1) antibodies, confirmed by a cell-based assay. A whole-body computed tomography scan showed progression of the lymphoma. Despite treatment with prednisone and intravenous immunoglobulins, the patient passed away.
Conclusion: ITPR1, an intracellular antigen in Purkinje cells, is targeted by antibodies in paraneoplastic RPCS. This is the first described case related to NHL.
Disclosure: None of the authors has any conflict of interest to disclose.

EPR-291 | Sleep disturbances in patients with myasthenia gravis A cross-sectional study

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Background and aims: To explore sleep dysfunction among patients with clinically stable patients with Myasthenia Gravis and seek to identify sleep disturbances and uncover their associated risk factors.
Methods: A cross-sectional study was conducted, involving the recruitment of 306 patients with MG from three MG centers. Participants completed an online self-report questionnaire covering demographics, clinical characteristics, and assessments using the Pittsburgh Sleep Quality Index (PSQI) scale, Stop-Bang scale, 15-item quality-of-life instrument for myasthenia gravis (MG-QOL 15) scale, patient health questionnaire (PHQ-9), and self-rating anxiety scale (SAS) to evaluate sleep quality among patients with MG.
Results: Approximately 68% of patients with MG experienced sleep disturbances (PSQI ≥6). Univariate analysis revealed that older age (>60 years), lower education level (≤12 years), unfavorable marital status, late disease onset (>55 years old), generalized subtype, myasthenia crisis, positive AchR-antibody, thymoma, thymectomy, and pathological type B thymoma were risk factors for sleep dysfunction in patients with MG. Within the sleep disturbance group, 51% of patients scored ≥3 on the Stop-Bang scale, indicating a higher risk of obstructive sleep apnea. Global PQSI scores showed significant linear correlations with MG-QOL 15, Stop-Bang, PHQ-9, and SAS scores ($p < 0.001$). Multivariate analysis revealed that sex, marital status, Stop-Bang score, SAS score, and MG QOL-15 score exhibited correlations with the PQSI score.

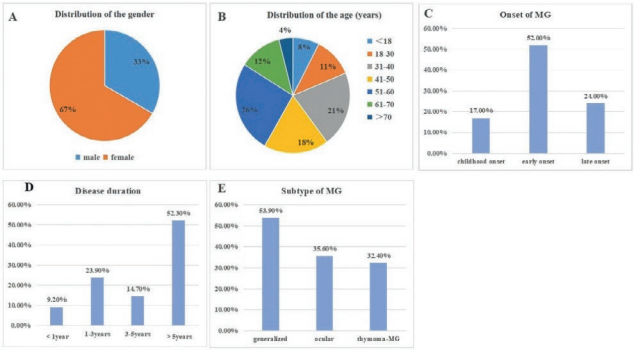

FIGURE 1 Demographics and Clinical Characteristics of myasthenia gravis patients.

TABLE 1 Comparison of clinical characteristics of MG patients between the non-sleep disturbances group and sleep disturbances group (*n*, %).

	Non-Sleep Disturbances (N=98)	Sleep Disturbances (N=208)	X^2	P value
Gender			0.120	0.729
Female	64(65.3%)	140(67.3%)		
Male	34 (34.7%)	68(32.7%)		
Age (years)				
< 18	18(18.4%)	5(2.4%)	24.420	7.740
18-60	72(73.5%)	162(77.9%)	0.722	0.396
> 60	8(8.2%)	41(19.7%)	6.610	**0.01**
BMI (kg/m²)				
< 18.5	15(15.3%)	19(9.1%)	2.57	0.109
18.5-23.9	54(55.1%)	105(50.5%)	0.570	0.450
≥24.0	29(29.6%)	84(40.4%)	3.331	0.067
Education level			4.71	**0.030**
< 12 years	58(59.2%)	149(71.6%)		
≥ 12 years	40(40.8%)	59(28.4%)		
Marital status			24.080	**< 0.001**
Single	44(44.9%)	38(18.8%)		
Coupled /Married	54(55.1%)	170(81.7%)		
Residence			0.581	0.446
Rural	31(31.6%)	57(27.4%)		
Town/City	67(68.4%)	151(72.6%)		
Monthly family income			1.925	0.165
Low (< ￥5000)	58(59.2%)	140(67.3%)		
Moderate-high (≥￥5000)	40(40.8%)	68(32.7%)		
Monthly treatment costs (percent of monthly income)				
< 10%	20(20.4%)	36(17.3%)	0.428	0.513
10-20%	31(31.6%)	62(29.8%)	0.105	0.746
> 20%	47(48.0%)	110(52.9%)	0.647	0.421
Disease duration of MG				
< 1 year	10(10.2%)	18(8.7%)	0.193	0.661
1-3 years	20(20.4%)	53(25.5%)	0.944	0.331
3-5 years	13(13.3%)	32(15.4%)	0.239	0.625
> 5 years	55(56.1%)	105(50.4%)	0.849	0.357
Onset of MG				
Childhood onset	32(32.7%)	20(9.6%)	23.46	1.272
Early onset	51(52.0%)	108(51.9%)	64.56	9.36
Late onset	15(15.3%)	78(37.9%)	14.843	**0.0001**
MG subtypes			14.583	**< 0.001**
Ocular MG	49(50.0%)	60(28.8%)		
Generalized MG	49(50.0%)	146(71.2%)		
History of myasthenia crisis	22(22.4%)	79(38.0%)	7.267	**0.007**

Conclusion: Sleep disturbances are prevalent among patients with MG, even in clinically stable cases. Psychological factors such as anxiety and health-related quality of life warrant increased attention in the management of these patients.

Disclosure: All authors claim that there are no conflicts of interest.

EPR-292 | Fc-glycosylation reveals brain-specific antibody profiles in NMDARe, tracking post-herpetic, tumor or idiopathic origin.

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Background and aims: Anti-NMDA receptor encephalitis (NMDARe) is driven by pathogenic IgG1 antibodies, sometimes accompanied by IgG2/3, leading to neuronal dysfunction. These antibodies are always present in CSF and may be present in serum.Triggers include tumors (mainly ovarian teratomas) and herpes simplex virus encephalitis, though many cases remain idiopathic. Prior B-cell receptor studies suggest compartmentalized antibody responses in the brain, but differences in Fc-glycosylation between serum and CSF, or by disease trigger, are unknown. This study aimed to identify Fc-glycosylation profiles in NMDARe that reflect antibody compartmentalization and disease triggers.

Methods: Using liquid-chromatography-mass-spectrometry we determined the Fc-glycosylation profiles of IgG1 and IgG2/3 in paired serum and CSF samples from (age- and sex-matched) patients with NMDARe ($n = 50$). Patients were classified based on disease trigger into post herpetic, tumor-related or idiopathic. Glycoprofiles were determined by quantification of fucosylation, sialylation, galactosylation and bisecting N-glucosamination.

Results: CSF IgG1 and IgG2/3 displayed a more inflammatory Fc-glycan profile than serum, with lower sialylation and galactosylation ($p < 0.001$). Post-herpetic NMDARe showed the most inflammatory glycoprofile, with reduced sialylation, lower galactose levels, and increased bisecting N-glucosamination ($p < 0.001$), differences absent in serum. Fucosylation levels remained stable across compartments and triggers.

Conclusion: In patients with NMDARe, CSF shows distinct Fc-glycosilation profiles, supporting a compartmentalized antibody response within the brain. Post-herpetic NMDARe is associated with more inflammatory glycoprofiles than other triggers. As glycan signatures determine different interactions with the innate immunity (e.g., complement, NK cells), these findings suggest distinct pathogenic mechanisms that might be harnessed to develop compartment-specific and trigger-specific therapeutic strategies in NMDARe

Disclosure: Nothing to disclose.

EPR-293 | Types and prognosis in peripheral nervous system involvement related to immune checkpoint inhibitors

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Background and aims: This study aimed to identify the frequency and types of peripheral nervous system involvement, clinical features, treatment options, and prognosis in patients receiving immune checkpoint inhibitors (ICIs) due to malignancy.
Methods: This study is a retrospective cross-sectional study. We included data of patients who presented to our electromyography laboratory with neurological complaints and were using ICIs between January 2019 and August 2024. We retrieved medical and electrophysiological records. Patients with complaints before the use of ICIs were excluded. In cases with multiple examinations, the first appropriate examination was included. Demographic data, oncological and neurological diagnosis, and medications used were detected from patient files.
Results: During the study, we reviewed the records of 31 patients. Seven were excluded. Two of the remaining 24(female=11, male=13; age:34-78) had multiple examinations. The most commonly used ICIs were pembrolizumab($n=7$) and nivolumab($n=6$). The most frequent malignancies were non-small cell lung cancer($n=13$) and breast cancer($n=3$). Electrophysiologically, sensory or sensory-motor axonal polyneuropathy was detected in 13(5 accompanied by myopathy), demyelinating polyneuropathy in 1, isolated myopathy in 4, and anterior root/anterior horn involvement in 1. The drugs most commonly used were nivolumab, pembrolizumab, atezolizumab. The treatment option was immune modulation in cases with demyelinating neuropathy and myopathy. The prognosis was poor in myopathies due to cardiovascular complications and complications related to malignancy.
Conclusion: ICIs have been increasingly used in cancer treatment and can cause immune-related effects. As demonstrated here, the most common peripheral nervous system involvement is axonal polyneuropathy, followed by myopathy.
Disclosure: Nothing to disclose.

EPR-294 | Immune checkpoint dysregulation in multiple sclerosis: Insights into AhR-driven regulatory B cell function

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Background and aims: This study aimed to characterize regulatory B cell populations in MS patients, assessing disease-related changes in these subsets. Given recent evidence linking regulatory B cells to immune checkpoint molecules regulated by the aryl hydrocarbon receptor (AhR), we investigated the correlation between regulatory B cell populations, AhR serum levels, and the expression of co-inhibitory molecules.
Methods: Peripheral blood mononuclear cells (PBMCs) were analyzed using high-dimensional flow cytometry from the serum of patients with relapsing-remitting MS (RRMS, $n=68$), secondary progressive MS (SPMS, $n=17$), and non-inflammatory neurological diseases (NINDS, $n=76$). Regulatory B cells were identified through subset-specific markers and examined for immune checkpoint molecule expression. AhR serum levels were quantified using a Dual-Luciferase Reporter Assay.
Results: Regulatory B cell subsets ($CD24^{+}CD38^{hi}$, $CD5^{+}CD1d^{+}$, and $CD39^{+}CD73^{+}$) were significantly reduced in MS patients compared to individuals with NINDS, alongside altered checkpoint molecule expression. Conversely, $CD27^{-}IgD^{-}$ "double-negative" (DN) B cells were increased. Moreover, a positive correlation was observed between AhR serum levels and Tim-1 expression on B cells.
Conclusion: This study elucidates MS-specific alterations in B cell subsets, demonstrating impaired regulatory properties mediated by immune checkpoint dysfunction. The observed reduction in co-inhibitory molecule expression suggests that AhR signaling, known for its immunomodulatory effects, may restore regulatory B cell function. These findings position AhR as a potential therapeutic target for selectively modulating B cell populations, offering a more precise alternative to broad-spectrum B cell depletion in MS. The study's insights could have meaningful clinical implications, enhancing diagnostic precision and guiding therapeutic strategies for MS management.
Disclosure: Nothing to disclose.

Muscle and neuromuscular junction disorder 3

EPR-295 | Improvement in myasthenia gravis-specific outcome subdomain scores with zilucoplan: RAISE-XT 120-week post hoc analysis

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Background and aims: In the Phase 3 RAISE study (NCT04115293), zilucoplan, a complement component 5 inhibitor, demonstrated clinically meaningful improvements in

Myasthenia Gravis Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) total scores versus placebo in patients with anti-acetylcholine receptor antibody-positive generalized myasthenia gravis. Improvements were sustained during long-term use in the ongoing open-label extension, RAISE-XT (NCT04225871). Treatment may have differential effects across different muscle groups; this post hoc analysis evaluated the effect of zilucoplan on MG-ADL and QMG subdomain scores.

Methods: Patients who completed a qualifying double-blind study (NCT03315130/RAISE) could enter RAISE-XT to self-administer once-daily subcutaneous injections of zilucoplan 0.3mg/kg. Mean changes from double-blind baseline to Week 120 in MG-ADL and QMG subdomain scores (ocular, bulbar, respiratory and limb/gross motor) in patients with baseline scores $>=1$ in that subdomain were assessed post hoc (interim data cut-off: 11 November 2023).

Results: Overall, 200 patients entered RAISE-XT; 183 received placebo or zilucoplan 0.3mg/kg in the double-blind studies. At Week 120, mean (standard error [SE]) change from baseline (CFB) was −7.14 (0.44; $n=86$) for MG-ADL and −9.84 (0.65; $n=83$) for QMG total scores. Mean (SE) CFB in MG-ADL subdomain scores were: ocular, −1.37 (0.27; $n=41$); bulbar, −1.32 (0.32; $n=22$); respiratory, −0.07 (0.11; $n=30$); and limb/gross motor, −0.87 (0.17; $n=39$). Mean (SE) CFB in QMG subdomain scores were: ocular, −2.52 (0.30; $n=52$); bulbar, −1.00 (0.45; $n=16$); respiratory, −0.06 (0.18; $n=33$); and limb/gross motor, −4.27 (0.43; $n=79$).

Conclusion: Treatment with zilucoplan for up to 120 weeks demonstrated sustained improvements in all MG-ADL and QMG subdomain scores.

Disclosure: This study was funded by UCB. Babak Boroojerdi, Fiona Grimson and Natasa Savic are employees and shareholders of UCB. Full disclosure of all industry relationships will be made during congress presentation if accepted.

EPR-296 | Centers of excellence: Establishing a harmonized, holistic approach for managing Pompe disease with gene therapy

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Background and aims: Emerging gene therapies have substantial logistical and clinical challenges requiring specialized centers with defined protocols. A scientific steering committee of 8 European experts deliberated the requirements for establishing centers of excellence (CoEs) for Pompe disease capable of incorporating gene therapy into patient management.

Methods: A modified think-tank approach was used to develop a consensus based on nominal group techniques, whereby discussions were led by a chairperson and informed by qualitative research (Figure 1).

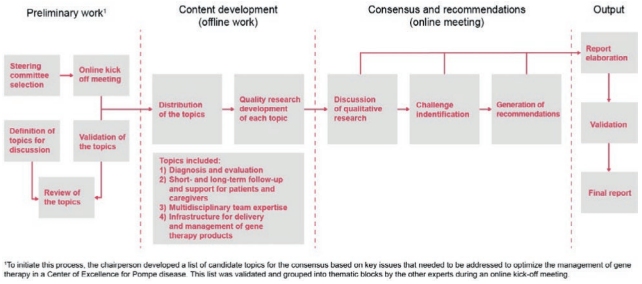

FIGURE 1 Methodological process used to develop the consensus.

Results: Improving the diagnosis and evaluation of Pompe disease is crucial for optimizing patient management and ensuring timely access to treatment. The committee recommended expanding newborn screening programs for infantile-onset Pompe disease and developing and implementing protocols for presymptomatic late-onset Pompe disease follow-up. A specialized multidisciplinary team trained in Pompe disease and gene therapy management is necessary to manage all stages of the patient's journey effectively (Figure 2). Pre-gene therapy assessments were recommended to mitigate risks. During gene therapy infusions, patients are recommended to undergo continuous vital sign monitoring and be hospitalized for up to 1 week. Post-gene therapy guidelines encompass corticosteroid immunosuppression, monitoring of adverse events (including hepatoxicity, troponin-I levels, thrombocytopenia, and thrombotic microangiopathy), and monitoring of Pompe disease (eg, functional assessments, muscle and cardiac magnetic resonance imaging every 6–12 months, and patient-reported outcomes). CoEs may need infrastructure upgrades to meet standard operating procedures for gene therapy products.

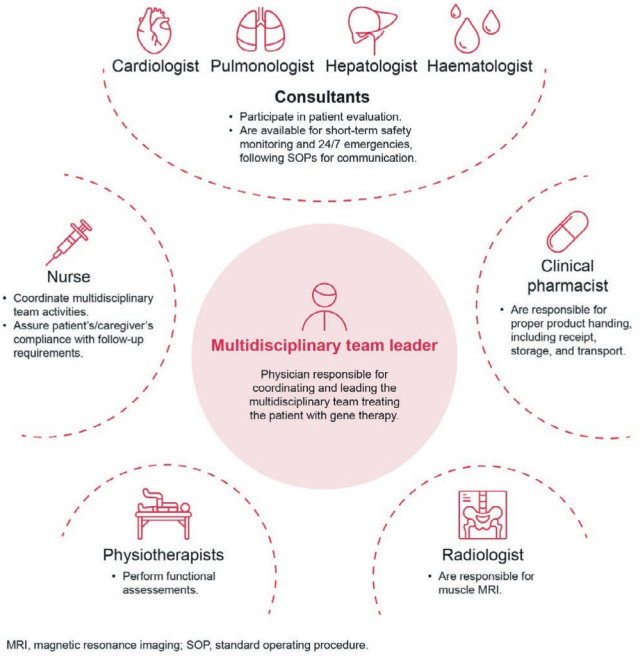

FIGURE 2 Multidisciplinary team profiles recommended by the experts for a center of excellence specializing in gene therapy for Pompe disease.

Conclusion: Successful implementation of gene therapy for Pompe disease requires a coordinated multidisciplinary effort to overcome existing gaps in knowledge, infrastructure, and care delivery.

Disclosure: Medical writing support was provided by Bassaam Mulk, PharmD, of Alpha (a division of Prime, Knutsford, UK), funded by Astellas. The authors disclose: BS: research grants from AMDA Foundation, Amicus, EU Horizon programs ComPaSS and PaLaDIn, Marigold Foundation, Roche Diagnostics; honoraria from Alexion, Amicus, Argenx, Astellas, Kedrion, Sanofi; and scientific advisorship for Amicus, Alexion, Astellas, Sanofi, Taysha. CDG: research grants from UCB, Pretzel Therapeutics; honoraria from Amicus, Sanofi, Astellas, Roche, UCB; and consulting fees from Amicus, Sanofi, Pretzel, UCB. PL: research grants from Amicus, Sanofi; advisory boards for Amicus, Astellas, Sanofi; honoraria from Amicus; and meeting attendance/travel support from Amicus, Sanofi. AH: Nothing to disclose. PG: consulting fees from BioMarin, Travere Therapeutics; honoraria from BioMarin; and share ownership in Bloomsbury Genetic Therapies; none in relation to the submitted work. AK-P: research grants from Biogen, Kedrion, Sanofi; honoraria from Alexion, AstraZeneca, Biogen, CSL Behring, Kedrion, Novartis, Roche, Takeda, UCB; meeting attendance/travel support from Alexion, AstraZeneca, Biogen, CSL Behring, Novartis, Roche, Takeda, UCB; and scientific advisorship for Merck. AT: consulting fees from Astellas, Roche. JV: research grant from Novo Nordisk Foundation; consulting fees/advisory boards from Dyne Therapeutics, Roche, Sanofi; and honoraria from Alexion, Edgewise Therapeutics, Janssen, UCB.

EPR-297 | Concomitant immunosuppressive therapy use with Ravulizumab: Analysis of a generalized myasthenia gravis global registry

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Background and aims: High-dose and long-term use of oral corticosteroids (OCS), including concomitant immunosuppressive therapies (con-ISTs), may be associated with short- and long-term adverse events and other health risks. The global MG SPOTLIGHT Registry (NCT04202341) assesses clinical practice outcomes with ravulizumab and eculizumab in adults with anti-acetylcholine receptor antibody-positive (AChR-Ab+) generalized myasthenia gravis (gMG). Here we describe changes in con-IST use after ravulizumab initiation.

Methods: This analysis included patients treated with ravulizumab for ≥6mo with available con-IST (azathioprine, mycophenolate mofetil, intravenous immunoglobulin/plasma exchange, methotrexate, and OCS) data. Descriptive analyses characterized treatment changes after ravulizumab initiation. No adjustment for covariates was performed. Safety was assessed in all patients.

Results: As of 01Jul2024, data from 44 patients fulfilled inclusion criteria for analysis (male: 70.5%; mean ± SD age at enrolment: 68.3 ± 13.0yrs; mean ± SD ravulizumab treatment duration: 1.3 ± 0.8yrs). At ravulizumab initiation, 19/44 (43.2%), 13/44 (29.5%), and 1/44 (2.3%) patients were receiving 1, 2, and ≥3 con-ISTs, respectively. Thereafter, 10/33 (30.3%) patients discontinued ≥1 con-IST, with 3/10 (30%) and 8/10 (80%) patients discontinuing within 3mo and 6mo of ravulizumab initiation, respectively. Following ravulizumab treatment, the number of patients receiving ≤5 and ≤10 mg/day OCS increased from 11/26 (42.3%) and 16/26 (61.5%), respectively, to 14/26 (53.8%) and 20/26 (76.9%) 3mo after ravulizumab initiation and 16/26 (61.5%) and 20/26 (76.9%) 6mo after ravulizumab initiation. Ravulizumab was well tolerated, consistent with previous analyses and clinical trial data.

Conclusion: Reduced con-IST and OCS burden was observed in patients with AChR-Ab+ gMG treated with ravulizumab in clinical practice, supporting a steroid-sparing role for ravulizumab.

Disclosure: RJN: research suppt/consultant/advisor: Alexion, Annexon, argenx, Cabaletta, Cour, Genentech, Grifols, Immunovant, MGFA, Momenta, NIH, Ra, S.A., Viela. AAH: research suppt: Alexion, AstraZeneca Rare Disease, argenx, Cabaletta, Genentech, Immunovant, Pfizer, Regeneron, UCB, Viela. AM: research suppt/speaker/consultant: Alexion, AstraZeneca Rare Disease, argenx, Octapharma, Grifols, Hormosan, Janssen, UCB; ad board chairman: German Myasthenia Gravis Society. CAS: ad board/speaker: Alexion, AstraZeneca Rare Disease, argenx, CSL Behring. LZ,CL,AY:employees/stock (options):Alexion, AstraZeneca Rare Disease. MTP: ad board: Alexion, AstraZeneca Rare Disease, Amgen, argenx, Catalyst, CSL Behring, Immunovant, UCB. GC:consultant/data&safety monitoring/ad boards:AI Therapeutics, Alexion, AstraZeneca Rare Disease, AMO, Antisense Therapeutics, Applied Therapeutics, AveXis, Avotres, Biogen, BMS, Clene Nanomedicine, Clinical Trial Solutions, CSL Behring, Entelexo, Genentech, Genzyme, GW Pharma, Hoya, Horizon Pharma, Immunic, Immunosis, Karuna, Kezar Life Sciences, Klein Buendel, Linical, Mapi, Merck/Serono, Mitsubishi Tanabe, NHLBI, Novartis, Opko Biologics, Perception Neuroscience, Protalix, Prothena, Reata, Regeneron, Roche, S.A., SAB Bio, Teva, UT Southwestern, UPenn, Visioneering Technologies. AJG: honoraria: Alexion, AstraZeneca Rare Disease, argenx, Janssen, UCB. PN:research/ad boards/data monitoring chair/speaker:Alexion, AstraZeneca Rare Disease, argenx, Momenta/Janssen, PCORI, Ra, Sanofi, UCB.

EPR-298 | Overcoming challenges in digital biomarker collection for myasthenia gravis: Insights from the ME&MGopen study

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Background and aims: Generalized myasthenia gravis (gMG) is a rare neuromuscular disorder causing fluctuating muscle weakness. Digital biomarkers (dBMKs) enable remote symptom tracking with potential benefits for gMG management, but challenges related to data quality and adherence remain. The ME&MGopen study evaluates the feasibility of using a smartphone app (ME&MGopenTM) to collect dBMKs that measure gMG symptoms under real-world conditions.
Methods: The decentralized ME&MGopen study enrolled 236 anti-acetylcholine receptor antibody-positive patients, with 125 included in analyses after one-year follow-up. ME&MGopenTM provided monthly tests to assess dBMKs for ptosis, limb fatigability, dysarthria, and respiratory impairment. DBMKs were compared with human-assigned annotations to evaluate precision and identify improvements. Adherence, satisfaction and perceived usefulness were assessed.
Results: The patients (70% female) spanned diverse gMG severity (MGFA Class II: 21%, III: 61%, IV: 18%), with mean age of 59 ± 16 years, and disease duration from symptom onset of 12 ± 13 years. Across > 1500 data points in each test, most data met quality criteria (% of tests meeting criteria: ptosis = 85%, dysarthria = 94%, respiratory = 94%, upper limb = 74%, lower limb = 82%). Correlation coefficients between dBMKs and manual annotations exceeded 0.7, indicating high accuracy. Factors affecting app performance were identified: arm compensation (upper limb test), face positioning (ptosis test). After one year, > 65% of patients remained adherent, most showing interest in ME&MGopenTM.
Conclusion: These data highlight the feasibility of dBMKs collection in gMG, addressing real-world challenges in a broad population and revealing opportunities for app improvements to support its ongoing validation study.
Disclosure: C.Barnett-Tapia: Research funding (paid to her institution) (Ad Scientiam, Alexion, Cartesian Therapeutics, US Department of Defence, Muscular Dystrophy Canada, MGNet, Grifols and Octapharma); Honoraria (consulting and/or Advisory board) fees (AcademicCME, Alexion AZ Rare Disease, argenx, Sanofi, Novartis, UCB Pharma and Janssen). S.Lehnerer has received speaker or consultancy honoraria or financial research support (paid to his institution) from Alexion, argenx, Biogen, Hormosan, HUMA, Johnson & Johnson, Merck, UCB and Roche. S.Bieuvelet, L.Carment, C.Gorin, N.Pesic-Heuvrard, D.Ravindra, N.Sellami, S.Zinaï: employees of Ad Scientiam. B.Dutta, A.Yegin: employees of Alexion Pharmaceuticals Inc. J.F.Howard: Research funding (paid to his institution) (Alexion AstraZeneca Rare Disease, argenx, Cartesian Therapeutics, Centers for Disease Control and Prevention, MGFA, Muscular Dystrophy Association, NIH, NMD Pharma, PCORI, UCB Pharma); honoraria/consulting fees (AcademicCME, Alexion AstraZeneca Rare Disease, Amgen, argenx, Biohaven Ltd, Biologix Pharma, CheckRare CME, F. Hoffmann-LaRoche Ltd, Horizon Therapeutics plc CoreEvitas, Curie.bio, Medscape CME, Merck EMD Serono, NMD Pharma, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, UCB Pharma, Zai Labs); non-financial support (Alexion AstraZeneca Rare Disease, argenx, Biohaven Ltd. Cartesian Therapeutics, Toleranzia AB, UCB Pharma and Zai Labs).

EPR-299 | The role of antisense oligonucleotides in Duchenne muscular dystrophy: A comprehensive meta-analysis

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Background and aims: Duchenne muscular dystrophy (DMD) is a severe X-linked disorder caused by mutations in the DMD gene, leading to dystrophin deficiency and progressive muscle degeneration. Antisense oligonucleotides (AONs) are a promising therapeutic strategy that induces exon skipping to restore the DMD reading frame, enabling production of functional dystrophin. Despite encouraging results, variability in outcomes highlights the need for comprehensive evaluation.
Methods: A systematic search of PubMed, Embase, Cochrane Library, and ClinicalTrials.gov identified preclinical and clinical studies published up to 2024. Eligible studies assessed AON therapies targeting exons 44, 45, or 51. Data were synthesized following PRISMA guidelines, and study quality was evaluated using risk of bias tools.
Results: Thirty-five studies (20 preclinical and 15 clinical trials) were included. Preclinical models showed dystrophin restoration levels of 30%–45% of normal, with significant improvements in muscle strength (mean increase: 40%, 95% CI: 32%–48%, $p < 0.001$). Clinical trials demonstrated dystrophin restoration levels of 5%–15%, accompanied by functional gains in the 6-minute walk test (mean increase: 25 meters, 95% CI: 15–35 meters, $p < 0.01$). Safety profiles were favorable, with common adverse events including mild injection site reactions and transient creatine kinase elevations. Subgroup analyses indicated improved outcomes with early treatment and optimized dosing.
Conclusion: AON therapies offer significant potential for treating DMD, achieving meaningful dystrophin restoration and functional improvements with manageable safety concerns. Further refinement of AON chemistries and delivery systems is essential to maximize therapeutic impact. These findings reinforce the role of AONs as a key pillar in the evolving landscape of DMD therapy.
Disclosure: Nothing to disclose.

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Background and aims: The global MG SPOTLIGHT Registry (NCT04202341) collects data on the real-world clinical safety/effectiveness of eculizumab and ravulizumab, complement component 5 (C5) inhibitor therapies (C5ITs), in adults with generalized myasthenia gravis (gMG). Here, we assess changes in MG Activities of Daily Living (MG-ADL) subdomain scores after C5IT initiation.

Methods: MG-ADL subdomain scores were assessed in Registry patients who received eculizumab (eculizumab subgroup), ravulizumab (ravulizumab subgroup), or transitioned from eculizumab to ravulizumab (switch subgroup) with data available prior to C5IT initiation and during treatment.

Results: This analysis (data cutoff: 01Jul2024) includes 178 Registry patients (male: 55.7%; mean ± SD age at MG diagnosis: 54.7 ± 19.0yrs) with 89, 49, and 40 patients in the eculizumab, ravulizumab, and switch subgroups, respectively. Statistically significant reductions ($p < 0.05$) in mean scores were observed for all MG-ADL subdomains after C5IT initiation (Figure 1). The proportions of patients with complete or partial improvement in individual MG-ADL subdomains during C5IT treatment were similar between the eculizumab and ravulizumab subgroups: 60.7% and 63.3% (ocular), 58.4% and 59.2% (bulbar), 51.7% and 49.0% (limbs), and 33.7% and 26.5% (respiratory), respectively. Among the switch subgroup, the proportions of patients with complete or partial improvement in individual subdomains were 67.5% (ocular), 67.5% (bulbar), 65.0% (limbs), and 45.0% (respiratory) at last assessment during ravulizumab treatment.

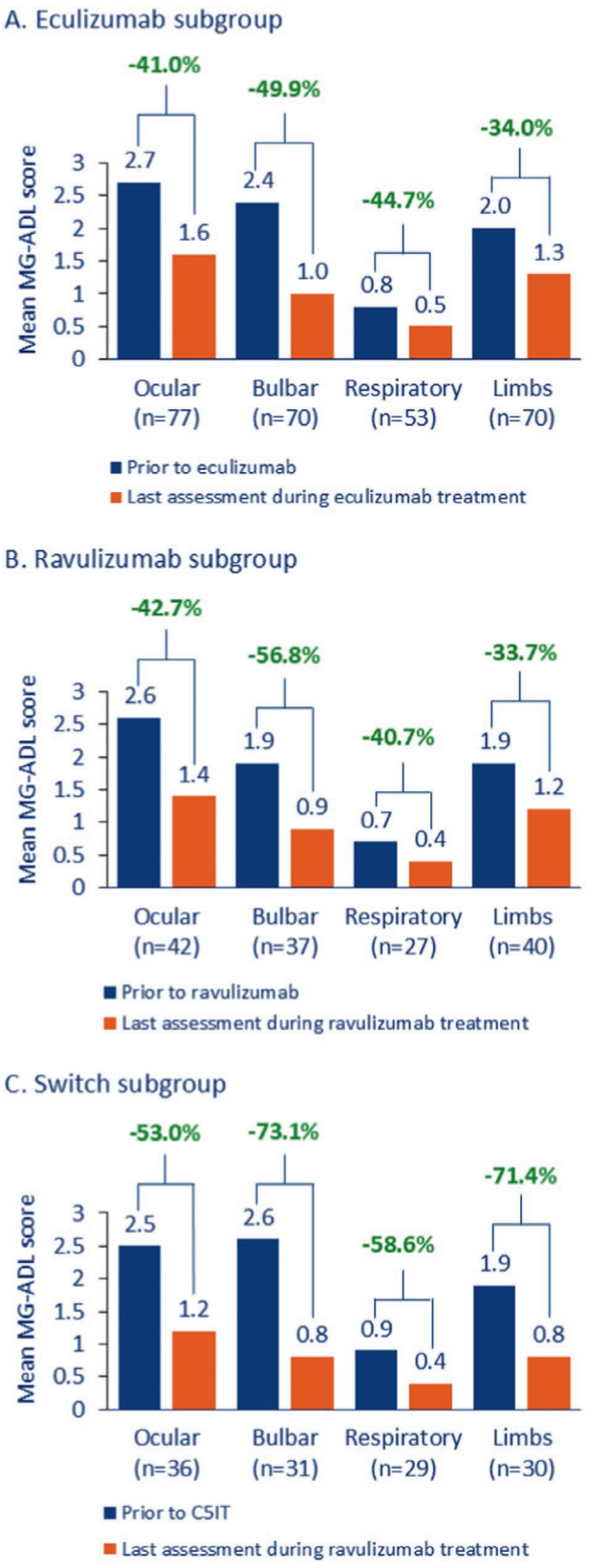

FIGURE 1 Change in MG-ADL subdomain scores after C5IT initiation. For each subdomain, *n* represents patients with nonmissing scores at both timepoints. Percent change in scores calculated for patients with nonzero scores prior to C5IT initiation. Max subdomain scores: 6 (ocular, limbs), 9 (bulbar), 3 (respiratory).

Conclusion: These results from clinical practice show the broad benefit of complement C5 inhibition with eculizumab and ravulizumab in improving ocular, bulbar, respiratory, and limb function as indicated by MG-ADL subdomain score in patients with gMG.

Disclosure: VJ: consultant/advisor/principal site investigator (PI): Alexion, AZ Rare Disease, Accordant, argenx, Immunovant, Janssen. SPM: consultant: AbbVie, Alexion, argenx, Catalyst, Grifols, Kabafusion, Supernus, UCB. FS: honoraria/consultant/PI: Alexion, Alexis, Amgen, argenx, Biogen, Dianthus, Genpharm, Johnson&Johnson, Leadiant, Lexeo, MedPharm, Medison, Neopharm Israel Pharma, Novartis, Prilenia, Reata, Remegen, Roche, Sandoz, Sanofi, Takeda, UCB, Zai Lab. AJG: honoraria: Alexion, AZ Rare Disease, argenx, Janssen, UCB. JMW: consultant: Alexion, AZ Rare Disease, Biogen, BMS, Teva. LZ, AY, CL: hold stock/options in AZ. GC: consultant/advisor: AITher., Alexion, AZ Rare Disease, AMO Pharma, Antisense Ther., Applied Ther., AveXis, Avotres, Biogen, BMS/Celgene, Clene Nanomedicine, Clinical Trial Solutions, CSL Behring, Entelexo Biother., Genentech, Genzyme, GW Pharma, Hoya Corp, Horizon Pharma, Immunic, Immunosis, Karuna, Kezar Life Sciences, Klein Buendel, Linical, Mapi Pharma, Merck/Serono, Mitsubishi Tanabe, NHLBI (Protocol Review Committee), Novartis, Opko Biologics, Perception Neurosci., Protalix BioTher., Prothena Biosci., Reata, Regeneron, Roche, SAB Biother., Sanofi-Aventis, Teva, UTSouthwestern, UPenn, Visioneering Technologies JA: speaker/consultant/PI: Alexion, argenx, UCB Pharma, Janssen, Amgen. RT: speaker/consultant/PI: Amylyx, Apellis, Alexion, Biogen, Cytokinetics, Mitsubishi Tanabe.

EPR-301 | Comparative efficacy of nipocalimab with other FcRn blocker therapies in generalized myasthenia gravis

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Background and aims: Nipocalimab demonstrated improved and sustained efficacy on Myasthenia Gravis Activities of Daily Living (MG-ADL) versus placebo (VIVACITY-MG3, NCT04951622) in generalized myasthenia gravis (gMG). Without available head-to-head comparisons, we indirectly compared nipocalimab efficacy versus other FcRn blockers, efgartigimod and rozanolixizumab, as measured by change from baseline (CFB) on MG-ADL.

Methods: Data were drawn from published registrational trials. Efgartigimod and rozanolixizumab have symptom-based cyclic dosing and nipocalimab has biweekly dosing. Indirect treatment comparisons (ITCs) were conducted using a placebo-anchored Bucher method to compare efficacy onset using 1-week timepoint, and for consistency of disease control, comparisons were at 8-weeks for efgartigimod (1-cycle duration) and 14-weeks for rozanolixizumab (final visit data reported). Unanchored population-adjusted indirect comparisons (without placebo) were also conducted given cross-trial differences in background standard-of-care. Differences <0 favored nipocalimab for all comparisons.

Results: Bucher Mean CFB difference [95% confidence interval (CI)] was comparable at 1-week versus efgartigimod [-0.04(-1.21,1.13)] and rozanolixizumab [7mg/kg = -0.11(-0.98,0.76); 10mg/kg = -0.02(-0.92,0.89)]. MG-ADL CFB was numerically greater versus efgartigimod at 8-weeks [-1.02(-2.51,0.47)] and significantly greater versus rozanolixizumab at 14-weeks [7mg/kg = -1.30(-2.40,-0.20), $p=0.021$; 10mg/kg = -1.40(-2.47,-0.34), $p=0.01$]. Unanchored ITCs showed statistically significant mean differences (95%CI) favoring nipocalimab versus efgartigimod at 8-weeks [-2.50(-4.02,-0.98), $p=0.001$] and versus rozanolixizumab at 14-weeks [7mg/kg = -3.36(-4.75,-1.96), $p<0.001$; 10mg/kg = -3.68(-6.18,-1.18), $p=0.004$].

Conclusion: Nipocalimab demonstrated comparable rapid onset of action and indicated favorable consistency of disease control versus symptom-based cyclic-dosed FcRn blockers. Future studies should investigate long-term sustained disease control, an essential consideration in managing a chronic condition like gMG.

Disclosure: S. Jacob has served as an international advisory board member or has been in the data monitoring committee for clinical trials for Alexion, Alnylam, Argenx, Johnson and Johnson, Immunovant, Merck, Novartis, Regeneron and UCB pharmaceuticals, is currently an expert panel member of Myasthenia Gravis consortium for Argenx pharmaceuticals and has received speaker fees from Argenx, Eisai, Terumo BCT and UCB pharmaceuticals. He is also a board member (trustee) of the UK myasthenia patient charity, Myaware. M. Hashim, K. Gandhi, R. Slowik, A. C. El Khoury, M. Ait-Tihyaty, M. J. Keng, and X. Lin are employees of Johnson and Johnson and may hold stock/stock options of Johnson and Johnson. B. Hutton has previously received honoraria from EVERSANA and Evidinno Outcomes Research Inc. for provision of methodologic advice related to the conduct of systematic reviews, meta-analyses and ITCs. C. Drudge and S. Singh are employees of EVERSANA. EVERSANA receives consultancy fees from pharmaceutical and device companies, including Johnson and Johnson. N. E. Gilhus has received consultative or speaker's honoraria from Johnson and Johnson, UCB, Argenx, Alexion, Merck, Dianthus, Amgen, Roche, Grifols, Immunovant, Huma, Denka, and Takeda.

EPR-302 | Cross-reactivity of glutamate transporter EAA1 and truncated EAA2 isoforms revealed via structural neuroinformatics

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Background and aims: The glutamate transporter subfamily is essential for maintaining neurotransmitter homeostasis and its dysregulations have been linked to the etiologies of many conditions, including neurodegenerative diseases. Our previous study indicated an inhibitory potential of truncated isoforms on glutamate transporter bio-assembly. However, EAA2 interactions

showed twofold higher binding affinity than EAA1 interactions (approximately -30 and -16 kcal/mol, respectively). In this study, we aimed to further understand these dynamics by focusing on the cross-reactions between EAA1 and isoforms of EAA2.

Methods: Utilizing a multi-level computational approach, including gene-centric isoform mapping and AlphaFold structural predictions, we identified several truncated isoforms of EAA2. Their complexes with canonical EAA1 were subjected to a wide range of multimer predictions/docking analyses, 50ns molecular dynamics simulations, and evolutionary coupling analyses. Accordingly, the root-mean-square-fluctuation (RMSF), Poisson-Boltzmann Surface-Area (MMPBSA) and trajectory analyses were conducted.

Results: Our findings reveal that EAA2 truncated isoforms (UniProt-IDs: A0A2R8Y642 and C9J9N5) form stable complexes with the canonical EAA1, with binding free energies of -23.16 and -22.83 kcal/mol after 50ns simulations (Figures 1 and 2). Subsequently, evolutionary conservation studies revealed these isoforms were not only structurally conserved but also demonstrates a significant evolutionary coupling with EAA1 (Figure 3). The conserved binding interfaces suggest a coevolutionary relationship that likely influences transporter oligomerization.

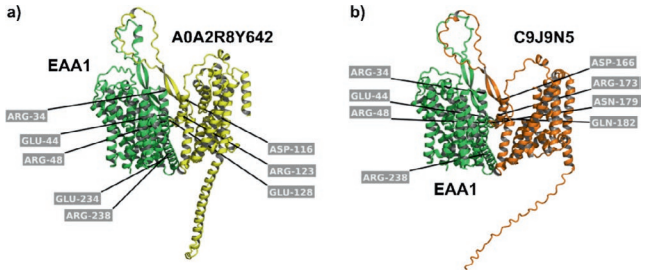

FIGURE 1 Heterodimeric complexes of EAA1 canonical structure and EAA2 truncated isoforms a) A0A2R8Y642 (yellow) and b) C9J9N5 (orange). The interface surface is displayed with the eight highest energy-contributing residues labeled.

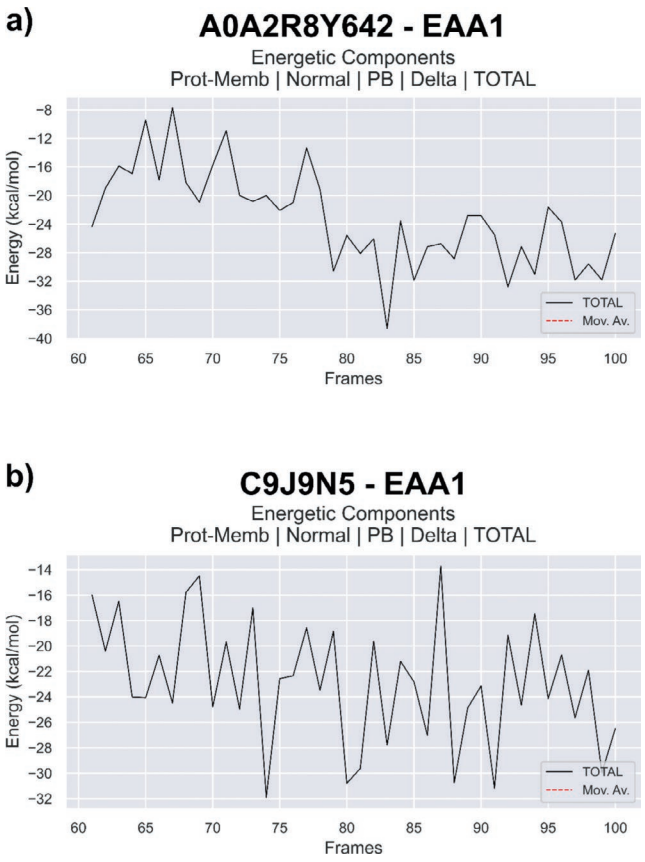

FIGURE 2 MMPBSA binding energy calculations of complexes a) A0A2R8Y642-EAA1 and b) C9J9N5-EAA1 through 30-50ns equilibrated molecular dynamics simulations.

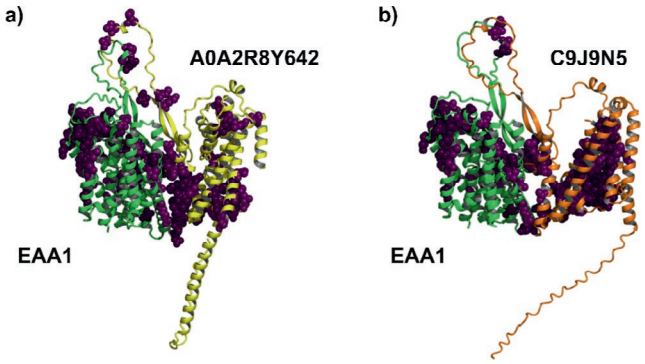

FIGURE 3 Evolutionary coupling analysis of EAA1 canonical protein, EAA2 truncated isoforms a) A0A2R8Y642 (yellow) and b) C9J9N5 (orange). A strong co-evolution (colored purple) of the residues contributing to the binding interfaces.

Conclusion: These findings not only deepen our understanding of glutamate transporter modulation but also identify promising therapeutic targets for neurological disorders. The study emphasizes the critical role of cross-reactivity in transporter function and provides a foundation for future research into their therapeutic and diagnostic potential.

Disclosure: Nothing to disclose.

EPR-303 | Computational models for new patient stratification strategies of neuromuscular disorders: The CoMPaSS-NMD project

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Background and aims: Hereditary Neuromuscular Diseases (HNMDs) are genetic disorders leading to progressive muscle wasting and weakness, affecting 111.9/100,000 individuals in the EU. Despite advances in diagnostics, over 60% of patients remain molecularly unsolved or misdiagnosed, hindering prognosis and treatment development. Artificial Intelligence (AI) offers transformative opportunities for data integration and precision diagnosis.
Methods: CoMPaSS-NMD employs AI-based tools for patient stratification through deep integration of clinical, genetic, histopathological, and imaging data. The study consists of: 1. Retrospective study: 3,900 genetic, 2,000 histopathological, 2,000 MRI existing data from European centers have been analyzed through unsupervised machine learning (ML) to develop stratification algorithms. 2. Prospective study: 500 undiagnosed HNMD patients undergoing standardized clinical, whole genome sequencing, histological, and MRI evaluations to generate new patient stratification means established on the ML-based algorithms. 3. Creation of CoMPaSS-NMD ATLAS as public repository of clinical, genetic, histopathological, and imaging data.
Results: Standard operating procedures have been developed to acquire robust datasets of uniform multimodal data. A new ranking tool for genetic variants has been proposed. Algorithms for histopathological and MRI analysis have been developed, addressing challenges such as data variability and identification of cluster-specific signatures. The platform of the ATLAS is a novel tool to address the fragmentation of information leading to delays in diagnosis and incomplete knowledge of multifaceted diseases.
Conclusion: CoMPaSS-NMD leverages AI to revolutionize the diagnosis of HNMDs, beyond the one gene-one phenotype paradigm. This multidimensional approach wil boost diagnostic rates by 30%, optimize healthcare strategies, and significantly improve the lives of patients and caregivers.
Disclosure: This project has received funding from the European Union (Horizon 2020) under Grant Agreement n° 101080874.

EPR-304 | Exploring the lived experiences and needs of people with generalized myasthenia gravis: A mixed methods study

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Background and aims: Generalized myasthenia gravis (gMG) is an autoimmune neuromuscular disorder with profound everyday impacts. This study aimed to understand the lived experiences and needs of people with gMG (PWgMG).
Methods: PWgMG and specialist healthcare professionals (HCPs) were interviewed to inform development of a survey of PWgMG (themes: pre-diagnosis, diagnosis, treatment, and living with gMG) in Germany, Italy, UK, and US. Interview data underwent thematic analysis. Statistics are descriptive.
Results: Fourteen PWgMG (71% female) and 10 neuromuscular specialists/neurologists were interviewed; 90 PWgMG were surveyed (64% female). PWgMG experienced several symptoms pre-diagnosis (Figure 1) and most (89%) reported daily life impacts. Time to seeking medical advice and diagnosis varied by country, symptoms, and age. PWgMG typically visited 2–3 HCPs pre-diagnosis; 25–65% were initially misdiagnosed, most commonly with mental health (40%) and neurological disorders (30%). Patients approached patient organizations (POs) for information at diagnosis more commonly in UK (68%) than Italy (26%), Germany (11%), or US (10%). PWgMG wanted PO resources to facilitate shared decision-making with HCPs and increased gMG awareness among primary care physicians (PCPs). At treatment initiation, side-effects and long-term safety were the most common concerns of PWgMG (54%). Despite treatment, gMG continued to impact daily life (Figure 2). HCPs identified needs for improved HCP/PCP awareness of gMG and reported challenges in MG-management related to insurance, comorbidities, speed-of-action and side effects of treatment, and family planning.

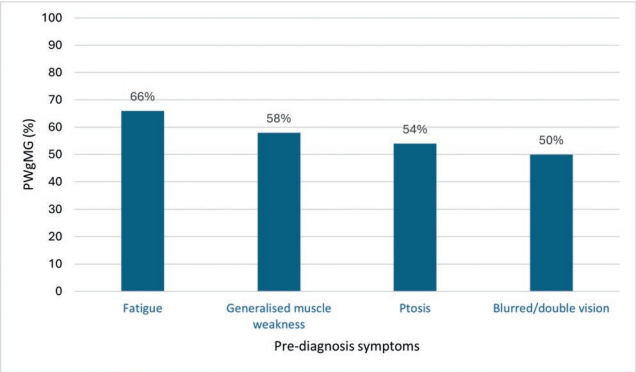

FIGURE 1 Symptoms experienced by PWgMG before diagnosis. N = 90. Symptoms reported by ≥50% of surveyed PWgMG shown.

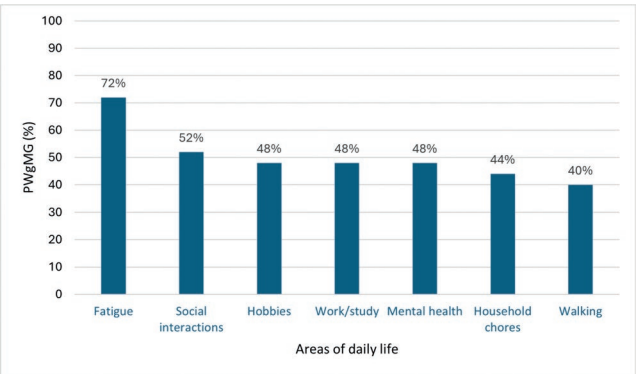

FIGURE 2 Areas of daily life 'always' or 'often' negatively affected by gMG despite treatment. N = 90. Areas of daily life impacted in ≥40% of surveyed PWgMG shown.

Conclusion: PWgMG have concerns around treatment side-effects/safety and experience limitations in daily activities. Resources to support shared decision-making and HCP communication are needed.

Disclosure: Acknowledgment: This study was sponsored by the healthcare business of Merck KGaA, Darmstadt, Germany (CrossRef Funder ID: 10.13039/100009945). Medical writing support was provided by Simon Stones, PhD, ISMPP CMPP™, of Amica Scientific, and funded by the healthcare business of Merck KGaA, Darmstadt, Germany. Author disclosures: Sophi Tatlock and Jana Raab are employees of the healthcare business of Merck KGaA, Darmstadt, Germany. Sophie Lehnerer has received speaker or consultancy honoraria or financial research support (paid to their institution) from Alexion, argenx, Biogen, Hormosan, HUMA, Johnson & Johnson, Merck KGaA, UCB, and Roche. Pushpa Narayanaswami has received research support from AHRQ, Alexion/AstraZeneca, Momenta/Janssen/J&J, PCORI, and Ra/UCB; has been involved in advisory boards/consultations with Alexion/AstraZeneca, Amgen, argenx, CVS, Dianthus, GSK, ImmuneAbs, Janssen/J&J, Novartis, Merck KGaA, Roche and UCB; is the Data Monitoring Committee Chair for argenx and NMD pharma, has served as DMC Chair for Sanofi; and receives royalties from Springer Nature. Kathryn Wiltz has received financial research support from Huma and Merck on previous work. Janet Smith is a paid adviser to the healthcare business of Merck KGaA, Darmstadt, Germany, unrelated to this study. Claudia Schlemminger has no financial conflicts of interest to disclose. They are a patient representative for the Gemeinsamer Bundesausschus.

EPR-305 | Efficacy of Nipocalimab in open-label extension in patients transitioned from placebo: Results from Vivacity-MG3 trial

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Background and aims: In the 24-week (W) double-blind phase-3 Vivacity-MG3 study (NCT04951622), nipocalimab+standard-of-care (SOC) demonstrated statistically significant and clinically meaningful improvements versus placebo+SOC in patients with generalized myasthenia gravis (gMG). After completing the double-blind phase, patients from placebo-arm may receive nipocalimab+SOC in ongoing open-label extension (OLE) to W24.

Methods: In OLE, 98 patients from placebo+SOC transitioned to nipocalimab+SOC. Data were collected up to OLE W24 (cut-off: 23-August-2024). Mean changes in MG-ADL and QMG scores from OLE baseline were evaluated. Within-group mean changes were examined using paired t-test. Percentage of patients achieving Meaningful Clinical Improvement (MCI >= 2-point within-patient improvement versus baseline in MG-ADL and sustained MCI (for >= 8W) and percentage-of-time spent in MCI were summarized.

Results: The mean (standard deviation [SD]) MG-ADL and QMG scores at OLE baseline were 6.33(3.37) and 13.47(5.70), respectively. Improvements in MG-ADL score were observed as early as OLE W2 in placebo+SOC patients transitioned to nipocalimab+SOC: mean (SD) change of −1.33(2.13), $n = 87$, $p < 0.001$, improving to −2.68(3.26), $n = 59$, $p < 0.001$ at OLE W24. At W24, 63.3% of patients achieved MCI, with 79.5% achieving it at any time during OLE phase; 51.1% of patients had sustained MCI. Similarly, as early as OLE W4, QMG improvement was observed with mean (SD) change of −2.65([3.95], $n = 79$, $p < 0.001$), continuing to −3.24([4.95], $n = 58$, $p < 0.001$) at OLE W24.

Conclusion: Placebo+SOC arm patients with gMG from Vivacity-MG3 who transitioned to nipocalimab+SOC exhibited improvements in MG-ADL as early as W2 after transition, with continued improvement through W24. This supports the potential of nipocalimab as an effective maintenance treatment option in this gMG population.

Disclosure: This work was funded by Johnson & Johnson. Kristl Claeys: Speaker/advisory board honoraria from Alexion, Alnylam, Amicus Therapeutics, argenx, Biogen, Ipsen, Johnson & Johnson Lupin, Pfizer, Roche, Sanofi-Genzyme, UCB, and Research funding from CSL Behring, Roche, Vertex. Maria Ait-Tihyaty, Kavita Gandhi, Ibrahim Turkoz, Zia Choudhry, Wim Noel, Charlotte Gary, and Sindhu Ramchandren: Employees of Johnson & Johnson, may hold stocks/stock options in Johnson & Johnson. Tuan Vu: MG related research or grant support from Alexion/AstraZeneca Rare Disease, Amgen, argenx, Cartesians, COUR, Dianthus, Johnson & Johnson, Immunovant, NMD Pharma, Regeneron, and UCB; consultant and/or speaker

bureau for Alexion, argenx, CSL Behring, Johnson & Johnson, ImmunAbs, and Dianthus.

EPR-306 | Efficacy of Nipocalimab in adult patients with moderate to severe ocular manifestations of gMG in phase 3 VIVACITY-MG3

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Background and aims: In generalized myasthenia gravis (gMG), 15-50% patients have ocular manifestations (ptosis, diplopia) limiting daily-activities and impacting quality-of-life. Nipocalimab+standard-of-care (SOC, nipocalimab) demonstrated sustained efficacy versus placebo+SOC (placebo) in VIVACITY-MG3 (NCT04951622). This analysis evaluated efficacy of nipocalimab versus placebo in the subgroup of patients with moderate-severe ocular manifestations (MSOM).

Methods: In this post-hoc analysis, MSOM was defined as baseline score of >=2-points on either diplopia or ptosis items of Myasthenia Gravis-Activities of Daily Living (MG-ADL) scale. Least-squares (LS) mean changes from baseline (CFB) to week 24 (W24) on the MG-ADL-ocular domain (MG-ADL-ocular) and total scores (MG-ADL-total) were analyzed using repeated measures models. Chi-square test statistics were used to evaluate the proportion of patients achieving meaningful within-person improvement (MWPI) of >=2-points at 24-weeks from baseline; logistic regression models were used to examine likelihood (OR) of achieving MWPI.

Results: At baseline, within MSOM subgroup, nipocalimab ($n=54/77$) and placebo ($n=51/76$) arms were comparable in mean age (52.5, 53.5 years), percentage of female patients (63%, 55%) and mean (Standard Deviation) MG-ADL-ocular (4.1[1.2]; 3.5[1.0]) and MG-ADL-total (10.1[2.8]; 9.4[1.9]) scores. At W24, the CFB LS mean differences (95%CI) for nipocalimab versus placebo were MG-ADL-ocular (-1.6[-2.6, -0.6]; -1.1[-2.0, -0.2]; $p=0.024$); and MG-ADL-total (-4.6[-5.4, -3.7]; -3.2[-4.1, -2.3], $p=0.010$), favoring nipocalimab. Greater proportion of patients achieved MWPI at W24 on MG-ADL-ocular (difference = 29.3%; OR = 3.6; $p=0.006$) and MG-ADL-total (difference = 24.4%; OR = 3.5; $p=0.01$), favoring nipocalimab.

Conclusion: Nipocalimab-treated patients with gMG and MSOM showed superior improvements on the MG-ADL-ocular and MG-ADL-total scores versus placebo-treated-patients and were significantly more likely to achieve MWPI at W24.

Disclosure: This work was funded by Johnson & Johnson. Kristl Claeys: Speaker/advisory board honoraria from Alexion, Alnylam, Amicus Therapeutics, argenx, Biogen, Ipsen, Janssen Pharmaceuticals, Lupin, Pfizer, Roche, Sanofi-Genzyme, UCB, and Research funding from CSL Behring, Roche, Vertex. Kavita Gandhi, Maria Ait-Tihyaty, Ibrahim Turkoz, Sheryl Pease, Charlotte Gary, Zia Choudhry, and Sindhu Ramchandren: Employees of Johnson & Johnson, may hold stocks/stock options in Johnson & Johnson.

EPR-307 | Analysis of long-term efficacy of nipocalimab in myasthenia gravis: Open-label extension of the Vivacity-MG3 trial

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Background and aims: New targeted treatments are needed to provide sustained disease control of generalized myasthenia gravis (MG). Nipocalimab+standard-of-care (SOC) demonstrated sustained efficacy over 24-weeks (W) in double-blind phase of the Vivacity-MG3 Phase-3 trial (NCT04951622); ongoing open-label extension (OLE) allows assessment of long-term efficacy of nipocalimab.

Methods: 98 patients from the Vivacity-MG3 nipocalimab+SOC arm transitioned from double-blind to OLE phase. Mean changes from double-blind baseline (CFB) in MG-ADL and QMG scores were computed for nipocalimab+SOC-treated patients at W24 and W48. Proportions of patients reaching Meaningful Clinical Improvement (MCI >=2-point within-patient improvement versus baseline in MG-ADL) were evaluated at post-baseline visits and W48. Proportions of patients with sustained response (MCI maintained for >=8W) were summarized. Similar analyses were conducted using QMG scores.

Results: The mean (standard deviation [SD]) MG-ADL and QMG scores at double-blind baseline (W0) were 9.51 (2.69) and 15.05 (4.80), respectively. The mean (SD) CFB in MG-ADL score in nipocalimab+SOC-treated patients was −4.46([3.59], $n=87$, $p<0.001$) at W24; improvement was maintained through W48 with a mean change of −5.56([3.72], $n=52$, $p<0.001$) in the OLE phase. 84.6% of the nipocalimab+SOC-treated patients achieved MCI at W48 and 93.9% at any time post-baseline. 77.6% of nipocalimab+SOC-treated patients sustained MCI for >=8W. Mean (SD) CFB in QMG score in nipocalimab+SOC-treated patients was −4.21([4.87], $n=81$, $p<0.001$) at W24; improvement was maintained through W48 with mean (SD) change in QMG score of −4.73([4.45], $n=47$, $p<0.001$) in the OLE.

Conclusion: Nipocalimab+SOC demonstrated significant and clinically meaningful efficacy at W24 from double-blind baseline. Disease control with nipocalimab+SOC was sustained up to 48-weeks.

Disclosure: This work was funded by Johnson & Johnson. Nicholas J. Silvestri: Consultant/advisor for Alexion, Amgen, Annexon, argenx, Immunovant, Johnson & Johnson, and UCB. Speaker for Alexion, argenx, Takeda, and UCB. Maria Ait-Tihyaty, Kavita Gandhi, Ibrahim Turkoz, Zia Choudhry, Wim Noel, Charlotte Gary, and Sindhu Ramchandren: Employees of Johnson & Johnson, may hold stocks/stock options in Johnson & Johnson.

EPR-308 | A real-life experience with zilucoplan in AChR-seropositive generalized myasthenia gravis

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Background and aims: Myasthenia gravis is a rare chronic autoimmune disease affecting the post-synaptic membrane of the muscle junction characterized by debilitating, and potentially fatal, muscle weakness. Treatment options available for generalized myasthenia gravis (gMG) have grown in recent years with the introduction of new drugs, such as the complement factor C5 inhibitors. The objective of the Compassionate Use Program (GM0025IT) is to provide early access to Zilucoplan for gMG patients with a high unmet medical need and severe disease burden.
Methods: Zilucoplan was administered by daily subcutaneous self-injection as for protocol. Efficacy was assessed by using the MG-ADL scale and QMG. The patients' baseline therapy remained unchanged during the entire course of treatment.
Results: Fifteen patients (F/M 12/3, mean age 55 y) affected by AChR-seropositive gMG received Zilucoplan. A reduction in MG-ADL scores was observed after one week from the first injection compared to baseline (MG-ADL 10.4 ± 3.5) with a mean change of – 1,67 points (ranging from -4 to 0). The main change at W4 was – 3,8 points and – 7,27 points at W24. Regarding QMG, a reduction of -3,86 points was achieved at W4 and – 7,28 points at W24, compared to baseline (QMG 16.5 ± 5.7).

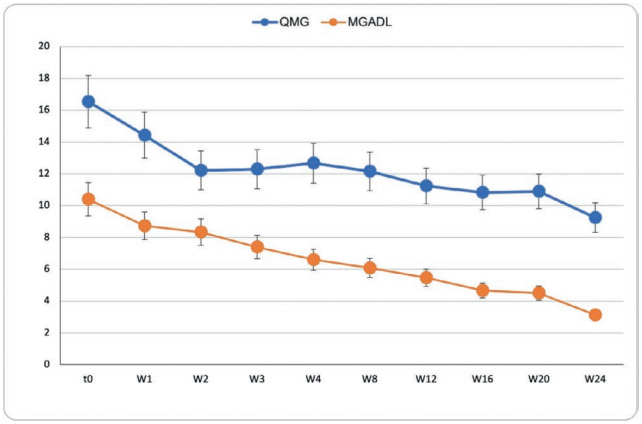

FIGURE 1 Treatment effect on the MG-ADL and QMG scales

TABLE 1 Patient demographics.

Variable	Zilucoplan (n=15)
Gender (F/M)	12/3
Ab-AChR+	15
Age	55.7±17.3
Previous Py use	15
Previous CS use	15
Previous NSIST = 0	0
Previous NSIST ≥1	15
Previous NSIST ≥2	3
Previous NSIST ≥3	0
Previous IVIG	14
Previous PLEX	5
Follow-up days	190.4
MG-ADL	10.4±3.5
QMG	16.5±5.7

AChR-Ab+ = anti-acetylcholine receptor antibody positive; PY = Pyridostigmine; CS = Corticosteroids; NSIST = Non-steroidal Immunosuppressants; MG-ADL = Myasthenia Gravis Activities of Daily Living scale; QMG = Myasthenia Gravis quantitative scale.

Conclusion: The decline in scores obtained testifies to the efficacy of treatment with Zilucoplan and the rapidity of its action onset. Also, Zilucoplan appears to be very easy to administer and has a favorable safety profile. Further data and longer observations are needed to confirm our data.
Disclosure: Nothing to disclose.

EPR-309 | A Bayesian ordinal transition model of Guillain-Barré syndrome (GBS) disability progression with anti-C1q treatment

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Background and aims: Guillain-Barré syndrome (GBS) is a complement-mediated peripheral neuropathy. In a double-blind, placebo-controlled phase 3 study (NCT04701164), ANX005 30 mg/kg rapidly inhibited C1q, demonstrating early and sustained improvements. Although the GBS Disability Scale (GBS-DS) tracks functional impairment, traditional analyses may overlook disability state transitions. We aimed to capture transitions in functional outcomes over time.
Methods: A Bayesian ordinal transition model with a first-order Markov transition structure was fit to the longitudinal ordinal GBS-DS data from the Phase 3 study (placebo, $n = 81$; 30 mg/kg, $n = 79$; 75 mg/kg, $n = 81$). Non-informative priors were used for all parameters. Baseline prognostic factors were used as covariates. The effect of treatment was allowed to vary over time by treatment group using splines. Conditional quantities were computed using covariate median values.
Results: ANX005 increased the number of visits spent in a good health status (GBS-DS 0 or 1) with a high probability (99.6%). Compared to placebo, ANX005 30 mg/kg increased the likelihood of transitioning to a better health state on the GBS-DS rapidly, starting in the first three weeks. The cumulative treatment effect assessed by model-based estimates of the probabilities of scores over time demonstrated a higher probability of having a good health status through 6 months of follow-up at each visit compared to placebo (Figure).

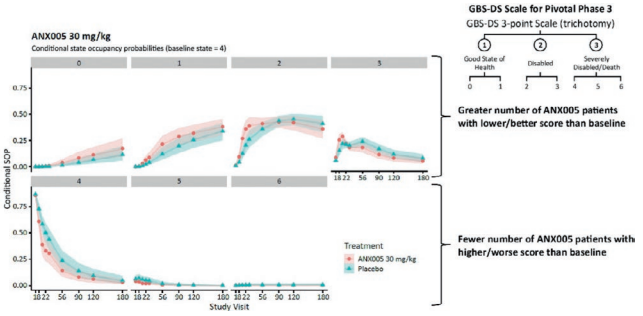

FIGURE 1 Conditional State Occupancy Probabilities (30 mg/kg) Baseline State = 4.

Conclusion: ANX005 30 mg/kg demonstrated rapid and sustained improvement, highlighting its potential benefit in GBS. This Bayesian ordinal transition model effectively uses the raw data, thereby increasing power, and presents a longitudinal view of treatment effect on disease progression compared to traditional cross-sectional methods.

Disclosure: The study was sponsored by Annexon Biosciences (Brisbane, CA, USA). PL: Employee and shareholder of Annexon Biosciences MR: Employee and shareholder of Annexon Biosciences HAK: Employee and shareholder of Annexon Biosciences ES: Consultancy/advisory role with Annexon Biosciences GM: Employee and shareholder of Annexon Biosciences KCG: Consultancy/advisory role with Annexon Biosciences, Argenx, Janssen, and Sanofi QDM: Consultancy/advisory role with Annexon Biosciences. ZI: Research funding from Fogarty International Center, National Institute of Neurological Disorders and Stroke of the National Institutes of Health, USA, and Annexon Biosciences. KAKA: No disclosures JN: Consultancy/advisory role with Annexon Biosciences PC: Employee and shareholder of Annexon Biosciences FEH: Consultancy/advisory role with Annexon Biosciences, Baylor Scott & White Research Institute, and Regeneron

EPR-310 | Long-term outcomes of steroid dosing regimens and withdrawal in myasthenia gravis: A single-center cohort study

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Background and aims: Corticosteroids (steroids) are the first-line immunotherapy for myasthenia gravis (MG). However, the optimal steroid dosing regimen and the effects of discontinuing immunotherapy remain unclear. This study aimed to investigate the impact of different steroid regimens and steroid withdrawal in MG with steroid monotherapy.

Methods: This is a cohort study based on a single-center prospective registry, including patients who achieved sustained minimal manifestations or better status with steroid monotherapy. The primary outcome was relapse. Group-based trajectory modeling (GBTM) identified distinct steroid regimens, and Cox proportional hazards models and propensity score matching (PSM) assessed the impact of regimens and steroid withdrawal.

Results: In 209 patients (median follow-up 54.0 months), 113 (54.1%) experienced relapse, and 65 (31.1%) discontinued steroids. GBTM identified three regimens: "High Start, Fast Taper" (Regimen 1), "Low Start, Slow Taper" (Regimen 2), and "Moderate Start, Gradual Taper" (Regimen 3). Compared to Regimen 1, Regimen 2 (HR = 0.15, 95% CI 0.07-0.32, $p < 0.001$) and Regimen 3 (HR = 0.28, 95% CI 0.15-0.53, $p < 0.001$) had significantly lower relapse risks. In patients who withdrew steroids, the median time to relapse was 7.0 (3.0, 22.0) months. After PSM, the steroid withdrawal group had a significantly higher 1-year relapse risk (HR = 1.58, 95% CI 1.03-2.44, $p = 0.039$) compared to the low-dose maintenance group.

Conclusion: High initial dose, rapid-tapering regimen increases relapse risk, while steroid withdrawal also significantly raises relapse risk compared to low-dose maintenance. Therefore, caution is advised when rapid tapering or discontinuing steroids in patients on steroid monotherapy.

Disclosure: Nothing to disclose.

EPR-311 | Evaluating the efficacy of nonviral gene delivery systems in DMD: A comprehensive meta-analysis

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[1]MME Foundation; [2]Newgiza University, Giza, Egypt; [3]Badr University in Cairo, Egypt

Background and aims: Duchenne muscular dystrophy (DMD) is a progressive neuromuscular disorder caused by mutations in the dystrophin gene, resulting in a complete absence of the dystrophin protein. Nonviral gene delivery systems have emerged as promising alternatives to viral vectors, offering reduced immunogenicity and improved safety profiles.

Methods: A systematic search of PubMed, Embase, Cochrane Library, and ClinicalTrials.gov identified relevant randomized controlled trials (RCTs), non-randomized studies, and preclinical research. Data were extracted and analyzed per PRISMA guidelines using R and Python. Risk of bias was assessed with the Cochrane Risk of Bias 2.0 and SYRCLE tools.

Results: The analysis included 20 studies with 1,325 participants and animal models. Nonviral systems, including liposomes, nanoparticles, and polymer-based carriers, significantly increased dystrophin expression (mean increase: 18.7%, 95% CI: 12.4–24.9%, $p < 0.001$). Functional outcomes, evaluated through grip strength and locomotion tests, improved significantly (mean increase: 2.6 points, 95% CI: 1.8–3.4, $p < 0.001$). Safety analysis showed a lower incidence of immune-related adverse events with nonviral systems (RR: 0.42, 95% CI: 0.29–0.59, $p < 0.001$) compared to viral vectors. Polymer-based carriers achieved the highest dystrophin expression, while lipid-based systems exhibited superior safety profiles.

Conclusion: Nonviral gene delivery systems demonstrate significant potential for dystrophin restoration, functional improvement, and enhanced safety in DMD therapy. Further research is needed to optimize delivery methods, dosing, and long-term outcomes to facilitate clinical application.

Disclosure: Nothing to disclose.

ABSTRACT

ePoster

Saturday, June 21 2025

Infectious Diseases

EPO-001 | Convulsivant status epilepticus over the course of HHV-6 encephalitis in a type 2 diabetic patient

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Background and aims: Human Herpes Virus 6 (HHV-6) is an omnipresent virus in the pediatric population, often associated with an exanthematic disease. HHV-6 encephalitis in immunocompetent adults is exceptional, with the main clinical and radiological features frequently resembling limbic encephalitis.
Methods: A 68-year-old patient with a history of type 2 diabetes, arterial hypertension, and hypercholesterolemia, presented to the emergency room for two new-onset bilateral tonic-clonic seizures (during the day of admission), confusion, fever, headache, photophobia (insidious progression over the last four days). Non-contrast brain computed tomography was unremarkable. Recent medical history included contact with a two-year-old who showed symptoms of acute upper respiratory tract infection. The patient also reported significant voluntary weight loss (approximately 13 kilograms in one month). The spinal tap revealed increased CSF (cerebrospinal fluid) protein levels (1,33g/L). CSF cultures were positive for HHV-6 and antiviral therapy with Ganciclovir was initiated. HIV (human immunodeficiency virus) serology was negative. Five days after admission, the patient developed convulsive status epilepticus and was transferred to Acute Critical Care where he received anti-seizure medication and required mechanical ventilation. Brain imaging by contrast magnetic resonance (performed six days after admission) revealed a T2/FLAIR hypersignal (gliotic) lesion in the central midbrain, but no abnormalities of the temporal lobes/limbic structures.
Results: The clinical progression was favorable after receiving anti-viral, supportive, and anti-seizure medication (no epileptic seizures and extubation after 5 days).
Conclusion: Although rare and most frequently associated with hematopoietic stem cell transplantation, HHV-6 primary infection/reactivation can cause severe neurological complications in adults, albeit sometimes lacking radiologic findings of limbing encephalitis.
Disclosure: Nothing to disclose.

EPO-002 | Early recognition of cerebral neuroschistosomiasis: Diagnostic and therapeutic insights in endemic regions

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Background and aims: Cerebral neuroschistosomiasis is a rare complication of Schistosoma mansoni infection, which is highly prevalent in Brazil, particularly in endemic regions like Pernambuco. - Although spinal cord involvement is more common, cerebral manifestations can occur and pose diagnostic challenges. - This study discusses the diagnostic and therapeutic challenges of cerebral neuroschistosomiasis, illustrated by a unique clinical case.
Methods: This study analyzes the clinical presentation, diagnostic process, imaging findings, and therapeutic outcomes of a rare case of cerebral schistosomiasis. A comprehensive review of the literature was conducted to contextualize the case findings and provide an evidence-based discussion on diagnostic challenges and therapeutic strategies in endemic regions.
Results: Clinical Features: A 16-year-old female presented with a 2-week history of right hemicranial headache, nausea, vomiting, and left homonymous hemianopia, with no systemic symptoms, highlighting the importance of isolated focal neurological signs. - Imaging Findings: Brain MRI revealed characteristic cortical and subcortical signal changes with linear and micronodular enhancement. - Differential Diagnosis: Included neoplasms, brain abscesses, and demyelinating diseases. However, epidemiological history and characteristic imaging patterns strongly suggested cerebral neuroschistosomiasis. - Treatment: Praziquantel and corticosteroids led to complete symptom resolution, underscoring the efficacy of this approach.

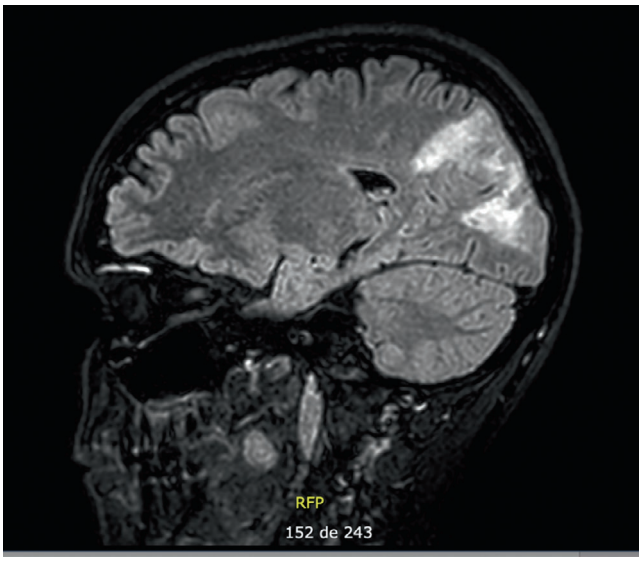

FIGURE 1 Brain MRI in sagittal flair

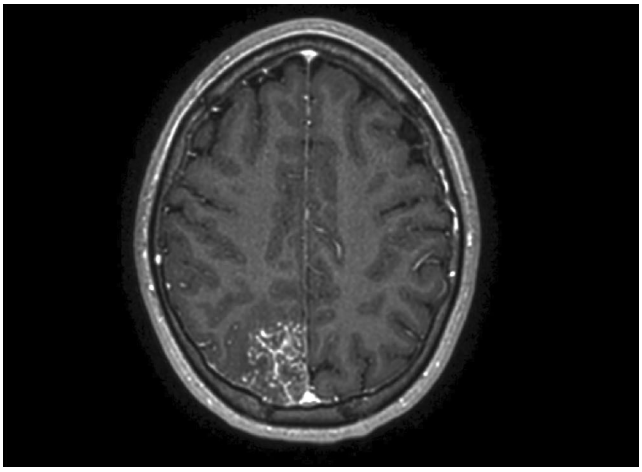

FIGURE 2 Brain MRI in axial T1

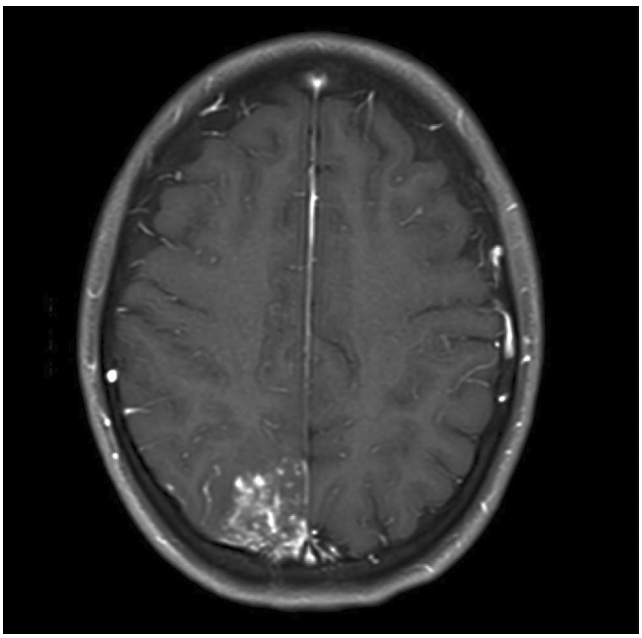

FIGURE 3 Brain MRI in axial T1-weighted post-contrast

Conclusion: - Cerebral neuroschistosomiasis should be considered in patients from endemic regions presenting with atypical neurological symptoms. - The combination of clinical history, characteristic imaging findings, and serology is essential for early diagnosis. - Proper treatment can prevent severe complications and significantly improve patient outcomes.
Disclosure: Nothing to disclose.

EPO-003 | EBV encephalitis in disguise: Navigating diagnostic obstacles in a polyallergic patient with severe hyponatremia

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[1]Department of Neurology, Central Military Emergency University Hospital "Dr. Carol Davila", Bucharest, Romania; [2]Clinical Neuroscience Department, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Background and aims: Epstein-Barr virus (EBV) is a rare cause of encephalitis in immunocompetent adults, with diagnosis often complicated by nonspecific clinical presentation that overlaps with other neurological conditions. In this case, the diagnostic process was complicated by severe hyponatremia, which raised suspicion of a paraneoplastic SIADH, delaying the identification of the cause of encephalopathy.
Methods: A 54-year-old polyallergic female presented with confusion and worsening general condition over 6 days, without fever or elevated inflammation markers. Initial head CT suggested an expansive process in the parieto-temporo-occipital region. Non-contrast brain MRI performed 6 days later showed cerebellar and occipital lesions, suggesting an ischemic event. Severe hyponatremia raised suspicion of paraneoplastic SIADH, prompting a chest-abdomen-pelvis CT that revealed a possible pancreatic tumor. Due to progressive ventricular dilation lumbar puncture was contraindicated, delaying the diagnosis; cerebrospinal fluid was later obtained through an external ventricular drain.
Results: Following a contrast-enhanced MRI with prior desensitization for allergic reactions, both encephalitis and cerebral metastases were considered, as the lesions were non-enhancing. Based on clinical suspicion, antiviral therapy, corticosteroids and cephalosporins were initiated. Serology showed positive EBV IgG and IgM, and EBV was detected in the cerebrospinal fluid, confirming EBV encephalitis. Despite aggressive treatment, the patient's condition worsened and she ultimately succumbed to the disease.
Conclusion: This case highlights the challenges in diagnosing EBV encephalitis, particularly when paraneoplastic SIADH complicate the clinical picture. It underscores the importance of a comprehensive differential diagnosis and the critical role of a multidisciplinary approach in overcoming diagnostic challenges and facilitating accurate treatment.
Disclosure: Nothing to disclose.

EPO-004 | The role of cognitive reserve in mediating HANDs in older adults living with-treated HIV in Tanzania

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[1]Department of Epidemiology, Bio-Statistics and Clinical Research, University of Dar es Salaam-Mbeya College of Health and Allied Sciences, UDSM-MCHAS, Mbeya, Tanzania; [2]Newcastle University, Newcastle Upon Tyne, UK; [3]Division of Psychiatry, University College London, London, UK, [4]5Northumbria Healthcare NHS Foundation Trust, North Tyneside General Hospital, North Shields, UK

Background and aims: HIV-associated neurocognitive disorders (HAND) are a spectrum of cognitive impairments in chronic HIV infection. HAND is common in sub-Saharan Africa (SSA), despite combination antiretroviral therapy (cART). Older people appear to be at increased risk. It is unknown if cognitive reserve (CR), which is protective in neurodegenerative dementias, protects against HAND.
Methods: Cross-sectional observational study completed in hospital outpatient clinics in Southwest Tanzania. We assessed HIV-positive participants aged ≥50 years established on cART using a neuropsychological test battery, functional assessment, informant history and depression screen. Control participants were HIV-negative individuals attending chronic disease clinics. We used operationalised Frascati criteria for HAND diagnosis. CR was measured using the Cognitive Reserve Index (CRI) and other proxy measures.
Results: The prevalence of HAND was 64.4% (n = 219/343). Lower CRI score [odds ratio (OR) = 0.971, p = 0.009] and less formal education (OR = 4.364, p = 0.026) were independent risk factors for HAND but HIV-severity measures were not. Unemployment and low-skilled manual work were associated with increased risk of HAND in bivariate analysis but not in multivariable analysis.
Conclusion: Higher total CRI score and more formal education appeared to be protective against HAND, in this cohort. Potentially, cognitively and socially stimulating activities and exercise could increase cognitive reserve in later life. Cognitive reserve could possibly be more important than HIV-disease severity in risk of HAND in older people with treated HIV.
Disclosure: Nothing to disclose.

EPO-005 | Clinical and neurological outcomes in patients with confirmed west Nile Virus: A descriptive study

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Background and aims: West Nile Virus (WNV) is a mosquito-borne infection that can lead to severe neurological complications. Pre-existing conditions such as arterial hypertension and diabetes mellitus may affect the severity and outcomes of WNV infection. This study examines the clinical and neurological outcomes in WNV patients, with a focus on the impact of comorbidities
Methods: The study included 22 patients diagnosed with WNV through serological and PCR testing. Demographic data, including age and comorbidities (arterial hypertension and diabetes mellitus), were collected. Patients were monitored for acute neurological complications such as encephalitis, meningitis, and paralysis. A three-month follow-up assessed the long-term effects of the infection
Results: The cohort had a mean age of 63 years, with a balanced male and female distribution. Comorbidities were prevalent, with 54.5% diagnosed with arterial hypertension and 36.4% with diabetes mellitus. These conditions were linked to more severe WNV-related complications. During the acute phase, encephalitis was the most common neurological complication, followed by axonal neuropathy. At the one-month follow-up, several sequelae were observed, including cognitive and behavioral disorders (18.2%), myalgia (27.3%), persistent axonal neuropathy (4.5%), tremor (4.5%), and cranial nerve paralysis (4.5%). Additional rare complications included epilepsy (4.5%) and subacute thyroiditis (4.5%).

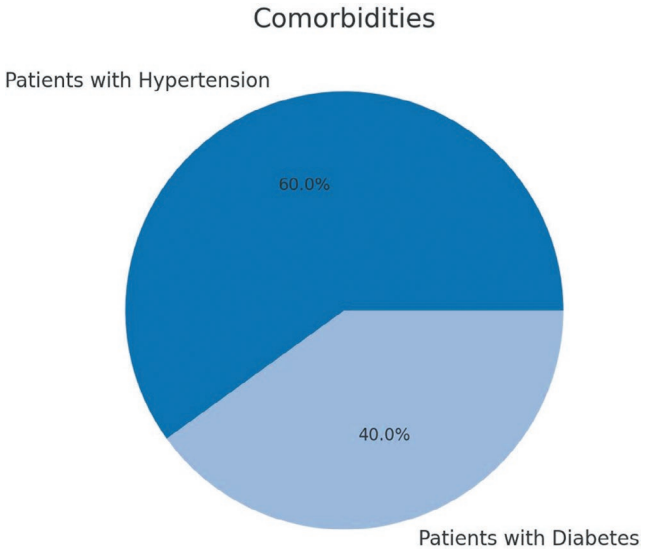
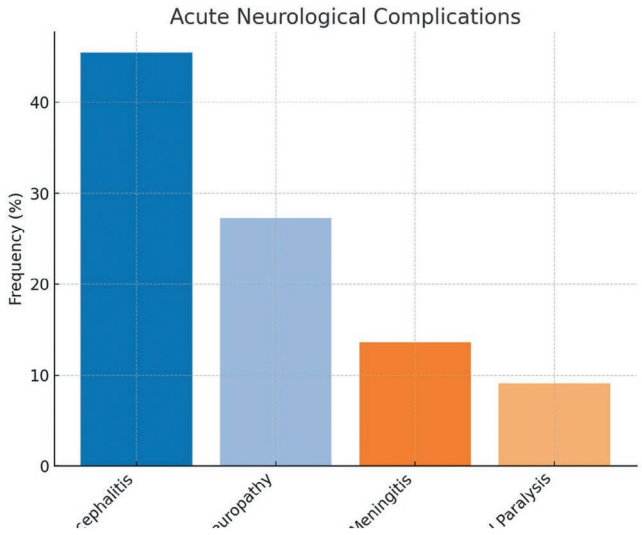
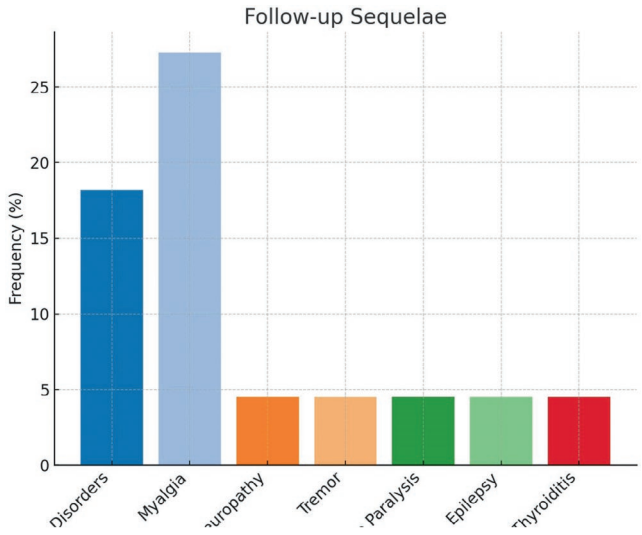


FIGURE 1 Comorbidities Prevalent in WNV infection



Acute Neurological Complications in WNV infection



Follow up Sequelae in WNV infection

FIGURE 2

Conclusion: Pre-existing health conditions contributed to more severe WNV complications and slower recovery. The study emphasizes the need for ongoing neurological care and monitoring for individuals with comorbidities

Disclosure: Nothing to disclose.

EPO-006 | Cerebrospinal fluid findings in patients with acute COVID-19 delirium: a multicenter retrospective data study

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[1]Department of Neurology and Experimental Neurology, Charité – Universitätsmedizin Berlin, Berlin, Germany; [2]Institute of Medical Informatics, Charité – Universitätsmedizin Berlin, Berlin, Germany; [3]Institute of Biometry and Clinical Epidemiology, Charité – Universitätsmedizin Berlin, Berlin, Germany; [4]Department of Anesthesiology and Intensive Care Medicine, Germany

Background and aims: Delirium is a frequent neuropsychiatric complication in critically ill COVID-19 patients. Pathophysiological mechanisms leading to delirium remain unclear, with hypothesized contributors including systemic inflammation, blood-brain barrier disruption, and neuroinflammation. Cerebrospinal fluid analysis (CSF) could be crucial to better understand underlying mechanisms, but CSF data on delirium are limited.

Methods: We retrospectively analyzed the clinical and CSF data of 55 critically ill COVID-19 patients with delirium admitted to one of the seven COVID-19 intensive care units of Charité - University Medicine Berlin between February 2020 and December 2021. Delirium was diagnosed using the Confusion Assessment Method for the ICU. CSF parameters assessed included pleocytosis, blood-brain barrier integrity, intrathecal immunoglobulin synthesis, total protein, lactate, neurofilament light chain protein, and anti-neuronal autoantibodies.

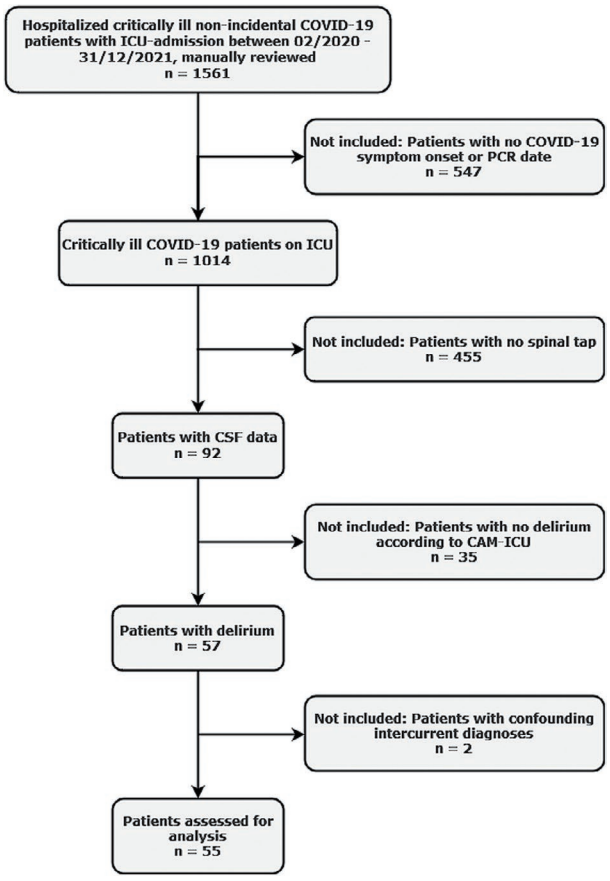

FIGURE 1 Flowchart of patient selection

Results: Blood-brain barrier disruption was observed in 53% of patients, while pleocytosis occurred in only 4%. Elevated CSF total protein and lactate were noted in 43% and 22% of patients. Intrathecal immunoglobulin synthesis was rare (4%). Anti-neuronal autoantibodies were infrequent in CSF (2%), but more common in serum (41%). Notably, CSF neurofilament light chain protein levels were elevated in 81% of patients, indicating significant axonal injury.
Conclusion: Our findings highlight CSF alterations in critically ill COVID-19 patients with delirium, characterized by frequent blood-brain barrier disruption, neuronal injury, and protein leakage, but minimal cellular immune response or intrathecal immunoglobulin synthesis. The presence of anti-neuronal autoantibodies in serum suggests a potential autoimmune contribution, though their direct pathogenic role remains uncertain. These results suggest that multifactorial mechanisms, including systemic inflammation and blood-brain barrier dysfunction drive COVID-19-related delirium.
Disclosure: Nothing to disclose.

EPO-007 | Lyme radiculoneuritis presenting with hyperacute lower limb weakness and a benign course, an atypical Bannwarth Syndrome

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Cork University Hospital, Cork, Ireland

Background and aims: We present a 49-year-old lady who presented with an episode of acute lower limb weakness. The patient reported instantaneous bilateral lower limb weakness, resulting in a fall to the ground. The patient did not have any pre-existing medical conditions and did not take any regular medications. There were no sensory symptoms and no upper limb weakness. She denied any recent illnesses or trauma. Examination demonstrated bilateral lower limb weakness and hyporeflexia. There were no sensory deficits and upper limb examination was unremarkable.
Methods: Neurophysiological evaluation was requested, which demonstrated reduced right common peroneal motor amplitude, but otherwise motor amplitudes and conduction velocities were within accep limits. Sensory responses were normal. Electromyography demonstrated florid acute denervation in both lower limbs in an L2-S2 distribution as well as upper limbs to a lesser degree. MRI brain and whole spine were unremarkable. Cerebrospinal fluid analysis demonstrated mildly elevated protein.
Results: Following review at a tertiary neurology centre 8 months following initial presentation, motor strength had normalised with no residual deficits. Further review noted frequent international travel and subsequent Borrelia burgdorferi serology revealed positive IgG and IgM suggesting recent infection. The patient completed a course of doxycycline. Subsequent neurophysiology showed complete resolution of previous features.
Conclusion: This case highlights an atypical hyperacute presentation of Lyme radiculoneuritis. While this frequently presents with concurrent neuropathic pain and sensory symptoms, both were absent in this case, broadening the clinical spectrum of this condition and highlighting Lyme disease as a rare but important differential in acute flaccid paresis.
Disclosure: Nothing to disclose.

EPO-008 | The accuracy of Bacterial Meningitis (BMS) in identifying pediatric patients high risk for bacterial meningitis

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[1]Department of Pediatrics, Mariano Marcos Memorial Hospital and Medical Center/Batac City, Philippines; [2]Department of Pediatrics, Mariano Marcos Memorial Hospital and Medical Center/Batac City, Philippines

Background and aims: Bacterial and aseptic meningitis have similar presentations but vastly different treatments and outcomes. Early identification of bacterial meningitis is crucial for appropriate evaluation and antibiotic therapy. The Bacterial Meningitis Score (BMS) helps clinicians distinguish between the two.
Methods: This cross-sectional single-center study involved 75 pediatric patients, aged 29 days to 18 years, suspected of meningitis, seen in the Emergency Room from March to November 2023 at a tertiary hospital in the Philippines. Eligible patients were selected based on inclusion and exclusion criteria. Lumbar punctures were performed to obtain cerebrospinal fluid (CSF) for analysis. High-risk predictors were scored using the Bacterial Meningitis Score (BMS): positive CSF Gram (2 points), CSF absolute neutrophil count ≥1000 cells/μL (1 point), CSF protein ≥80 mg/dL (1 point), peripheral absolute neutrophil count ≥10,000 cells/μL (1 point), and seizures prior to or during presentation (1 point). Predictors were classified as very low risk (BMS=0) or not very low risk (BMS ≥1).

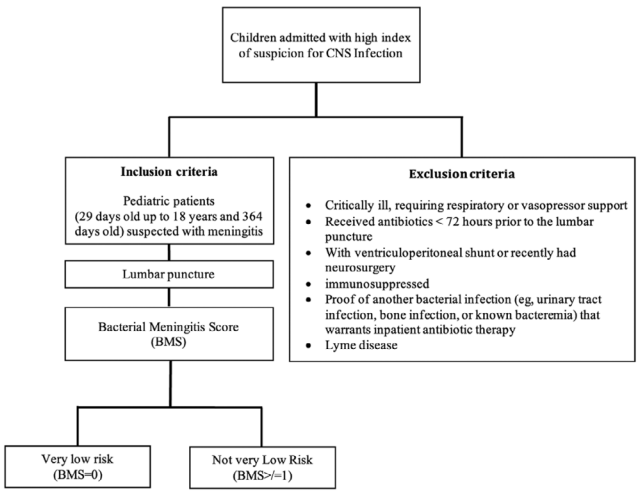

FIGURE 1 Patient Flow Diagram

Results: The sensitivity of the Bacterial Meningitis Score (BMS >/=1) for bacterial meningitis is 100% (95% CI), and the specificity is 19.70% (95% CI). The positive and negative likelihood ratios were 1.23 (positive predictive value 24%, 95% CI, 1.10 – 1.53) and 0 (negative predictive value 100%, 95% CI, 0.01 – 1.68), respectively.

BMS PREDICTORS PRESENT	HIGH-RISK PREDICTORS	NO. OF PATIENTS *WITH NOT VERY LOW RISK*	NO. OF PATIENTS *WITH BACTERIAL MENINGITIS*
1 Predictor	Seizure before or at the time of presentation	25	4
	Peripheral ANC >/=10,000 cells/uL	1	0
	CSF Protein >/= 80mg/dL	4	0
	CSF ANC >/1000 cells/uL	2	1
2 Predictors	Seizure before or at the time of presentation *and* Peripheral ANC >/=10,000 cells/uL	11	4
	Seizure before or at the time of presentation *and* CSF Protein >/= 80mg/dL	1	0
	Seizure before or at the time of presentation *and* CSF ANC >/1000 cells/uL	1	1
	Seizure before or at the time of presentation *and* Positive CSF Gram	2	2
	Peripheral ANC >/=10,000 cells/uL *and* CSF ANC >/1000 cells/uL	1	1
>/=3 Predictors	All combinations	13	5

Total patients with >/=1 predictors: 61; Abbreviations: ANC, absolute neutrophil count; CSF, cererbrospinal fluid

FIGURE 2 Risk of Bacterial Meningitis for Patients with 1, 2, or 3 or more Bacterial Meningitis Score Predictors

Sensitivity [95% CI]	**100%**
Specificity [95% CI]	**19.70%**
Negative predictive value [95% CI, 0.01 – 1.68]	**100%**
Positive predictive value [95% CI, 1.10 -1.53]	**24%**
Positive likelihood ratio [95% CI, 0.62,1.74]	**1.23**
Negative likelihood ratio [95% CI, 0.06, 11]	**0.0**
Prevalence bacterial meningitis	**6-18%** *(Kulik et al., 2013)*

Pretest Probability: 0.25 (25%) | Posttest Odds: 0.33 | Posttest Probability: 0.70 (70%) | Posttest Odds: 0.41

FIGURE 3 Performance of Bacterial Meningitis Score (BMS)

Conclusion: The BMS's high sensitivity and negative predictive value effectively rule out bacterial meningitis. However, its low specificity and positive predictive value require cautious interpretation of positive results. It's a useful initial screening tool, but further evaluation and testing are necessary for diagnosis
Disclosure: Nothing to disclose.

EPO-009 | Bridging the gap: Uncovering cardiovascular risks in HIV patients – A pilot study

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Yaounde Central Hospital, Yaounde, Cameroon

Background and aims: The advent of Highly Active Antiretroviral Therapy (HAART) has significantly improved the life expectancy of HIV-positive patients, yet it has also coincided with a rising prevalence of cardiovascular disease (CVD), particularly among this population. HIV itself is a recognized independent risk factor for CVD. This study aims to identify cardiovascular risk factors in HIV-infected individuals at diagnosis and evaluate the feasibility of dual diagnosis.
Methods: Conducted over nine months at the Day Hospital of Etoug-ebe Baptist Hospital in Yaoundé, this cross-sectional study enrolled patients who tested positive for HIV during screening campaigns. We used adapted questionnaires and simple body measurements to assess cardiovascular risk factors.
Results: The study included 73 participants, predominantly female, with an average age of 35.6 years. Notably, hypertension was prevalent in 16.4% of participants, while 8.2% were classified as obese, and 26% demonstrated abdominal obesity. Conversely, 9.6% of participants were underweight. Age and sex had no significant impact on hypertension prevalence, and no clinical signs of atherosclerosis were observed.
Conclusion: The high prevalence of cardiovascular disease risk factors among HIV-positive patients highlights the need for concurrent diagnosis of both conditions. Implementing dual diagnosis is feasible and essential for guiding effective care strategies, ultimately reducing morbidity and mortality.
Disclosure: Nothing to disclose.

EPO-010 | West Nile Virus: An uncommon cause of meningoencephalitis in Ukraine: A case report

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[1]Department of Neurology, LLC "Dobrobut-Clinic", Kyiv, Ukraine; [2]Department of Neurology, Bogomolets National Medical University, Kyiv, Ukraine

Background and aims: The West Nile virus (WNV) is an RNA virus from the Flaviviridae family, transmitted by mosquitoes. WNV neuroinvasive disease is a rare life-threatening complication of WNV infection that is becoming more common in Europe in summertime.
Methods: A single case presentation.
Results: A 67-year-old man was transferred from a local clinic with impaired level of consciousness with a two-week history of fever, nausea, vomiting, general weakness. The patient lives in a lakeside locality. A papular rash on the skin and bilateral subconjunctival hemorrhages were detected. Neurological examination revealed: disorientation, aphasia and positive meningeal signs. Brain MRI showed signs of leptomeningeal post-contrast enhancement. In CSF: cytosis – 20 cells/mm^3, predominantly lymphocytes, protein 1020 mg/L, glucose 3.0 mmol/L. However, the IV acyclovir was started, the patient developed rapid deterioration with a short episode of critical bradycardia and asystole, which led to the mechanical ventilation. The blood tests for sarcoidosis, tick-borne encephalitis, syphilis, and HIV were negative. The cerebrospinal fluid analyses for Herpesviruses were also negative and acyclovir was withdrawn. Pulse therapy with methylprednisolone was started, which led to the restoration of consciousness and discontinuation of mechanical ventilation. On day 10, WNV infection was diagnosed by positive serology (IgG and IgM). Two weeks later patient was discharged, asymptomatic except for mild ataxia and hearing loss.

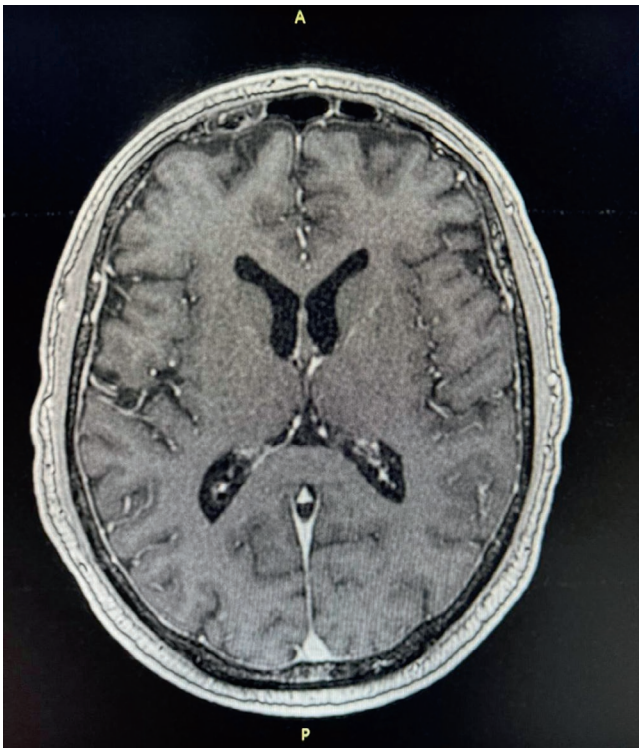

FIGURE 1 Patient's brain MRI T1 post contract sequence, axial projection -leptomeningeal post-contrast enhancement.

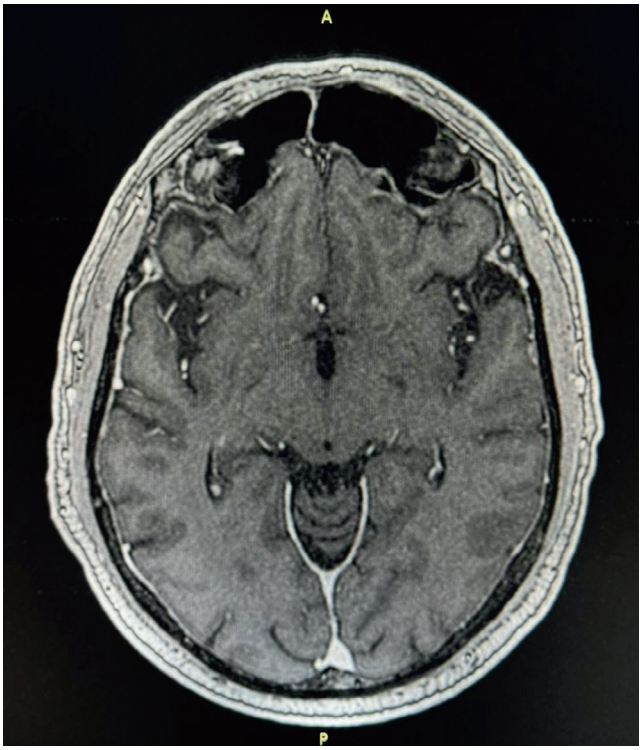

FIGURE 2 Patient's brain MRI T1 post contract sequence, axial projection -leptomeningeal post-contrast enhancement.

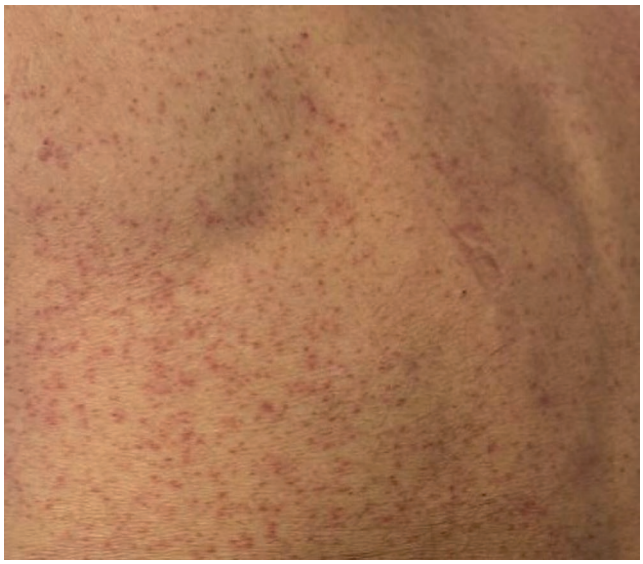

FIGURE 3 A maculopapular rash on a patient's back.

Conclusion: We report this case to emphasize that elderly male patients have a higher risk of developing WNV neuroinvasive disease with high mortality rate. Despite its rarity, WNV is becoming endemic in Europe, highlighting the need for increased awareness.
Disclosure: Nothing to disclose.

EPO-011 | An unexpected "Souvenir"

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Background and aims: Melioidosis is a rare infection caused by the bacteria Burkholderia pseudomallei. It is an endemic infection in Southeast Asia and Northern Australia. Its diagnosis can be challenging because it is an imported pathogen that can mimick other diseases. This is why it is crucial to know this entity and its connection to recent travel history to high-risk areas.
Methods: We describe the case of a 42-year-old woman with no relevant medical history. She was referred to the emergency department following a generalized tonic-clonic epileptic seizure while sleeping. The neurological exam showed a right upper quadrantanopia. The medical history highlighted a recent travel to Vietnam, where she swam in rivers and the sea. In the final days of the trip, she experienced headache, cough, and a mild feverish sensation, treated with amoxiciline.
Results: A brain MRI revealed a heterogeneous left temporoparietal lesion with irregular anular gadolinium enhance; a pyogenic abscess or a high-grade glial neoplasm were the main differential diagnoses. A brain biopsy was performed and microbiological culture showed growth of Burkholderia pseudomallei. The patient was treated with Meropenem for 8 weeks, followed by Cotrimoxazole for 6 months. No further seizures were reported and a 3-month follow-up MRI showed persistent radiological improvement.

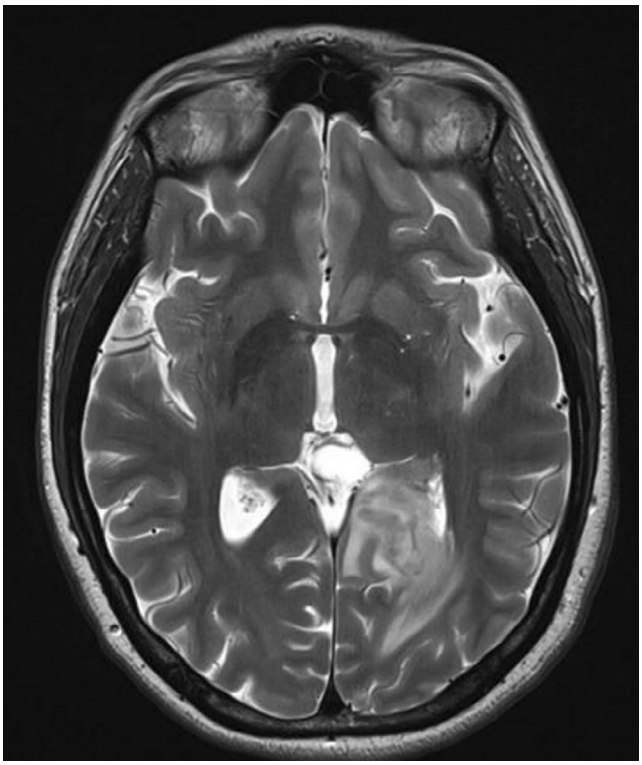

FIGURE 1 MRI

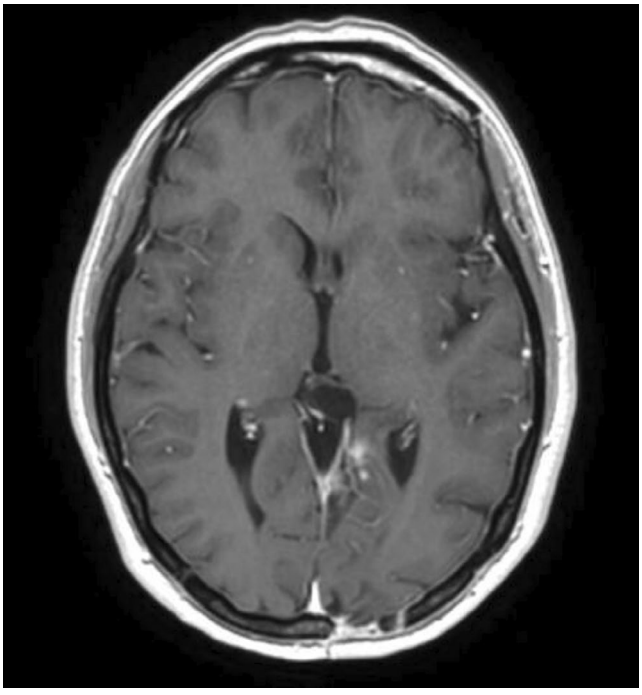

FIGURE 2 Follow up MRI

Conclusion: The case underscores the importance of addressing abscess microbiology with brain biopsy, crucial to diagnose Melioidosis. In closing, we want to raise awareness among Occidental clinicians about the growing number of cases in European regions due to the continued tourism to endemic countries.
Disclosure: Nothing to disclose.

EPO-012 | Gender-related differences in subjects with persisting COVID-19 loss of smell: baseline data from the SMELL-trial

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Background and aims: Olfactory dysfunction is one of the most common symptoms of COVID-19. Indeed, incidence of loss of smell after SARS-CoV-2 infection has been estimated by meta-analysis to be around 50% with subjective recovery rates ranging from around 3 to 90%. Moreover, recent studies have shown that up to 7% of patients remain anosmic for more than 12 months after the onset of COVID-19 infection.
Methods: The SMELL-trial is a monocentric RCT evaluating the efficacy of olfactory training in individuals with persisting COVID-19 associated loss of smell (>3 months post-infection). Olfactory performance was measured using the identification and discrimination subscales of the Sniffin' Sticks. Data regarding demographics, comorbidities, Quality of Life (QoL,), mental health, well-being and subjective olfactory impairment (olfactory visual analogue scale, patient global impression of severity) were collected.
Results: A total of 70 individuals were included. There were more female (64%) participants. Mean age was 54 years (SD: 14.5) and mean OD duration of 20 months (SD: 11.4). No differences between both sexes were seen for age, BMI, or symptom duration, neither for comorbidities nor smoking history. There were no gender-related differences for QoL or health, nor for well-being and mood. No differences were seen for subjective olfactory impairment. However, men had lower scores on both subscales of the Sniffin' Sticks (identification: 6.85 vs. 9.16, discrimination: 8.81 vs. 10.11).
Conclusion: In the SMELL-trial cohort, there were no gender-related differences in QoL, well-being and mood as well as measures of subjective olfactory impairment, while objective assessment of olfactory function was worse in men compared to women.
Disclosure: NDC reports no financial disclosures. BH reports honoraria from Novartis AG, BIAL, AbbVie and grants from the Austrian science fund (FWF) outside the submitted work. KS reports honoraria from the International Parkinson and Movement Disorders Society, grants from the FWF Austrian Science Fund, the Michael J. Fox Foundation, and the International Parkinson and Movement Disorder Society, as well as personal fees from Teva, UCB, Lundbeck, AOP Orphan Pharmaceuticals AG, AbbVie, Roche, and Grünenthal outside the submitted work.

EPO-013 | The gut-brain axis in Post-COVID-19 condition: a cross-sectional microbiome and neuroimaging study

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Department of Neurology, University Hospital RWTH Aachen, Aachen, Germany

Background and aims: Post-COVID-19 condition (PCC) affects 15% of people worldwide previously infected with SARS-CoV-2, having a lasting impact on society, with fatigue and

cognitive impairment as the most common symptoms. While the pathogenic mechanisms remain unclear, gut dysbiosis is increasingly recognized to play a key role in PCC pathogenesis, disrupting proper gut-brain communication and serotonin metabolism. Here, we investigated gut microbiota of PCC patients in relation to neurological manifestations and neuroimaging changes.

Methods: In this cross-sectional study, consisting of 42 subjects (29 females, 46.7±11.3 years) and 30 healthy controls (22 females, 53.9±17.8 years) we analyzed gut microbiota using 16S rRNA gene amplicon sequencing and its relation to neuropsychological performance, reported symptoms and neuroimaging alterations of resting-state functional and structural magnetic resonance imaging (MRI).

Results: We observed significantly altered gut microbiota in PCC patients (PERMANOVA, $p<0.001$) with a higher abundance of the genera Bacteroides and Alistipes, and a lower abundance of Blautia and Agathobacter compared to healthy controls (Kruskal-Wallis test, $p<0.05$, LDA score>2.5). Moreover, we detected brainstem alterations that strongly correlated with both self-reported fatigue and microbiome dysbiosis.

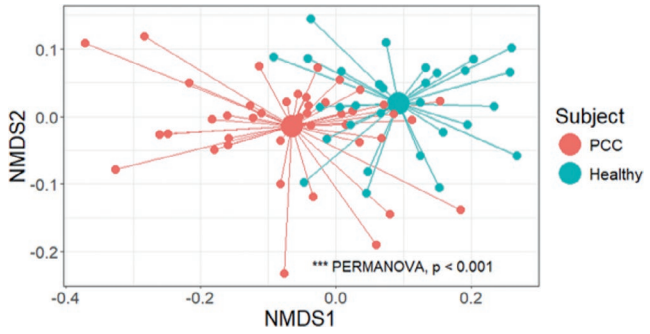

FIGURE 1 Non-metric Multi-dimensional Scaling Plot (NMDS) of gut composition of PCC patients and of a healthy control group, based on weighted Unifrac as dissimilarity measure.

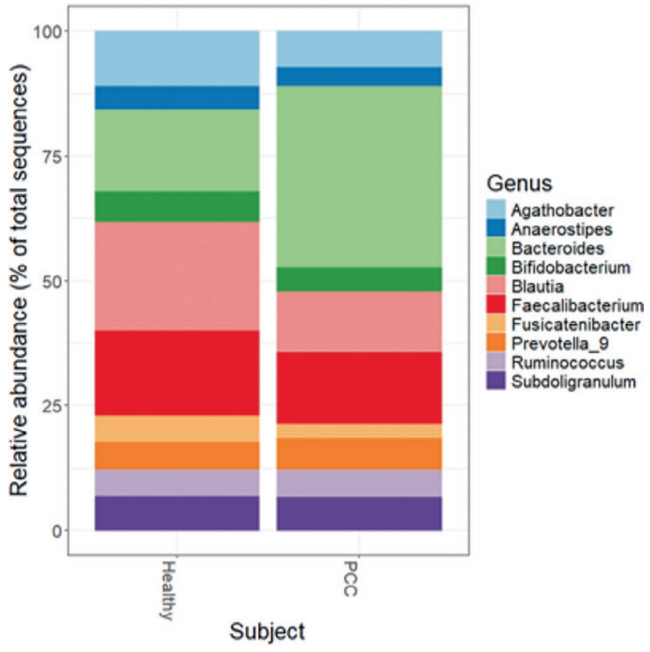

FIGURE 2 Average relative abundance of top 10 genera found in gut microbiota in PCC patients and a healthy control group.

Conclusion: This pioneering study comprehensively investigates the gut-brain axis in PCC linking gut microbiome alterations to both neurological symptoms and MRI-detectable brain changes. Our results suggest a significant role of microbiome disruptions in the manifestation of brain changes and key neurological symptoms in PCC. These findings highlight the potential for microbiome-targeted interventions including dietary modifications, pre- and probiotics, selective serotonin reuptake inhibitors, and vagus nerve stimulation, to restore gut-brain homeostasis and alleviate symptoms.

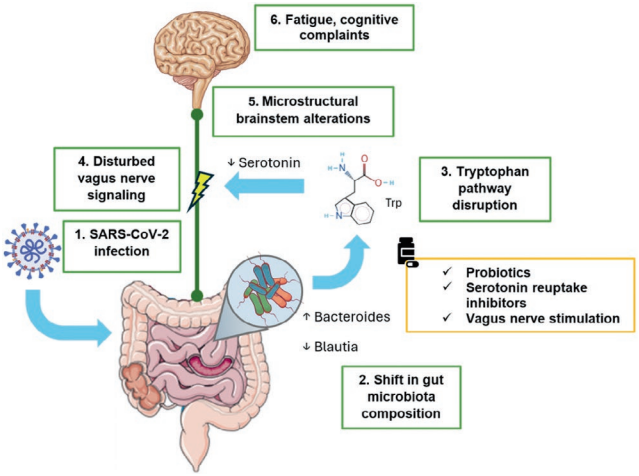

FIGURE 3 Hypothesized mechanism of gut dysbiosis in Post COVID pathogenesis.

Disclosure: Sophie Wetz and Dr. Julia Walders are funded by the Else-Kröner-Fresenius Grant (2022_EKEA.58). Dr. Ravi Dadsena and Prof. Dr. Kathrin Reetz have nothing to disclose.

EPO-014 | Rapid progression and fatal outcome of HHV-6 encephalitis in an immunocompromised adult: A case report

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Background and aims: Human herpesvirus 6 (HHV-6) is a neurotropic virus with a strong affinity for the central nervous system (CNS). While primary infection is typically self-limited during childhood, the reactivation of HHV-6 can lead to serious neurological conditions, particularly in immunocompromised individuals.

Methods: We report the case of a 67-year-old female with a history of end-stage kidney disease who developed progressive neurological symptoms, beginning with speech difficulties, quickly evolving into motor deficits, and altered mental status. Diagnostic workup included cerebrospinal fluid (CSF) analysis, revealing positive polymerase chain reaction (PCR) results for HHV-6, along with findings suggestive of inflammation. Serological testing showed a high viral load of HHV-6. Magnetic resonance imaging (MRI) demonstrated non-enhancing hyperintensities on fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) sequences in the left

hemisphere, particularly in the cortical regions, with associated cortical hemorrhages. Abnormal signal changes indicative of encephalitis were also observed in the right frontal and temporal lobes.

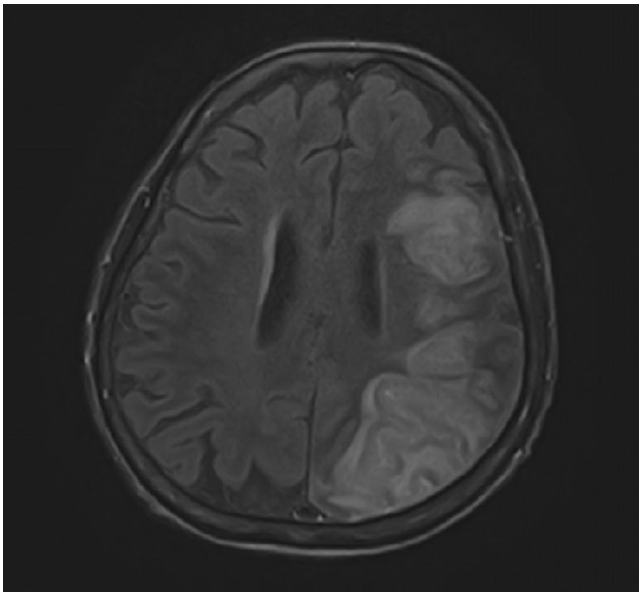

FIGURE 1 MRI axial FLAIR image

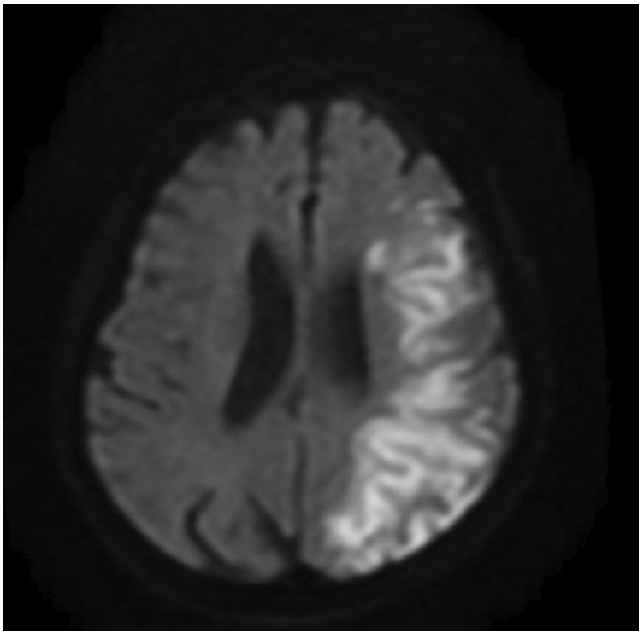

FIGURE 2 MRI axial DWI image

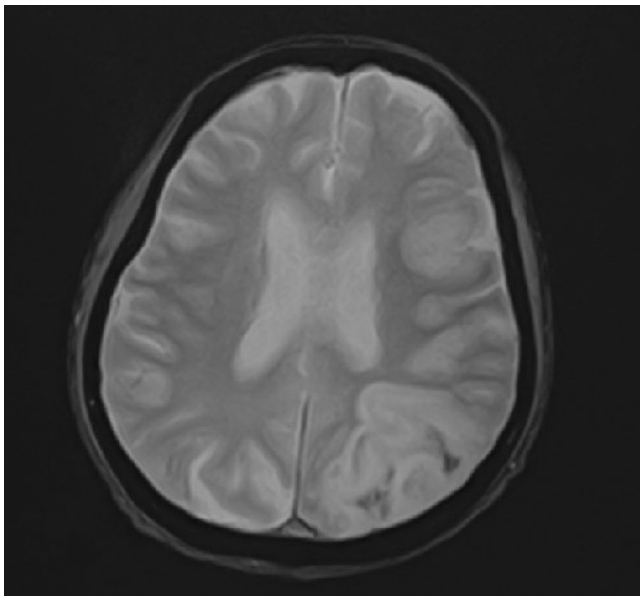

FIGURE 3 MRI axial SWI image

Results: The patient was promptly initiated on antiviral therapy, in addition to antibiotics and supportive care. Despite these interventions, the patient's condition continued to deteriorate, showing a poor response to treatment, and she ultimately succumbed to the illness.
Conclusion: This case highlights the significant threat posed by HHV-6 encephalitis, particularly in immunocompromised patients, underscoring the importance of early detection, comprehensive diagnostic workup, and timely therapeutic intervention. Although early diagnosis and treatment are critical, the prognosis may remain poor in cases with extensive neurological involvement.
Disclosure: Nothing to disclose.

EPO-015 | Heidenhain variant of Creutzfeldt-Jakob disease: A diagnostic challenge in patients with visual disturbances

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Department of Neurology, Faculty of Medicine, Ondokuz Mayıs University, Samsun, Turkey

Background and aims: Creutzfeldt-Jakob disease (CJD) is a rare, fatal neurodegenerative disorder caused by misfolded prion proteins. The Heidenhain variant of CJD (HvCJD) is characterized by early visual disturbances, including visual impairment, altered color perception, and cortical blindness, often preceding cognitive and motor symptoms. This variant poses a diagnostic challenge, as patients typically seek ophthalmologic evaluation before a neurological diagnosis is made.
Methods: This report presents two cases of HvCJD with varying clinical manifestations. Both patients underwent cranial MRI, EEG, and CSF analysis, including testing for 14-3-3 protein. The diagnostic criteria of the World Health Organization for probable CJD were used.

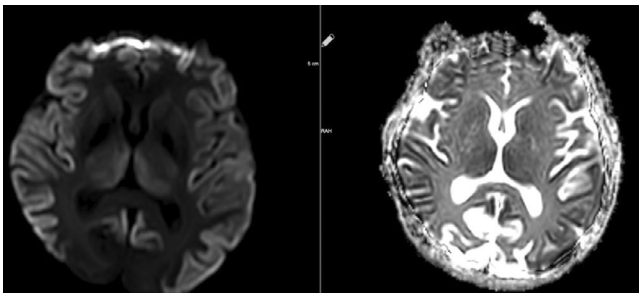

FIGURE 1 Diffusion restrictions in the bilateral frontoparieto-occipital lobes and bilateral thalami

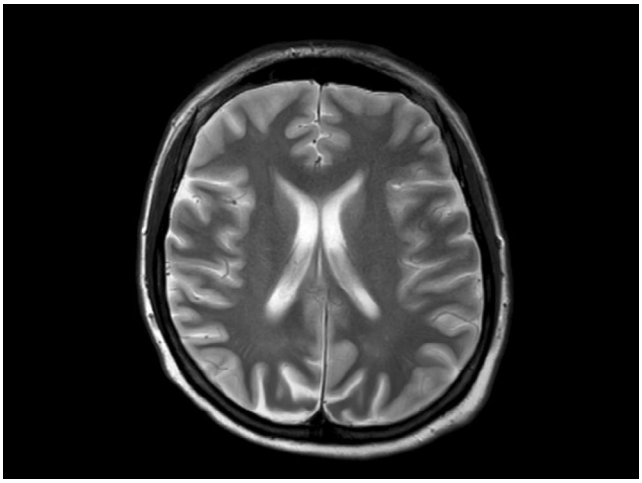

FIGURE 2 FLAIR hyperintensities in the bilateral cortical surfaces of frontoparietooccipital lobes

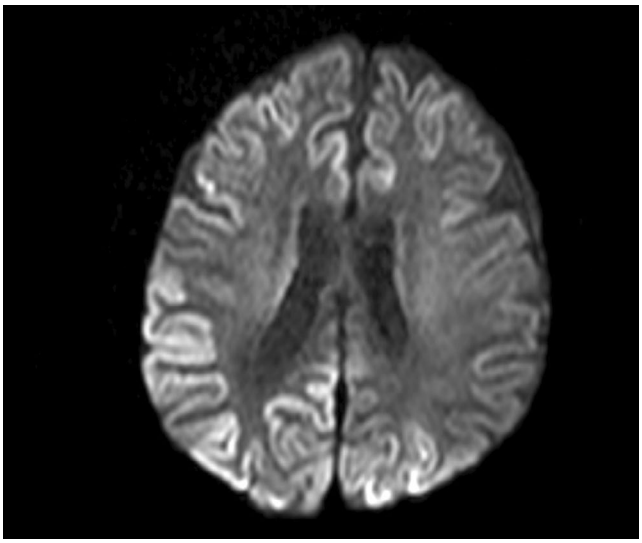

FIGURE 3 Diffusion-restricted signal changes in the bilateral frontoparietal and temporo-occipital cortical surfaces, with more pronounced involvement in the right parieto-occipital region

Results: The first case is a 35-year-old female with progressive visual impairment, behavioral changes, and cortical blindness, progressing to akinetic mutism. The second case is a 74-year-old male with visual impairment, ataxia, and rapidly progressive dementia. Both patients showed characteristic MRI, EEG, and CSF findings, supporting the diagnosis of probable CJD.

Conclusion: These cases emphasize the clinical heterogeneity of HvCJD and the importance of considering it in the differential diagnosis of unexplained visual disturbances and rapid neurological decline. Early recognition is critical to reduce diagnostic delays and the risk of prion disease transmission. Increased awareness among healthcare providers, especially ophthalmologists, is essential for timely diagnosis and management.
Disclosure: Nothing to disclose.

Epilepsy 1

EPO-016 | Progression of negative myoclonus

A. Sinokki[1]; L. Säisänen[2]; J. Hyppönen[2]; K. Silvennoinen[3]; R. Kälviäinen[4]; E. Mervaala[2]; P. Karjalainen[1]; S. Rissanen[1]
[1]Department of Technical Physics, University of Eastern Finland, Kuopio, Finland; [2]Kuopio Epilepsy Center, Department of Clinical Neurophysiology, Kuopio University Hospital, Full Member of ERN EpiCARE, Kuopio, Finland; [3]Institute of Clinical Medicine, School of Medicine, Faculty of Health Sciences, University of Eastern Finland, Kuopio, Finland; [4]Kuopio Epilepsy Center, Neurocenter, Kuopio University Hospital, Full Member of ERN EpiCARE, Kuopio, Finland

Background and aims: Negative myoclonus (NM) is characterized as a short absence (<500 ms) of muscle tone and is one of the main motor symptoms in progressive myoclonus epilepsies. NM may result in dropping items or falling. NM can be quantified by measuring silent periods (SP) in electromyography (EMG). The aim of the study is to determine whether progression of NM over one year can be detected using an EMG-based analysis method.
Methods: One-year follow-up study was conducted for 18 progressive myoclonus epilepsy type 1 (EPM1) patients. SPs in EMG were detected from a 15-minute segment from the beginning of Unified Myoclonus Rating Scale (UMRS) assessment. NM severity was rated using a standardized scoring system (0 = no NM, 3 = severe NM) during the UMRS assessment. Three EMG features were calculated: number of SPs, average SP duration, and ratio of SP to muscle activity.

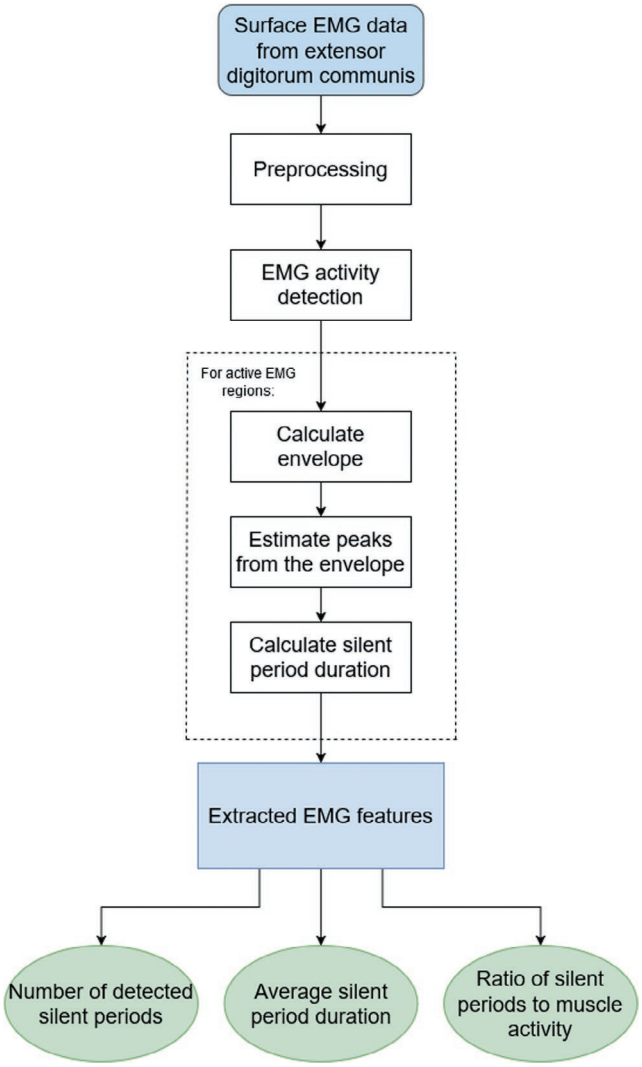

FIGURE 1 Flowchart of the electromyography analysis method and silent period detection.

Results: NM severity increased in seven subjects. Among these, two showed an increase in EMG features, while others showed no significant change or a decrease. Subjects with higher NM severity (2 – 3) had higher ratio of SP to muscle activity on both visits. Nine patients scored as "no NM" had average SP duration below 100 ms in both assessments.

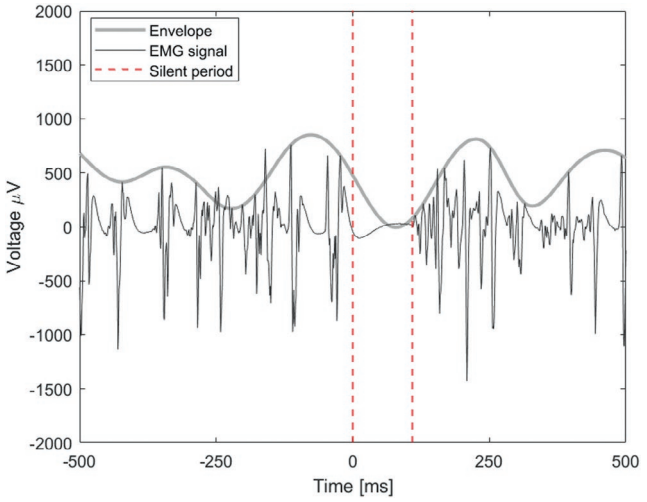

FIGURE 2 Example of a silent period detected from electromyography signal (black), extracted envelope curve (gray), and silent period starting from t=0s.

Conclusion: Results suggest that one year may be too short time to observe meaningful NM progression. Additionally, the observed decrease in SPs may reflect natural fluctuations seen during short-term evaluations such as UMRS. EMG-based measurements during long-term home monitoring would most probably improve reliability and provide greater clinical relevance.

Disclosure: A.S. Nothing to disclose. L.S. Nothing to disclose. J.H. Nothing to disclose. K.S. has received speaker's honorarium by Jazz Pharma. R.K. has received speaker's honoraria from Eisai, Jazz Pharmaceuticals, Orion, and UCB and honoraria for membership of the advisory boards/consultation of Angelini Pharma, Eisai, Jazz Pharmaceuticals, Orion and UCB. E.M. Nothing to disclose. P.A.K. is a co-founder in Adamant Health Ltd. He is an inventor in patent applications WO2019166557A1 and WO2020174122A1. S.M.R. is a co-founder in Adamant Health Ltd that develops EMG-based analysis software. She is an inventor in patent applications WO2019166557A1 and WO2020174122A1.

EPO-017 | Treatment patterns in adult patients with focal-onset seizures initiating cenobamate in USA

A. Iovera[1]; J. Leach[1]; E. Alvarez-Baron[1]; P. Lipone[1]; C. Benoist[1]; R. Bosan[2]; E. Eworuke[2]; A. Comandini[1]; E. Salvatori[1]; A. Cattaneo[1]
[1]Global Medical Department, Angelini Pharma S.p.A., Rome, Italy; [2]IQVIA, Falls Church, USA

Background and aims: Antiseizure medications (ASMs) are a mainstay for patients with epilepsy. Cenobamate is a novel ASM indicated for adults with focal onset seizures (FOS). Real-world data on the treatment patterns associated with cenobamate use will shed light on its efficacy and safety.

Methods: Retrospective analysis of IQVIA PharMetrics Plus database was conducted on US adult patients with FOS and a cenobamate claim (index date) between 1/4/2020 to 30/4/2023. Patients had a minimum of 6-month continuous enrolment pre- and post-index date. Patients were on cenobamate monotherapy (≥90 days prescription claims) or polytherapy (overlapping

≥90 days' supply cenobamate and other ASMs). All other patients were categorized as undetermined. Then, a 90-day window was used to determine patients that continued, switched, augmented (prescription for an additional ASM) or discontinued cenobamate regimen.

Results: Among the 1,132 patients included, 45.1% were on polytherapy, 1.5% on monotherapy, and 53.5% on undetermined regimen. In the polytherapy group, the largest proportion of patients were on cenobamate and 1 additional ASM (47%), followed by 2 additional ASMs (36%) and 3+ additional ASMs (17%). Most patients continued the identified treatment regimen (66.2%), did not augment (91.5%), and did not switch (97.7%). 11.2% discontinued cenobamate, 20.6% discontinued additional ASMs.

Conclusion: Most patients used cenobamate with only 1 additional ASM. Our study showed high patient adherence and minimal changes in treatment regimen (low rates of augmentation and switching). As seen here, cenobamate discontinuation rate was in line with the literature and lower than the one of co-ASMs.

Disclosure: Angelini is the sponsor and funded IQVIA to conduct the study.

EPO-018 | Long-term outcomes in patients with generalized tonic-clonic seizures following VNS therapy: Interim CORE-VNS 36 months

A. Suller-Marti[1]; M. Keezer[2]; R. Verner[3]; A. Andrade[1]; M. Veilleux[4]; K. Myers[5]; J. Burneo[6]; G. Giannicola[3]; M. Dibue[3]; P. Roncon[3]

[1]Department of Clinical Neurological Sciences, Schulich School of Medicine and Dentistry, Western University, London, Ontario, Canada and Department of Pediatrics, Schulich School of Medicine and Dentistry, Western University, London, Ontario, Canada; [2]Department of Neurosciences and School of Public Health, Université de Montréal, Montreal, Quebec, Canada; [3]LivaNova PLC (or a subsidiary), Houston, USA; [4]Department of Neurology and Neurosurgery, Montreal Neurological Institute and Hospital, Montreal, Quebec, Canada; [5]Research Institute of the McGill University Medical Center, Montreal, Quebec, Canada; [6]Department of Clinical Neurological Sciences, Schulich School of Medicine and Dentistry, Western University and Department of Epidemiology and Biostatistics, Schulich School of Medicine and Dentistry, Western University, London, Ontario, Canada

Background and aims: Generalized tonic-clonic seizures (GTCs) are substantially devastating with considerable health risks. This study examines the long-term outcomes of VNS in patients with GTCs.

Methods: Patients were enrolled into a prospective, multicenter observational registry called CORE-VNS (NCT03529045). Participants with primary GTCs were selected for analysis (focal seizures at baseline and LGS were excluded). Selected study participants completed a 3-month retrospective baseline period and after the VNS implant, were followed for up to 36 months.

Results: Fifty-nine participants received an initial VNS implant, with 12 implanted within 5 years of epilepsy diagnosis and 47 after more than 5 years. Earlier implant recipients were younger (median age 9.7 vs. 25.9 years). Participants had previously failed a median of 6 antiseizure medications (ASMs). Among 40 participants completing 36 months of follow-up, the responder rate (≥50% seizure reduction) was 70% (N=28; 95% CI: 56.0–81.7%), with a median seizure frequency change (MSFC) of -83.2% (95% CI: -100% to -53.3%). Earlier implant recipients demonstrated a higher responder rate (83.3% vs. 67.7%) and greater MSFC (-94.3% vs. -76.4%). Quality of life improved for 27% of participants, regardless of implant timing. Adverse events were reported by 35.6% (N=21), with the most frequent being dysphonia (11.9%, N=7), dyspnea (6.8%, N=4), implant site pain (5.1%, N=3), and cough, oropharyngeal pain, and implant site infection (3.4%, N=2).

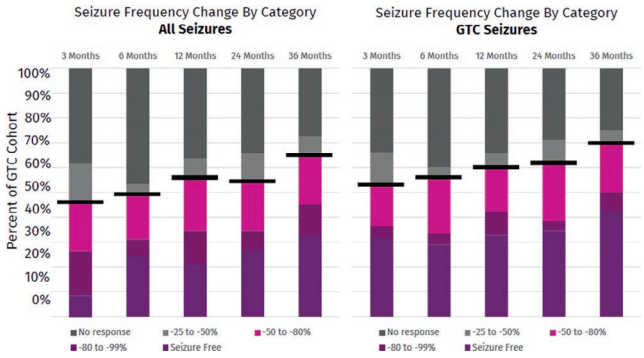

FIGURE 1 Seizure Frequency Change by Category

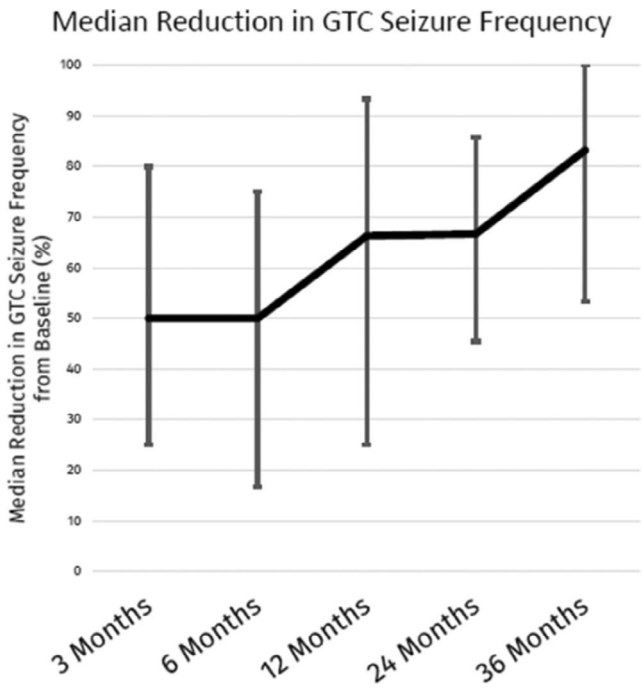

FIGURE 2 Median Reduction in GTC Seizure Frequency

Conclusion: Adjunctive VNS was well-tolerated and effective in reducing GTC frequency, with a 36-month responder rate of 70% and an MSFC of up to -94.3%. These findings reflect the modern experience of VNS in GTC management.

Disclosure: RV, PR, MD, GG are employees of LivaNova PLC (or a subsidiary) and hold stock or stock options with the company, who is the manufacturer of the VNS Therapy System. All other authors are investigators associated with the CORE-VNS

Study, and in that capacity they or their institutions receive compensation from LivaNova for study-related activities. No author received direct compensation from LivaNova related to this abstract.

EPO-019 | Prediction of short-term outcome in non-convulsive status epilepticus: External validation of the SACE score

C. Silvestri[1]; G. Giovannini[3]; N. Orlandi[3]; L. Taruffi[2]; M. Burani[2]; M. Malerba[3]; A. Padvani[1]; S. Meletti[3]
[1]Department of Continuity of Care and Frailty, U.O. Neurologia 2, University of Brescia, Brescia, Italy; [2]Department of Biomedical Metabolic Sciences and Neurosciences, University of Modena and Reggio Emilia, Italy; [3]Neurophysiology Unit and Epilepsy Centre, Azienda Ospedaliera-Universitaria of Modena, Italy

Background and aims: Non-convulsive status epilepticus (NCSE) lacks prominent motor symptoms, making initial diagnosis critical for improved outcomes. This study evaluated the SACE (Seizures, Age, Coma, EEG evolution) score in predicting NCSE outcomes and compared it with other prognostic tools (STESS, mSTESS, EMSE-EACE). The primary outcome was 30-day survival.
Methods: In a single-center, retrospective study, 276 NCSE patients were analyzed from an initial cohort of 423. Bivariate logistic regression was used to identify which EEG patterns from Salzburg Consensus Criteria are significantly associated with in-hospital and 30-day survival. We tested performance of the SACE score in our NCSE population. Spearman's correlation coefficient examined the relationship between the SACE scores and the modified Rankin Scale (mRS) at 30 days.
Results: The cohort's mean age was 71.7 years (60% female), 27% of patients presented with coma at NCSE onset. Patients with EEG typical spatio-temporal ictal (TSE) patterns (n=37) had higher survival rates (86.5% in-hospital, 81.1% at 30 days) than those without (70.7% and 61.5%, respectively). The original SACE score demonstrated sensitivity of 0.508, specificity of 0.737, Youden's Index (YI) of 0.246, and AUC of 0.623. We developed a refined SACE score by adjusting parameter (sensitivity 0.39, specificity 0.758, YI 0.147, AUC 0.661) outperforming existing tools in predicting 30-day outcomes.

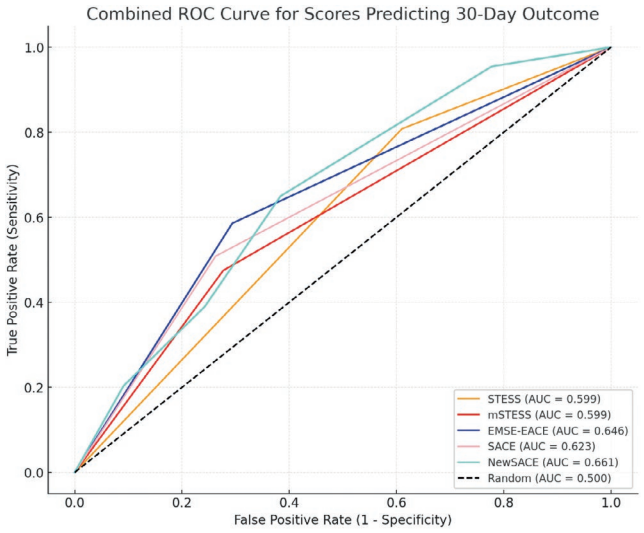

FIGURE 1

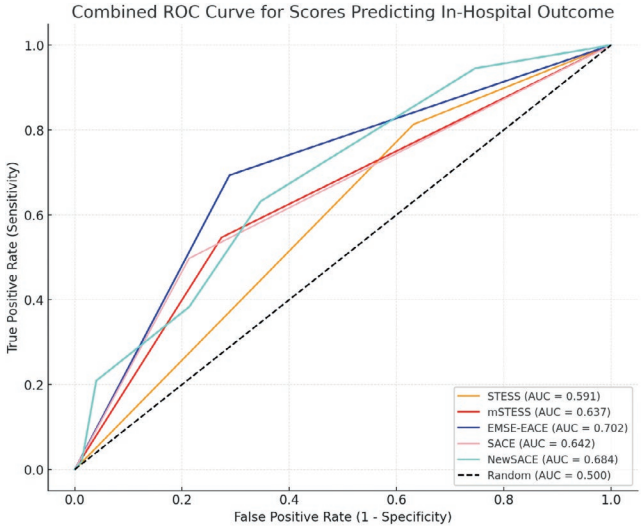

FIGURE 2

Conclusion: We confirmed that EEG TSE patterns predicted 30-day survival. A refined SACE scores, which assigns two points for a history of seizures, showed a slightly better performance. A moderate correlation was identified between the SACE score and mRS 30-day (Spearman correlation coefficient 0.508; $p < 0.001$).
Disclosure: Nothing to disclose.

EPO-020 | Perampanel as the only add-on adjunctive therapy in highly active epilepsy

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Background and aims: People with highly frequent seizures often show resistance to therapy and poor prognoses, posing significant challenges for clinicians. Perampanel (PER) is a new generation antiseizure medication effective in focal and generalized seizures. This study aimed to evaluate the 12-month effectiveness of PER as only add-on treatment for people with highly active epilepsy in a real-world setting.
Methods: Data from the Italian retrospective, longitudinal, multicenter perampanel as Only Concomitant Antiseizure Medication (PEROC) study were analyzed. Patients were grouped by baseline seizure frequency in a) <5, b) 5–20, and c) >20 seizures/month. Outcomes included PER retention, responder rates (>=50% seizure reduction), seizure-free rates, and adverse events (AEs).
Results: The study included 485 patients: 354 with <5, 79 with 5–20, and 52 with >20 seizures/month at baseline, respectively. Retention rates at 12 months were 75.1%, 65.3%, and 58.1% respectively, without significant differences (p=0,077). Poor tolerability was the main reason for treatment withdrawal. At the 1-year follow-up, seizure frequency significantly decreased in all groups (p<0.001), with responder rates of 71.2%, 61.8%, and 63.2% in the three subgroups, showing no significantly differences between the groups. Seizure-free rates were lower in patients with >20 (15.8%) and 5–20 seizures/month (23.5%) compared <5 seizures/month (49.5%; p=0.001). AEs, mainly dizziness, irritability, and drowsiness, occurred in 30% of patients, with similar rates across groups (p= 0.092).

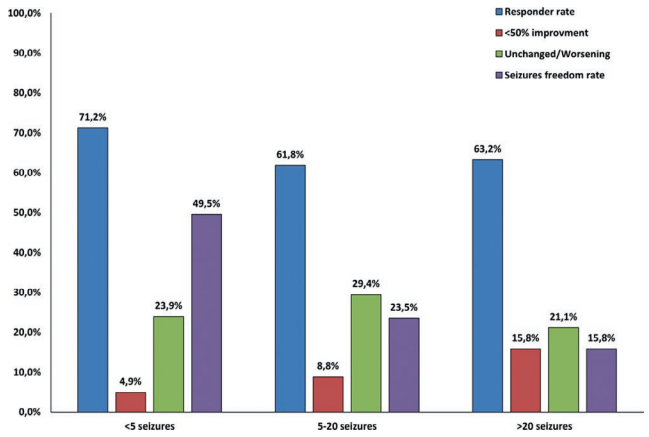

FIGURE 1 Proportion of responder patients, patients achieving seizure freedom, patients with 20 per month)

Conclusion: PER demonstrated good efficacy and tolerability as only concomitant antiseizure medication in a real-world setting in patients with highly active epilepsy, revealing a valuable treatment option in this population.
Disclosure: Nothing to disclose.

EPO-021 | What matters most to people living with epilepsy? A review of published qualitative research relating to health outcomes

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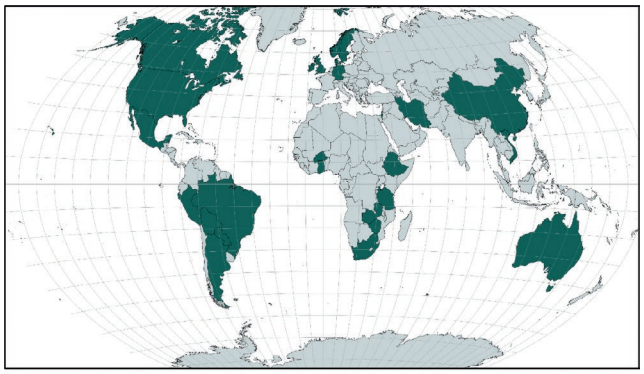
Background and aims: There is a wealth of research examining the lived experience perspective from adults living with epilepsy across a range of geographical and cultural contexts. This review synthesises outcomes discussed by adults when asked about their lived experience.
Methods: MEDLINE was searched using an established qualitative methodological search filter. Studies reporting qualitative primary evidence of the views and experiences of adults living with epilepsy were included. Two independent researchers identified, screened and extracted data from relevant articles. Population and study characteristics were extracted in addition to verbatim quotes relevant to outcomes.
Results: Database searching returned 614 articles, of which 74 were included for outcome synthesis. The views of over 2474 people with epilepsy and 658 caregivers were identified (median 20 per study, range 4-632) from 6 continents. Of included studies, 77% used in-depth interviews, 12% used focus groups, 4% used a mixture of focus groups and in-depth interviews, and 7% used mixed methods approaches. A total of 140 granular outcomes were coded from the included studies. 'Social and role functioning' and 'emotional functioning' outcomes were the most frequently coded, supporting the notion that living with epilepsy represents more than living with seizures.



Dark green shading represents country of residence of study participants from included studies. Map generated using mapchart.net

FIGURE 1 Geographical location of adults with epilepsy in included qualitative studies

Conclusion: The results have wide-reaching implications, providing new insights on what matters most to people living with epilepsy in a diverse range of geographic, societal and cultural settings. The results should be used to inform clinical practice,

research, and inform which patient-centric outcomes should be measured in future clinical trials.
Disclosure: Nothing to disclose.

EPO-022 | Safety, efficacy and pharmacokinetic analysis of intravenous VAL-1221 treatment in Lafora disease

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Background and aims: Lafora Disease (LD) is a progressive myoclonus epilepsy with onset in previously healthy adolescents leading to death in young adulthood, with no effective treatments currently available. This study investigates the safety, efficacy and pharmacokinetics of intravenous VAL-1221, the first potentially disease-modifying treatment administered to LD patients.
Methods: Monocentric analysis of a 12-month compassionate use program for VAL-1221 (20 mg/kg every other week) in LD patients. Safety was assessed through adverse events (AE) monitoring. Efficacy was evaluated using clinical scales (including the Lafora disease clinical performance scale-LDPS) and neuroimaging. Pharmacokinetic studies were performed using liquid chromatography-high resolution mass spectrometry (LC-HRMS) to analyze plasma and CSF samples.
Results: Five patients (range: 17-24 years; 3 females) at intermediate to advanced stages of LD received VAL-1221. Four patients completed the 12-month treatment course, while one discontinued after 8 months due to status epilepticus. We observed 5 mild infusion-related AEs (skin rash, n=1; hypotension, n=4) and no other treatment-related AEs. Efficacy analyses showed a trend of deterioration from baseline to 12 months across various measures. The pharmacokinetic of VAL-1221 was characterized by plasma concentrations (Cmax 100-150 ug/mL; T1/2 60 min), but the drug was undetectable in CSF in all three assessed patients.

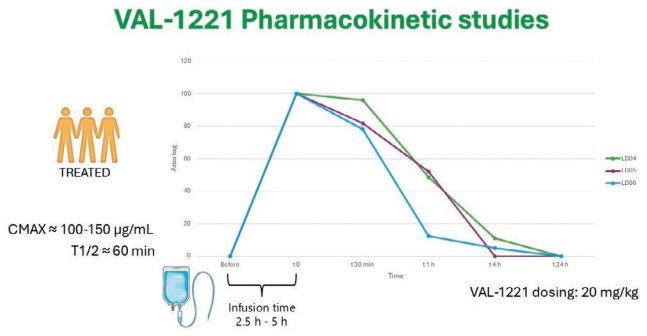

FIGURE 1 VAL-1221 pharmacokinetics

Conclusion: VAL-1221 drug demonstrated an acceptable safety and tolerability profile. Evidence of disease progression and the lack of identification of the drug in CSF suggest that intravenous VAL-1221 does not cross the blood-brain barrier and is therefore ineffective for treating LD in this formulation. Further studies are needed to explore alternative administration methods.

Disclosure: Nothing to disclose.

EPO-023 | MOGAD spectrum and epilepsy: A review on age-dependent radiologiacal and clinical profiles

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Background and aims: Anti-MOG antibody-associated disease (MOGAD) is a rare acute demyelinating syndrome presenting differently across lifespan. Albeit frequent, epilepsy remains a relatively understudied MOGAD-related symptom. We aimed to characterize age-dependent imaging, biohumoral and clinical signatures in MOGAD patients with epilepsy.
Methods: We systematically reviewed online repositories up to April 2024, selecting 126 case reports/series on MOGAD patients with seizures/epilepsy (Figure 1). Data were reported as percentages or medians with interquartile ranges, and comparisons were performed using Chi-square and Mann-Whitney U tests, as appropriate.

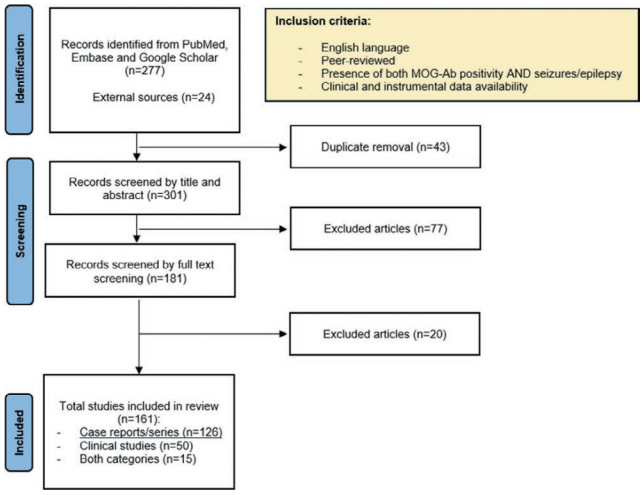

FIGURE 1 Flowchart of the screening process. The keywords used for the searches were ("myelin oligodendrocyte glycoprotein" OR "MOG" OR "MOGAD") AND ("epilepsy" OR "seizure"). Adapted from Page MJ et al, BMJ 2021.

Results: We included 273 MOGAD patients, 124 presenting with adult-onset and 149 with pediatric-onset disease. Pediatric-onset patients were more often female (p=0.012), presented more commonly with acute demyelinating encephalomyelitis (p<0.001), and experienced encephalopathy more frequently (p=0.001). Adult-onset patients more often presented with cortical encephalitis and typical MOGAD onset (p<0.007) and had higher cerebrospinal fluid pleiocytosis (p=0.005). Antibody co-positivity was seen in 30% of patients, predominantly with anti-NMDAR IgG (87%). MRI revealed no significant age-related differences in temporal lobe involvement or leptomeningeal enhancement. Both groups exhibited epileptic manifestations primarily at disease onset, with no significant age-related difference concerning generalized manifestations, but pediatric patients more likely experiencing status epilepticus (p=0.003). Despite no significant differences in immunotherapy, antiseizure medication (ASM) and ASM polytherapy use, pediatric-onset patients showed higher rates of residual deficits and chronic epilepsy at follow-up (p<0.007) (Figure 2).

	Adult	Pediatric	Total	Adult vs pediatric p-value
N	124	149	273	
Female sex, n/tot (%)	42/124 (34)	79/149 (49)	121/273 (44)	**0.012**
Age at onset (years), median (IQR)	29 (38-23)	8 (4-12)	13 (7-28)	-
Phenotype*, n/tot (%)				
ADEM	11/124 (9)	55/149 (37)	66/273 (24)	**<0.001**
ADEM + CCE	6/124 (5)	13/149 (9)	19/273 (7)	0.203
CCE	60/124 (48)	48/149 (32)	108/273 (40)	**0.007**
MOGAD	16/124 (16)	6/149 (4)	22/273 (8)	**<0.001**
MOGAD + ADEM	2/124 (2)	1/149 (1)	3/273 (1)	0.493
MOGAD + CCE	24/124 (19)	22/149 (15)	46/273 (17)	0.379
Other	5/124 (4)	4/149 (3)	9/273 (3)	0.653
Disease course, n/tot (%)				
Monophasic	46/124 (37)	52/149 (35)	98 (36)	0.732
Relapsing	78/124 (63)	97/149 (65)	175 (64)	0.732
Prodromal fever, n/tot (%)	65/124 (52)	69/149 (46)	134/273 (49)	0.324
Encephalopathy, n/tot (%)	70/115 (61)	117/148 (79)	187/263 (71)	**0.001**
CSF features				
Pleiocytosis, n/tot (%)	89/110 (81)	80/105 (76)	160/215 (74)	0.323
Cell number in patients with pleiocytosis (cell/mm^3), median (IQR)	95 (37-190)	53 (20-129)	67 (30-157)	**0.005**
Lymphocytic predominance, n/tot (%)	39/43 (91)	23/29 (79)	62/72 (86)	0.150
Oligoclonal bands, n/tot (%)	23/80 (29)	21/62 (34)	44/142 (31)	0.525
Antibody co-positivities, n/tot (%)	41/124 (33)	41/149 (28)	82/273 (30)	0.371
Anti-NMDAR IgG co-positivity, n/tot (%)	34/41 (83)	37/41 (90)	71/82 (87)	0.356
MRI features, n/tot (%)				
Temporal lobe involvement	43/102 (42)	34/86 (40)	77/188 (41)	0.678
Leptomeningeal enhancement	35/86 (41)	30/95 (32)	65/181 (36)	0.122
Epilepsy features				
Age of epilepsy onset (years), median (IQR)	29 (23-37)	8 (5-12)	14 (7-29)	-
Generalized manifestations, n/tot (%)	76/96 (82)	55/79 (70)	131/175 (75)	0.062
Status epilepticus, n/tot (%)	13/98 (13)	31/105 (30)	44/203 (22)	**0.003**
Therapy, n/tot (%)				
Acute immunetherapy use	116/121 (96)	121/123 (98)	237/244 (97)	0.360
Chronic immunetherapy use	65/111 (59)	74/125 (59)	139/236 (59)	1.000
Acute ASM use	37/75 (49)	25/51 (49)	62/126 (49)	1.000
Chronic ASM use	39/79 (49)	43/77 (56)	82/156 (53)	0.382
Chronic ASM polytherapy use	10/39 (26)	9/43 (21)	19/82 (23)	0.595
Outcome, n/tot (%)				
Time of follow-up (months), median (IQR)	14 (6-28)	24 (12-48)	21 (8-37)	**0.008**
Residual deficits, n/tot (%)	39/121 (32)	60/123 (49)	99/244 (41)	0.007
Severe residual deficits**, n/tot (%)	8/39 (21)	7/60 (12)	15/99 (15)	0.229
Chronic epilepsy, n/tot (%)	10/91 (11)	35/91 (38)	45/182 (25)	**<0.001**

*Acute demyelinating encephalomyelitis (ADEM) phenotypes were defined according to the International Pediatric Multiple Sclerosis Study Group criteria (Krupp et al. 2013). Cortical encephalitis (CCE) phenotype were classified according to Valencia-Sanchez et al., 2022, including cases previously described as FLAIR-hyperintense lesions in anti-MOG-associated encephalitis with seizures (FLAMES). Patients were included in the MOGAD category if they met the 2023 international MOGAD Panel criteria (Banwell et al. 2023). If the patient presented with overlapping phenotypes were classified accordingly. Other phenotypes included meningitis, pachymeningitis and cortical vasculitis.

**Defined as: EDSS≥3, FSS≥10, mRS≥1

Abbreviations. ADEM=acute demyelinating encephalomyelitis; ASM=anti-seizure medication; CCE=cortical encephalitis; CSF=cerebrospinal fluid; EDSS=Expanded Disability Status Scale; FSS=Functional Status Scale; IQR=interquartile range; MOGAD=myelin-oligodendrocyte glycoprotein-associated disease; MRI=magnetic resonance imaging; mRS=Modified Rankin Scale; N=number, NMDAR=N-methyl-D-aspartate receptor, tot=total.

FIGURE 2 Demographic, clinical, biohumoral, MRI and electroclinical characteristics in patients with MOGAD and epilepsy, according to age of onset. For each feature, analyses were performed on the total number of patients with available data.

Conclusion: Current literature addresses epilepsy as a significant comorbidity in MOGAD, with relevant rates of chronic progression. Significant age-dependent differences in clinical presentation and outcomes underscore the importance of age-specific approaches.

Disclosure: MR, GC, VV, AB nothing to disclose. CZ consulting or speaking fees from Alexion, Astrazeneca, Biogen, Bristol Myers Squibb, Janssen, Merck, Novartis, Roche, Sandoz, Sanofi. MM grants and personal fees from Sanofi Genzyme, Merck Serono, Roche, Biogen, Amgen and Novartis. PP speaker fees from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon and Sanofi; grants from Italian Ministry of Health (MSAL) and FISM. MF received compensation for consulting services or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, MSAL, the Italian Ministry of University and Research (MUR), and FISM. MAR received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche, and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva, she receives research support from the MS Society of Canada, MSAL, MUR, and FISM.

EPO-024 | Changes in antiseizure medications and their serum concentrations during pregnancy in women: A real-world experience

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[2]Neurophysiopathology Unit and Regional Centre for Epilepsy, Department of Continuity of Care and Frailty, ASST Spedali Civili di Brescia, Brescia, Italy

Background and aims: Pregnancy is known to impact on pharmacokinetics of antiseizure medications (ASMs) due to changes of absorption, distribution, metabolism and catabolism. This is particularly relevant for women with epilepsy (WWE), as these changes can contribute to worsening or recurrence of seizures and consequent risks for the fetus. We retrospectively evaluated the pharmacokinetics of ASMs and the clinical course of WWE over three years with focusing on how dosage variation affects the circulating drug levels.

Methods: 47 pregnant WWE with at least one visit to the Regional Epilepsy Center were considered. Data collected included demographics, epilepsy type, seizure frequency 9 months before and during pregnancy, ASMs dosage and serum concentrations. Complete data for all trimesters were available for 24 patients. The concentration-to-dose (C/D) ratio was calculated at four time points: before pregnancy and during each trimester. Repeated measures ANOVA was used to analyze the C/D ratio changes between the timepoints (before pregnancy vs each trimester).

Results: C/D ratio showed a mean significant decrease (-38.5%) in the first trimester (p<0.05). The variation of C/D ratio in the first trimester for levetiracetam and lamotrigine was -20% and -52.2% respectively. Despite most of the patients underwent an

increase in ASM dosage during pregnancy, a persistent reduction in the C/D ratio was observed ($p<0.05$). Nevertheless, seizure frequency did not increase.

Conclusion: Our study suggests that pregnancy induces changes in ASM concentrations, which are not fully mitigated by therapeutic adjustments. Nevertheless, seizure frequency appeared to be stable, suggesting that other biological factors may contribute to seizure control.

Disclosure: Nothing to disclose.

EPO-025 | The effect of the vigilance state on the epileptogenic network: An SEEG study

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Background and aims: Unlike interictal anomalies, it's unclear how sleep modulates seizures and thalamo-cortical connectivity during seizures. This study aims to clarify how vigilances states influence the epileptogenic network, and its relations with thalamus during ictal/interictal periods

Methods: 36 patients with SEEG implantation presenting seizures during sleep (S) and wakefulness (W), characterized by low voltage fast activity pattern (LVFA) and thalamic electrode, were selected. EI was used to identify contacts belonging to 3 network zones (EZN, PZN, NIZ) and to assess S/W's epileptogenicity variations. Nonlinear correlation coefficient(h^2) evaluated functional connectivity (FC) differences, comparing S/W, within zones and between zones and the thalamus. FC analysis was performed across four periods: Background (BG), Pre-LVFA, LVFA, and Post-LVFA, based on their relationship to rapid discharge.

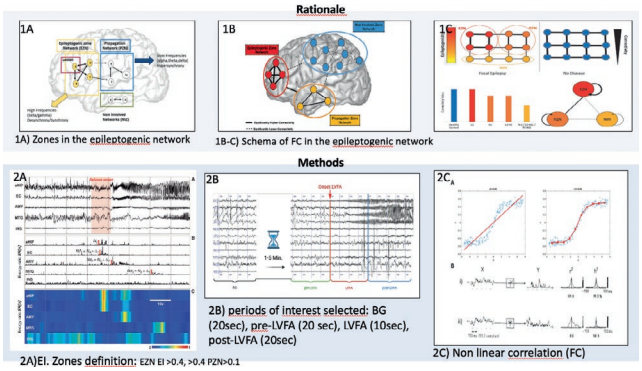

FIGURE 1 Rationale: Schematic representation of the epileptogenic network and FC changes. Methods: representation of the various methods used (EI with cut-off, periods of interest, and non-linear correlation)

Results: No differences found in the number of contacts across the zones between S/W. During the preictal period, no FC differences were observed in EZN between S/W, a significant increase in FC during S was detected during BG and Pre-LVFA in the PZN ($p<0.001$, $p=0.028$) and in the NIZ ($p<0.001$). Inter-zone analysis revealed increased FC during sleep in BG and Pre-LVFA across all comparisons performed ($p<0.001$). An increase in FC during S was observed only in BG for EZN-thalamus and PZN-thalamus ($p=0.004$, $p=0.001$) and in BG and Pre-LVFA for NIZ-thalamus ($p<0.001$, $p<0.001$). No FC differences between S/W were observed during ictal periods (LVFA and post-LVFA).

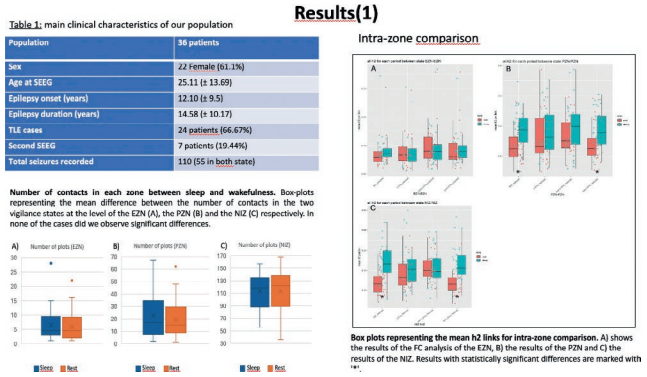

FIGURE 2 Result (1): Table of population, number of plots and intra-zone comparison of FC between S/W

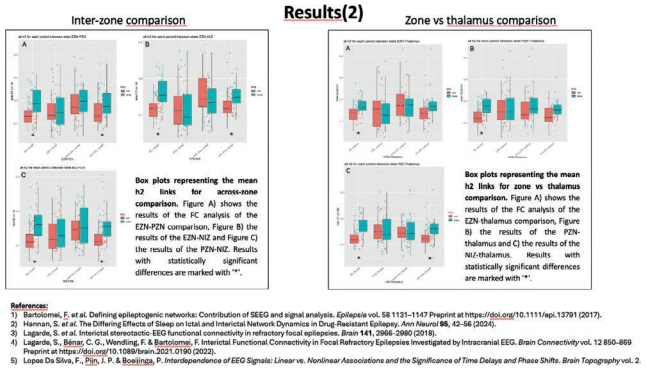

FIGURE 3 Result (2): Inter-zone and zones vs thalamus comparison of FC between S/W, bibliography

Conclusion: Sleep does not appear to modulate seizures. EZN exhibits a distinct FC profile that remains unaffected by vigilance state, unlike other zones. This may aid in differentiating it for pre-surgical evaluation.

Disclosure: Nothing to disclose.

EPO-026 | Simultaneous SEEG and Scalp-EEG for precise localization of epileptogenic zone in MRI-negative temporal lobe epilepsy

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Background and aims: MRI-negative focal epilepsy presents challenges in localizing the epileptogenic zone (EZ), crucial for achieving surgical seizure freedom. Simultaneous stereo-electroencephalography (SEEG) and scalp-electroencephalography (ScEEG) provide complementary insights by comparing ictal and interictal patterns, improving EZ delineation for diagnostic and therapeutic strategies.
Methods: This retrospective analysis included 10 adult patients with MRI-negative drug-resistant temporal lobe epilepsy (TLE) who underwent simultaneous SEEG and ScEEG at the Department of Neurology, Medical University of Vienna, between 2016 and 2023. SEEG electrodes were placed based on electroclinical hypotheses, and ScEEG according to the 10-20 system. Seizures were classified based on ictal EEG latency of ScEEG and SEEG onset in: Group 1 (≤10 seconds), Group 2 (>10 seconds), and Group 3 (no ScEEG changes). Seizure onset patterns (SOP) were categorized as ictal paroxysmal fast activity (iPFA), high-amplitude polyspikes (HAP), or rhythmic sharp waves (rSW). Interictal epileptiform discharges (IEDs) were analyzed for morphology, amplitude, and distribution. The study was approved by the local Ethics Committee (EK 2161/2024).
Results: Median seizure onset latency was 6 seconds (range: 0–43). Group 1 SOPs showed iPFA and HAP (40.9%), Group 2 - HAP (45.4%) and rSW (27.3%) and in Group 3 HAP and rSW was represented equally (44.4%). Scalp-detected interictal populations were observed in 50% of SEEG-recorded events, with sharp waves most frequent (33.3%). Interictal and ictal activity on deeper SEEG contacts rarely corresponded with ScEEG.
Conclusion: Deep epileptic discharges in MRI-negative TLE often remain confined to SEEG. Combining SEEG and ScEEG enhances EZ delineation and supports optimized therapeutic planning.
Disclosure: Nothing to disclose.

EPO-027 | Unraveling the role of IL-1β and PIP3 in epilepsy and sleep disturbances: Insights into the PI3K/AKT pathway

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Background and aims: Epilepsy, a neurological disorder affecting 1% of the global population, is characterized by recurrent seizures and closely linked to sleep disturbances such as reduced sleep efficiency and sleep deprivation. These disturbances exacerbate seizure recurrence, creating a vicious cycle. The PI3K/AKT signaling pathway, critical for cellular survival and inflammation, has been implicated in epilepsy, with interleukin-1β (IL-1β) playing a central role. IL-1β interacts with its receptor IL-1R1, activating pathways such as NF-κB, which are linked to seizures. However, the role of phosphatidylinositol-3,4,5-trisphosphate (PIP3) in this cascade and its connection to sleep disturbances remain unclear.
Methods: Using a pentylenetetrazol (PTZ)-induced mouse model of epilepsy, we investigated the roles of IL-1β signaling and PIP3. IL-1R1 knockout mice were compared with wild-type controls. Pharmacological inhibitors of the PI3K/AKT pathway were employed to study PIP3's function. Sleep parameters were assessed using polysomnography and behavioral analyses.
Results: IL-1R1 knockout suppressed PIP3 expression and reduced NMDA receptor activity, mitigating epileptogenesis. Sleep disturbances, including fragmented sleep and reduced efficiency, were significantly improved by targeting IL-1β signaling or inhibiting the PI3K/AKT pathway.
Conclusion: IL-1β and PIP3 are pivotal in the PI3K/AKT pathway underlying epilepsy and associated sleep dysfunction. Suppression of IL-1R1 or inhibition of the PI3K/AKT pathway not only mitigates seizures but also improves sleep disturbances. These findings highlight promising therapeutic strategies to address epilepsy and its comorbid sleep issues.
Disclosure: Nothing to disclose.

EPO-029 | From phenotype to genetics and back: A longitudinal study of monogenic developmental and epileptic encephalopathies

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Background and aims: Developmental and epileptic encephalopathies (DEEs) are neurodevelopmental disorders characterized by early-onset and drug-resistant seizures, significant developmental delay or regression and distinctive EEG abnormalities. This study aimed to investigate the correlations between electro-clinical phenotype and genetic findings and evaluate the natural history of persons with monogenic DEEs.
Methods: Between January 2023 and December 2024, 155 persons with DEEs underwent a comprehensive clinical-instrumental study at the Neurology Unit of the Fondazione IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo (FG), Italy, including detailed epilepsy history, 24-hour video electroencephalography, neuropsychological assessment, brain 3T MRI and genetic analysis.
Results: The mean age at the time of genetic diagnosis was 6.26 years. NGS sequencing identified a genetic etiology in 61 patients, while SNP-arrays analysis in 13. Pathogenic or likely pathogenic variants were identified in genes with an autosomal dominant inheritance pattern in 73.3% of patients, X-linked inheritance in 6.6% and autosomal recessive inheritance in 20%. The most frequently reported genes were SCN1A (20%), followed by TSC1 (8%) and CACNA1A (5%). MRI findings included cortical atrophy in 15 patients, cerebellar atrophy in 8 and focal lesions in 13. Neuropsychological assessments demonstrated severe intellectual disability in 34.7% of patients. In 37% of patients, 24-hour video electroencephalography revealed specific seizure types (e.g. "tonic seizures" in 7 patients) and facilitated the optimization of antiseizures medications.

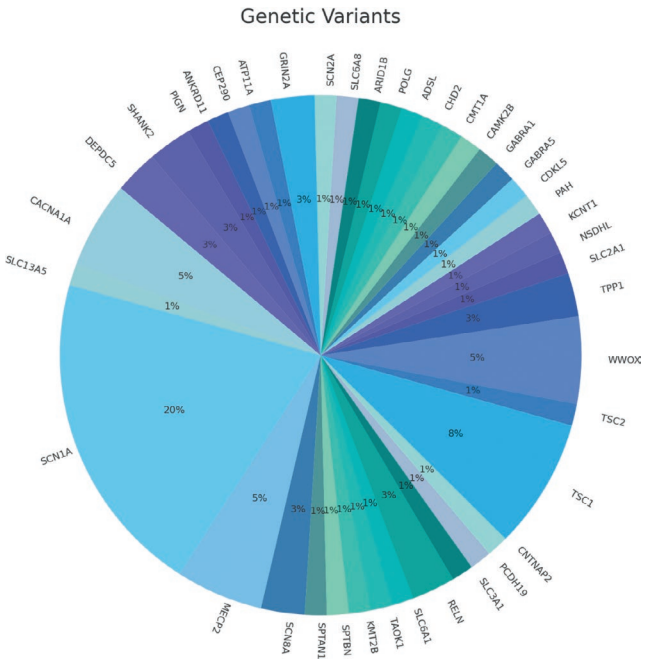

FIGURE 1 An overview of gene's variants identified.

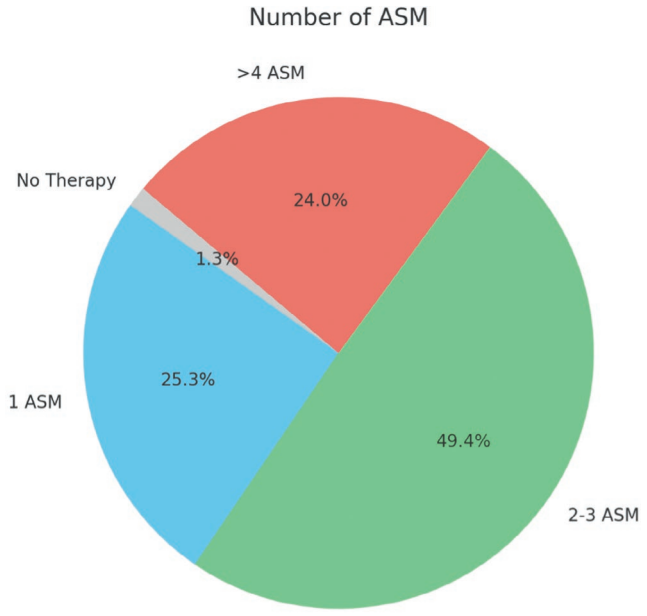

FIGURE 2 Percentage of drug resistant epilepsy.

Conclusion: This longitudinal study highlights the crucial role of phenotype and genetic testing in the diagnostic workup of DEEs. Molecular diagnosis facilitated personalized treatments and improved our understanding of the underlying pathophysiology in a significant proportion of patients.
Disclosure: Nothing to disclose.

EPO-030 | Efficacy and tolerability of Cenobamate: Real-world experience from a tertiary Italian centre

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Background and aims: To evaluate real-world efficacy and tolerability of cenobamate (CNB) in patients with drug-resistant epilepsy (DRE) in an Italian tertiary hospital.
Methods: We conducted a single-centre, retrospective, observational study collecting data from clinical records at Bellaria Hospital. Inclusion criteria were age ≥18 years, focal seizures and DRE. Primary effectiveness endpoints included seizure reductions (≥50-80%, ≥80.1-99%, 100%) or worsening at 3, 6 and 12 month visits. Safety endpoints included rates of adverse events (AEs) at 3, 6 and 12 month visits.
Results: The study included 96 patients with DRE, of whom 13.5% had developmental and epileptic encephalopathy (DEE). Etiology was known in 69% (11.5% genetic, 9.4% vascular malformation, 3% autoimmune, 3% infectious, 36.5% structural, 5% genetic and structural). Median number of prior and concomitant antiseizure medications (ASMs) were 6 and 2.5, respectively. Retention rates were 95%, 92% and 88.7%, and mean CNB dosages/day were 112.76 mg, 149.08 mg and 180.95 at 3, 6 and 12 months, respectively. At the last available visit, 28.6%, 20.6% and 15.9% had response rates of ≥50-80%, ≥80.1-99% and 100%, 17.5% did not respond and a further 17.5% worsened. At baseline, median epilepsy duration was 25.95 years and median number of seizures/month was 12.50, with a significant reduction ($P < 0.001$) at all timepoints. The cumulative percentages of patients with AEs and AEs leading to discontinuation were 46%, 39.6% and 38.7% at 3, 6 and 12 months.
Conclusion: In this highly refractory population, CNB demonstrated good efficacy regardless of etiology, prior and concomitant ASMs. AEs were frequent but mostly mild-to-moderate.
Disclosure: Nothing to disclose.

EPO-031 | Acute kidney injury in patients with spontaneous intracerebral hemorrhage – Is it a real problem?

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Background and aims: Acute kidney injury (AKI) is common in critically ill intensive care unit patients, including those with intracerebral hemorrhage (ICH). Spontaneous ICH accounts for 10-15% of all strokes and is the leading cause of death and long-term disability in people over 40 years of age worldwide, and the development of AKI in these patients further worsens their outcomes. The aim of the study was to determine the incidence and risk factors for AKI, as well as short-term outcomes in patients with spontaneous ICH.
Methods: In this single-center study, we retrospectively analyzed the data of consecutive patients diagnosed with spontaneous ICH.
Results: Of the 237 patients with spontaneous ICH included in the study, 13.5% of patients developed AKI. Risk factors for AKI were: severity of neurological deficit as measured by the National Institutes of Health Stroke Scale (NIHSS), larger hematoma volume, as well as higher baseline mean systolic and diastolic blood pressure. Furthermore, patients who developed AKI had higher levels of serum glucose, urea, serum creatinine and lower estimated glomerular filtration rate (eGFR) on hospital admission. In addition, the overall and in-hospital mortality were much higher in patients with AKI than in those without AKI. Finally, adjusted regression analysis identified the in-hospital use of nephrotoxic antibiotics as a major risk factor, increasing the likelihood of AKI by eightfold.
Conclusion: These findings highlight the importance of early identification of high-risk patients and careful management of nephrotoxic agents to reduce the incidence and adverse outcomes of AKI in ICH patients.
Disclosure: Nothing to disclose.

EPO-032 | Complex post-closure hallucinations as a sign of posterior callosal stroke: A case-report

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Background and aims: Visual hallucinations triggered by eye closure are a very rare finding in clinical practice. Underlying pathomechanisms include cortex irritation and cortical release phenomenon caused by suppression of inhibitory cortical input to visual association areas.
Methods: We describe the case of a 77-year-old female with transient visual hallucinations at closed eyes after a posterior ischemic stroke due to basilar artery occlusion.
Results: At admission the patient presented with altered consciousness state and NIHSS scored 23 points. CT-Angiography showed basilar artery occlusion, and patient underwent thrombectomy. The following day neurological examination was dramatically improved (NIHSS 0), and the patient complained only of complex visual hallucinations occurring at closed eyes. CT-scan and EEG were negative while brain MRI (6th day) showed DWI restriction in splenium of corpus callosum, and FDG-PET (8th day) revealed hypometabolism in right temporo-occipital area. On day 10, visual hallucinations disappeared, and the patient was discharged.
Conclusion: Splenium of Corpus callosum is involved in integration network mainly for occipital cortex. Posterior callosal stroke might result in right temporo-occipital area hypometabolism suggesting that closed-eye hallucinations may be related to loss of inhibitory cortical input to visual association areas as described in Charles Bonnet Syndrome.
Disclosure: Nothing to disclose.

EPO-033 | Terson syndrome secondary to cerebral intraparenchymal haemorrhage

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Background and aims: Terson syndrome was first described as a vitreous haemorrhage secondary to subarachnoid haemorrhage (SAH). It is associated with worse prognosis in these patients. More recently, intracerebral haemorrhage and neoplasms have also been associated with this syndrome.
Methods: Case report.
Results: A 28-year-old male was admitted due to an explosive headache with nausea, vomiting and, 10 minutes later, altered mental status. He was sedated and intubated due to inefficient respiratory pattern in the pre-hospital setting. Neurological examination showed absence of eye opening, anisocoria due to right mydriasis, unreactive pupils, motor response with flexion of the right upper limb and pathologic extension of the left upper limb (Glasgow Coma Scale 6). He had previous history of amblyopia secondary to congenital periocular hemangioma and

strabismus, surgically corrected during childhood. Head-CT showed a right temporal hematoma with significant mass effect. Decompressive craniectomy and hematoma evacuation were performed. Aetiological investigation, including analytical evaluation, and digital cerebral angiography were negative. Brain MRI showed a small haemorrhage on the posterior surface of the right eye. Ophtalmologic evaluation confirmed vitreous haemorrhage. There was progressive clinical improvement. At discharge, the patient presented left hemiparesis and was autonomous in activities of daily living (mRankin 2).

Conclusion: In this case, the acute intracerebral haemorrhage was responsible for a rapid increase in intracranial pressure that extended to the optic nerve sheath leading to vitreous haemorrhage. There was no impact on visual acuity, possibly due to previous amblyopia. In this case, MRI was essential for diagnosis the vitreous haemorrhage.

Disclosure: Nothing to disclose.

EPO-034 | Neglecting neglect: Optimising FASTED assessment for Prehospital LVO-stroke prediction

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Background and aims: FAST-ED is a validated screening tool for large vessel occlusion (LVO) ischaemic stroke detection. The London Prehospital Video Triage (PVT) service enables stroke specialists to assist in on-scene assessment, but examining neglect via video remains challenging and may introduce delays. We evaluate the utility of neglect within FAST-ED score.

Methods: We retrospectively analysed patients assessed via PVT between January and June 2023 and admitted to the National Hospital for Neurology and Neurosurgery. FAST-ED's accuracy for LVO prediction was compared with two alternative models: neglect field excluded, and double weighting eye-deviation. LVO was defined based on thrombectomy eligibility, including M1, proximal M2, P1, A1, and basilar occlusions.

Results: 424 patients were analysed: including 52 LVO stroke, 177 non-LVO stroke, and 125 non-strokes. Conventional FAST-ED≥4 as LVO prediction demonstrated sensitivity 0.65 and specificity 0.86 among stroke patients, and specificity 0.89 among all patients. Mimics with FAST-ED≥4 included functional (3), seizures related to sepsis (2), new mass lesion (1) and hyperglycaemia (1). If only MCA-implicated LVOs are considered, FAST-ED≥4 showed improved sensitivity of 0.74. Full FAST-ED, FAST-ED with neglect excluded, and FAST-ED with neglect excluded while eye-deviation score doubled, all showed similar predictive accuracies (AUC of 0.82, 0.82, and 0.81 respectively). For patients with confirmed neglect on admission, 69% were missed on PVT assessment.

TABLE 1 Case numbers for various final diagnosis groups and their FASTED score.

	Stroke LVO with MCA involvement	Stroke LVO with no MCA involvement	Stroke non-LVO	Non-Stroke
FASTED <4	12	6	153	114
FASTED >=4	34	0	24	13

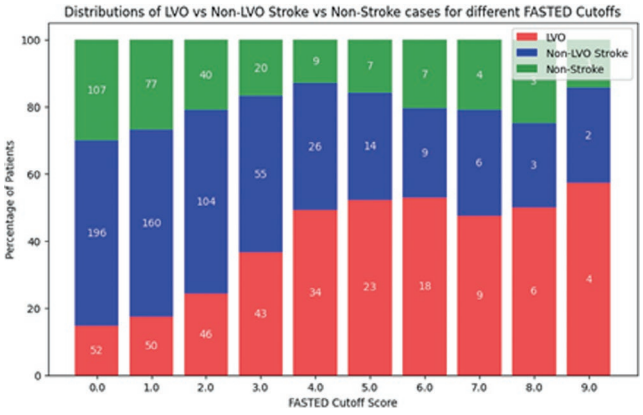

FIGURE 1 Distribution of cases for various FASTED cut-off scores

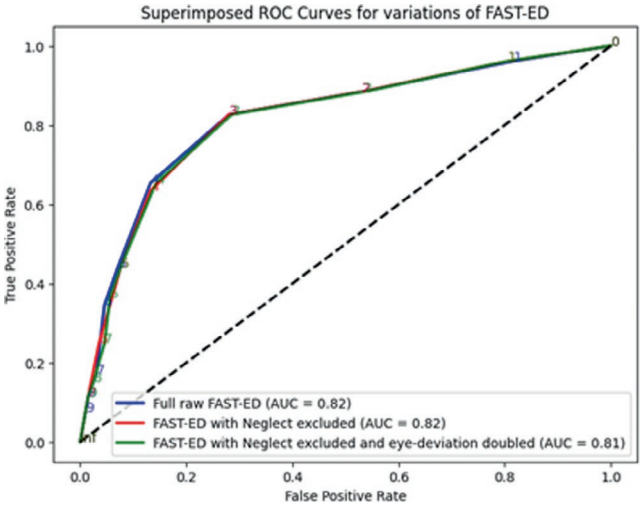

FIGURE 2 Superimposed ROC curves for variations of FASTED scores

Conclusion: FAST-ED is an effective tool for LVO identification, particularly for MCA LVO. Excluding neglect assessment does not significantly impact its accuracy. Specialist assessment via PVT would enhance the exclusion of clear non-stroke with high FAST-ED, and inclusion of non-MCA LVO.

Disclosure: Nothing to disclose.

EPO-035 | NOTCH3 protein EGFr domain and white matter lesions effects on brain volume in CADASIL patients

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Background and aims: Epidermal growth factor-like repeat domains (EGFrs) of the NOTCH3 protein have been classified into three risk groups that may predict disease severity in cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL) patients. Extensive white matter hyperintensities (WMHs) in CADASIL patients are associated with increased brain volume. Still, no correlation has been explored when considering the EGFr risk category.
Methods: 70 CADASIL patients were classified into three risk groups with similar mean age according to the NOTCH3 EGFr domain altered: 26 high-risk, 23 medium-risk, and 21 low-risk. Normalized brain volume (brain parenchyma volume/intracranial cavity volume) and normalized white matter (WM) lesion volume (WM lesion volume/intracranial cavity volume) were calculated using VolBrain DeepLesionBrain from volumetric T1w and FLAIR brain MRI sequences. A multivariate linear regression model was used to model the relationship between normalized brain volume and normalized WM lesion volume, considering the effect of EGFr risk category, age and sex.
Results: The regression analysis showed that brain volume significantly decreases with increasing age ($p=0.001$), while it increases in individuals with higher EGFr risk categories ($p=0.010$) and greater WM lesion volumes ($p<0.001$). Sex does not have a significant effect ($p=0.298$).
Conclusion: Our study confirms previous reports that greater WMH volumes are associated with increased brain volume in CADASIL patients, which may be caused by an overall increase in water content within cerebral tissue despite the loss of white matter components, while adding the EGFr risk category as another factor that seems to influence this correlation.
Disclosure: Nothing to disclose.

EPO-036 | Does emergency conversion to general anesthesia during mechanical thrombectomy increase the risk of poor outcome?

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Background and aims: The consequences of emergency conversion (EC) from non-general anesthesia (non-GA) to general anesthesia (GA) during mechanical thrombectomy (MT) are unknown. This study aimed to explore the functional outcomes of patients who underwent EC during MT.
Methods: We included consecutive patients with anterior large vessel occlusion and pre-mRS ≤2 treated with MT in 3 thrombectomy capable centers between January 2022 and December 2023. Inverse probability weighting (IPW) reduced bias by indicating the anesthesia type on study outcomes. We used a weighted ordinal robust logistic regression analysis to explore the primary outcome of modified Rankin Scale (mRS) shift at 90 days in EC versus GA versus non-GA. Secondary outcomes included 90-day poor outcome, defined as an mRS >2, 90-day mortality, symptomatic intracranial hemorrhage (sICH), and successful recanalization.
Results: We included 669 patients: 395 underwent GA, 189 non-GA, and 85 EC. There was no significant shift for worse mRS scores at 90 days in EC versus GA (cOR 1.17, 95% CI 0.97-1.41; $p=0.091$) and versus non-GA (cOR 0.88, 95% CI 0.72-1.07, $p=0.201$). Secondary outcomes were not different among the three groups, but the GA technique was an independent predictor of successful recanalization (aOR 1.90, 95% CI 1.30–2.80; $p=0.001$).

	mRS shift (univariate)		
Predictors	*Common Odds Ratio*	*CI*	*p*
Type of anesthesia			
EC	1*		
GA	1.17	0.97-1.41	0.091
Non-GA	0.88	0.72-1.07	0.201
	mRS shift (multivariate)		
Predictors	*Adjusted Common Odds Ratio*	*CI*	*p*
Type of anesthesia			
EC	1*		
GA	1.29	0.93-1.37	0.215
Non-GA	0.83	0.68-1.01	0.062
Age	1.02	1.01-1.03	**0.001**
Sex (female)	0.96	0.97-1.12	0.563
NIHSS (per unitary increase)	1.09	1.08-1.11	**0.001**
Glucose at admission (per unitary increase)	0.99	0.99-1.01	0.314
ASPECT score (per unitary increase)	1.06	0.99-1.13	0.084
IVT	0.82	0.69-0.96	**0.014**
GTR (per unitary increase)	1.01	1.00-1.01	**0.001**
Number of passes more than 3	1.74	1.44-2.10	**0.001**

FIGURE 1 Weighted shift analysis for mRS at 90 days. EC= emergency conversion; GA= general anaesthesia; NIHSS= National Institutes of Health Stroke Scale; ASPECT = Alberta Stroke Program Early CT; IVT= intravenous thrombolysis; GTR= groin-to-reperfusion. *Reference

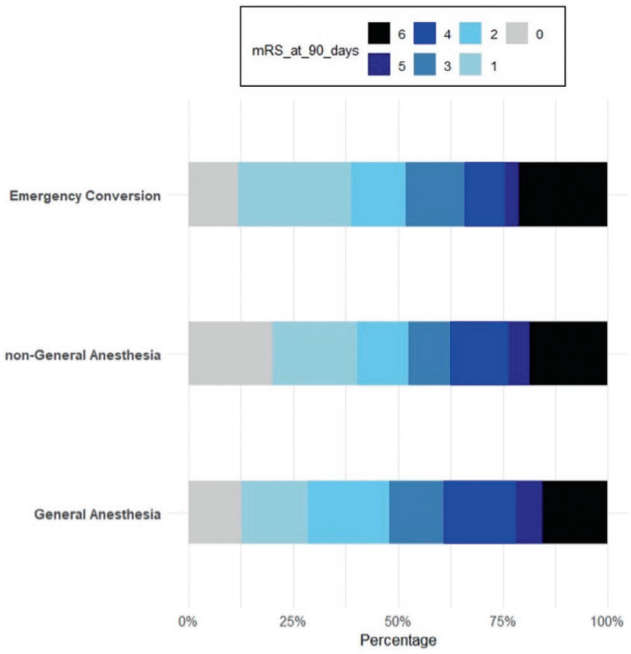

FIGURE 2 Distribution of modified Rankin Scale (mRS) scores at 90 days in patients underwent Emergency Conversion (EC), non-General Anesthesia (non-GA), and General Anesthesia (GA).

Conclusion: Our study suggests that EC is not associated with worse functional outcome compared to patients undergoing primary GA or non-GA.
Disclosure: Nothing to disclose.

EPO-037 | In-hospital course of ischemic stroke without LVO treated with thrombolysis: Impact of Fazekas score, location, and size

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Background and aims: Whether leukoaraiosis worsens prognosis in acute ischemic stroke patients undergoing intravenous thrombolysis (IVT) remains debated. We aimed to assess how IVT influences outcomes in minor ischemic stroke without large vessel occlusion (LVO) and whether stroke size, location, or leukoaraiosis severity affects in-hospital improvement.
Methods: We included acute ischemic stroke patients without LVO and confirmed by brain MRI. Demographic data, NIHSS at admission (NIHSS_in) and discharge (NIHSS_out), stroke location and size, and Fazekas score (sum of periventricular/subcortical values, range 0–6) were collected. Two-way ANOVA was performed.
Results: Among 207 patients, 126 (60.9%) met inclusion criteria. 58.7% female, mean age was 76.6 ± 11.4 years, 17.5% IVT-treated, mean NIHSS_in 4.55 ± 3.29, NIHSS_out 1.2 ± 1.87, hospital stay 11.65 ± 7.55 days. IVT and non-IVT groups were similar in age/sex. Fazekas scores: 25.4% mild (0–2), 35.7% moderate (3–4), 37.3% severe (5–6). Stroke locations: 19.8% infratentorial, 19.8% deep, 50.8% hemispheric, 9.5% multifocal. IVT patients had significantly lower NIHSS_out ($p < 0.001$, covariate: NIHSS_in). Those with severe Fazekas scores showed greater NIHSS_out improvement with IVT (mean -1.7 ± 0.55; $p = 0.002$, covariate: NIHSS_in). Stroke location and size had no impact.

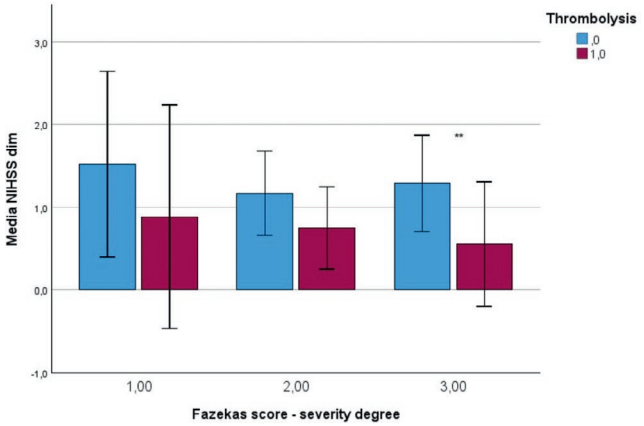

FIGURE 1 NIHSS at discharge according to Fazekas score (1: mild, 2: moderate, 3: severe) in patients treated with intravenous thrombolysis (IVT) and those not treated with IVT.

Conclusion: In IVT-treated patients, severe leukoaraiosis does not worsen outcomes. Instead, IVT appears particularly beneficial in these patients with reduced functional reserve.
Disclosure: F. Tazza, M. Pizzorno, E. Scarsi, C. Finocchi have nothing to disclose.

EPO-039 | Efficacy and safety of reteplase versus alteplase for the treatment of acute ischemic stroke: A meta-analysis

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Background and aims: Reteplase rise as a possible alternative to Alteplase in managing patients presenting with acute ischemic stroke within the eligible therapeutic window.
Methods: We systematically searched Medline, Scopus, and Cochrane Library up to August 2024. We Included RCTs comparing the efficacy and safety of Reteplase to that of Alteplase in adult patients who received thrombolytic therapy within 4.5 hours of symptoms onset and had excellent functional status before the onset of their stroke. Primary efficacy outcome was an excellent functional outcome, defined as a modified Rankin scale score of 0 or 1 within 90 days. Primary Safety outcome was assessed using the incidence of symptomatic intracranial hemorrhage within 36 hours. Other safety outcomes were the incidences of any adverse event, serious adverse event, and death within 90 days.
Results: Out of 376 records identified, 3 studies were included in this review, comprising 1772 patients, Reteplase showed higher excellent functional outcome (RR=0.89 95% CI= [0.84,0.94], P=<0.0001), higher dramatic recovery at 7-30 days (RR=1.11, 95% CI=[1.04,1.18], p=0.002), and Barthel Index score of ≥61 at 90 days (RR=1.06, 95% CI=[1.01,1.12], P=0.02) in comparison to Alteplase. Symptomatic intracranial hemorrhage within 36 hours and mortality were not significantly different between the two arms (RR=1.06, 95% CI=[0.62,1.81], p=0.83), (RR=1.18, 95% CI=[0.72,192], p=0.51]

respectively. However, the incidences of any adverse event or serious event within 90 days were significantly higher in the Reteplase arm (RR=1.12, 95% CI=[1.07,1.18], p=<0.00001), (RR=4.12, 95% CI=[2.79,6.07], p=<0.00001) respectively.

Conclusion: Reteplase seems to be more effective and less safe than Alteplase.

Disclosure: Nothing to disclose.

EPO-040 | Safety and efficacy of factor XIa inhibitors for prevention of thromboembolism: Systematic review and meta-analysis

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Background and aims: Stroke and thromboembolism remain the leading causes of mortality worldwide. Factor Xia (FXIa) might prevent thromboembolism without interfering with hemostasis, thus leading to a lower risk of bleeding compared to direct oral anticoagulants (DOACs).

Methods: We conducted a systematic search using PubMed, Embase, and Clincaltrials.gov to retrieve randomized controlled trials comparing FXIa inhibitors to placebo or DOACs in patients at risk of stroke or thromboembolism. All statistical analyses were carried out using RevMan 5.4, using a random effects model.

Results: Our meta-analysis included 14 RCTs involving 30,952 patients. FXIa inhibitors significantly decreased the risk of major bleeding (RR 0.47, 95% CI: 0.33-0.66, I2=46%) with no significant change in systemic embolism or thromboembolism (RR 0.82, 95% CI: 0.66-1.03, I2=60%). There was no significant change between two groups when assessing the rate of all bleeding events (RR 0.78, 95% CI: 0.55-1.11, I2=73%), all-cause mortality (RR 0.89, 95% CI: 0.70-1.13, I2=0%), ischemic stroke (RR 1.01, 95% CI: 0.47-2.15, I2=83%). FXIa inhibitors were associated with a reduced risk of intracranial hemorrhage (RR 0.44, 95% CI: 0.21-0.95, I2=1%). Although there was a higher rate of all adverse events in the FXIa inhibitors group (RR 1.58, 95% CI: 1.03-2.40, I2=95%), risk of serious adverse events (RR 1.16, 95% CI: 0.86-1.55, I2=74%) remained comparable between two groups.

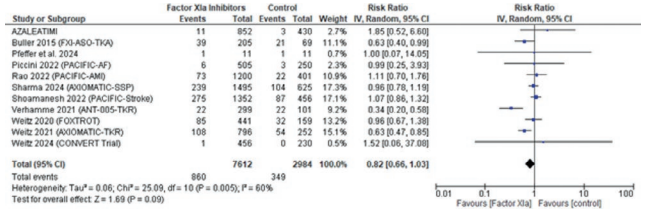

FIGURE 1 Forrest plot for thromboembolism/systemic embolism.

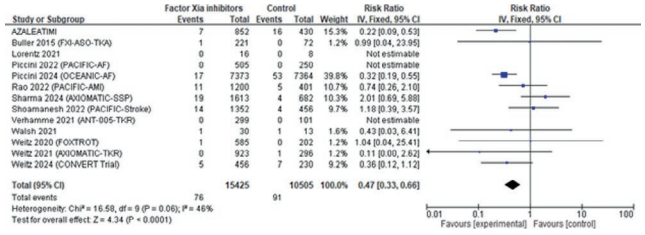

FIGURE 2 Forrest plot for Major bleeding.

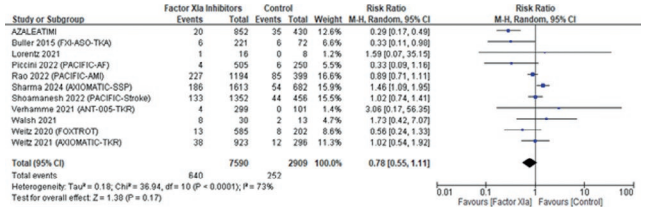

FIGURE 3 Forrest plot for All bleeding events.

Conclusion: When compared with DOACs, FXIa inhibitors demonstrate favorable bleeding outcomes without changing thromboembolism, mortality, or other safety outcomes. Data from high-quality, large-scale RCTs is warranted for evidence of its clinical benefit.

Disclosure: Nothing to disclose.

EPO-041 | Left atrial appendage occlusion versus anticoagulant therapy alone after ischemic stroke despite anticoagulation

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Background and aims: Recurrent ischemic stroke in patients with atrial fibrillation (AF) despite oral anticoagulation remains a clinical challenge. Left atrial appendage occlusion (LAAO) is a potential mechanical intervention to mitigate this risk. We aim to compare the efficacy and safety of LAAO plus anticoagulation versus continued oral anticoagulant (OAC) therapy alone in secondary major events prevention.

Methods: This retrospective cohort study included patients with nonvalvular AF who experienced ischemic stroke despite

anticoagulation. Outcomes were compared between two groups: LAAO recipients (mean follow-up 4.7±3.3 years) and controls on OAC therapy (mean follow-up 1.1±1.0 years). Multivariate Cox regression evaluated time to a first event, a composite of stroke, bleeding, and other systemic embolisms. Safety of the LAAO procedure was also evaluated.

Results: The study enrolled 108 patients, 45.4% women, with a mean age of 77.2±9.8 years. Both cohorts exhibited elevated CHA2DS2-VASc scores, with a mean of ≥5±1.2. During the follow-up, 20 patients experienced an event (4 in the LAAO group and 16 in the OAC group). The event rate was significantly lower in the LAAO group (0.082 vs 0.82 events per 100 patient-years) with an aHR of 0.10 (CI 95% 0.01-0.79, p=0.03). Multivariate analysis was adjusted for age and CHA2DS2-VASc. Individually, each of the composite variables was not significant. Major procedural complications occurred in two patients (6%) undergoing LAAO (cardiorespiratory arrest and major bleeding).

Conclusion: LAAO showed superior event prevention compared to OAC alone in patients with nonvalvular AF, albeit with low-frequency procedural risks. These findings support LAAO as an effective secondary prevention strategy in high-risk population.

Disclosure: Nothing to disclose.

EPO-042 | Efficacy and safety of recombinant human prourokinase vs. alteplase in acute ischemic stroke: A meta-analysis

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Background and aims: Intravenous Alteplase at 0.9 mg/kg is the standard treatment for acute ischemic stroke in patients presenting within 4.5 hours. The role of recombinant human Prourokinase (rhPRO-UK) in stroke management is less understood. This meta-analysis evaluates the efficacy and safety of rhPRO-UK compared to Alteplase.

Methods: A systematic search of PubMed and Cochrane databases identified randomized controlled trials (RCTs) comparing rhPRO-UK to Alteplase in acute ischemic stroke. Outcomes assessed included: (1) Modified Rankin Scale (mRS) scores of 0–2 (good functional outcomes) at 90 days; (2) systemic bleeding; (3) symptomatic intracranial bleeding (as defined by SITS-MOST); and (4) serious adverse events within 90 days. Heterogeneity was assessed using the I^2 statistic, and random-effects models were applied.

Results: Three RCTs including 1,179 patients treated with rhPRO-UK were analyzed. At 90 days, rhPRO-UK was non-inferior to Alteplase in achieving mRS 0–2 outcomes (OR 1.01; 95% CI 0.83–1.23; p = 0.93; I^2 = 0%). Risks of symptomatic intracranial bleeding (RR 0.53; 95% CI 0.18–1.59; p = 0.26; I^2 = 25%) and serious adverse events (RR 0.95; 95% CI 0.78–1.16; p = 0.60; I^2 = 0%) were comparable. The risk of systemic bleeding was lower with rhPRO-UK (RR 0.73; 95% CI 0.58–0.92; p = 0.009; I^2 = 57%).

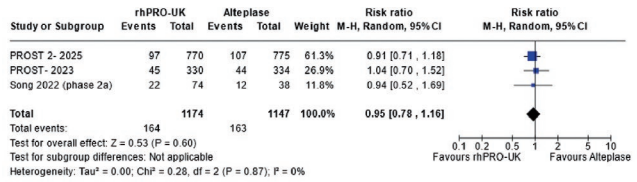

Figure 4. The risk of serious adverse events post ischemic stroke treatment with rhPRO-UK was neither inferior nor superior to standard care with Alteplase (RR 0.95; 95% CI 0.78-1.16; p=0.60).

Figure 4.Serious Adverse Events Within Post-Stroke 90 Days: Recombinant human prourokinase (rhPRO-UK) versus Alteplase.

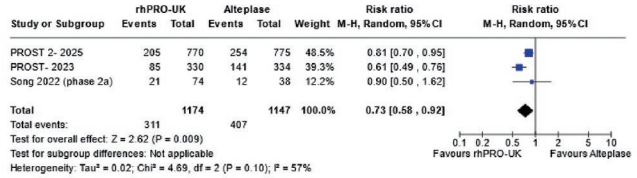

Figure 1A. There was lower risk of systemic bleeding (both minor and major bleeding outcomes) for patients treated with rhPRO-UK within 4.5 hours of ischemic stroke, compared to Alteplase therapy (RR 0.73; 95% CI 0.58-0.92; p=0.009). High heterogeneity was detected.

Figure 1B.Leave-one-out analysis to detect heterogeneity.

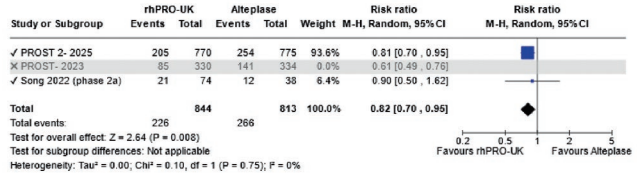

Figure 1B. There was no heterogeneity as we removed PROST RCT. In our opinion, the reason is in the study, PROST used long term follow up for this outcome, within 90 days; while the other two RCTs more short-term follow-up, within 7 days.

Forest plots of Alteplase versus rhPRO-UK in management of acute ischemic stroke within 4.5hours

Figure 1.Systemic Bleeding Outcomes: Recombinant human prourokinase (rhPRO-UK) versus Alteplase.

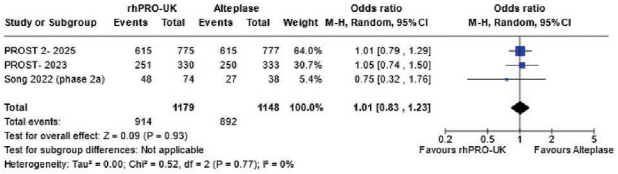

Figure 2. There were no noticeable differences in chance of gaining good functional outcomes (defined as modified Rankin Scale Score between 0 and 2; mRS 0-2) 90 days post ischemic stroke for patients with rhPRO-UK, compared to standard care (OR 1.01; 95% CI 0.83-1.23; p=0.93).

Figure 2.Good Functional Outcomes At 90 Days: Recombinant human prourokinase (rhPRO-UK) versus Alteplase.

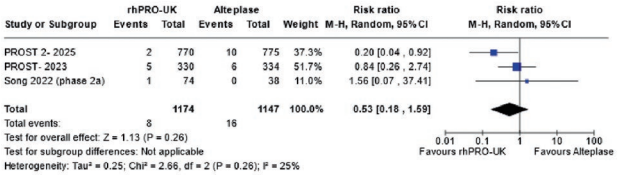

Figure 3. There were no differences in the risk of symptomatic intracranial bleeding post ischemic stroke treatment with rhPRO-UK, compared to standard care with Alteplase (RR 0.53; 95% CI 0.18-1.59; p=0.26).

(*)Symptomatic intracranial hemorrhage defined in SITS-MOST*

SITS-MOST=Safe Implementation of Thrombolysis in Stroke-Monitoring Study defines as Symptomatic intracranial bleeding is defined as the presence of intracranial hemorrhage (ICH) detected on brain imaging, which is associated with neurological deterioration (i.e., an increase in the National Institutes of Health Stroke Scale (NIHSS) score by 4 or more points) or leads to a clinical worsening of the patient's condition.

Figure 3.Symptomatic Intracranial Hemorrhage Defined In SITS-MOST*: Recombinant human prourokinase (rhPRO-UK) versus Alteplase.

Symptomatic Intracranial Hemorrhage and Good Functional Outcomes at 90 Days: Recombinant human prourokinase (rhPRO-UK) versus Alteplase.

Conclusion: RhPRO-UK offers similar efficacy and safety to Alteplase in acute ischemic stroke, with a reduced risk of systemic bleeding. These findings, limited by potential biases such as sample size reductions, warrant further RCTs to confirm rhPRO-UK's safety profile and explore its potential superiority.
Disclosure: Nothing to disclose.

EPO-043 | Predictive value of ABCD2 score and Canadian TIA Score for outpatient management of vascular neurological deficits

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Background and aims: The safety of outpatient management for transient ischemic attack (TIA) and minor acute ischemic stroke (MAIS) remains controversial. This study aimed to evaluate the predictive value of the ABCD2 score and the Canadian TIA Score (CTS) for acute ischemic lesions (AIL) and to identify independent predictors of recurrence in patients presenting with TIA or MAIS, to guide admission to stroke units.
Methods: We retrospectively reviewed medical records of patients with suspected TIA or MAIS between June 2022 and December 2023. ABCD2 and CTS scores were considered positive at cut-offs of ≥4 and ≥9 points, respectively, indicating high acute ischemic stroke risk. Univariate and multivariate analyses compared patients with and without AIL, while ROC analysis assessed the predictive value of both scores.

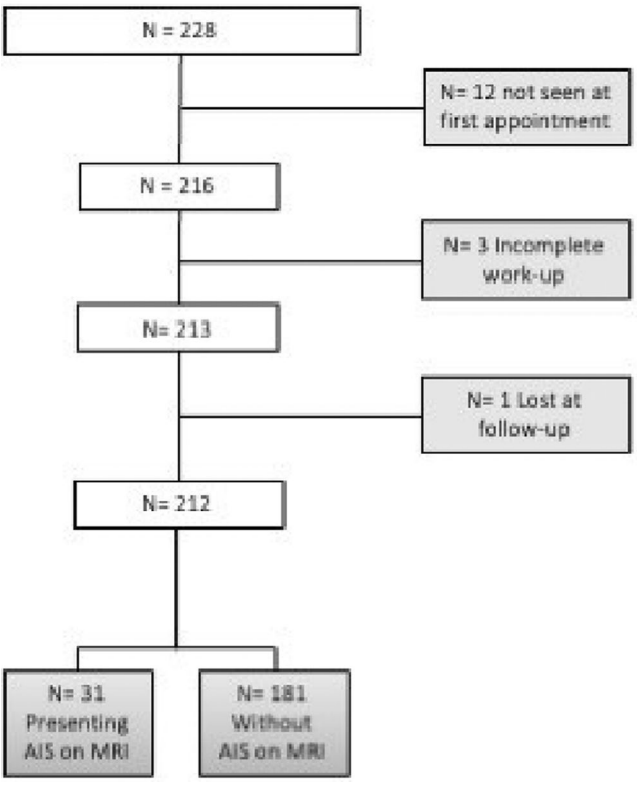

FIGURE 1 Flowchart

Results: From 212 patients analyzed, thirty-one (14.6%) had AIL and presented more often with motor deficits (29% vs. 11%, p=0.02), symptom duration ≥24 hours (41.9% vs. 9.9%, p<0.001), and shorter delays to MRI (8 vs. 16 days, p=0.03). Multivariate analysis identified early MRI acquisition (per day: OR=0.96, p=0.013), symptom duration ≥24 hours (OR=7.77, p<0.001), and motor deficits (OR=3.93, p=0.008) as independent predictors of AIL. Both ABCD2 and CTS scores demonstrated high negative predictive value (NPV) (90% and 88.7%, respectively) but moderate predictive accuracy (60% vs. 69.8%). Among 28 patients with recurrence, no significant differences were observed compared to the overall population.

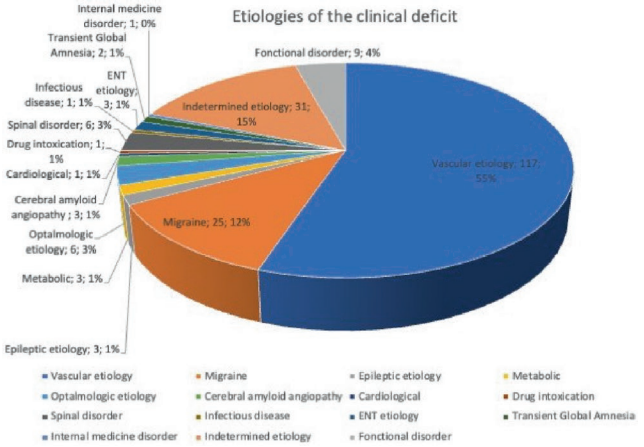

FIGURE 2 Etiologies

Conclusion: ABCD2 score and CTS exhibit moderate accuracy for predicting AIL but provide high NPV, supporting their use in safely discharging patients with presumptive negative MRI findings.
Disclosure: Nothing to disclose.

EPO-044 | Management of unruptured intracranial aneurysms: 10-year experience of a multidisciplinary committee

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Background and aims: ESO guidelines report a risk of rupture for unruptured intracranial aneurysms (UIA) of 0.8%/patient-year. Endovascular or surgical treatment is often indicated in UIAs with high-risk features, with reported treatment failure of 10-18% and disabling procedural complications of 4%. We analyzed the characteristics and prognosis of patients with UIA evaluated by a multidisciplinary committee.
Methods: Retrospective observational study of patients with UIA evaluated by a multidisciplinary committee (neurology,

neurosurgery, neuroradiology) between 2011 and 2019. We compared basal characteristics and outcomes of treated and untreated patients.
Results: Seventy-five patients were included, median age 60 years (71% women), with median follow-up of 8.4 (6.5-11.4) years after UIA diagnosis. Most frequent risk factors were hypertension (56%) and smoking (51%). Most common aneurysm locations were middle cerebral (36%) and internal carotid arteries (35%). Ten patients (13%) presented with compressive symptoms, while 87% were considered incidental UIAs. Thirty-eight patients (51%) underwent intervention (25 endovascular and 13 surgical treatment), while 37 (49%) were managed conservatively. No significant differences were found between treatment groups in terms of age, maximum aneurysm diameter or PHASES score. Treated aneurysms were more frequently irregular (21% vs 5%). One (2.6%) fatal complication (and 2 non-disabling) occurred in the treated group and 4 (10%) required reintervention. One fatal hemorrhage (global rupture rate of 0.3%/patient-year) occurred in the conservative group. Significant aneurysm growth was reported in 4 patients during follow-up, one of whom underwent embolization.
Conclusion: Evaluation of UIA management by a multidisciplinary committee is associated with low rates of fatal complications and rupture during follow-up.
Disclosure: Nothing to disclose.

EPO-045 | Laboratory and radiological findings associated with increased stroke risk in atheosclerotic carotid disease

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Background and aims: The aim is to identify inflammatory and radiological biomarkers that can predict ischemic stroke risk.
Methods: 62 cases were examined in three groups: asymptomatic carotid stenosis (ACS), symptomatic carotid stenosis (SCS), and control group. In serum samples, inflammatory markers and natural immune system activity were evaluated by ELISA and flow cytometry. In the SCS group, they were repeated in the acute phase and at 6-months. While all patients underwent vascular imaging, white matter lesions were classified according to the Fazekas scale using MR, and the presence of intraplaque hemorrhage was evaluated with MPRAGE. Cognitive functions of patients were determined using the ACE-R and MMSE tests.
Results: In the SCS group, levels of IL-6, IL-1 beta, and M1 monocytes were higher compared to the ACS and control groups ($p < 0.01$, $p < 0.05$, $p < 0.05$, respectively). IL-8 levels in the SCS group were higher than the control group ($p < 0.05$). In the ACS group, IL-8 levels were higher in patients with heterogeneous plaques than homogeneous plaques ($p = 0.04$). CitH3 and PMN in the SCS and IL-6 in the ACS were higher in patients with advanced carotid stenosis ($p = 0.008$, $p = 0.009$, $p = 0.043$, respectively). In the ACS group, MMSE and ACE-R scores were found to be lower than the control group ($p = 0.045$, $p = 0.005$).
Conclusion: Increased inflammation and neutrosis in atherosclerotic carotid disease were associated with stroke. No clear relationship was demonstrated between severe white matter disorder and increased systemic inflammation.
Disclosure: Nothing to disclose.

Cognitive Neurology/Neuropsychology

EPO-046 | Loneliness and prescription drug misuse in older patients: A study of patients on potentially addictive medication

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Background and aims: Medications with addictive potential are commonly prescribed to older patients despite consensus recommendations advocating caution. Studies have shown a link between loneliness and medication use, but rarely evaluate substance use disorder-related outcomes in real-life clinical settings. We explored the association between loneliness prolonged drug use and severity of drug dependence.
Methods: With a clinical sample including 246 consenting older patients, we conducted a consecutive cross-sectional study at a large public regional hospital in Norway. We measured loneliness, using the De Jong-Gierveld Loneliness Scale, and severity of prescription drug dependence by the Severity of Dependence Scale (SDS), and defined prolonged use as medication use exceeding duration recommended by clinical guidelines. We cross-checked information from both patient interviews and electronic hospital registries. Multivariable logistic and linear regression models were used.
Results: The adjusted odds ratio of prolonged use for overall, social and emotional loneliness were 1.32 (95% CI: 1.07–1.61), 1.52 (95% CI: 1.05–2.20) and 1.41(95% CI: 1.05–1.91), respectively. The odds were higher for female and multimorbid patients, and lower for those with higher education. Loneliness was positively associated with the SDS score, adjusting for sociodemographic and clinical characteristics. The association was stronger when Z-hypnotics were co-used with opioids or benzodiazepines.

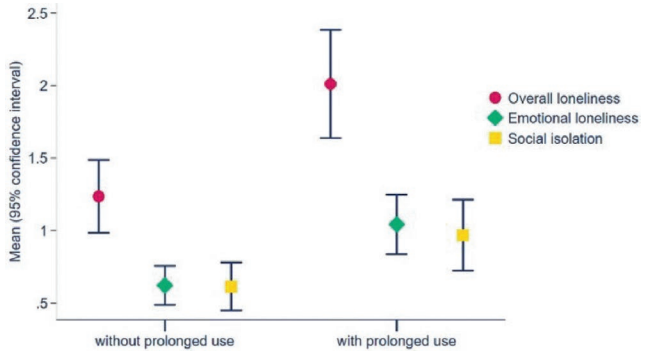

FIGURE 1 Loneliness score in older patients with vs without prolonged use of potentially addictive meds.

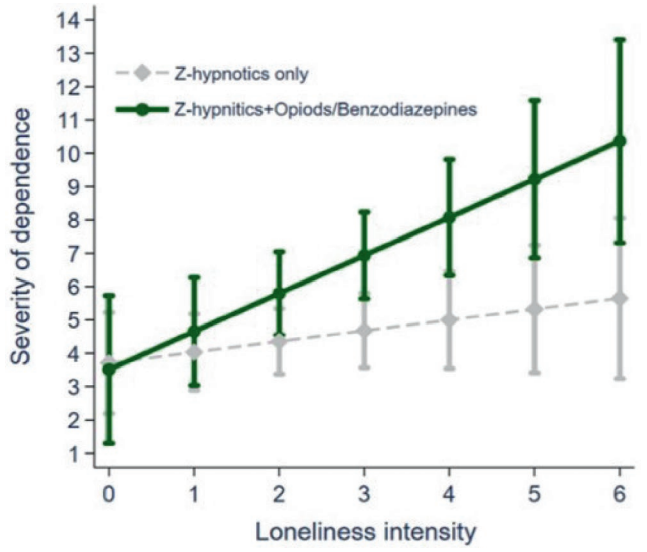

FIGURE 2 Association between loneliness score and severity of dependence in older patients using potentially addictive meds.

Conclusion: In older patients, physicians should be aware that prolonged use and dependence on central nervous system inhibitory drugs are more probable when loneliness intensifies. A particular focus on female, lower-educated, multimorbid patients, and those receiving concomitant medications is suggested.

Disclosure: CL has participated on an advisory board and received payment for lectures arranged by Abbvie Pharma AS, Novartis AS, and Roche AS, Norway. He has also received research sponsorship from Abbvie pharma. All other authors declare that they have no conflicts of interest.

EPO-047 | Emotion recognition deficits and brain functional network connectivity in frontotemporal degeneration

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Background and aims: We investigated emotion recognition (ER), functional brain connectivity of ER-related networks and their relationship in a frontotemporal degeneration (FTD) cohort.

Methods: 109 FTD patients [46 bvFTD, 10 sbvFTD, 13 nfvPPA, 18 svPPA, 22 PSP] and 114 HC underwent the Comprehensive Affect Testing System-abbreviated version (CATS-A). Accuracy scores for basic and combined positive and negative emotions were compared across groups. Structural and resting-state functional MRI were obtained for 79 patients and 49 HC. In 50 young HC, functional connectivity of six ER networks was reconstructed from key nodes: salience (SN), semantic appraisal, anterior default mode (aDMN), visuo-associative, sensorimotor (SMN), and basal ganglia networks. Intra-network direct functional connectivity (dFC) and graph-based nodal properties were compared among groups and correlated with CATS-A scores.

Results: FTD groups showed deficits in recognizing positive and, mainly, negative emotions compared to HC. SvPPA recognized happiness better than bvFTD and nfvPPA, while sbvFTD recognized worse disgust than svPPA. Compared to HC, all FTD patients exhibited altered dFC nodal properties, including higher path length, reduced nodal strength, local efficiency and clustering coefficient within the SN, SMN and aDMN. Lower

accuracy in recognizing negative emotions correlated with altered aDMN properties in FTD and SMN in HC.

Conclusion: Our data confirmed ER deficits in FTD and suggested a differential role in ER valence based on the temporal FTD subtypes (svPPA vs sbvFTD). While HC relied on the SMN in processing negative emotions, FTD patients showed a shift to the aDMN, reflecting loss of specificity and compensatory mechanisms.

Disclosure: Funding. European Research Council (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer Disease. Co-funding Next Generation EU [DM 1557 11.10.2022]. Disclosures: AG, CT, VC, ES, FF, EGS, GM, FC, ENA, GDL, PC, SP, CV, LT, IA, FV, MLGT nothing; EC, SB grants from Italian Ministry of Health (MSAL); GC speaker fees from Neopharmed Gentili; NT consulting fees from Amylyx Pharmaceuticals and Zambon Biotech SA. VS consulting or speaking fees from AveXis, Cytokinetics, Italfarmaco, Liquidweb srl, Novartis Pharma AG, Amylyx Pharmaceuticals, Biogen, Zambon Biotech SA; grants from MSAL, AriSLA, and E-Rare Joint Transnational Call; BP consulting or speaking fees from Liquidweb srl; MF consulting or speaking fees from Alexion, Almirall, Bayer, Biogen, Bristol-Myers Squibb, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, TEVA; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; research support from Biogen Idec, Merck-Serono, Novartis, Roche. FA speaker honoraria from Biogen Idec, Roche, Eli Lilly and GE Healthcare, and grants from MSAL, the Italian Ministry of University and Research, AriSLA, the ERC, the EU Joint Programme – Neurodegenerative Disease Research, Foundation Research on Alzheimer Disease.

EPO-048 | Neuropsychological tests predict amyloid status in MCI and mild dementia: Real-world memory clinic insights

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Background and aims: Alzheimer's disease (AD), the leading cause of dementia, necessitates accessible diagnostic tools to complement amyloid-PET imaging and cerebrospinal fluid (CSF) analysis, particularly with the advent of disease-modifying therapies. This study evaluated the predictive accuracy of individual and combined neuropsychological assessments for amyloid-PET status in patients with mild cognitive impairment (MCI) or mild dementia, considering age and education level.

Methods: A retrospective analysis (2015–2019) included 118 adults aged 45–85 years with cognitive deficits. Exclusion criteria were CDR >1, MMSE <20, clinically significant neuroimaging abnormalities, or a history of major cerebrovascular events. Neuropsychological assessments. Amyloid-PET was conducted within six months of baseline testing. Statistical analyses evaluated test performance using ROC curves and logistic regression and were conducted using the open-source statistical software Jamovi (v. 2.3.21.0).

Results: The FCSRT immediate free-recall (IFR) component (AUC = 0.70) and the recall of Rey-Osterreith Complex Figure (AUC = 0.63) showed predictive value for amyloid positivity. While FCSRT displayed high sensitivity and Rey recall high specificity, combined test performance was modestly improved by including verbal fluency and age (AUC = 0.76). Subgroup analyses showed better predictive accuracy in patients younger than 75 years and with higher education levels (AUC = 0.88 for IFR; AUC = 0.78 for Rey recall).

TABLE 1 Predictive performance of neuropsychological tests and predictive model within the global cohort.

	Sensitivity	Specificity	PPV (%)	NPV (%)	AUC (CI 95%)
Amyloid positive status in the global cohort (N = 76)					
FCSRT (cut-off score)					
IFR (≤ 17)	59.21%	80.95%	84.91%	52.31%	0.70 (0.60-0.80)
ITR (≤ 31)	48.68%	78.57%	80%	45.21%	0.67 (0.57-0.77)
DFR (≤ 6)	68.06%	59.52%	74.24%	52.08%	0.65 (0.55-0.75)
DTR (≤ 10)	50%	71.43%	75%	45.45%	0.63 (0.53-0.73)
ISC (≤ 0.8)	58.73%	74.36%	78.72%	52.73%	0.66 (0.56-0.76)
Rey-Osterrieth Complex Figure (cut-off score)					
Immediate (≤ 33)	79.71%	26.32%	66.27%	41.67%	0.50 (0.39-0.61)
Recall (≤ 13)	90.91%	36.11%	72.29%	68.42	0.63 (0.53-0.73)
Verbal fluency (cut-off score)					
≥ 21	69.23%	58.97%	73.77%	53.49%	0.66 (0.56-0.76)
Semantic fluency (cut-off score)					
≤ 20	79.69%	38.89%	69.86%	46.67%	0.55 (0.45-0.65)
Digit span forward (cut-off score)					
≥ 6	44.68%	73.08%	75%	42.22%	0.58 (0.48-0.68)
Stroop (cut-off score)					
Time (≥ 30.5)	67.19%	50%	69.35%	47.5%	0.56 (0.46-0.66)
Errors (≤ 11)	93.85%	21.62%	67.78%	66.67%	0.55 (0.45-0.65)
Multiple Features Targets Cancellation (MFTC) (cut-off score)					
Accuracy (≥ 0.92)	76.47%	46.88%	69.64%	55.56%	0.59 (0.49-0.69)
Time (≥ 47)	88.14%	32.43%	67.53%	63.16%	0.59 (0.49-0.69)
Predictive model (IFR – delayed Rey Figure – verbal fluency, age)					
≥ 1	100%	11.11%	67.35%	100%	0.76 (0.67-0.85)
≥ 2	92.42%	27.78%	70.11%	66.67%	
≥ 2.5	71.21%	66.67%	79.66%	55.81%	
≥ 3	69.7%	69.44%	80.7%	55.56%	
≥ 3.5	54.55%	83.33%	85.71%	50%	
≥ 4.5	28.79%	100%	100%	43.37%	

TABLE 2 Predictive performance of neuropsychological tests within the cohort ≤75 years and with high education (>8 years)

	Sensitivity	Specificity	PPV (%)	NPV (%)	AUC (CI 95%)
Amyloid positive status ≤ 75 years and high education (> 8 years) (N = 28)					
FCSRT (cut-off score)					
IFR (≤ 17)	*71.43%*	*100%*	*100%*	*68%*	*0.88 (0.79-0.95)*
ITR (≤ 29)	*57.14%*	*94.12%*	*94.12%*	*57.1%*	*0.80 (0.71-0.89)*
DFR (≤ 4)	*68%*	*88.24%*	*89.47%*	*65.22%*	*0.81 (0.72-0.90)*
DTR (≤ 10)	*64%*	*82.35%*	*84.21%*	*60.87%*	*0.78 (0.69-0.87)*
ISC (≤ 0.63)	*61.11%*	*100%*	*100%*	*68.18%*	*0.79 (0.70-0.88)*
Rey-Osterrieth Complex Figure (cut-off score)					
Immediate (≤ 34)	*86.96%*	*23.53%*	*60.61%*	*57.14%*	*0.50 (0.40-0.60)*
Recall (≤ 13)	*95.45%*	*53.33%*	*75%*	*88.89%*	*0.78 (0.69-0.87)*
Verbal fluency (cut-off score)					
≥ 21	*83.33%*	*43.75%*	*68.97%*	*63.64%*	*0.64 (0.54-0.74)*
Semantic fluency (cut-off score)					
≥ 26	*71.43%*	*42.86%*	*65.22%*	*50%*	*0.50 (0.40-0.60)*
Digit span forward (cut-off score)					
≥ 5	*70%*	*69.23%*	*77.78%*	*60%*	*0.71 (0.61-0.81)*
Stroop (cut-off score)					
Time (≥ 32.5)	*60%*	*68.75%*	*70.59%*	*57.89%*	*0.61 (0.51-0.71)*
Errors (≤ 2)	*95.45%*	*29.41%*	*63.64%*	*83.33%*	*0.57 (0.47-0.67)*
Multiple Features Targets Cancellation (MFTC) (cut-off score)					
Accuracy (≥ 0.95)	*68.75%*	*50%*	*64.71%*	*54.55%*	*0.55 (0.45-0.65)*
Time (≥ 57)	*86.36%*	*62.5%*	*76%*	*76.92%*	*0.72 (0.62-0.82)*

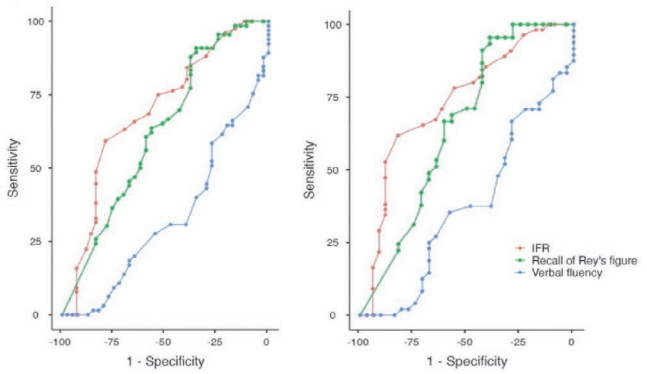

FIGURE 1 ROC curves of IFR, recall of Rey's figure, and verbal fluency. On the left in the global cohort, on the right in the cohort ≤75 years.

Conclusion: These results emphasize the utility of neuropsychological assessments as non-invasive, cost-effective tools for identifying individuals requiring advanced diagnostic confirmation of AD, particularly in younger and more educated patients.
Disclosure: Nothing to disclose.

EPO-049 | Investigating the reality of functional neurological disorder diagnosis: A case study from a UK neurological centre

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Background and aims: This study investigates diagnostic rates and clinical attitudes towards Functional Neurological Disorder (FND) at a large UK neurological centre without a dedicated FND service.
Methods: Inpatient episodes, outpatient appointments, and emergency department attendances from 1 January 2018 to 30 June 2024 were reviewed to determine FND diagnosis rates. A total of 9,698 medical records were assessed for coding accuracy, while a clinician survey explored neurologists' understanding of the condition within the neurological centre. These findings were contextualised with historical understandings of functional disorders.
Results: FND was diagnosed in 19 patients over the study period. A diagnosis rate of 0.0135% was found in outpatient appointments and a rate of 0.0145% in emergency department attendances. Survey responses highlighted the influence of historical stigmas, outdated perceptions, and insufficient institutional support in shaping clinical attitudes and treatment decisions.
Conclusion: Despite accounting for 5-15% of neurology patients and an estimated 8,000 new diagnoses in the UK annually, FND remains a marginalised condition at this centre. Persistent stigma and systemic underinvestment contribute to low diagnosis rates and inadequate care. Addressing these cultural and institutional barriers in essential for improving diagnosis and treatment for FND.
Disclosure: Nothing to disclose.

EPO-050 | Rubber hand illusion in Parkinson's disease

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Background and aims: To investigate the rubber hand illusion (RHI) in patients with Parkinson's disease (PD) compared to healthy controls (HC).

Methods: 37 PD and 30 HC underwent neuropsychological evaluation, RHI, and RHI-questionnaires, and a functional MRI (fMRI) during a virtual reality motor task (VR-motor task). VR-motor-task consisted in hand-moving while observing a virtual hand in three conditions (synchronous, demultiplied, mismatch). We compared PD and HC with multivariate analyses examining the proprioceptive localization of the participant's index finger (PLIF) before stimulations, post-stimulation RHI-questionnaire scores, and fMRI activity. Linear regressions were used to analyze the relationship between proprioceptive drifts and RHI-questionnaire scores. Linear mixed-effects models examined PLIF changes after each stimulation and between pre-stimulation phases.

Results: No PLIF differences were observed between groups in each pre-stimulation phase. Compared to HC, PD patients showed higher RHI-questionnaire scores. In all participants, we observed a positive relationship between RHI-questionnaire scores and proprioceptive drifts toward the RH. Both groups showed significant PLIF changes toward the RH after the first left-hand synchronous stimulation. In PD, we observed PLIF changes also after second synchronous left-hand stimulation and after both first and second synchronous right-hand stimulation. During fMRI, PD patients showed reduced left temporal-parietal junction activity in the demultiplied condition.

Conclusion: In both groups, we confirmed the RHI after a first synchronous left-hand stimulation. In PD, the RHI effect increased after a second stimulation and extended to the dominant hand. PD patients also showed higher subjective RH ownership in both conditions and hands. These findings suggest impaired self-agency in PD.

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EPO-051 | Cognitive performance in healthy females: A comparative study of menopause and non-menopause groups

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Background and aims: After age, sex is a major risk factor for Alzheimer's disease with lower lifetime exposure to ovarian hormones being the strongest cause. The cognitive effects of menopause are not fully understood, and studies on healthy females are lacking. This study aimed to explore differences in cognitive performance in healthy menopausal and non-menopausal women.

Methods: We recruited 114 healthy female volunteers aged 30-65 years among Belgrade University employees. The exclusion criteria were difficulties in communicative ability and/or safe engagement in interventions, and presence of any neurological, psychiatric, medical condition, or iatrogenic cause known to affect the brain structure and/or function. All participants underwent a detailed assessment including basic demographic data, data on vascular risk factors, mood scales, comprehensive neuropsychological assessment, and Cognitive Reserve Index Questionnaire.

Results: Among participants, 48 reached menopause at the mean age of 48.6 ±4.89 years, while 66 were not yet in menopause. The mean age/education of the menopause group was 54.91 ±4.8/18.60 ±4.16 years, respectively, and 43.11 ±6.91/19.31 ±4.13 years in the non-menopausal group. The menopausal group had significantly more subjective complaints in general (median 7.00 vs. 3.50, p=0.005 for positive answers on the MyCog scale), especially in the memory domain (median 3.00 vs. 1.00, p=0.038). Differences in raw scores of neuropsychological tests (MMSE, MOCA, ROCF memory score) did not persist after age correction.

Conclusion: The menopausal group reported more cognitive complaints, however, cognitive performance did not differ. Further research on healthy women is needed to understand the cognitive burden of menopause better.

Disclosure: This research was supported by Alzheimer's Association grant AACSFD-17-533520.

EPO-052 | An Italian scale for the assessment of motor speech disorders in patients with PPA and PSP

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Background and aims: This study provides an Italian scale to assess motor speech disorders (MSD) in patients with primary progressive aphasia (PPA) and progressive supranuclear palsy (PSP).
Methods: The motor speech evaluation scale (MSE) evaluates: sustained /a/, alternating and sequential motion rates (AMR, SMR), counting, and repeating 8 words 5 times each. MSE was administered to 75 patients (59 PPA, 16 PSP) and 63 healthy controls (HC-MSE). Sixty-seven patients and 61 matched HC (HC-MRI) also underwent an MRI scan. Analysis included duration, voice quality, articulatory rate (AR), and accuracy, along with the average number of syllables (ANS) per repeated word. Patients were classified as having apraxia of speech (AOS, N=20), dysarthria (DYS, N=11), mixed conditions (MIX, N=7), or non-MSD (N=37). Sequential Feature Selection (SFS) identified parameters differentiating MSD subtypes. Voxel-based morphometry assessed grey matter (GM) atrophy in MSD cases.
Results: SFS distinguished AOS from non-MSD considering age, AR of microscopico, and accuracy of artiglieria and segregazione (R^2=1.00). Non-MSD and DYS differed in AR of pagoda and ANS of artiglieria (R^2=0.92). Age, ANS of pagoda, and AR of microscopico differentiated non-MSD and MIX (R^2=1.00). AOS and DYS differed in voice quality, AR of /papa/, SMR and spaghetti tasks, accuracy for /papa/, and ANS of artiglieria (R^2=0.90). Compared to HC-MRI, AOS cases showed left motor and premotor atrophy, while MIX cases left inferior frontal damage.
Conclusion: This study provides the first Italian scale to evaluate MSD in PPA and PSP. The MSE distinguishes AOS, DYS, and their co-occurrence, supporting its use in neurodegenerative conditions.
Disclosure: Funding. European Research Council (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer Disease. Co-funding by the Next Generation EU [DM 1557 11.10.2022]. Disclosures. LL, AR, VC, ES, CT, FF, TG, EGS, MLGT nothing to disclose; EC grants from Italian Ministry of Health (MSAL); GC speaker fees from Neopharmed Gentili; MF consulting or speaking fees from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, MSAL, Italian Ministry of University and Research (MUR), and FISM. FA is Associate Editor of NeuroImage: Clinical, has received speaker honoraria from Biogen Idec, Roche, Eli Lilly and GE Healthcare, and receives or has received research supports from MSAL, MUR, AriSLA, ERC, the EU Joint Programme – Neurodegenerative Disease Research, and Foundation Research on Alzheimer Disease (France).

EPO-053 | Obstructive sleep apnea severity is associated with operation but not maintenance deficits in working memory

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Background and aims: Obstructive sleep apnea (OSA) is a highly prevalent sleep disorder often linked to cognitive deficits, particularly impairments in working memory (WM). Baddeley's model suggests WM involves maintaining and operating information, with distinct functional characteristics and neural underpinnings. However, it remains unclear how OSA compromises WM, particularly its key components. Hence, we explored the association of OSA severity and deficits in different aspects of WM.

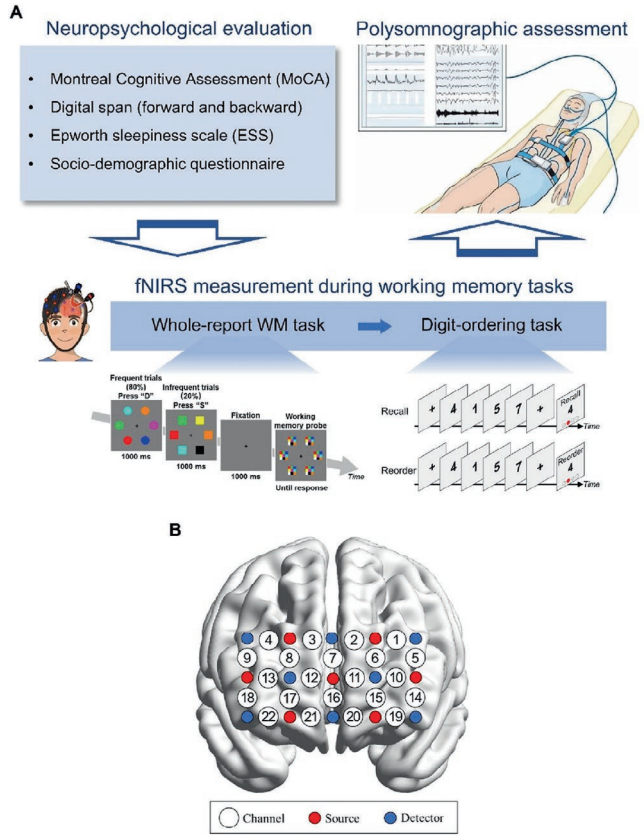

FIGURE 1 (A) Study procedures and experimental design. (B) Spatial profiles of fNIRS channels.

Methods: Twenty-three male participants with suspected OSA (Mage = 34.0 years) sequentially underwent neuropsychological evaluation, WM tasks, and polysomnographic assessment (Fig. 1A). During the WM tasks, prefrontal cortex activities were recorded using a 22-channel functional near-infrared spectroscopy (fNIRS), and quantified via fractional amplitude of low-frequency fluctuations (fALFF) (Fig. 1B). WM maintenance and operation were evaluated using the whole-report WM task and the digit-ordering task, respectively. The apnea-hypopnea index (AHI), nadir of oxygen saturation (SpO2), and the Epworth Sleepiness Scale (ESS) were used to quantify the severity of OSA.
Results: The severity of OSA was found to be significantly associated with deficits in WM operation (rESS = 0.476, p = 0.026), but not with WM maintenance (Fig. 2). A hierarchical regression model, including demographic characteristics, SpO2 nadir, and fALFF of channel 22, explained a significant proportion of the variance in WM operation (Adj. R2 = 0.40, p = 0.004).

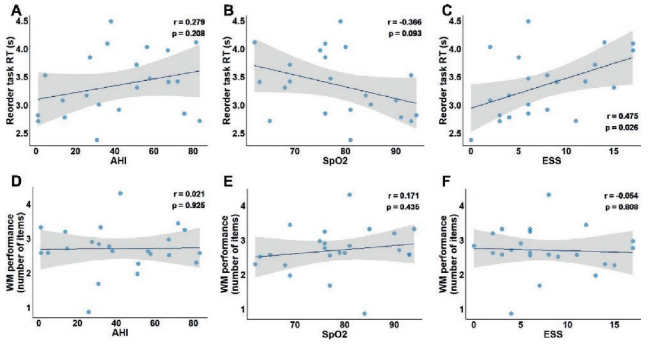

FIGURE 2 Correlation analysis of the severity of OSA and participants' performance in the digit-ordering task (A-C) and the whole-report WM task (D-F).

Conclusion: Worsen OSA is associated with slower response during WM operation, but not with the maintenance of WM, potentially due to reduced spontaneous activity in the prefrontal cortex.
Disclosure: Nothing to disclose.

EPO-054 | French version of the Northwestern Anagram Test to assess syntactic impairment in primary progressive aphasias

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Background and aims: Primary progressive aphasias (PPA) are neurodegenerative conditions including three main variants: nonfluent/agrammatic (nfa), semantic, and logopenic PPA. Several tests allow for assessing the linguistic core features for stringently classifying semantic and logopenic PPA, but there is no internationally available tool to quantify grammatical-syntactic disorders guaranteeing correct classification of nfa-PPA. The Northwestern Anagram Test (NAT) aimed at filling this gap. We aimed at validating its French version (NAT-F).
Methods: The NAT-F was applied to 10 PPA patients, 10 Alzheimer's disease (AD) patients and 50 healthy controls, using a digital tablet application (Figure 1). The NAT-F was adapted from the initial English and Italian versions to probe for different French syntax structures (items) including canonical/active and non-canonical/passive sentences. To provide a rapid testing procedure, we shortened the original English version generating and comparing two 22-item versions (NAT-F1, NAT-F2).

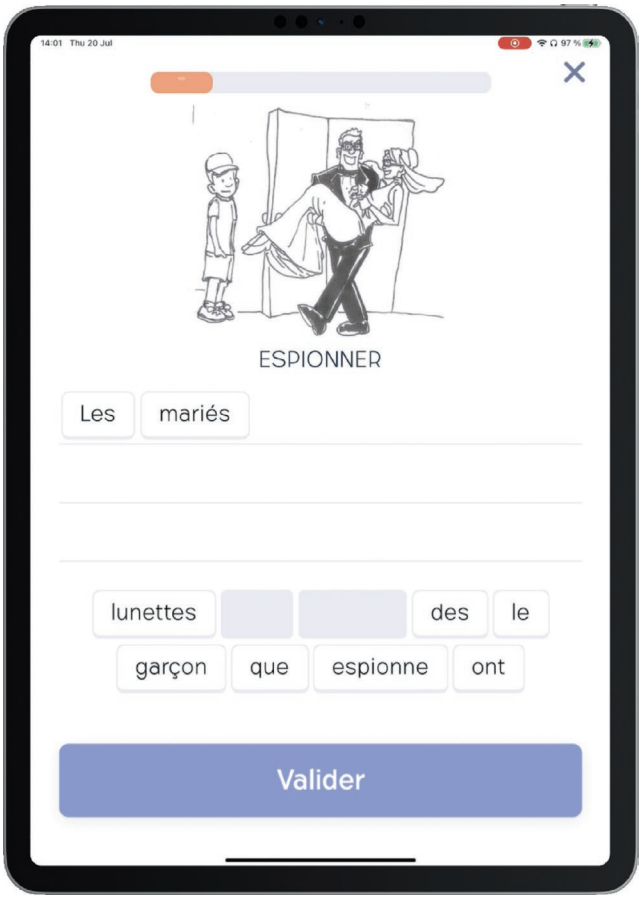

FIGURE 1 Example of a NAT-F item, featuring a non-canonical object-related sentence. The infinitive form of the verb is indicated and the words are provided in scrambled order. The task consists in reordering then within 60 seconds.

Results: Patients and controls were comparable for age (p=0.07), sex (p=0.56) and educational level (p=0.47). Performance of controls was correlated between NAT-F1 and NAT-F2 for both total scores (rho=0.61, p<0.0001) and item-specific scores (p<0.001). NAT-F scores of both versions were lower in PPA and AD patients compared to controls (p<0.001, Figure 2), especially for non-canonical items. Within non-canonical items, performance with passive sentences was poorer in PPA than in AD patients (p=0.002), and within PPA variants there was a trend for poorest performance in nfa-PPA with passive and object-relative sentences.

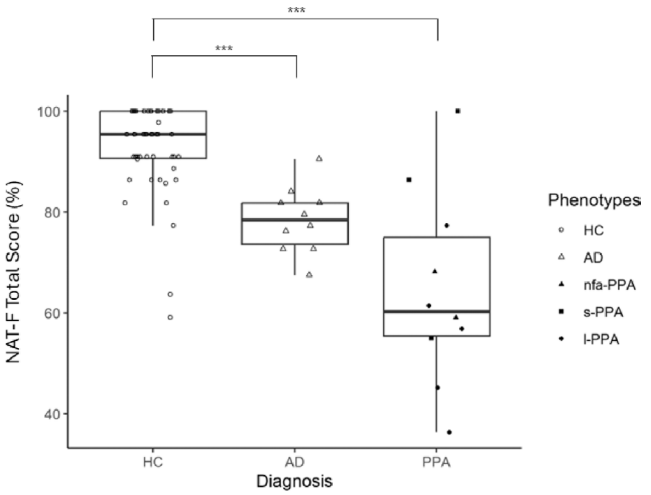

FIGURE 2 Comparisons of NAT-F total scores between the diagnostic groups (Kruskal-Wallis and Dunn's post hoc test). ***: p <0.0001. AD: Alzheimer's disease; HC: healthy controls; l-PPA: logopenic PPA; nfa-PPA: nonfluent/agrammatic PPA; s-PPA: semantic PPA.

Conclusion: NAT-F provides an international and clinically-relevant tool for test-based classification of nfa-PPA. Definitive validation requires the assessment and comparison of larger populations of the three PPA main variants.
Disclosure: Nothing to disclose.

EPO-055 | Towards a functional protective model for the prodromal stage of alpha-synucleinopathies

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Background and aims: Isolated Rapid Eye Movement Sleep Behavior Disorder (iRBD) is an early stage of synucleinopathies. While Slow Wave (SW) sleep is renowned for its protective effects against degeneration, its specific role in synucleinopathy-related neurodegeneration remains poorly understood. Parkinson's disease-related pattern (PDRP) expression on 18fluorodeoxyglucose PET ([18F]FDG-PET) is a marker of neurodegeneration in iRBD. We aimed to investigate between SW and PDRP alongside cognitive performance in iRBD, with an exploratory focus on cognitive reserve (CR).
Methods: 41 polysomnography-confirmed iRBD patients underwent [18F]FDG-PET, neuropsychological assessment and CR Index questionnaire (CRIq). The PDRP expression was computed for each patient. SW density (SWd) and Slow Oscillations density (SOd) were calculated on frontal EEG derivations in N2 and N3 sleep with an automated algorithm.
Results: SWd and SOd (in N2 and N3 sleep) were positively correlated with cognitive screening and visuospatial abilities domains. PDRP was positively correlated with the TMT A score and negatively correlated with SWd in N3 sleep (all p<0.05).

iRBD with Mild Cognitive Impairment (MCI) showed a reduction in SWd and SOd in both N2 and N3 sleep in comparison to patients without MCI (all p<0.05), but no difference in PDRP expression. Patients with MCI showed a non-significant reduction at CRIq in comparison to cognitively normal patients.

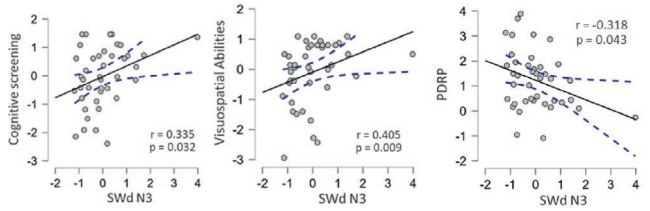

FIGURE 1 Correlation analysis between SW sleep indexes, neuropsychological data and PDRP.

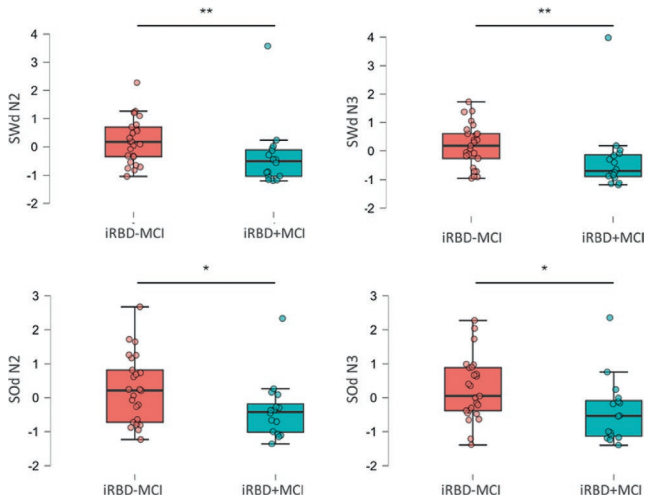

FIGURE 2 Comparisons between iRBD-MCI and iRBD+MCI patients on SW sleep indexes.

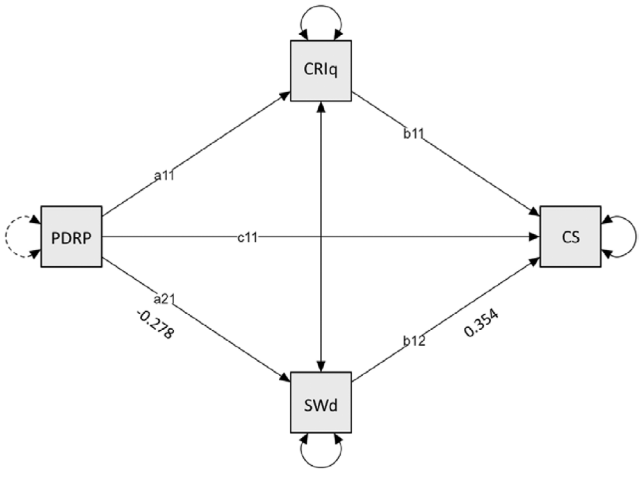

FIGURE 3 Putative model for testing CR.

Conclusion: Our findings highlight a novel interaction between pathological burden and SW sleep dynamics in iRBD, which is also closely tied to cognitive deficits manifestation. Future longitudinal studies should investigate whether these associations might be moderated by CR as a possible protective factor against neurodegeneration.

Disclosure: Nothing to disclose.

EPO-056 | Associations between spatial navigation performance and Alzheimer's disease biomarkers

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Background and aims: Spatial navigation impairment is among the earliest cognitive deficits in Alzheimer's disease (AD). This study investigated the association between spatial navigation performance and AD biomarkers in individuals with amnestic mild cognitive impairment (aMCI).
Methods: This study included 80 amnestic MCI participants with AD (AD aMCI), 66 aMCI participants without AD (non-AD aMCI), and 72 cognitively normal (CN) adults. Spatial navigation performance was assessed using real-space and computerized versions of the human analogue of the Morris Water Maze task, which measured allocentric, egocentric, and delayed allocentric navigation performance. All participants underwent neuropsychological and brain assessments. Biomarker data for cerebrospinal fluid (CSF) levels of amyloid-beta1-42, total tau, phosphorylated tau181, and amyloid PET imaging were collected for all aMCI participants.
Results: On the real and virtual allocentric and delayed allocentric tasks, both AD and non-AD aMCI participants performed worse than the CN group (p<=0.018), with AD aMCI participants performing worse than non-AD aMCI participants (p=0.014). On the real and virtual egocentric tasks, AD aMCI participants performed worse than the CN group (p<=0.015), while the non-AD aMCI and CN groups showed similar performance. On the virtual egocentric task, AD aMCI participants performed worse than the non-AD aMCI participants (p<0.001), Performance on the real, virtual, and delayed allocentric tasks and the virtual egocentric task was associated with lower amyloid-beta1-42 levels and a higher p-tau181/amyloid-beta1-42 ratio (beta≥0. 174, p<=0.015).
Conclusion: Spatial navigation impairments, particularly allocentric, are strongly linked to AD biomarkers in aMCI. These tasks are promising non-invasive tools for early detection and monitoring of AD-related pathology.
Disclosure: National Institute for Neurological Research (Programme EXCELES, ID Project No. LX22NPO5107) – Funded by the European Union – Next Generation EU, and the Institutional Support of Excellence 2 2. LF UK (Grant No. 6980382).

EPO-057 | Preoperative magnesium levels and risk of postoperative delirium in elderly non-cardiac surgery patients: A cohort study

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Background and aims: Postoperative delirium (POD), common in elderly patients, is linked to neuroinflammation,

oxidative stress, and synaptic dysfunction. This study explored the association between preoperative magnesium (Mg) levels and POD risk, aiming to identify optimal levels and underlying mechanisms.

Methods: This retrospective cohort study included patients ≥65 undergoing non-neurosurgical, non-cardiac procedures (2014–2021). Preoperative Mg levels were measured within 30 days before surgery, and POD occurrence within seven days post-surgery was assessed using standardized criteria. Logistic regression adjusted for confounders (via DAG) examined the Mg-POD relationship. Mg levels were divided into quintiles, with RCS analyses for nonlinear associations and subgroup analyses by sex, age, renal dysfunction, and diabetes.

Results: 53445 patients were analyzed, with 1,551 (2.9%) developing POD. Multivariable logistic regression showed Mg as a continuous variable was inversely associated with POD (OR=0.89, 0.85–0.93, p<0.001). Quintile analysis revealed a linear trend, with the lowest POD risk at Mg=0.89 mmol/L. Below it, each SD increase reduced POD risk (OR=0.75, 0.71–0.79); above it, risk increased (OR=1.04, 0.97–1.12). Adjusting for albumin transformed the U-shaped association into a linear one, identifying albumin as a key confounder. Mediation analysis demonstrated albumin partially mediated the Mg-POD relationship (direct effect c'=−0.047, indirect effect a*b=−0.022, both p<0.001), explaining 31.88% of the effect. Mediation was stronger in patients with renal insufficiency (57.14%) and diabetes (21.84%).

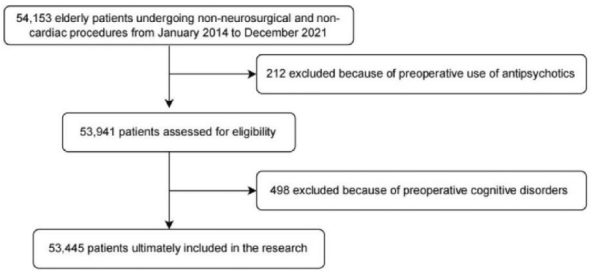

Figure 1. Flowchart of study population. POD, postoperative delirium.

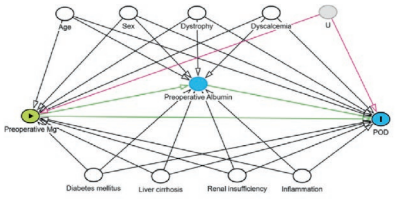

Figure 2. Directed acyclic graph represents associations between covariates and primary exposure and outcome.
White circles denote ancestors of both the exposure and outcome that have been controlled as confounders, blue circles represent the outcome and its causal direct determinants, green circle symbolizes the exposure variable, while the gray circle denotes variables that are unobserved. The causal relationships are depicted by green lines, whereas gray lines illustrate paths of bias that have been accounted for. Conversely, pink lines highlight the biasing paths that remain unadjusted due to latent variables. Mg, serum magnesium; POD, postoperative delirium;U, unmeasured confounders.

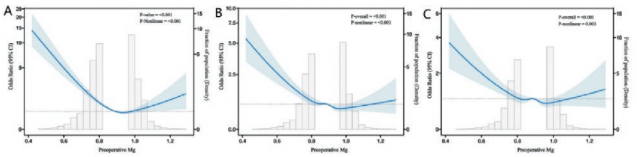

Figure 3. Association between Mg and POD with the restricted cubic splines function.
(A) Unadjusted model. (B) Multivariable model adjusted for Multiadjusted model adjusted for age, sex, BMI, BUN, NLR, Ca, renal insufficiency, liver cirrhosis and diabetes mellitus. (C): Multivariable model additionally adjusted for albumin levels as a potential mediator.
ORs are indicated by blue solid lines and 95% CIs by light blue dotted lines. Reference lines for no association are indicated by the gray dotted lines at an odds ratio of 1.0. Density plot are presented by gray shadow area to show the fraction of the population with different levels of Mg. Model with 5 knots located at 5th, 28th, 50th, 72th and 95th percentiles. Y-axis represents the OR to present POD for any value of Mg compared to individuals with reference value (50th percentile) of Mg.
Abbreviations: Mg, serum magnesium; BMI, body mass index; BUN, blood urea nitrogen; NLR, neutrophil-to-lymphocyte ratio; Glu, blood glucose; Ca, serum calcium; POD, postoperative delirium; OR, odds ratio; CI, confident interval.

Conclusion: Maintaining optimal Mg levels may reduce POD risk, particularly in vulnerable populations.

Disclosure: Nothing to disclose.

EPO-059 | Machine Learning Prediction of non-dementia cognitive symptoms using clinical, genetics, cognitive and imaging data

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Background and aims: Non-neurodegenerative disorders can present with cognitive symptoms and superficially resemble dementia. Current diagnostic methods lack precision and standardisation. We assessed whether Machine learning (ML) models accurately predict non-dementia-related cognitive symptoms (functional cognitive disorder, FCD).

Methods: The UK Biobank contains 500,000 participants and clinical, cognitive and physical measurements, and imaging data. Participants were followed between 2006 and 2023. Participants with daily or almost daily cognitive symptoms were selected, excluding patients with dementia at baseline and other neurological disorders. Dementia at follow-up was derived using linked health records. Five machine learning methods (random forest, decision tree, c50, logistic regression and Extreme Gradient Boosting) were developed, with ten-fold cross-validation. Performance metrics (internal validation) included accuracy, area under the receiver operating characteristic curve (AUC), sensitivity, specificity, and F1 score. The effect of individual qualitative and quantitative features in correctly predicting FCD was explored.

Results: 11862 participants (1407 dementias, 10455 FCD), with a mean age of 57-years-old (46% male). The optimal model (random forest) demonstrated an accuracy of 0.85, AUC of 0.87, sensitivity of 0.88, specificity of 0.61, PPV of 0.95, and an F1 score of 0.91. Age at recruitment, traumatic and adverse life events, and polygenic risk score were the most important predictors among 38 best performing variables.

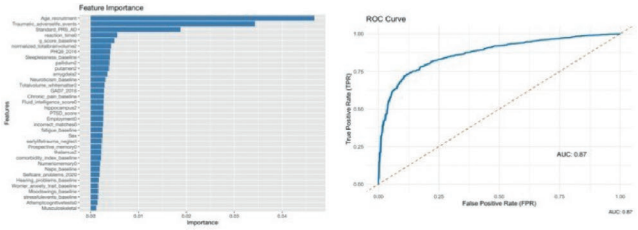

FIGURE 1 A, Feature importance graph for the Random Forest classification model. B, The receiver operating characteristic curve for the best-performing random forest model. AUC: area under the curve.

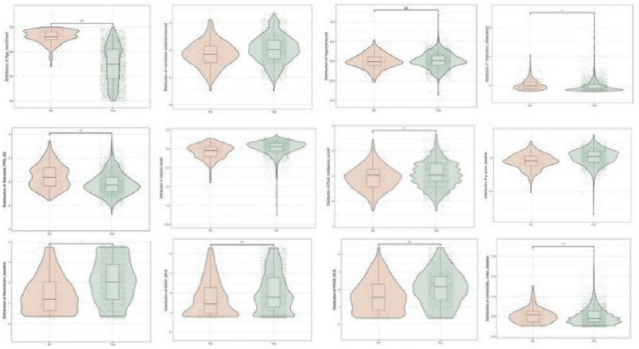

FIGURE 2 Quantitative measures. Differences in age at recruitment, normalized total brain volume, hippocampal volume, total volume of white matter changes, polygenic risk scores (PRS) for Alzheimer's disease, reaction time, fluid intelligence score, global cognitive function (g-score), neuroticism score, anxiety (GAD-7), depressive symptoms (PHQ-9) and comorbidity index.

TABLE 1 Performance of Machine learning models on a dataset of clinical history, cognitive, imaging and genetic data to discriminate dementia from FCD among participants with disabling cognitive symptoms.

ML model	Accuracy	AUC	Sensitivity	Specificity	PPV	NPV	F1 score
Decision tree	0.74	0.80	0.50	0.98	0.99	0.21	0.67
C50 decision tree	0.56	0.76	0.97	0.14	0.89	0.49	0.24
Random forest	0.85	0.87	0.88	0.61	0.95	0.42	0.91
Logistic regression	0.74	0.88	0.98	0.24	0.90	0.63	0.38
XGBoost	0.86	0.87	0.91	0.54	0.97	0.54	0.94

Conclusion: Robust machine learning model performance may allow for early identification of individuals with non-progressive cognitive symptoms (FCD). The use of routine clinical data is promising to aid clinical decision-making with prognostic implications, and research studies. Prospective validation of these models in independent datasets is required to improve generalizability.
Disclosure: Nothing to disclose.

EPO-060 | Is cognitive dysfunction an inevitable outcome in migraine?

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Background and aims: Cognitive dysfunction, though not traditionally considered a core symptom of migraine, significantly impacts patients' daily lives, particularly during attacks. This study evaluates the neuropsychological performance of patients with episodic and chronic migraine by comparing their baseline and attack-period performance with healthy controls.
Methods: Thirty-two patients with episodic migraine, 32 with chronic migraine, and 30 age- and gender-matched healthy controls were included. Demographic data, HIT-6 scores and headache characteristics were recorded. The Mini-Mental State Examination, Beck Depression Inventory (BDI), Stroop Test, Clock Drawing Test, Forward and Backward Digit Span Tests (DST) were administered during attacks and repeated interictally. Healthy controls completed the same tests. Statistical evaluation included frequentist statistics, Spearman correlations, and beta regression.
Results: HIT-6 scores were higher in the chronic migraine group compared to the episodic group. Chronic migraine patients had higher baseline BDI scores and lower DST scores than controls. All six tests showed significantly worse performance during attacks in both migraine groups (Figure 1). Attack severity correlated with cognitive impairment, particularly in the episodic migraine group (Figure 2). Beta regression revealed each monthly attack added 1.58 points to HIT-6 scores, peaking at 20 attacks per month.

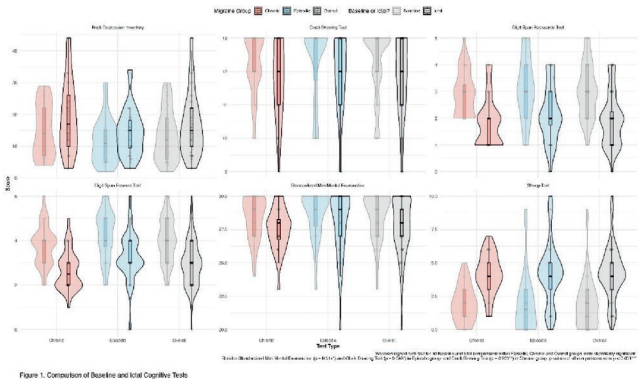

Figure 1. Comparison of Baseline and Ictal Cognitive Tests

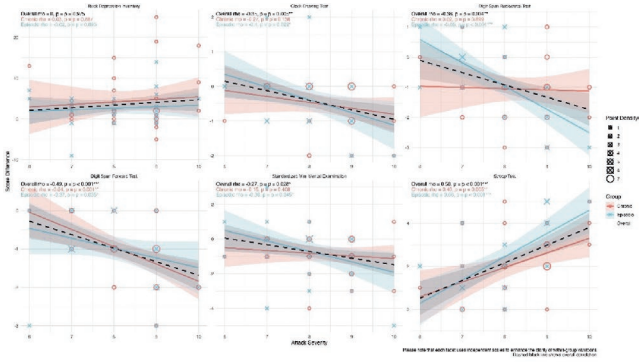

Figure 2. Correlation between the attack's severity and the score difference between baseline and ictal cognitive test results

Conclusion: Cognitive impairment during ictal and interictal periods significantly contributes to migraine-related disability, with attack frequency worsening the burden. Clinicians should monitor cognitive performance and adjust treatment plans to address this impact.
Disclosure: Nothing to disclose.

EPO-061 | Headache acceptance and migraine-related disability: Validation of the Turkish headache acceptance questionnaire

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Department of Neurology, Prof. Dr. Cemil Taşcıoğlu City Hospital, Istanbul, Turkey

Background and aims: Mindfulness-based therapies, such as Acceptance and Commitment Therapy (ACT), show promise in helping individuals lead active lives despite chronic pain. While pain acceptance has been studied in chronic pain, headache-specific tools are needed due to the unique features of headaches. This study evaluated the validity and reliability of the Turkish version of the Headache Acceptance Questionnaire (HAQ), designed to measure headache-related pain acceptance, and examined its relationship with migraine-related disability.
Methods: From February to December 2024, migraine patients were assessed using the HAQ, HIT-6, and MIDAS scales. Validation incorporated content validity, structural validity through factor analyses, and reliability testing using Cronbach's alpha and ICC. Correlations between HAQ scores and migraine-related disability were analyzed.
Results: Among 184 patients (156 females) the Turkish HAQ demonstrated excellent content validity and strong structural validity (KMO=0.89, Bartlett's p<0.001). Reliability was excellent, with a Cronbach's alpha of 0.909 and ICC of 0.99 (p<0.001). HAQ scores were strongly and negatively correlated with HIT-6 (r=-0.86, p<0.001) and MIDAS (ρ=-0.73, p<0.001).

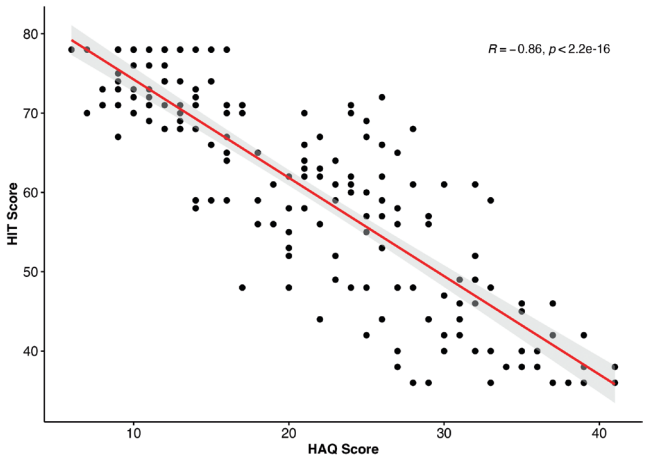

FIGURE 1 Correlation between HAQ Score and HIT-6 Score.

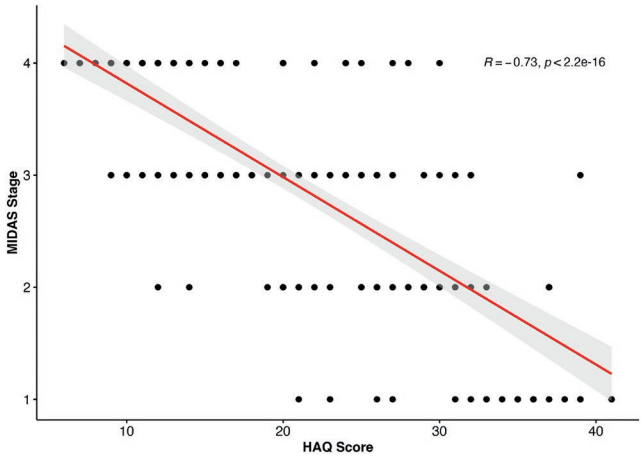

FIGURE 2 Correlation between HAQ Score and MIDAS Stage.

Conclusion: The Turkish HAQ is a valid and reliable tool for assessing headache-specific pain acceptance. The strong inverse relationship between headache acceptance and disability highlights the clinical importance of acceptance-based therapies, such as ACT, in managing migraine.
Disclosure: Nothing to disclose.

EPO-063 | Real-world safety and tolerability of fremanezumab in migraine prevention: Final outcomes of the PEARL study

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Background and aims: PEARL (EUPAS35111) is a 24-month observational, prospective, Phase 4 study evaluating the real-world effectiveness and safety of fremanezumab for episodic

and chronic migraine (EM, CM) prevention. Here we present safety and tolerability outcomes from the PEARL study after 24 months of follow up.

Methods: Eligible participants were adults with EM or CM receiving fremanezumab for migraine prevention, who maintained a daily headache diary prior to and throughout the study period. Primary endpoint: the proportion of participants with >=50% reduction in monthly migraine days (MMD) during the 6-month period after fremanezumab initiation. Safety and tolerability were assessed by adverse event (AE) reporting.

Results: In total, 637/1128 (56.5%) participants with available data achieved the primary endpoint. All enrolled participants (N=1140) were included in the safety analysis. Overall, 642/1140 (56.3%) participants reported >=1 AE (Table 1). Drug-related AEs were reported by 376 (33.0%) participants; the most common being general disorders and administration site conditions (n=253, 22.2%) and gastrointestinal disorders (n=79, 6.9%; Table 1). Drug-related serious AEs were infrequent, occurring in four (0.4%) participants; the most common was drug hypersensitivity (n=2, 0.2%). AEs leading to treatment discontinuation were reported by 61 (5.4%) participants; the most frequent reasons were drug ineffectiveness (n=36, 3.2%), injection site erythema (n=5, 0.4%) and injection site pruritus (n=4, 0.4%).

TABLE 1 Safety analysis.

	SAS (N=1140)
Participants with >=1 AE, n (%)	642 (56.3)
Common AEs, n (%)*	
General disorders and administration site conditions	280 (24.6)
Infections and infestations	268 (23.5)
Nervous system disorders	134 (11.8)
Gastrointestinal disorders	127 (11.1)
Participants with >=1 drug-related AE, n (%)†	376 (33.0)
Participants with drug-related serious AEs, n (%)†	4 (0.4)
Participants with AEs leading to discontinuation, n (%)	61 (5.4)
Common drug-related AEs, n (%)†,‡	
General disorders and administration site conditions	253 (22.2)
Injection site erythema	98 (8.6)
Drug ineffective	75 (6.6)
Injection site pruritus	61 (5.4)
Injection site swelling	47 (4.1)
Injection site pain	30 (2.6)
Fatigue	21 (1.8)
Injection site rash	17 (1.5)
Injection site warmth	15 (1.3)
Gastrointestinal disorders	79 (6.9)
Constipation	58 (5.1)
Nervous system disorders	38 (3.3)
Migraine	14 (1.2)
Skin and subcutaneous tissue disorders	24 (2.1)
Psychiatric disorders	21 (1.8)
Infections and infestations	18 (1.6)
Musculoskeletal and connective tissue disorders	14 (1.2)

*Includes MedDRA system organ class reported in >=5.0% of the study population.
†Drug-related AEs that have been classified by the investigator to be related to fremanezumab treatment.
‡Includes MedDRA system organ class and associated preferred terms reported in >=1.0% of the study population.
AE, adverse event; MedDRA, Medical Dictionary for Regulatory Activities; SAS, safety analysis set.

Conclusion: The favourable long-term safety and tolerability of fremanezumab demonstrated in this analysis are consistent with the known safety profile of fremanezumab from previous PEARL interim analyses and randomised controlled trials, supporting its continued clinical use for migraine prevention.

Disclosure: MA: AbbVie, Amgen, AstraZeneca, Eli Lilly, GlaxoSmithKline, Lundbeck, Novartis, Novo Nordisk Foundation, Pfizer, Teva Pharmaceuticals. DM: Allergan, Amgen, Bayer, Biogen, Cefaly, electroCore, Eli Lilly, Genesis Pharma, Merck Serono, Merz, Mylan, Novartis, Roche, Sanofi Genzyme, Specifar, Teva Pharmaceuticals. FMA: AbbVie, Eli Lilly, Lundbeck, Novartis, Pfizer, Teva Pharmaceuticals. CJS: AbbVie, Allergan, Almirall, Amgen, Eli Lilly, Grünenthal, Lundbeck, MindMed, Novartis, Pfizer, Teva Pharmaceuticals, Zynnon, Baasch-Medicus Foundation, Eye on Vision Foundation, German Migraine and Headache Society. GS: AbbVie, Lundbeck, Novartis, Pfizer, Teva Pharmaceuticals, Vinnova, Lund University, Swedish Neurological Association. PPR: AbbVie, Amgen, Biohaven EraNet NEURON, Chiesi, Eli Lilly, Lundbeck, Instituto Investigación Carlos III, MINECO, Novartis, Pfizer, RIS3CAT FEDER, Teva Pharmaceuticals. PJD: AbbVie, electroCore, Eli Lilly, Lundbeck, Novartis, Pfizer, Teva Pharmaceuticals. TN: AbbVie, Amgen, Eli Lilly, Glenmark, Lundbeck, Neurocrine Novartis, Organon, Pfizer, Teva Pharmaceuticals, UCB. IPM: AbbVie, Allergan, Eli Lilly, Lundbeck, Novartis, Organon, Pfizer, Teva Pharmaceuticals. MLS: AbbVie, Eli Lilly, Lundbeck, Novartis, Pfizer, Teva Pharmaceuticals. CT: AbbVie, Chordate, Dompé, Eli Lilly, Ipsen, Lundbeck, Novartis, Pfizer, Teva Pharmaceuticals, European Commission, Italian Ministry of Health, Migraine Research Foundation. PK, VRC, HA, study funding: Teva Pharmaceuticals.

EPO-064 | sNfL and GFAP levels in idiopathic intracranial hypertension: an exploratory study

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Background and aims: Idiopathic intracranial hypertension (IIH) is a systemic disorder marked by increased intracranial pressure carrying the risk of blindness due to optic nerve damage. Serum neurofilament light chain (sNfL) and glial fibrillary acidic protein (GFAP) are emerging biomarkers of axonal damage and astrocytic activation, respectively.

Methods: From an ongoing prospective observational study including pwIIH, sNfL and GFAP levels were measured at baseline using single-molecule array (Simoa) technology, and analyzed as Z-scores adjusting for age, BMI and – for GFAP – sex. The ophthalmological outcomes included papilledema degree, visual outcomes (visual acuity, visual field), optical coherence tomography and transbulbar sonography.

Results: We included 23 pwIIH (mean age 34.3 years (SD 8.1), 95.7% female, median cerebrospinal fluid (CSF) opening

pressure 33.0 cmCSF (IQR 26.9–35.4), median body mass index (BMI) 35.7 kg/m2 (IQR 31.1–43.3)). Mean sNfL and GFAP Z-scores at baseline were 1.0 (1.0) and 0.5 (1.4), respectively. sNfL Z-scores at baseline exhibited a non-significant positive correlation with the GCL volume of the worse eye (r=0.38, p=0.079), whereas GFAP Z-scores showed no correlation with any ophthalmological outcomes. Additionally, neither sNfL nor GFAP Z-scores correlated with the CSF opening pressure.

Conclusion: sNfL might be associated with GCL volume, an established sensitive marker of optic nerve damage. In contrast, GFAP does not appear to correlate with any ophthalmological outcomes. Given that IIH entails impaired CSF homeostasis, the lack of correlation might be attributable to impaired outflow of biomarkers from the CSF into the bloodstream.

Disclosure: All authors declare no conflict of interest relevant to this study.

EPO-065 | Acute Trigeminal Autonomic Cephalalgia headache service: An effective rapid-access pathway for headache patients

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Background and aims: An acute trigeminal autonomic cephalalgia (TAC) headache service is a rapid access consultation service for patients with TACs offering urgent advice and treatment. We conducted a service evaluation of the interventions offered to assess the effectiveness of this service.

Methods: Data from successive consultations (n=419) in the acute TAC headache service from 19/02/2018 to 29/07/2024 were collected from clinic letters as part of a service evaluation. Data were summarized as percentages or as medians with interquartile ranges.

Results: Data from 419 consultations of 190 patients were analyzed. Their median age was 49 years (IQR: 38-58) and 67% were male. The highest number of referrals were received in March (11.5%) and November (9.8%) and 19% were new referrals. The distance to patients' home ranged from 1 - 423 kms (median 32, IQR: 8 - 103). The majority were due to cluster headache (79%), followed by other primary headache (20%) and secondary headache (1%) disorders. In TAC patients, the median duration of the bout at the time of review was 3 weeks (IQR: 1-8). Interventions included treatment revisions (51%), greater occipital nerve (GON) injections (13%), a combination of GON injection and treatment revisions (24%) or advice alone (11%). Interventions were effective in 62% of patients.

Conclusion: An acute TAC headache service is effective for patients with primary headache disorders, especially for cluster headache. This service effectively provides urgent and tailored guidance and treatment to patients with TAC headaches, minimizing the need to visit the emergency department.

Disclosure: PA, LA, MN, WS, MV and NK have nothing to disclose relevant to this submission. PJG reports, over the last 36 months, grants from Celgene and Kallyope, and personal fees from Aeon Biopharma, Abbvie, Aurene, CoolTech LLC, Dr Reddy's, Eli-Lilly and Company, Linpharma, Lundbeck, Pfizer, PureTech Health LLC, Satsuma, Shiratronics, Teva Pharmaceuticals, Tremeau, and Vial, and personal fees for advice through Gerson Lehrman Group, Guidepoint, SAI Med Partners, Vector Metric, and fees for educational materials from CME Outfitters and WebMD, and publishing royalties or fees from Massachusetts Medical Society, Oxford University Press, UptoDate and Wolters Kluwer, and a patent magnetic stimulation for headache (No. WO2016090333 A1) assigned to eNeura without fee.

EPO-066 | Do EHF Criteria reflect response to acute treatments in resistant and refractory migraine? The REFINE study

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Background and aims: The European Headache Federation (EHF) defines resistant and refractory migraine by failure of ≥3 (resistant) or all (refractory) pharmacological preventive treatment classes, without considering acute treatments. This study aimed to evaluate whether these definitions also correlate with response to acute treatment.

Methods: We conducted a multicenter, prospective, international study (REFINE) to test the EHF definitions in a real-life setting in 15 European headache centers. The Headache Under Response to Treatment (HURT) Questionnaire assessed the impact of migraine on daily activities and effectiveness of acute medications in patients with resistant, refractory, and non-resistant non-refractory (NRNR) migraine.

Results: We included 689 patients, of whom 261 (37.9%) had resistant, 73 (10.6%) refractory, and 355 (51.5%) NRNR migraine. Patients with refractory migraine experienced more significant impairment in daily activities (HURT-2) and social activities (HURT-3) versus those with resistant and NRNR migraine (46 [63.0%] vs 110 [42.2%] vs 51 [14.4%], p<0.001; 37 [50.7%] vs 67 [25.7%] vs 25 [7.0%], p<0.001). Regarding acute medication efficacy (HURT-5), more patients with refractory migraine stated

that one dose "never" relieved their headache, and delayed or avoided taking acute medication due to concerns about adverse events (HURT-7), versus those with resistant and NRNR migraine (29 [39.7%] vs 28 [10.7%] vs 25 [7.0%], p<0.001; 16 [21.9%] vs 7 [2.7%] vs 11 [3.1%], p<0.001).
Conclusion: Patients with refractory and resistant migraine report poorer acute treatment response compared with those with NRNR migraine, which significantly affect daily lives. Management of difficult-to-treat migraine should focus on optimizing acute treatments, alongside preventive therapies.
Disclosure: Nothing to disclose.

EPO-067 | Profile of triptan use and efficacy in migraine patients treated with Anti-CGRP monoclonal antibodies

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Background and aims: Anti-CGRP monoclonal antibodies (mAbs) are migraine-specific preventive drugs. Evidence suggests they may reduce the need for acute medications, such as triptans. Even so, some anecdotal cases have reported a loss of triptan efficacy during treatment with these agents.
Methods: Ongoing ambispective study involving migraine patients from a tertiary center treated with anti-CGRP mAbs. The primary outcomes were the necessity and efficacy of triptans before and after starting mAbs therapy; a Likert scale was created to assess the latter.
Results: A total of 86 patients were included, predominantly women (84,88%), with a mean age of 42±12 years. Fremanezumab was the prevailing mAb (66,28%). Satisfactory to excellent results were reported by 71 patients (82.56%). Before starting mAbs, 69 patients (80.29%) used triptans, mainly zolmitriptan (36.23%) and eletriptan (34.78%). Among these, 57.97% (n=40) experienced some benefit: 27.54% satisfactory, 18.54% good, and 11.59% excellent. After initiating mAbs, 34.78% (n=24) no longer required triptans, indicating a significant reduction in the need for abortive treatments. Among patients continuing triptan use, 33.33% (n=15) reported a difference in efficacy, with 86.67% (n=13) noting improvement (p=0.004).
Conclusion: As previously suggested in other studies, preliminary findings indicate that anti-CGRP mAbs may reduce the need for triptans in migraine management. Despite anecdotal reports of triptan efficacy loss, so far our data did not support this. Further studies are needed to explore this interaction.
Disclosure: Nothing to disclose.

EPO-068 | Consistency of response to rimegepant: A patient-level interim analysis of a prospective real-world observational study

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Background and aims: This study evaluated real-world consistency of response to rimegepant for acute treatment of migraine at the individual patient level.
Methods: This prospective observational study was conducted using the Migraine Buddy® app with adults experiencing 3–14 headache days in the last 30 days and planning to use rimegepant during the next 30 days. Using a custom-made interface, participants completed: a baseline survey; a 28-day daily diary assessing time to meaningful pain relief (relief considered meaningful by the patient), time to meaningful functional improvement, and treatment satisfaction; and a questionnaire at study completion. Interim analyses assessed consistency of response, defined as achieving response in ≥2 of the first 3 rimegepant-treated attacks or in ≥3 of the first 4 rimegepant-treated attacks. Response was assessed via meaningful pain relief within 2 hr, meaningful functional improvement within 2hr, and report of satisfied/extremely satisfied with rimegepant.
Results: Among 118 participants with ≥3 rimegepant-treated attacks, 62.7% achieved meaningful pain relief within 2 hr in ≥2 of the first 3 attacks, 60.2% achieved meaningful improvement in functioning within 2 hr in ≥2 of the first 3 attacks, and 75.4% reported treatment satisfaction. Among 95 participants with ≥4 rimegepant-treated attacks, 48.4% achieved meaningful pain relief within 2 hr in ≥3 of the first 4 attacks, 48.4% achieved meaningful improvement in functioning within 2 hr in ≥3 of the first 4 attacks, and 69.5% reported treatment satisfaction.
Conclusion: Many patients with ≥3 or ≥4 rimegepant-treated attacks achieved consistent response to rimegepant within 2 hr on endpoints of meaningful pain relief and functional improvement.
Disclosure: LA, FD, and KHB are employed by, and own stock in, Pfizer. AU is an employee of Aptar Digital Health, paid consultants to Pfizer. GL has received fees from Abbvie, TEVA, Lundbeck, Eli Lilly, Novartis, Pfizer, and Dr Reddy's. RBL received research support, grants, or fees from the NIH, FDA, NHF, Aeon, Allergan/AbbVie, Amgen, Axsome, Dr Reddy's, Eli Lilly, GlaxoSmithKline, Ipsen, Lundbeck, Pfizer, Merck, Teva and Vedanta; and holds options in Axon, Biohaven Pharmaceuticals, CoolTech, and Manistee. PJG received a grant from Kallyope;

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EPO-069 | Migraine patients treated with Fremanezumab: What happens when treatment is discontinued? Experience in a single center

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Background and aims: To describe the effect of discontinuing Fremanezumab in a cohort of patients with chronic migraine (CM) or episodic migraine (EM), following the European Headache Federation guidelines (2022).
Methods: Inclusion criteria: patients with CM or EM treated with monthly Fremanezumab for 12 to 18 months (December/2020-December/2024) and follow-up after discontinuation >6 months. Sample: 61 patients, two groups: patients who after discontinuation required restarting treatment (F1) and patients who did not (F0). Additionally, F1 is subdivided into patients who reinitiated treatment early (<=4 months) (F1.1) or late (F1.2). Demographic characteristics, disability scores (MIDAS and HIT-6) and migraine days/month (MMD) were analyzed quarterly. Descriptive analysis of the total and analytical analysis between F0 and F1 and between F1.1 and F1.2 were performed (χ^2, Mann-Whitney U). The response to Fremanezumab, both initially and upon reinitiation in F1, was compared (Wilcoxon).
Results: Sixty-one patients, mean age 53.1±10 years and age at onset 17.6±7.5 years, mostly women (n=56, 91.8%), 57 (93.4%) suffered from CM. Treatment reinitiation was required in 54 patients (88.5%), 46.3% early, without a significant loss of efficacy (p>0.05) after restart. Three patients required treatment reinitiation twice. At baseline, the mean MMD was 16.8±6.9, the mean HIT-6 score was 67.7±6.3 and MIDAS score was 91.6±50.3. No statistically significant differences were found between F0 and F1 in demographic characteristics or baseline scores, except gender.

Comparison of demographic factors, migraine characteristics and baseline scores between F0 and F1

	F0 (no reinitiation) N= 7 (11,5%)	F1 (reinitiation) N = 54 (88,5%)	TOTAL N = 61 (100%)	P < 0,05
Gender (women)	5 (71,4%)	51 (94,4%)	56 (91,8%)	0,037
Mean age	57,7±9,5	52,4±10	53,1±10	0,171
Age at onset	17,2±4,4	17,7±7,8	17,6±7.5	0,588
History of depression and/or anxiety	4 (57,1%)	25 (46,3%)	29 (47,5%)	0,589
Cardiovascular risk factors	2 (28,6%)	11 (20,4%)	13 (21,3%)	0,618
Chronic migraine	7 (100%)	50 (92,6%)	57 (93,4%)	0,456
Migraine with aura	2 (28,6%)	24 (44,4%)	4 (50%)	0,424
Number of preventives tested	6,4±4,4	5,6±1,4	5,7±2	0,627
MMD baseline	18,7±6,2	16,5±7	16,8±6,9	0,376
HIT-6 baseline	68,3±6,3	67,6±6,3	67,7±6,3	0,872
MIDAS baseline	97,1±44,9	90,9±51,3	91,6±50,3	0,542
Medication overuse baseline	7 (100%)	46 (85,2%)	53 (86,9%)	0,275
NSAIDs/month baseline	21,6±8,4	14,6±11,8	15,4±11,6	0,106
Triptan/month baseline	13,7±13,8	14,3±9,8	14,2±10,2	0,793

FIGURE 1

Comparison of demographic factors, migraine characteristics and baseline scores between F1.1 and F1.2

	F1.1 (reinitiation <= 4th month) N= 25 (46,3%)	F1.2 (reinitiation > 4th month) N = 29 (53,7%)	TOTAL (F1) N = 54 (100%)	P < 0,05
Gender (women)	23 (92%)	28 (96,6%)	51 (94,4%)	0,467
Mean age	51,5±9,6	53,2±10,4	52,4±10	0,310
Age at onset	17,8±8,2	17,6±7,6	17,7±7,8	0,900
History of depression and/or anxiety	13 (52%)	12 (41,4%)	25 (46,3%)	0,435
Cardiovascular risk factors	2 (8%)	9 (31%)	11 (20,4%)	0,036
Chronic migraine	23 (92%)	27 (93,1%)	50 (92,6%)	0,877
Migraine with aura	10 (40%)	14 (48,3%)	24 (44,4%)	0,542
Number of preventives tested	5,8±1,4	5,5±1,5	5,6±1,4	0,393
MMD baseline	17,6±6,8	15,6±7,1	16,5±7	0,258
HIT-6 baseline	67,4±6,7	67,8±6,2	67,6±6,3	0,900
MIDAS baseline	96±46	86,3±56,1	90,9±51,3	0,542
Medication overuse baseline	20 (80%)	26 (89,7%)	46 (85,2%)	0,319
NSAIDs/month baseline	14,1±12	14,9±11,8	14,6±11,8	0,791
Triptan/month baseline	15,6±9,4	13,1±10,2	14,3±9,8	0,335
Median months until reinitiation	3 (1-4)	8 (5-29)	5 (1-29)	-

FIGURE 2

Conclusion: 88.5% of migraine patients had to reintroduce Fremanezumab, recovering its efficacy after reinitiation. This led to a change in our protocol, consisting of avoiding treatment discontinuation in patients with chronic migraine.
Disclosure: Nothing to disclose.

EPO-070 | "Comorbidities" of idiopathic intracranial hypertension: An Austrian population based cohort study

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Background and aims: Idiopathic intracranial hypertension (IIH) is a rare disorder characterized by headaches and papilledema. While a variety of diagnoses is frequently observed with IIH, population-based data on comorbidities and co-medication in IIH is scarce.
Methods: The Austrian health insurance register (>99% population coverage) was queried for patients discharged between 2016 and 2021 with ICD-10 code G93.2 and/or acetazolamide (AZM) prescription. IIH was considered confirmed if G93.2 was assigned ≥2 times and AZM was prescribed ≥ once. Five obese controls (OBC, ICD-10: E65/66/68) and five general population controls (GPC) were drawn from the register for each patient. Comorbidities and prescribed analgesics as well as antidepressants were extracted.
Results: Of 5,969 patients identified, 114 fulfilled the criteria for confirmed IIH. Compared to 114 OBC and 114 GPC matched for age and sex, IIH patients had significantly higher rates of any headache comorbidity (17.5%; 1.8% OBC, 0% GPC), migraine (10.5%; 1.8% OBC, 0% GPC), and depression (14.9%; 7.0% OBC, 0.9% GPC). Analgesic use was high (88.6%), with increased prescriptions of opioids (30.7%; 15.8% OBC, 5.3% GPC), antimigraine medications (19.3%; 5.3% OBC, 2.6% GPC), and CGRP inhibitors (8.8%; 0% OBC, 0% GPC).

TABLE 1 Demographics and frequency of invasive/non-invasive therapies (SD = standard deviation, m = male, f = female).

	IIH patients	obese controls (OBC)	general population (GPC)	test statistic	p
N	114	114	114		
mean age in years (SD)	34.2 (10.9)	34.5 (10.9)	33.2 (10.9)		
sex (m:f) in %	12:88	12:88	12:88		
headache comorbidities					
any headache comorbidity N (%)	20 (17.5%)	2 (1.8%)	0 %	$X_{(2)} = 36$	< .001
migraine N (%)	12 (10.5%)	2 (1.8%)	0 %	$X_{(2)} = 19$	< .001
tension headache N (%)	9 (7.9%)	0 %	0 %		
cluster headache N (%)	0 %	0 %	0 %		
medication overuse headache N (%)	1 (.9%)	0 %	0 %		
psychiatric comorbidities					
depression N (%)	17 (14.9%)	8 (7.0%)	1 (.9%)	$X_{(2)} = 16$	< .001
Suicide attempts or self-inflicted injuries N (%)	1 (.9%)	0 %	0 %		
analgesics use					
any analgesic N (%)	101 (88.6%)	98 (86.0%)	29 (25.4%)	$X_{(2)} = 131$	< .001
nonsteroidal anti-inflammatory drugs N (%)	91 (79.8)	95 (83.3%)	29 (25.4%)	$X_{(2)} = 103$	< .001
opioids N (%)	35 (30.7%)	18 (15.8%)	6 (5.3%)	$X_{(2)} = 26$	< .001
other analgesics N (%)	77 (67.5%)	59 (51.8%)	8 (7.0%)	$X_{(2)} = 92$	< .001
antimigraine medication N (%)	22 (19.3%)	6 (5.3%)	3 (2.6%)	$X_{(2)} = 22$	< .001
CGRP N (%)	10 (8.8 %)	0 %	0 %	$X_{(2)} = 20$	< .001
antidepressant use					
antidepressant N (%)	64 (56.1 %)	44 (38.6%)	8 (7.0%)	$X_{(2)} = 63$	< .001

Conclusion: IIH patients had more headache and psychiatric comorbidities than controls and relied more on symptomatic treatments. Frequent use of analgesics, antidepressants, and antimigraine medications highlights the disease burden. As the dataset is based on hospital discharge records, headache comorbidities are likely underreported in GPC. Outpatient data are needed for a more comprehensive assessment.
Disclosure: Funding There was no funding to this research. Competing interests Nina Müller1,2, Nik Krajnc1,2, Sina Zaic1,2, Stefan Macher1,2, Christian Wöber1,2, Wolfgang Marik2,3, Klaus Novak2,4, Berthold Pemp5, Berthold Reichardt6, and Gabriel Bsteh1,2 NM: declares no conflict of interest relevant to this study NK: has participated in meetings sponsored by, received speaker honoraria or travel funding from BMC/Celgene, Merck, Novartis, Roche and Sanofi-Genzyme. SZ: declares no conflict of interest relevant to this study SM: declares no conflict of interest relevant to this study CW: has received honoraria consultancy/speaking from Apomedica, Curelator, Eli Lilly, Grünenthal, Hermes, Novartis, Pfizer, Ratiopharm/Teva, and Stada WM: declares no conflict of interest relevant to this study. KN: declares no conflict of interest relevant to this study. BP: has received honoraria for consultancy/speaking from Chiesi, GenSight and Santen. BR: declares no conflict of interest relevant to this study. GB: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene/BMS, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting Biogen, Celgene/BMS, Novartis, Roche, Sanofi-Genzyme and Teva. He has received unrestricted research grants from Celgene/BMS and Novartis.

EPO-071 | Optical nerve sheath diameter for prediction of post-dural puncture headache: A pilot prospective observational study

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Background and aims: Post-puncture headaches are a frequently distressing complication for patients after diagnostic lumbar puncture (LP). We aimed to determine whether decreased ONSD after diagnostic LP can be used as a predictor for patients with post-lumbar puncture syndrome (PDPH).
Methods: In this prospective observational study 87 patients, who received a diagnostic LP, ONSD measurements were recorded before (T0) and 1 hour after LP (T1). 76 patients became an additional value 24 hours after LP (T2). ONSD measurements were performed 48 hours (T3) and 72 hours (T4) after LP in patients, who presented with symptoms related to intracranial hypotension. Demographic data such as age, gender, BMI and chronic headaches were recorded at different times.
Results: All included patients showed a physiological reduction in ONSD after diagnostic LP, but no more substantial decrease in the PDPH group could be shown (Fig. 1). The PDPH group decreases significantly at T2 and T3 (Fig. 2). No statistical difference was found in terms of BMI, gender, liquor volume, needle size or previous headaches between the PDPH and Non-PDPH groups (Table 1). Younger female patients were more likely to experience PDPH symptoms. The rate of PDPH development was 9.20% (n = 7). The ROC curve analysis showed the optimal ONSD cutoff value at 4.9 mm for predicting PDPH. Adopting this cutoff value, the sensitivity and specificity were 92.9 % and 85.7%, respectively.

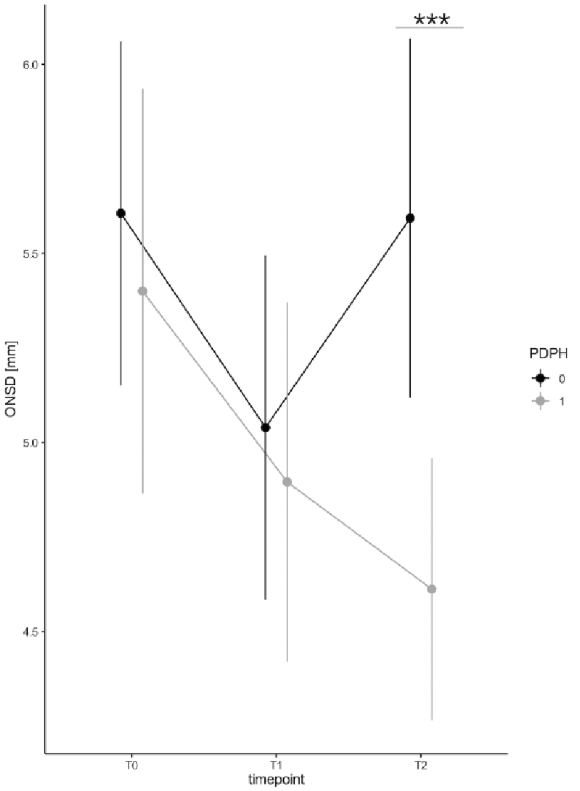

FIGURE 1 The ONSD measures values of the PDPH group and Non-PDPH group at different times.

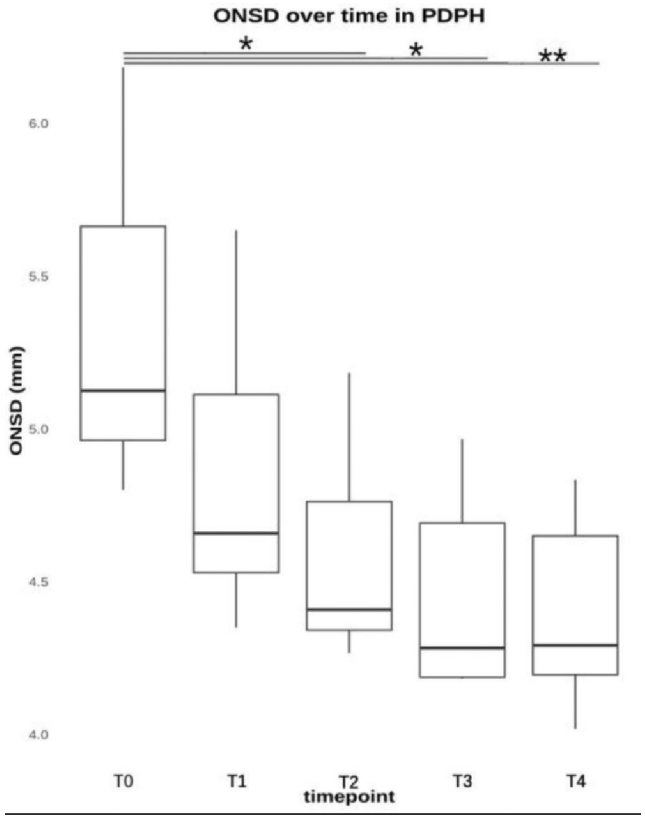

FIGURE 2 The ONSD measurement values of the patients with post-dural puncture headache (PDPH) at different times.

TABLE 1 Demographic data of the PDPH and Non-PDPH groups.

Characteristic	Non-PDPH group n = 69		PDPH group n = 7		P-value
	Number (%)	Mean ± SD Median (Min-Max)	Number (%)	Mean ± SD Median (Min-Max)	
Age (years)		56,35 ± 17,54 60 (19-88)		34,00 ±12,32 30 (21-53)	<0.001
Sex (F/M)	31/38 (44,90/55,10)		5/2 (71,40/28,60)		NS
BMI (kg/m²)		25,25 ± 5,12 25,00 (13,70-37,40)		22,51 ± 4,08 23,20 (16,60-27,10)	NS
Chronic headaches (yes/no)	12/57 (17,40/82,60)		2/5 (28,60/71,40)		NS
Liquor volume (mL)		9,00 ± 7,12 5,50 (3-35)		11,43 ± 8,52 10,00 (5-30)	NS
Gauge		20,35 ± 1,26 20,00 (20-27)		20,57 ± 0,98 20,00 (20-22)	NS

Conclusion: In conclusion, we showed that non-invasive ultrasound can be an objective method for diagnosing headaches caused by intracranial hypotension after LP.
Disclosure: Nothing to disclose.

EPO-072 | Is there still a role for detoxification strategies in migraine therapeutic scenario?

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Background and aims: Medication overuse headache (MOH) management relays on detoxification strategies able to withdraw

from overused drugs but also to improve the responsiveness to treatments. Recent evidence supported the effectiveness of monoclonal antibodies acting on the CGRP pathway (CGRP-mAbs) regardless withdrawal from overused drugs and detoxification. Since MOH can be distinguished in simple (MOH Type I) and complex (MOH Type II) phenotypes, we evaluated whether detoxification strategy can still have a role in patients with complex MOH to improve the response to preventive treatment with CGRP-mAbs compared to simple MOH.

Methods: Two hundred chronic migraine patients affected by MOH and treated with subcutaneous CGRP-mAbs underwent an extensive interview to assess clinical parameters of disease severity. The primary endpoint of the study was the differences in the percentage of patients achieving a >50% reduction in monthly headache days at the end of the first, third and sixth month of treatment with CGRP-mAbs compared with the baseline among simple and complex MOH groups based on previous detoxification strategy.

Results: Dividing patients based on the diagnosis of MOH types and detoxification strategy (4 groups: patients with MOH type I performing or not detoxification strategy and patients with MOH type II performing or not detoxification strategy), no differences were found in the percentage of patients showing a >50% response in monthly headache attacks frequency nor after one month (p=0.132) nor after the third (p=0.184) and sixth month of treatment (p=0.113).

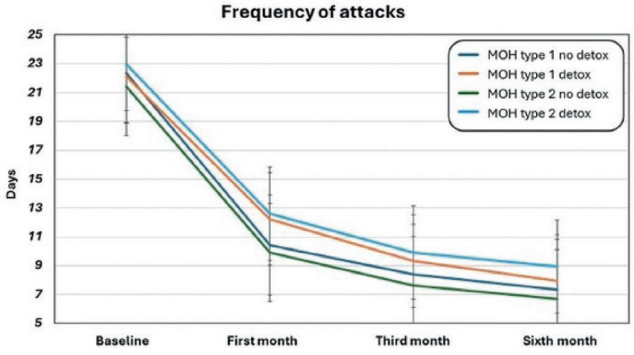

FIGURE 1

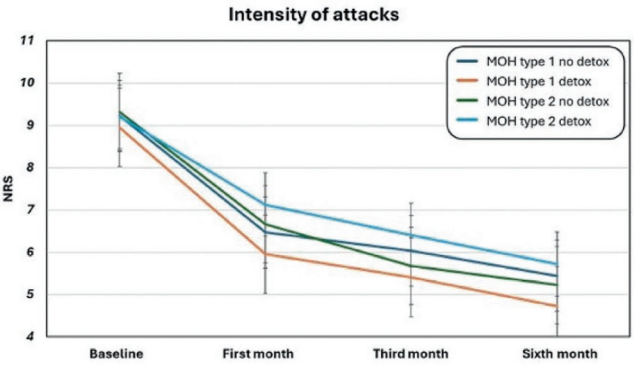

FIGURE 2

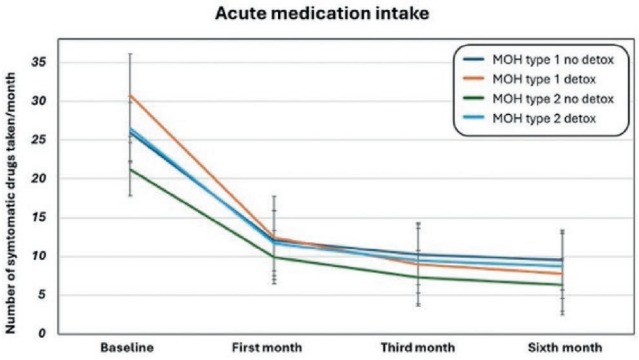

FIGURE 3

Conclusion: CGRP-mAbs may be effective in MOH patients irrespective from both detoxification strategies and "complexity" of MOH.

Disclosure: Nothing to disclose.

EPO-073 | Impact of atogepant on patient-reported outcomes for the preventive treatment of migraine in Japanese participants

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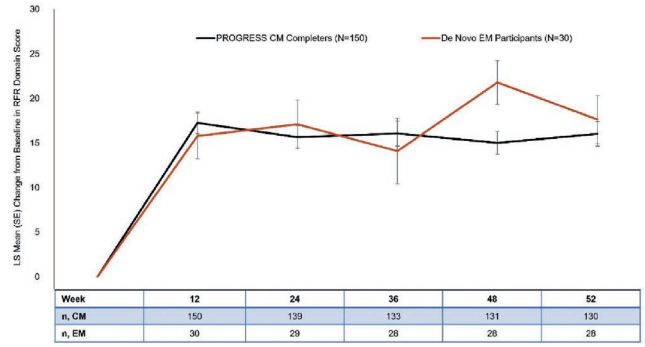
Background and aims: Atogepant is an oral calcitonin gene–related peptide receptor antagonist approved in the US and EU for the preventive treatment of migraine in adults.

Methods: This open-label, 52-week, long-term safety study evaluated atogepant 60 mg once daily (QD) for the preventive treatment of migraine in Japanese participants. The study enrolled participants with chronic migraine (CM) who completed the Phase 3 PROGRESS trial and de novo participants with episodic migraine (EM), aged 18–80 years with a >1-year history of migraine and a history of 4–14 migraine days per month. The study included a 4-week screening period (EM only), 52-week open-label treatment period of atogepant, and 4-week safety follow-up period. The primary endpoint was the safety and tolerability of atogepant. Exploratory health outcomes evaluated in the trial included change from baseline in the Migraine Specific Quality of Life Questionnaire v2.1 (MSQv2.1) Role Function-Restrictive (RFR) domain score, the Activity Impairment in Migraine-Diary (AIM-D) Performance of Daily Activities (PDA) and Physical Impairment (PI) domain scores, and Headache Impact Test-6 (HIT-6) total score over 52 weeks.

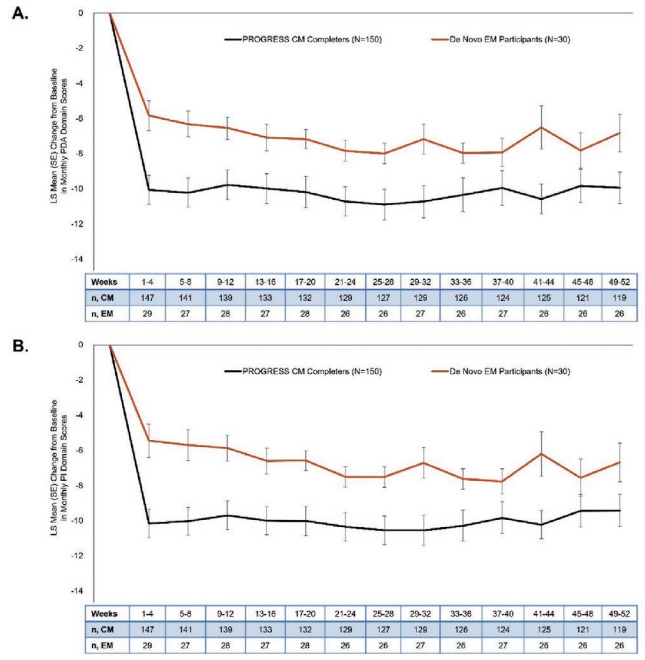
Results: The modified intent-to-treat population included 150 CM PROGRESS completers and 30 de novo EM participants. Least-square mean change from baseline at each time point assessed over the 52-week treatment period demonstrated improvement in the MSQv2.1 RFR domain score (Figure 1),

AIM-D PDA and PI domain scores (Figure 2), and HIT-6 total score (Figure 3) in CM and EM participants.



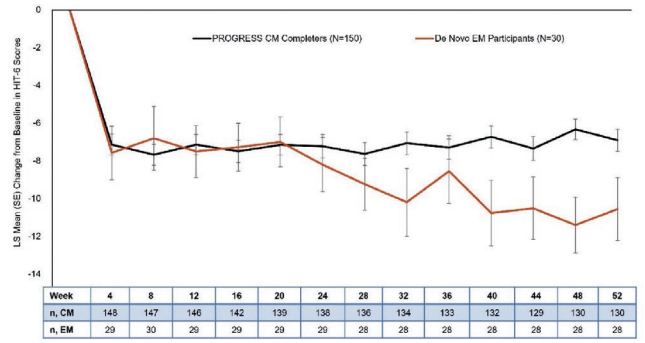
Week	12	24	36	48	52
n, CM	150	139	133	131	130
n, EM	30	29	28	28	28

FIGURE 1 Least Square Mean Change From Baseline in the MSQv2.1 RFR Domain Score Over 52 Weeks in PROGRESS CM Completers and De Novo EM Participants



Weeks	1-4	5-8	9-12	13-16	17-20	21-24	25-28	29-32	33-36	37-40	41-44	45-48	49-52
n, CM	147	141	139	133	132	129	127	129	126	124	125	121	119
n, EM	29	27	28	27	28	26	26	27	26	27	28	26	26

FIGURE 2 Least Square Mean Change From Baseline in AIM-D PDA (A) and PI (B) Domain Scores Over 52 Weeks in PROGRESS CM Completers and De Novo EM Participants



Week	4	8	12	16	20	24	28	32	36	40	44	48	52
n, CM	148	147	146	142	139	138	136	134	133	132	129	130	130
n, EM	29	30	29	29	29	29	28	28	28	28	28	28	28

FIGURE 3 Least Square Mean Change From Baseline in HIT-6 Total Score Over 52 Weeks in PROGRESS CM Completers and De Novo EM Participants

Conclusion: Patient-reported outcomes showed improvements from baseline with atogepant 60 mg QD treatment and these persisted over 52 weeks.

Disclosure: Yasuhiko Matsumori reports personal consultancy fees from Amgen, Astellas, BioPharma K.K., Daiichi Sankyo Co., Ltd, Eli Lilly Japan K.K., and Otsuka Pharmaceutical Co., Ltd. Takao Takeshima has been on the speakers' bureau for Amgen K.K., Daiichi Sankyo Co., Ltd., Eli Lilly Japan K.K., and Otsuka Pharmaceutical Co., Ltd., and has received research funding/collaborative research expenses from AbbVie GK., Amgen K.K., Eli Lilly Japan K.K., Eisai Co., Ltd., Lundbeck Japan K.K., and Pfizer Japan Inc. Takao Takeshima also acted as an advisor to Hedgehog MedTech, Inc., Sawai Pharmaceutical Co., Ltd., and TEIJIN Pharma Ltd. Fumihiko Sakai is a consultant for Amgen, Eli Lilly, and Otsuka. Toshimasa Yamamoto has received honoraria from Eisai Co., Ltd., and Takeda Pharmaceutical Co., Ltd. Noboru Imai reports being an advisor for Sawai and received speaker fees from Daiichi Sankyo, Eli Lilly, Otsuka, and Amgen. Gina Ahmadyar, Colleen Castro, Karen Carr, Krisztian Nagy, and Jia Bao are employees of AbbVie and may own AbbVie stock.

EPO-074 | Low pulse pressure and high serum complement C1q are risk factors for hemodialysis headache

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Background and aims: Hemodialysis headache (HDH) is a common complication in dialysis patients, affecting their quality of life. The etiology and triggering factors are not well understood. This study aimed to assess the prevalence and characteristics of HDH in Chinese patients undergoing hemodialysis and identify potential risk factors.
Methods: The study included two phases: a cross-sectional observational study and a case-control study. Participants underwent neurological exams, and demographic and medical data were collected. Serum levels of creatinine, uric acid, glucose, electrolytes, inflammatory markers (TNF-α, IL-1β, IL-6, etc.), and blood pressure were measured before and after dialysis.
Results: he prevalence of HDH was 37.7% (183/485). HDH was typically a bilateral, moderate-intensity tightening headache lasting less than 2 hours. In the case-control study (50 HDH patients, 84 controls), pre-dialysis pulse pressure (PP) was lower in the HDH group (51.5 ±18.2 vs. 67.9 ±14.9, p=0.027). Pre-dialysis C1q levels were significantly higher in the HDH group (201.5 vs. 189.0, p=0.021). Lower pre-dialysis PP (OR=0.96) and body weight (OR=0.95) decreased HDH risk, while higher C1q levels (OR=1.02) increased the odds of HDH.
Conclusion: Low PP, low body weight, and high blood complement C1q may be potential risk factors associated with HDH.
Disclosure: Nothing to disclose.

EPO-075 | Plasma NfL and extracellular vesicles profile predict cognitive impairment in Parkinson's disease

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Background and aims: The mechanisms underlying cognitive decline in PD remain largely unclear. We investigated the relative contribution of a selected panel of biomarkers of neurodegeneration and variants in the GBA and APOE genes in driving cognitive dysfunction in PD.
Methods: We enrolled 222 PD patients in a multicentric, cross-sectional study. The cohort was stratified in PD with normal cognition (PD-NC, n = 119), PD with mild cognitive impairment (PD-MCI, n = 82) and PD with dementia (PDD, n = 21). GBA and APOE genotypes were characterized in the whole cohort (Table 1). Plasma levels of neurofilament light chain (NfL), tau, p-tau181, Aβ1-40, Aβ1-42, α-synuclein, glial fibrillar acidic protein (GFAP), and small extracellular vesicles (EVs concentration and mean size) were analyzed using SIMOA and Nanoparticle Tracking Analysis.

TABLE 1 Demographics and clinical characteristics of the study cohort. a One-way ANOVA; b Chi-Square test; c Kruskal-Wallis test; d Two-way ANCOVA with group and sex as factors, age as covariate.

	PD-NC (n = 119)	PD-MCI (n = 82)	PDD (n = 21)	PD all (n = 222)	p
Age, years	60.3 ± 9.1	62.9 ± 9.6	65.5 ± 9.4	61.8 ± 9.5	0.032[a]
Females, n (%)	49 (41.2)	31 (37.8)	11 (52.4)	131 (59.0)	0.479[b]
Disease duration, years	10.2 ± 6.6	11.1 ± 6.8	13.0 ± 8.3	10.8 ± 6.9	0.304[c]
MDRS	139 ± 4.7	134 ± 6.8	121 ± 12.1	136 ± 8.3	< 0.001[d]
Education, years	12.4 ± 4.0	10.9 ± 3.9	10.7 ± 4.6	11.7 ± 4.1	0.025[c]
ApoE4 (≥ 1 allele)	21 (18.3)	19 (23.5)	8 (38.1)	48 (22.1)	0.146[b]
GBA1 variants carriers, n (%)	18 (15.7)	11 (13.8)	3 (14.3)	32 (14.8)	0.932[b]

Results: Age-adjusted ANCOVA showed higher Aβ1-40, Aβ1-42, NfL, p-Tau, t-Tau in PDD than PD-NC. PD-MCI showed higher NfL, p-Tau and EVs mean size compared to PD-NC (Fig. 1). A multinomial logistics regression model adjusted for demographics and genetic variables showed higher EVs mean size (p=0.023) and NfL concentration (p=0.037) associated to PD-NC and PDD group, respectively (Table 2). There were no differences in plasma biomarker profiles between GBA-PD and non-GBA-PD.

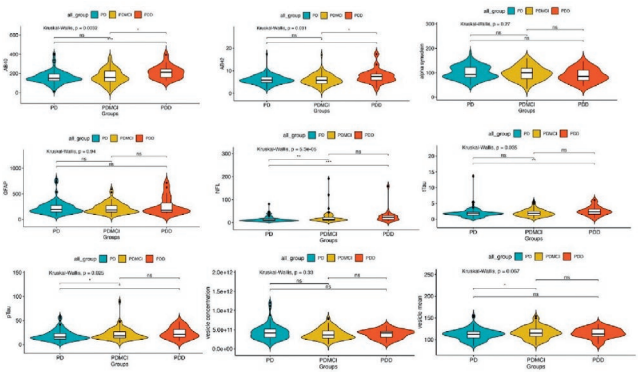

FIGURE 1 Plasma biomarkers levels in PD-NC, PD-MCI e PDD groups.

TABLE 2 Multinomial logistic regression model for prediction of PD cognitive status.

	Predictor	β	SE	p	OR
PD-MCI vs PD-NC	Intercept	-4.55193	2.0318	0.025	0.0105
	Aβ1-42	-0.08255	0.0809	0.308	0.9208
	Age (y)	0.03349	0.0178	0.060	1.0341
	Disease duration (y)	0.00778	0.0242	0.748	1.0078
	Sex (F vs M)	-0.31852	0.3393	0.348	0.7272
	Education (y)	-0.07364	0.0394	0.062	0.9290
	t-Tau	0.15369	0.1430	0.283	1.1661
	NfL	0.02354	0.0132	0.074	1.0238
	p-Tau	-8.00e−4	0.0160	0.960	0.9992
	EVs mean size (nm)	**0.02835**	**0.0124**	**0.023**	**1.0288**
	GBA+	-0.12640	0.4637	0.785	0.8813
	APOE4+	0.17552	0.3854	0.649	1.1919
PDD vs PD-NC	Intercept	-10.65701	3.7289	0.004	2.35e-5
	Aβ1-42	0.18121	0.1163	0.119	1.1987
	Age (y)	0.05646	0.0314	0.073	1.0581
	Disease duration (y)	0.01467	0.0390	0.707	1.0148
	Sex (F vs M)	0.71265	0.5907	0.228	2.0394
	Education (y)	-0.04503	0.0687	0.512	0.9560
	t-Tau	0.22073	0.1936	0.254	1.2470
	NfL	**0.03149**	**0.0151**	**0.037**	**1.0320**
	p-Tau	0.01434	0.0275	0.602	1.0144
	EVs mean size (nm)	0.02812	0.0210	0.180	1.0285
	GBA+	-0.12116	0.8831	0.891	0.8859
	APOE4+	1.39093	0.5967	0.020	4.0186

Conclusion: We identified plasma NfL and EVs mean size as independent predictors of cognitive dysfunction in PD, independently from GBA and APOE status. The longitudinal follow-up of this well-characterized cohort holds promises in identifying novel biomarkers able to identify clusters of PD patients with distinct cognitive trajectories.
Disclosure: Nothing to disclose.

EPO-076 | Post Hoc analysis: Impact of prior catechol-o-methyltransferase Inhibitor use on foslevodopa/foscarbidopa optimization

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[1]Edmond J Safra Program in Parkinson's Disease, Morton & Gloria Shulman Movement Disorders Clinic, Toronto Western Hospital, UHN; Division of Neurology, University of Toronto; Krembil Brain Institute, Ontario, Canada; IRCCS Humanitas Research Hospital, Milan, Italy; [2]AZ St-Jan Brugge, Brugge, Belgium and Ghent University Hospital, Ghent, Belgium; [3]Neurology Department, University General Hospital of Elche, Carrer Almazara, Elche, Spain; [4]Lund University, Lund, Sweden; [5]AbbVie Inc, North Chicago, USA; [6]Institute of Psychiatry, Psychology & Neuroscience, King's College Hospital, London, UK

Background and aims: Prior (until conversion) catechol-O-methyltransferase inhibitors (COMTi) use may affect foslevodopa/foscarbidopa (LDp/CDp) dose conversion and optimization due to COMT inhibition and related pharmacodynamic effects. This post hoc analysis explored impacts of prior COMTi on dosage, efficacy, and safety of 24-hour continuous subcutaneous LDp/CDp infusion.

Methods: Patients from a 52-week open-label study of LDp/CDp (NCT03781167) were grouped by prior COMTi (opicapone or entacapone) or no prior(non-COMTi) use. Outcomes included dosing, change from baseline (CFB) in OFF-time and ON-time without troublesome dyskinesia (PD diary), CFB in dyskinesia time/impact (MDS-UPDRS 4.1/4.2), and adverse events ([AE] including special interest: hallucinations and dyskinesia).

Results: Prior opicapone users had shorter PD duration and more OFF-time at baseline than non-COMTi (Table 1). Both prior COMTi groups had higher baseline levodopa(LD) equivalent doses (Table 1). Prior entacapone users showed longer optimization (Table 2). From weeks 1–2, median daily LD dose slightly decreased for prior opicapone but increased for prior entacapone and non-COMTi (Figure 1). Dyskinesia time scores increased from baseline–day 2 in prior COMTi vs non-COMTi(mean[SD]:prior opicapone,0.4[0.9],p=.066; prior entacapone, 0.3[1.0],p=.049; non-COMTi,0.0[0.9]). No other relevant CFB differences were observed for dyskinesia, OFF time, or ON time without troublesome dyskinesia. Groups reported similar proportions of any AE (Table 2). Table 2 shows hallucination, dyskinesia, and serious AEs; however, sample sizes are a limitation. LDp/CDp discontinuation was similar among groups; most common reason was AE for prior opicapone and non-COMTi, and withdrawn consent for prior entacapone (Table 2).

TABLE 1 Demographics and Baseline Characteristics by Prior COMT Inhibitor Use.

	Prior Opicapone (N=25)	Prior Entacapone (N=46)	Non-COMTi (N=172)
Age, years, LS mean [95% CI]	65.5 [61.9, 69.1]	64.2 [61.5, 66.9]	63.7 [62.3, 65.1]
p-value[a]	.363	.741	-
PD Duration, years, LS mean [95% CI]	10.4 [8.3,12.4]	12.3 [10.6, 13.7]	12.6 [11.8, 13.4]
p-value[a]	.048*	.627	-
Motor Fluctuation Duration, years, LS mean [95% CI]	5.2 [3.4, 7.1]	6.4 [5.1, 7.8]	6.9 [6.2, 7.6]
p-value[a]	.099	.574	-
LEDD, mg			
Median (min-max)	1419 (575-3225)	1370 (416-3039)	1108 (150-3513)
LS mean [95% CI]	1484 [1261,1706]	1490 [1326,1654]	1228 [1143,1313]
p-value[a]	.036*	.006**	-
OFF time, h, LS mean [95% CI]	6.9 [6.0, 7.8][b]	5.9 [5.2, 6.5][c]	5.8 [5.4, 6.1][d]
p-value[a]	.018*	.767	-
ON time without troublesome dyskinesia, mean (SD)	8.1 (2.4)[b]	9.3 (2.4)[c]	9.2 (2.5)[d]
MDS-UPDRS Part 4.1, time spent with dyskinesias, mean (SD)	1.5 (1.0)	1.1 (0.9)	1.2 (1.0)
MDS-UPDRS Part 4.2, functional impact of dyskinesias, mean (SD)	1.0 (1.1)	0.8 (1.2)	1.1 (1.2)

LEDD, levodopa equivalent daily dose; LS, least-squares; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; PD, Parkinson's disease.
[a]p-values were obtained from ANOVA comparing group LS means. * p<.05, ** p<.01.
[b]n=24; [c]n=45; [d]n=166.

TABLE 2 Dose Adjustments During the Initial Optimization Period and Overall AE Profile.

	Opicapone (N=25)	Entacapone (N=46)	Non-COMTi (N=172)
Optimization Duration[a]			
Overall, days, median (min-max)	8 (1-39)	15 (1-50)	8 (1-59)
Number of visits, mean (SD)	3.7 (2.3)	3.6 (2.4)	3.5 (2.5)
Dose Adjustments			
Initial base rate, LD mg/hr, mean (SD)	68.1 (18.8) n=25	75.1 (29.7) n=46	63.4 (27.6) n=172
End of optimization base rate, LD mg/hr, mean (SD)	78.9 (24.4) n=21	85.2 (30.8) n=41	74.1 (29.3) n=141
Increased from initial, no. of patients (%)	13 (61.9)	27 (65.9)	93 (66.0)
Decreased from initial, no. of patients (%)	6 (28.6)	6 (14.6)	20 (14.2)
No change, no. of patients, %	2 (9.5)	8 (19.5)	28 (16.3)
AEs and Discontinuation During Optimization and Treatment			
Any AE, no. of patients (%)	23 (92.0)	44 (95.7)	162 (94.2)
AESI: hallucinations	5 (20.0)	12 (26.1)	39 (22.7)
AESI: dyskinesia	4 (16.0)	1 (2.2)	13 (7.6)
Any SAE, no. of patients (%)	7 (28.0)	15 (32.6)	40 (23.3)
Premature LDp/CDp discontinuation, no. of patients (%)	11 (44.0)	17 (37.0)	78 (45.3)
Reasons for discontinuation			
AE	8 (32.0)	8 (17.4)	47 (27.3)
Withdrew consent	4 (16.0)	10 (21.7)	25 (14.5)
Lack of Efficacy	3 (12.0)	3 (6.5)	12 (7.0)

AE, adverse event; AESI, adverse event of special interest; LD, levodopa; LDp/CDp, foslevodopa/foscarbidopa; SAE, serious adverse event.
[a]Optimized infusion rate was considered achieved when no changes to the prescribed base rate were made for 15 days

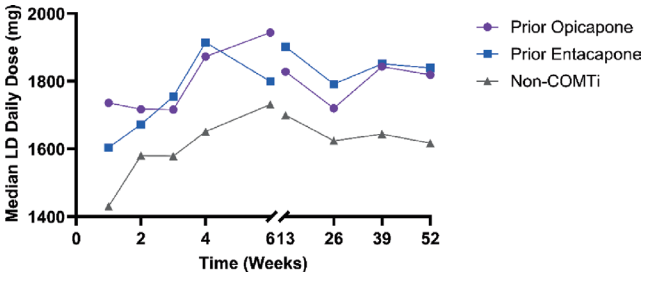

FIGURE 1 Daily LD Dose from LDp/CDp Infusion Over 52 Weeks.

Conclusion: Prior COMTi use does not impact overall efficacy and safety of LDp/CDp. During initial days after conversion, closer monitoring for dosing-related effects like dyskinesias may be advised.

Disclosure: AF received consulting fees from AbbVie, Abbott, Boston Scientific, Medtronic, and UCB; research support from Boston Scientific, Medtronic, Michael J. Fox Foundation for Parkinson's Research, and University of Toronto; honoraria

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EPO-077 | Retinal asymmetrical degeneration in Parkinson's disease and rem sleep behavior disorder

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Background and aims: According to the Synuclein Origin and Connectome (SOC) model, Rem Sleep Behavior Disorder (RBD) patients represent the prodromal phase of "body first" Parkinson's Disease (PD) patients, characterized by a more symmetric disease presentation due to a more symmetric alpha-synuclein spreading. Conversely, "Brain first" PD patients are predicted to have an asymmetrical spreading and clinical presentation, and no prodromal RBD. Thinning of the retinal layers has been described in both RBD and PD patients, however no study has ever assessed the presence of asymmetrical retinal degeneration.
Methods: Early PD "brain first" patients diagnosed according to the MDS-PD diagnostic criteria were recruited, absence of RBD was assessed using the RBDSQ questionnaire (score <6). Isolated RBD patients were diagnosed via videopolysomnography. Macula layer's thickness was evaluated using Spectral-Density Optical Coherence Tomography (SD-OCT). Asymmetry index (AI) was computed for each macular layer.
Results: Thirteen RBD patients and 15 PD "brain first" were recruited. Mean disease duration for PD patients was 25.6 ± 13.5 months, with a mean UPDRS-ME score of 25.5 ± 7.3. There was no difference in age, sex, and Moca score between the groups. Concerning macular layers, there was a significant higher AI in the outer plexiform layer (OPL) in PD vs RBD patients (10.7±8.5 vs 4.3±3.2; p=0.02). No differences were found in the other macular layers.
Conclusion: Our findings suggest a more asymmetrical retinal degeneration in "brain first" PD patients and a more symmetrical pattern in prodromal "body first" patients supporting the SOC model.
Disclosure: Nothing to disclose.

EPO-078 | OGA inhibition as a potential therapeutic approach for tauopathies: The prosper study, a phase 2 trial in PSP

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Background and aims: Progressive supranuclear palsy (PSP) is a primary tauopathy characterized by the pathological aggregation of tau protein. Tau hyperphosphorylation and other post-translational modifications contribute to its accumulation. O-GlcNAcylation, a dynamic modification that competes with phosphorylation, is regulated by O-GlcNAcase (OGA), which removes O-GlcNAc moieties from tau. OGA inhibition has been shown to elevate tau O-GlcNAcylation and to reduce the pathological aggregation of tau. Studies using different OGA inhibitors have consistently shown a reduction in tau-related pathology in multiple tau models. FNP-223, a selective orally administered OGA inhibitor, shows promise as a disease-modifying therapy for PSP based on preclinical evidence.

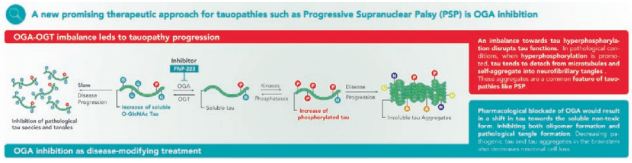

FIGURE 1 FNP-223 Mechanism of Action. FNP-223 is a reversible, substrate-competitive inhibitor of OGA, blocking O-GlcNAc removal from tau. This inhibition increases glycosylated tau, preventing pathological aggregation while maintaining structure and function.

Methods: The PROSPER study is a Phase 2 randomized, double-blind, placebo-controlled trial assessing the efficacy, safety, and pharmacokinetics of FNP-223. Eligible participants include patients diagnosed with possible or probable PSP-Richardson's syndrome within three years of symptom onset. 220 participants are being recruited across 44 sites in Europe and the U.S. Participants are randomized 1:1 to receive oral FNP-223 or placebo three times daily for 52 weeks. The primary endpoint is the change in the total PSPRS score. Secondary and exploratory endpoints will evaluate effects on progression rates of functionality, cognition, quality-of-life, neurodegeneration fluid biomarkers, and brain volume.
Results: Recruitment is ongoing. The study aims to provide critical data on the safety and efficacy of FNP-223 in slowing disease progression.
Conclusion: FNP-223 represents a promising therapeutic approach targeting tau pathology in PSP. The PROSPER study will

determine its potential as a disease-modifying agent for PSP, addressing an urgent unmet need in this population.

Disclosure: Prof. Dr. Med. Günter Höeglinger, Dr. Lawrence I. Golbe, Dr. Adam Boxer, Dr. Yaroslau Compta Hirnyj, Dr. Huw Morris are coordinating investigators for the PROSPER Study. Anna Colomé, Marta Nicolás, Lubia Álvarez, Begoña Fernández, Carla Varona, Carlos Sastré are employees of Ferrer, the sponsor of the PROSPER Study.

EPO-079 | Apomorphine sublingual film's efficacy in elderly patients with Parkinson's disease: Post-hoc analysis of study CTH-301

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Background and aims: Apomorphine sublingual film (SL-APO) is indicated for the on-demand treatment of OFF-episodes in patients with Parkinson's disease (PD). This study evaluated the efficacy of SL-APO in elderly (≥70 years) and younger (<70 years) patients over the long term.

Methods: The Phase 3, multicentre, non-randomised, open-label Study CTH-301 assessed the long-term (≥3 years) safety, tolerability and efficacy of SL-APO. This post-hoc analysis evaluated the efficacy of SL-APO in patients aged <70 and ≥70 years. Assessments included SL-APO dose, discontinuation rate due to lack of efficacy, changes in Movement Disorder Society-Unified PD Rating Scale (MDS-UPDRS) Part III scores from pre- to post-dose at Weeks 24, 36 and 48, and percentage of patients with a full-ON response within 30 minutes post-dose at Weeks 24, 36 and 48.

Results: Of the 369 de novo (not previously exposed to SL-APO) patients included in Study CTH-301, 253 (68.6%) were aged <70 years and 116 (31.4%) ≥70 years. The mean SL-APO optimised dose was similar for the <70 and the ≥70 years age groups (19.6 mg vs 21.2 mg; p=0.09). Both groups achieved a clinically meaningful reduction in MDS-UPDRS Part III at all time points (Figure 1). More than 75% of patients in both groups reported a full-ON response at all visits (Figure 2). The rate of discontinuation due to lack of efficacy was low and comparable across age groups (6.3% [16/253] vs 6.0% [7/116]).

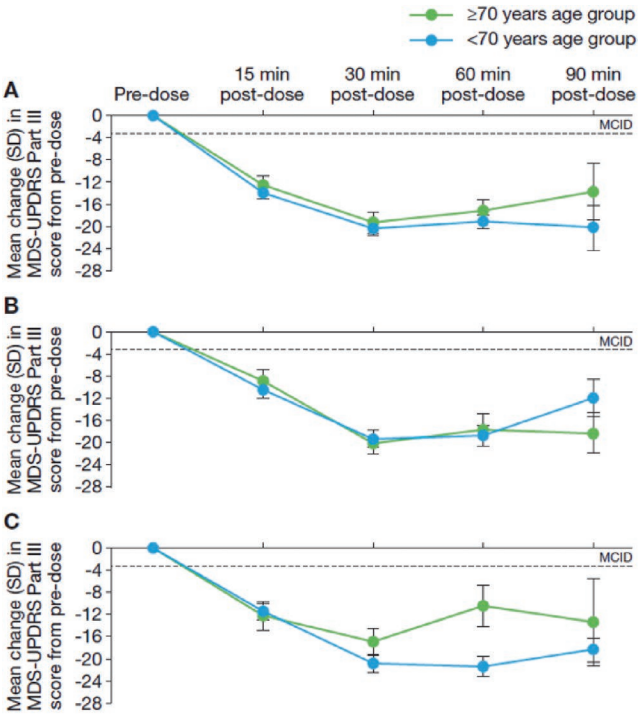

Figure 1. Mean (SD) change in MDS-UPDRS Part III score from pre-dose to 15, 30, 60, and 90 minutes post-dose in patients aged <70 years and in those aged ≥70 years at 24 Weeks (A); 36 Weeks (B); and 48 Weeks (C). The analysis included *de novo* patients only (i.e. those who were exposed to the study drug for the first time). MCID, minimal clinically important difference; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; SD, standard deviation.

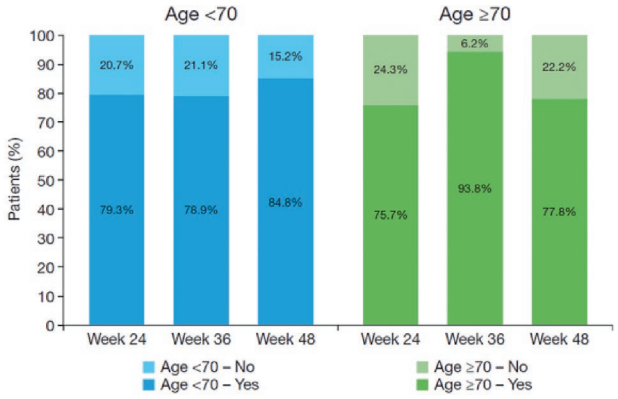

Figure 2. Patients achieving self-rated full-ON response within 30 minutes post-dose at 24, 36, and 48 Weeks. The analysis included *de novo* patients only (i.e. those who were exposed to the study drug for the first time).

Conclusion: SL-APO was efficacious over the long-term as an on-demand treatment for OFF episodes in elderly patients with PD.

Disclosure: FM is a consultant for Bial, AbbVie, and Zambon, and has received honoraria for educational presentations from Bial and Zambon. LW has received a speaker honorarium and travel payments from Bial. WHJ is a speaker and/or consultant for Bial, Britannia, Desitin and Zambon. DSG has received honoraria for educational presentations and advice service from AbbVie, UCB Pharma, Lundbeck, KRKA, Zambon, Bial, Italfarmaco, Archimedes, Esteve, Qualigen, Teva, Merz, Orionpharma and Stada. He also received grants from the Spanish Ministry of Economy and Competitiveness [PI16/01575] co-founded by ISCIII (Concesión de subvenciones de Proyectos de Investigación en Salud de la convocatoria 2020 de la Acción

Estratégica en Salud 2017-2020 por el proyecto "PROGRESIÓN NO MOTORA E IMPACTO EN LA CALIDAD DE VIDA EN LA ENFERMEDAD DE PARKINSON" y "Concesión de Contrato para la intensificación de la actividad investigadora en el Sistema Nacional de Salud, Convocatoria 2021, Instituto de Salud Carlos III"). JK has received honoraria or consultation fees from AbbVie, Bial, Biogen, Desitin, Esteve, Licher MT, Medtronic, NeuroDerm, Novartis, STADA, UCB Pharma, and Zambon; in addition, he is Specialty Chief Editor for Frontiers in Neurology (section Applied Neuroimaging) and Associate Editor (Neurology) for Therapeutic Advances in Chronic Disease. MMF, GH-J, and IP are employees of Bial. Study supported by Bial.

EPO-080 | Effect of opicapone on non-motor burden in people with Parkinson's disease-related sleep disturbances: The OASIS study

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Background and aims: Sleep disturbances are common and challenging to manage in Parkinson's disease (PD) and patients often present with a high non-motor symptoms (NMS) burden. This study's objective was to assess if enhancing levodopa effectiveness with the catechol-O-methyl transferase inhibitor opicapone (OPC) may alleviate NMS in patients with PD-related sleep issues and motor fluctuations.
Methods: This post-hoc analysis of the 6-week, open-label, single-arm OpicApone in Sleep dISorder (OASIS) study evaluated OPC 50 mg as levodopa add-on therapy. Changes from baseline to Week 6 in Movement Disorder Society Non-Motor Rating Scale (MDS-NMS) domains were analysed, as well as tolerability.
Results: Of the 16 patients in the OASIS, 15 completed treatment. At baseline, the mean (standard error; SE) MDS-NMS score was 131.3 (26). Following 6 weeks of OPC treatment, there was a significant reduction in the MDS-NMS score, with a mean change of -28.9 (95% confidence interval: -44.7 to -13.2; p=0.0015). The mean (SE) MDS-NMS sleep and wakefulness domain decreased by -6.4 (2.6) points (-31%; p=0.025) (Table 1), with significant improvements in insomnia (-2.8 [1.1]; -43%; p=0.03) and in unintentional daytime sleep episodes (-2.2 [0.8]; -41%, p=0.02) (Figure 1). Mean (SE) reductions were seen across other MDS-NMS domains, including depression, anxiety, apathy, gastrointestinal, pain and other symptoms (Table 1). OPC was well-tolerated.

MDS-NMS domains	Baseline (N=16)	OPC 50 mg (6 weeks) (n=15)	Change from baseline to Week 6	p-value
Depression, mean (SE)	11.3 (3.6)	8.3 (4.9)	-3.1 (1.7)	0.097
Anxiety, mean (SE)	**12.2 (3.3)**	**8.7 (3.9)**	**-4.3 (1.8)**	**0.035**
Apathy, mean (SE)	9.4 (2.2)	6.7 (2.8)	-2.9 (1.4)	0.057
Psychosis, mean (SE)	0.7 (0.5)	0.3 (0.3)	-0.4 (0.3)	0.253
Impulse Control and Related Disorders, mean (SE)	0.4 (0.3)	0.9 (0.5)	0.5 (0.4)	0.264
Cognition, mean (SE)	14.4 (3.9)	12.6 (3.2)	-1.8 (1.5)	0.247
Orthostatic Hypotension, mean (SE)	3.1 (1.0)	3.4 (1.6)	0.1 (1.1)	0.9
Urinary, mean (SE)	8.5 (3.0)	8.7 (3.0)	-0.3 (0.8)	0.744
Sexual, mean (SE)	9.4 (2.7)	7.4 (2.5)	-0.5 (0.8)	0.58
Gastrointestinal, mean (SE)	**8.3 (3.3)**	**6.1 (3.0)**	**-2.3 (0.9)**	**0.03**
Sleep and Wakefulness, mean (SE)	**20.4 (2.5)**	**13.7 (3.8)**	**-6.4 (2.6)**	**0.025**
Pain, mean (SE)	13.6 (3.0)	9.5 (2.3)	-3.6 (2.1)	0.102
Other, mean (SE)	**19.6 (4.1)**	**15.0 (4.3)**	**-4.1 (1.4)**	**0.013**

Table 1. MDS-NMS domains scores at baseline, after 6 weeks with opicapone (endpoint), and change from baseline to endpoint. Data are shown as mean (SE). 'Other' domain refers to unintentional weight loss, decrease in sense of smell, excessively physically and/or mentally tired, and excessive sweating. Numbers in bold indicate a significant p-value (<0.05), according to paired t-test analysis. MDS-NMS, Movement Disorder Society Non-Motor Rating Scale; SE, standard error.

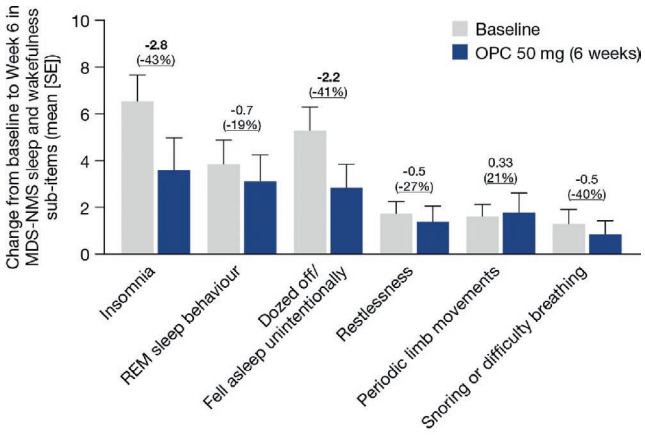

Figure 1. Change from baseline to Week 6 in MDS-NMS sleep and wakefulness sub-items.
Numbers in bold indicate a significant p-value (<0.05), according to paired t-test analysis. MDS-NMS, Movement Disorder Society Non-Motor Rating Scale domains; OPC, opicapone; SE, standard error; REM, rapid eye movement.

Conclusion: OPC significantly reduced NMS burden, particularly improving sleep-related issues, such as insomnia and daytime sleepiness, in PD patients with motor fluctuations and sleep disturbances, highlighting its potential to address both motor and non-motor challenges in this population.
Disclosure: JJF has received grants from GlaxoSmithKline, Grunenthal, Fundação MSD (Portugal), TEVA, MSD, Allergan, Novartis and Medtronic. JFF also received consultancy and speaker fees, and participated in advisory boards for GlaxoSmithKline, Novartis, TEVA, Lundbeck, Solvay, BIAL, Merck-Serono, Merz, Ipsen, Biogen, Acadia, Allergan, Abbvie, Sunovion Pharmaceuticals, Zambon, Affiris and Angelini. MFG has received payment/honoraria for lectures from Zambon, Bial Portugal, Takeda and Amicus Therapeutics, and payment/honoraria for advisory boards from Abbvie and Bial Portugal. MMF, RC, HB and JH are employees of Bial. CT has received consulting/independent contractor fees from AbbVie, UCB, Roche, Bial, Ono and Boehringer, speakers honoraria from AbbVie, STADA, Bial and Alexion, and receives royalties from Thieme

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EPO-081 | Evaluation of non-motor symptoms in Parkinson's disease with and without a GBA mutation: A cross sectional study

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Background and aims: Glucocerebrosidase gene mutations (GBA+) are the main genetic risk factor for Parkinson's disease (PD). Earlier onset and a higher burden of motor and non-motor symptoms (NMS) have been described, but the whole range of non-motor manifestations including balance have not been assessed.
Methods: A cross-sectional observational study was conducted on 40 non demented PD patients (20 GBA+), matched by age, sex and PD duration. Motor and non-motor variables were assessed using standardized tests and validated scales.
Results: Both groups were comparable in age and disease onset (5.05y GBA+ and 5.75y GBA-). Non-Motor Symptoms Scale score for GBA+ was higher (82.85 vs 71.05, p=0.914).Higher scores were also seen for GBA+ in King's Parkinson's Disease Pain Scale, modified Fatigue Impact Scale, Questionnaire for Impulsive Compulsive Disorders in Parkinson's Disease Rating Scale, Apathy Evaluation Scale and Beck Depression Inventory (see table 1). Instrumental posturography revealed lower global stability index and balance index in GBA+ patients (P=0.051 and P=0.091). Computerized reaction time tasks showed a tendency to slower execution and more mistakes in GBA+ patients with no statistically significant differences (see table 2).

TABLE 1 non motor symptoms assessment.

	GBA+	GBA-	P
KPPS	9.95	8.50	0.272
MFIS	56	49.3	0.316
QUIP-RS	21.1	13.5	0.127
AES	15	11.5	0.128
BDI	13.3	9.2	0.094

AES (Apathy Evaluation Scale), BDI (Beck Depression Inventory), KPSS (King's Parkinson's disease Pain Scale), MFIS (Modified Fatigue Impact Scale), QUIP-RS (Questionnaire for Impulsive-Compulsive Disorder in PD Rating Scale).

TABLE 2 Computerized cognitive processing tasks

	GBA+	GBA-	P
Selective response time	605	564	0.288
Selective response correct %	84%	92%	0.200
Go response time	439	437	0.728
Go response correct %	94%	96%	0.200
No go response correct %	78%	83%	0.185
Search response time	956	846	0.206
Search response % correct	88%	96%	0.473

Selective response (selection of presented stimulus between a square and a circle), go response (go-no go task), search response (finding a letter among 5 others and selecting whether the letter is present or not).

Conclusion: Higher burden of NMS in GBA+ was found as expected, as well as poorer balance performance, even though patients were in early stages and a tendency towards lower scores on cognitive processing speed. We will assess the progression of NMS and balance to identify potential markers to define a GBA+ phenotypic profile. These findings could guide the need for genetic testing in clinical practice.
Disclosure: Nothing to disclose.

EPO-082 | Expanding the clinical spectrum of STUB1-related disorder: Dystonia and GPi-DBS as therapeutic option

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Background and aims: STUB1 mutations cause hereditary ataxias, with additional features including dementia and extrapyramidal symptoms. There is no literature on the therapeutic role of deep brain stimulation (DBS) in this disorder.
Methods: We personally evaluated proband and her two siblings, and reviewed clinical records and videos of their mother. Genetic investigations included targeted assays for C9orf72, SCA1, 2, 3, 6, 7, 8, 12, 17, DRPLA, DYT6, and mitochondrial disorders. Exome sequencing was performed in the proband, followed by Sanger sequencing in her siblings and mother.
Results: Proband, a 50-year-old female, presented with cervical dystonia at age 33, which was generalized by age 45. Brain MRI showed marked cerebellar atrophy (Figure 1). Neuropsychological evaluation revealed cognitive deficits (ACE-III score: 80/100). CSF analysis found elevated total tau (181 pg/ml) with normal phospho-tau (29 pg/ml) and beta-amyloid (891 pg/ml). At 48, the

patient underwent bilateral GPi-DBS, resulting in moderate improvement (CGI=+2). Proband's mother developed dysarthria at 41, followed by spastic tetraparesis, cerebellar ataxia, and dementia. By age 80, she was significantly disabled, with limited verbal contact. Her brain MRI revealed pronounced cerebellar atrophy. Proband's brother reported muscle fatigue and tremulousness at 41, and electromyography indicated neurogenic involvement. The sister, aged 52, remained asymptomatic. Exome sequencing identified heterozygous STUB1 c.146A>G (p.Tyr49Cys) variant in the proband. Sanger sequencing confirmed the variant in the mother and brother, but not in the unaffected sister. Genetic testing for other hereditary conditions was negative.

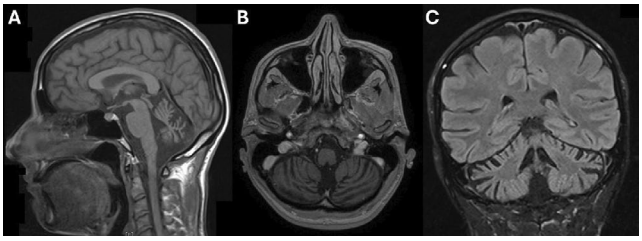

FIGURE 1 Brain MRI of the proband at 46 years old demonstrating cerebellum atrophy on T1-weighted sagittal (A) and axial (B), and T2-weighted coronal (C) sequences.

Conclusion: STUB1 mutations can present with dystonia and cognitive impairment without ataxia. GPi-DBS may offer therapeutic benefits in STUB1-related dystonia.

Disclosure: J. Kasprzak reports no disclosures relevant to the manuscript. A. Sulek reports no disclosures relevant to the manuscript. T. Janiszewska reports no disclosures relevant to the manuscript. J. Slawek serves as a co-editor-in-chief of Neurologia i Neurochirurgia Polska. He received consultancies from Allergan, Abbvie, Ipsen, Everpharma, Merz, Novartis, Biogen, Roche, TEVA. He received speakers' bureau honoraria from Allergan, Abbvie, Ipsen, Everpharma, Merz, Novartis, Biogen, Roche, TEVA. He has intellectual property rights for "Application of Hydrogen Peroxide and 17β -Estradiol and its Metabolites as Biomarkers in a Method of Diagnosing Neurodegenerative Diseases In Vitro" (WO/2023/234790). J. Dulski is partially supported by the Polish Minister of Science (Scholarship for Outstanding Young Scientists, SMN/19/1279/2023), and the Haworth Family Professorship in Neurodegenerative Diseases fund (90052067). He serves as an editorial board member of Neurologia i Neurochirurgia Polska. He received speakers' bureau honoraria from VM Media Ltd., Radosław Lipiński 90 Consulting, Ipsen. He has intellectual property rights for "Application of Hydrogen Peroxide and 17β -Estradiol and its Metabolites as Biomarkers in a Method of Diagnosing Neurodegenerative Diseases In Vitro" (WO/2023/234790).

EPO-083 | Effectiveness of opicapone added to different levodopa doses in Parkinson's: Post-Hoc analysis of the ADOPTION trials

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Background and aims: This study assessed the efficacy of opicapone 50 mg compared to an additional 100 mg dose of levodopa in reducing OFF-time in Parkinson's disease (PD) patients experiencing the first signs of motor fluctuations using different levodopa dosing regimens.

Methods: The ADOPTION clinical program included two 4-week, randomised (1:1), open-label studies in South Korea and Europe. PD patients with early wearing-off received opicapone 50 mg or an increased dose of levodopa (increased by 100 mg/day) as add-on to standard levodopa therapy. In this exploratory post hoc analysis, change from baseline in absolute OFF-time (primary endpoint) was evaluated in two subgroups: patients receiving ≤400 mg/day of levodopa (low-dose group) and those receiving >400–≤600 mg/day of levodopa (moderate-dose group) at baseline (Table 1).

TABLE 1 Baseline characteristics (randomised set). H&Y and Yahr; PD, Parkinson's disease; SD, standard deviation.

	≤400 mg/day levodopa at baseline		>400 mg/day levodopa at baseline	
	Opicapone 50 mg (n=73)	+100 mg levodopa (n=63)	Opicapone 50 mg (n=52)	+100 mg levodopa (n=55)
Age, year (SD)	63.08 (8.7)	63.3 (10.0)	65.4 (7.5)	66.1 (7.8)
PD Duration, years (SD)	4.57 (3.0)	4.83 (3.6)	5.7 (4.1)	5.9 (3.4)
H&Y (SD)	1.9 (0.5)	1.9 (0.5)	2.15 (0.5)	2.2 (0.5)
OFF-time at baseline, h (SD)	3.4 (1.1)	3.3 (1.0)	3.5 (0.9)	3.5 (1.0)
Levodopa dosage, mg/day				
Mean (SD)	317.8 (66.7)	318.6 (62.0)	513.5 (67.9)	519.8 (68.2)
Min, max	150, 400	150, 400	425, 600	450-650

Results: OFF-time reduction was consistently greater with opicapone 50 mg than the increased levodopa dose. In the low-dose group, mean (95% confidence interval) OFF-time reduction was -60.12 (-85.77, -34.47) minutes with opicapone versus -40.40 (-64.98, -15.83) minutes with levodopa. In the moderate-dose group, OFF-time reduction was -66.27 (-86.27, -46.18) minutes with opicapone and -24.91 (-55.22, 5,4) minutes with 100 mg levodopa (Figure 1). While opicapone maintained a consistent effect across levodopa dose ranges, the additional 100 mg

levodopa dose showed a trend toward reduced efficacy at higher baseline levodopa doses.

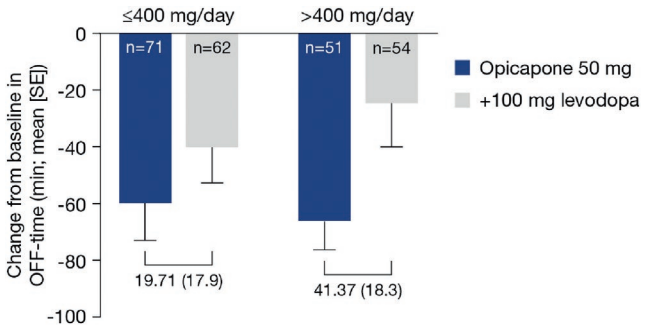

FIGURE 1 Mean (SE) change from baseline to end of study treatment in absolute OFF-time. SE, standard error; min, minutes.

Conclusion: Opicapone consistently reduced OFF-time by ~1 h independently from the total levodopa dose at baseline and was more efficacious than an increased levodopa dose, suggesting that it is an effective strategy for early motor fluctuations in PD patients.

Disclosure: JJF received grants/honoraria from GlaxoSmithKline, Grunenthal, Fundação MSD, TEVA, MSD, Allergan, Novartis and Medtronic, GlaxoSmithKline, Novartis, TEVA, Lundbeck, Solvay, BIAL, Merck-Serono, Merz, Ipsen, Biogen, Acadia, Allergan, Abbvie, Sunovion Pharmaceuticals, Zambon, Affiris and Angelini. JYL received grants/honoraria from NRF, SMG-SNU, Eisai Korea, Bial, SK Chemicals. BJ received grants from Peptron and Abbvie Korea. WP received honoraria from Alterity, AbbVie, Affiris, AstraZeneca, Axovant, BIAL, Biogen, Britannia, Lilly, Lundbeck, NeuroDerm, Neurocrine, Denali Pharma, Orion Pharma, Roche, Stada, Sunovion, Takeda, UCB, Zambon, Michael J. Fox Foundation, EU FP7 and Horizon 2020. AA received compensation/support from UCB, Boehringer Ingelheim, Britannia, AbbVie, Zambon, BIAL, NeuroDerm, Theravance Biopharma, Roche, Chiesi Pharma, Lundbeck, Horizon, Ministry of Education University and Cariparo Foundation. FS received honoraria from Lundbeck, UCB, Chiesi, Zambon, Britannia, Cynapsus, Sunovion, Kyowa, Abbvie, Neuroderm, Biogen and BIAL. OR provided consultancy for/received grants from institutions including AbbVie, Adamas, Acorda, Addex, AlzProtect, ApoPharma, AstraZeneca, Axovant, BIAL, Biogen, Britannia, Buckwang, CereSpir, Clevexel, Denali, INC Research, IPMDS, Lundbeck, Lupin, Merck, Novartis, CHU, France-Parkinson, INSERM, Michael J. Fox Foundation and Cure Parkinson UK. DMR, MMF, HB, GC-F and JH are Bial employees.

EPO-084 | PSMF1 variants: A rare cause of early-onset Parkinson's disease

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Background and aims: Biallelic Proteasome Inhibitor Subunit 1 (PSMF1) variants have been described in patients with early-onset Parkinson's disease (PD) mainly presenting with atypical aspects.

Methods: 1091 DNA samples (collected at the Parkinson Institute of Milan between 2002 and 2023) from early onset PD patients and/or positive family history were analysed with whole-exome sequencing.

Results: Biallelic PSMF1 variants were detected in one patient (estimated prevalence: 0.0009). This woman presented bradykinesia, rest tremor of the right hand, micrography started at the age of 46. She suffered from a depressive syndrome started at the age of 27. Her maternal grandmother was diagnosed with PD at the age of 80. No hyposmia, constipation, or rapid eye movement sleep behaviour disorder were referred. Brain MRI was unremarkable, 123I-FP-CIT single-photon emission computed tomography was compatible with parkinsonism. Ropinirole improved tremor but induced hallucinations and confusion at higher doses. Chronic treatment with levodopa was started with benefit. Two years later (four years from the first symptoms onset) she developed motor fluctuations (wearing-off, morning akinesia, peak-dose dyskinesia). At neurological examination no atypical signs were present. The patient died at the age of 64. Genetic analysis revealed the presence of two PSMF1 variants: c.129+2T>C (affecting position +2 of the donor splice site of exon 1) and c.725G>A (p. R242H). Both have already been reported; interestingly, the c.129+2T>C variant have not been associated to PD yet.

Conclusion: We confirm that biallelic PSMF1 variants cause a very rare form of early-onset PD, which may also present with a more typical clinical phenotype.

Disclosure: Nothing to disclosure.

EPO-085 | Drug use and long-term Parkinson's disease risk: A systematic screening approach

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Background and aims: A systematic drug-wide approach might be useful to identify drugs that (1) could be repurposed to treat Parkinson's disease (PD) or (2) could help explain PD pathogenesis (Romanowska 2023). The aim of this study was to investigate the drugs associated with a reduced or increased risk of PD in two

cohorts of the Bologna Local Health Trust (BLHT), identified by both clinical diagnosis and health administrative databases.
Methods: Historical cohort study design with time-dependent exposure. Population: residents in BLHT (680,000) aged ≥25 years without PD diagnosis, follow-up 2010-2023. Exposure: use of 94 drug classes (ATC codes, level 2) ascertained by administrative prescriptions data after at least 5 years. Endpoint: PD onset identified through (1) the ParkLink Bologna cohort or (2) a validated algorithm launched on healthcare databases. Associations between drug classes and PD risk estimated by means of Cox proportional hazard models.
Results: We identified 824 individuals with PD from ParkLink and 8,585 from algorithm. Protective association (Table 1) was found for ATC codes B03 "Antianemic", C01 "Cardiac", C03 "Diuretics", H02 "Corticosteroids for systemic use" M04 "Antigout preparations". Codes N06 "Psychoanaleptics" and G04 "Urologicals" showed an increased risk (Table 1).

Table 1. Drugs (by ATC codes) associated with a reduced or increased risk of Parkinson's disease in the ParkLink cohort (clinical diagnosis) and in the algorithm cohort (Zenesini 2022) of the Bologna Local Health Trust. Comparison with other drug-wide screening studies.

ATC code	Bologna cohorts*	Agreement with other drug-wide studies
B03 "Antianemic"	Protective association	
C01 "Cardiac"	Protective association	
C03 "Diuretics"	Protective association	French cohort (Courtois 2022)
G04 "Urologicals"	Increased risk	Norway cohort (Romanowska 2023)
H02 "Corticosteroids for systemic use"	Protective association	Norway cohort (Romanowska 2023)
M04 "Antigout preparations"	Protective association	Finland cohort (Koponen 2022)
N06 "Psychoanaleptics"	Increased risk	Norway cohort (Romanowska 2023)

*Agreement between ParkLink and algorithm cohorts.
Courtois et al. Mov Disord. 2022;37(12):2370-2385. doi:10.1002/mds.29205
Koponen et al. Clin Epidemiol. 2022;14:1217-1227. doi:10.2147/CLEP.S381280
Romanowska et al. Neurology. 2023;101(21):e2068-e2077. doi:10.1212/WNL.0000000000207899
Zenesini et al. Neuroepidemiology. 2023;57(5):336-344. doi:10.1159/000533362

Conclusion: Specific drug classes may impact PD onset and progression, as suggested by consistent findings among different geographic and healthcare settings (Courtois 2022, Koponen 2022, Romanowska 2023) (Table 1). Many classes with anti-inflammatory activity may have a protective role. Further studies exploring these associations at the 3rd to 5th level of ATC codes are warranted.
Disclosure: Nothing to disclose.

EPO-086 | sGFAP is elevated in essential tremor patients with late disease onset and short disease duration

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Background and aims: The role of neurodegeneration in essential tremor (ET) remains debated, particularly in patients with late disease onset. Neuropathological studies have identified structural changes in the Purkinje cells and its connections. Recent studies additionally suggested a role of cerebellar astrocytes. Increased levels of serum glial fibrillary acidic protein (sGFAP), an astrocytic intermediate filament, were found in various neuroinflammatory and neurodegenerative diseases. The objective of this case-control study was to investigate the role of sGFAP in ET focusing on early-stage late-onset patients.
Methods: sGFAP was quantified by single molecule array at baseline and 5-years-follow-up in 36 ET-patients and 36 age-matched healthy controls. ET-patients were assessed using the Fahn-Tolosa-Marin-Tremor-Rating-Scale. The ET group was stratified (1) by median age at onset and median disease duration in early-stage late-onset and early-onset/late-stage ET, and (2) by median sGFAP-level at baseline.
Results: Early-stage late-onset ET-patients had higher baseline-sGFAP than controls (p=0.023) and higher follow-up-sGFAP and annual sGFAP-increase than both controls (p=0.023; p=0.007) and early-onset/late-stage ET-patients (p=0.021; p=0.024). Baseline sGFAP-level correlated with tremor severity at follow-up in the early-stage late-onset (rs=0.704, p=0.011) but not in the early-onset/late-stage group. Patients with high compared to low sGFAP-baseline levels had later disease onset (p<0.001) and sGFAP-increase was associated to tremor progression only in high sGFAP-patients (p=0.041). ET-plus and pure-ET-patients did not differ in any of the sGFAP-parameters.
Conclusion: sGFAP is elevated in early stages of late-onset ET and associated to tremor progression, substantiating the role of a pathophysiological substrate in ET in this subgroup.
Disclosure: Nothing to disclose.

EPO-087 | The impact of antidopaminergic medications on assessment of function, cognition, and motor features on HD outcomes

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Background and aims: Antidopaminergics medications (ADMs; VMAT2 inhibitors and antipsychotics) are essential for Huntington's disease (HD) symptom management. However, potent anti-dopamine activity of ADMs is associated with faster progression in measures of HD, including function (TFC), cognition (SWR/SDMT), motor (TMS), and the composite measure of progression (cUHDRS). No prospective randomized controlled trials (RCT) have addressed the impact of ADMs in HD over time. The Phase 3 PROOF-HD trial (NCT04556656) evaluated the efficacy and safety of pridopidine in HD, and it is the first double-blind, placebo-controlled study presenting data assessing the impact of ADMs on a placebo group.
Methods: Participants on- or off-ADMs in the placebo arm were compared across HD outcome measures. The most frequently used ADMs included olanzapine (18%), risperidone (18%), deutetrabenazine (13%), tetrabenazine (9%), aripiprazole (8%), tiapride (11%), and quetiapine (5%).
Results: By week 78, on-ADM participants (n=133) showed greater declines across all measures compared with off-ADM participants (n=112): TFC (Δ = -1.31 vs. -0.46, p<0.0001), cUHDRS (Δ = -1.29 vs. -0.49, p<0.0001), SDMT (Δ = -2.36 vs. -0.38, p=0.0003), SWR (Δ = -4.12 vs. -0.73, p=0.02), and TMS (Δ=3.95 vs. 1.12, p=0.01).
Conclusion: These findings underscore the impact of ADMs on HD outcomes, highlighting the need for careful consideration in patient-care and clinical trial design. Future HD trials should account for ADM use, e.g., using natural history controls, to ensure accurate assessment of disease progression and treatment efficacy.
Disclosure: This study was sponsored by Prilenia Therapeutics.

EPO-088 | Patient profiles and first-line treatment in Parkinson's disease: Study on the 2/100th French Nationwide claims database

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Background and aims: The care pathways of patients with Parkinson's disease (PD) in France are poorly understood outside expert centers and clinical trials. What is the reality of their management? We describe the socio-demographic and clinical characteristics of PD patients, as well as the first-line antiparkinsonian treatment choices.
Methods: Retrospective cohort study of patients over 20 years of age identified has having PD in the sample of the French Nationwide claims database (ESND) from 01/01/2015 to 31/12/2021 by declaration of a long-term illness, hospitalization for PD, or at least three dispensations of antiparkinsonian drugs within one year. The demographic and clinical profiles of patients, as well as the first-line antiparkinsonian treatments, stratified by patient age at treatment initiation, was described.
Results: Among the 11,095 PD patients analysed, 50.1% were men. First-line treatments for patients aged ≥70 years (63.3%) included levodopa + decarboxylase inhibitor (64.9%), piribedil (9.8%), and pramipexole (9.2%), with an average duration of 2.8 years, and a single treatment in 69.9% of cases. For patients aged <70 years, first-line treatments included pramipexole (31.0%), levodopa + decarboxylase inhibitor (18.8%), and ropinirole (17.9%), with an average treatment duration of 3 years and a single treatment line in 53.6% of cases.
Conclusion: This study highlights differences in therapeutic strategies based on patient age at treatment initiation: a predominance of levodopa + decarboxylase inhibitor in patients over 70 years old and dopamine agonists in younger patients. These results are in line with the local recommendations of the time.
Disclosure: This research was conducted with support from Orion Pharma. BD, DD, CG, AS, OR and TR are members of Orion's advisory board. BD received honoraria for presentations from Merz and Ipsen. CG received honoraria from Abbvie and Ipsen. MB is president of the Contract Research Organization Qualees in charge of the study.

EPO-089 | Analysis of single PDQ-39 items comprising the PDQ-8 shows foslevodopa/foscarbidopa therapy improved PDQ-8 summary index

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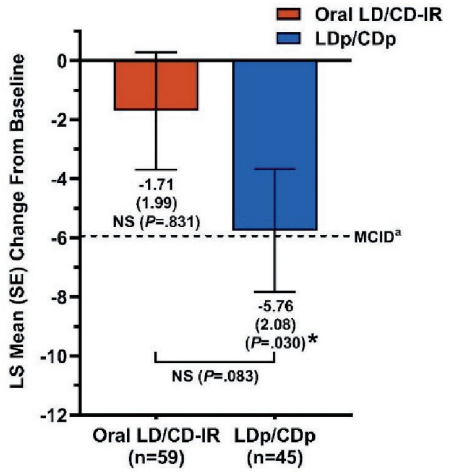
Background and aims: The 39-item Parkinson's Disease Questionnaire (PDQ-39) is a disease-specific instrument evaluating Parkinson's disease (PD) patients quality of life (QoL); however, this assessment is time-consuming. The shorter PDQ-8, comprised of 1 representative item from each of the 8 PDQ-39 domains, is reported to have similar validity and responsiveness as PDQ-39. Horváth et al. used the 8 representative items from PDQ-39 assessments to calculate the PDQ-8 Summary Index (PDQ-8-SI) and minimal clinically important difference (MCID) for PDQ-8-SI and PDQ-39-SI (5.94, 4.72, respectively). Our objective was to similarly derive and analyse PDQ-8-SI from PDQ-39 assessments in advanced PD patients treated with 24-hour foslevodopa/foscarbidopa (LDp/CDp) continuous subcutaneous infusion.
Methods: The PDQ-8-SI was calculated post hoc from 1 active-controlled and 1 open-label phase 3 trial using the approach above in patients treated with LDp/CDp or oral levodopa/carbidopa immediate-release therapy for 12 weeks (NCT04380142), or with LDp/CDp for 52 weeks (NCT03781167), respectively. Nominal P values were calculated via one-sample t-test and analysis of covariance, or two-sided paired-sample t-test.
Results: Figure 1 reports active-controlled trial within-group change from baseline and vs oral PDQ-8-SI improvement. Figure 2 reports open-label trial PDQ-8-SI change from baseline. Table 1 reports each trial's calculated PDQ-8-SI and previously reported PDQ-39-SI. LDp/CDp overall safety was previously reported as generally well tolerated.



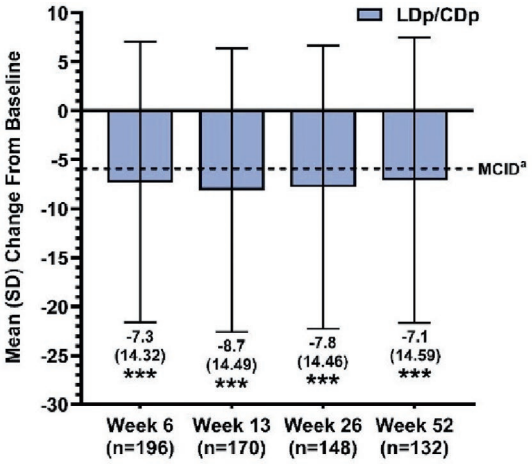
Abbreviations: ANCOVA, analysis of covariance; CD, carbidopa; CDp, foscarbidopa; IR, immediate-release; LD, levodopa; LDp, foslevodopa; LS, least-squares; MCID, minimal clinically important difference; n, number of patients included in the individual parameter analysis; NS, not significant; PDQ-8-SI, Parkinson's Disease Questionnaire 8-item Summary Index; SE, standard error

*$P \leq .05$
Within-group P values were calculated via one-sample t-test while between treatment groups P value was calculated via ANCOVA model including effects for treatment, country, and baseline.

Statistical significance of the active-controlled trial PDQ values is nominal due to the trial's prespecified hierarchical testing design not passing a higher-ranked endpoint. (Solleau MJ, et al. *Lancet Neurol.* 2022;21:1099–1109.)

[a] The accepted MCID for detecting improvement in the PDQ-8-SI is -5.94 (nonmodel-based mean) change from baseline (Horváth K, et al. *Neuroepidemiology.* 2017;48:1-8.)

Figure 1. Active-Controlled Trial Calculated PDQ-8-SI



Abbreviations: CDp, foscarbidopa; LDp, foslevodopa; MCID, minimal clinically important difference; n, number of patients included in the individual parameter analysis; PDQ-8-SI, Parkinson's Disease Questionnaire 8-item Summary Index; SD, standard deviation

***$P \leq .001$
Within-group P values were calculated via two-sided paired-sample t-test.

[a] The accepted MCID for detecting improvement in the PDQ-8-SI is -5.94 (nonmodel-based mean) change from baseline (Horváth K, et al. *Neuroepidemiology.* 2017;48:1-8.)

Figure 2. Open-Label Trial Calculated PDQ-8-SI

Table 1: The Currently Calculated PDQ-8-SI and Previously Reported PDQ-39-SI Mean Changes From Baseline in the Active-Controlled and Open-Label Phase 3 Clinical Trials

Parameter	PDS-8-SI Mean Change	PDQ-39-SI Mean Change
Active-Controlled Trial Change from Baseline to Week 12, LS mean (SE)		
Oral LD/CD-IR, n/N=59/59	-1.71 (1.99)	-2.28 (1.75)[a]
LDp/CDp, n/N=45/45	-5.76 (2.08)*	-6.38 (1.83)***[a,b]
Treatment Difference Between Groups, LS mean (SE) of Difference	-4.05 (2.31)[c]	-4.10 (2.04)*[a]
Open-Label Trial Change from Baseline to Indicated Timepoint, mean (SD)		
Week 6, n/N=196/243	-7.3 (14.32)***[b]	-7.6 (12.81)***[b,d]
Week 13, n/N=170/243	-8.7 (14.49)***[b]	-8.3 (13.57)***[b,d]
Week 26, n/N=148/243	-7.8 (14.46)***[b]	-7.3 (12.62)***[b,d]
Week 52, n/N=132/243	-7.1 (14.59)***[b]	-7.2 (13.65)***[b,d]

Abbreviations: ANCOVA, analysis of covariance; CD, carbidopa; CDp, foscarbidopa; IR, immediate-release; LD, levodopa; LDp, foslevodopa; LS, least-squares; MCID, minimal clinically important difference; N, total number of patients included in the analysis; n, number of patients included in the individual parameter analysis; PDQ-39-SI, Parkinson's Disease Questionnaire 39-item Summary Index; PDQ-8-SI, Parkinson's Disease Questionnaire 8-item Summary Index; SD, standard deviation; SE, standard error

*$P \leq .05$; **$P \leq .01$; ***$P \leq .001$
Within-group P values in the active-controlled trial were calculated via one-sample t-test while between treatment groups P values were calculated via ANCOVA model including effects for treatment, country, and baseline. Any statistical significance observed in the active-controlled trial PDQ values is nominal due to the trial's prespecified hierarchical testing design not passing a higher-ranked endpoint.[a]

Within-group P values in the open-label trial were calculated via two-sided paired-sample t-test.

[a] Previously reported in the active-controlled trial's primary results paper by Solleau MJ, et al. *Lancet Neurol.* 2022;21:1099–1109.
[b] Greater than or equal to the accepted MCID of -5.94 and -4.72 (nonmodel-based mean) change from baseline for detecting improvement in the PDQ-8-SI and PDQ-39-SI, respectively (Horváth K, et al. *Neuroepidemiology.* 2017;48:1-8.)
[c] $P = .0829$
[d] Previously reported in the open-label trial's primary results paper by Aldred J, et al. *Neurol Ther.* 2023;12(6):1937-1958.

Conclusion: Both trial's calculated PDQ-8-SI showed similar nominally significant improvements vs baseline near/over MCID in LDp/CDp-treated patients, as previously reported for PDQ-39-SI. These results suggest evaluating QoL in PD patients using PDQ-8 could obtain results similar to PDQ-39 with reduced patient/caregiver assessment time burden.

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EPO-090 | First results of the Multiple Sclerosis Autonomy Scale (MSAS) questionnaire

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Background and aims: Many MS patients have symptoms that impact on their autonomy, defined as being able to perform the roles that are most important to oneself, with or without help. MSAS is a new questionnaire that aims at evaluating patient autonomy in multiple sclerosis. Our current study's primary objective is to validate the psychometric properties of the MSAS questionnaire.
Methods: The FOCAL-MS2 study will confirm the psychometric properties of the short version of the questionnaire. 210 pairs of healthcare professionals and patients were recruited to test the questionnaire for 1 year. This analysis describes the characteristics of patients and MSAS questionnaire results at inclusion. MSAS scores are standardized on 0-100 scale, higher scores representing higher burden of autonomy.
Results: From the 210 patients included from January to April 2024, 199 completed the MSAS questionnaire at baseline: 74% women, mean age at diagnosis 34.3 +/- 9.9 years; 132 (66.3%) had a relapsing remitting form of MS (RRMS), 23 (11.5%) with primary progressive (PPMS) and 44 (22.1%) with secondary progressive (SPMS). The most important dimension for patients was support from their partner (mean score: 89.5±15.6) and consideration from the care team (mean score: 86.5±14.8). The least important dimension was the image projected to others (mean score: 69.7±24.0).
Conclusion: The population included in the study covers the different profiles of MS patients. Not all the dimensions are equally important for each patient, making it possible to identify individualised priorities that have a real impact on autonomy.
Disclosure: The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: Cecile Donze: consulting and speaking honoraria from Biogen, BMS, Coloplast, Merck, Novartis, Roche, Sanofi, and Teva; Claude Mekies: honoraria for scientific advisory boards participation or contribution to scientific meetings from Bayer, Biogen, BMS, Celg`ene, Eisai, Genzyme, GSK, Janssen, Lilly, Merck, Novartis, Pfizer, Roche, Sandoz, Sanofi, and Teva; Geraud Paillot: no conflict of interest; Patrick Vermersch: honoraria, contribution to meetings from AB Science, Biogen, BMS-Celgene, Imcyse, Janssen, Merck, Novartis, Roche, Sanofi-Genzyme, Teva, and research supports from Merck, Novartis, and Sanofi-Genzyme; Guillaume Montagu: as an employee of unknowns SAS, consulting for Alexion, Astellas, BMS, Celltrion, Chiesi, Gilead, Novo Nordisk, Pfizer, and Roche; Lucie Brechenmacher, Alexandre Civet and David Pau are employees from Roche SAS, France; Catherine Mouzawak: honoraria for consulting, scientific advisory boards participation, or other activities from Biogen, Janssen, Merck, Novartis, Sanofi, and Roche; Mikael Cohen: consulting honoraria from Ad Scientiam, Alexion, Biogen, BMS, Horizon Therapeutics, Merck, Novartis, and Roche.

EPO-091 | Inter-network connectivity and consolidated resilience in adult and pediatric multiple sclerosis patients

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Background and aims: Consolidated resilience (CR) is a measure that combines cognitive reserve and cognitive resilience. Our aim was to assess whether CR moderates the association between inter-network functional connectivity and cognition in different age groups of multiple sclerosis (MS) patients.
Methods: A total of 268 MS patients underwent cognitive and 3.0T MRI assessment. CR scores were computed using a partial least-squares path model combining proxy-based measures of cognitive reserve (years of education and intelligence quotient) with residual-based measures of cognitive resilience. Resting state fMRI scans were acquired from 25 adult MS patients, 24 sex- and disease duration-matched pediatric MS patients. MS patients were re-evaluated after a median follow-up of 2.4 years (interquartile range 1.6–3.3 years). We identified the main cognitive networks by independent component analysis and calculated inter-network connectivity through pairwise correlations. As a summary measure of connectivity strength for each network, we calculated the degree, i.e., the weighted sum of inter-network correlation coefficients. Linear mixed models were used to evaluate the effect of CR and degree on cognitive changes.
Results: Linear mixed models showed significant three-way interactions (CR x time x network degree) for verbal memory scores (frontoparietal network [$\beta = 1.42$, $p = 0.010$]) in pediatric MS patients, and for attentional/executive scores (salience network [$\beta = 1.42$, $p = 0.010$]; executive control network [$\beta = -0.70$, $p = 0.008$]) in adult MS patients.
Conclusion: The association between higher CR and better cognitive outcomes in MS patients is moderated by specific RS FC patterns between cognitive networks, which change with age.
Disclosure: DM, PV, AM have nothing to disclose. MM reports grants and personal fees from Sanofi Genzyme, Merck Serono, Roche, Biogen, Amgen and Novartis. MF received

compensation for consulting services or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM. MAR received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche, and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva, she receives research support from the MS Society of Canada, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM.

EPO-092 | Incidence of infection in 500 adults 55 years and older with multiple sclerosis treated with ocrelizumab

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Background and aims: Phase III clinical trials for Ocrelizumab, a disease modifying therapy for multiple sclerosis (MS), excluded patients >55 years; however, Ocrelizumab is widely used to treat people with MS 55 years and older.
Methods: A retrospective, observational cohort study was conducted at a high-volume academic medical center in Boston, USA. The electronic medical records of 500 randomly selected adults aged 55 and older, who received at least one dose of Ocrelizumab IV (June 2017-April 2024).
Results: Participants were 65% female, 92% White and, at last follow up, were aged: 55–59 years (n=133), 60–64 years (n=151), 65–69 years (n=105), 70–74 years (n=70), 75–79 years (n=29), and ≥80 years (n=12). Presentations were RRMS (45%), SPMS (22%), PPMS (15%), and atypical (2%). Average MS duration was 20 years. The median number of Ocrelizumab doses was 6. Ocrelizumab was a third-line or later treatment in 55%. Hypogammaglobulinemia (IgG<600 mg/dL) occurred at least once in 52%. 30% of those tested (n=117) were JCV-antibody seropositive (index level >1.5). During 21867.1 person-months of observation, there were 882 infections, including urinary tract infections (n=420), COVID-19 (n=172), upper respiratory tract infections (n=104), sepsis (n=12) and PML (also exposed to natalizumab, n=1). 105 hospitalizations and 1 death were related to infections. There were 32.5 non-COVID infections per 1,000 person-months of Ocrelizumab IV in older adults.
Conclusion: We depict a cohort of older adults clinically selected to take Ocrelizumab for MS and their safety profile.
Disclosure: F. Mateen has received research funding from EMD Serono, Genentech, Horizon Therapeutics, Novartis, and TG Therapeutics. S. Lee and R. Scheu have nothing to disclose.

EPO-093 | Cord lesion burden and atrophy in late-onset multiple sclerosis: A comparative study with adult-onset multiple sclerosis

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Background and aims: Late-onset multiple sclerosis (LOMS) is defined when clinical onset starts after age 50. This study aimed to characterize LOMS patients in terms of cervical cord lesions and atrophy, compared to disease duration (DD)-matched adult-onset MS (AOMS), and correlate their cord damage with clinical scores.
Methods: A total of 101 MS patients (81 AOMS/20 LOMS, mean DD=2.1 years in both groups) and 83 healthy controls (HC, 57/26 matched with AOMS and LOMS, respectively) underwent following 3T MRI scans: (i) sagittal/axial cord T2-weighted scans for cord lesion count and volume; (ii) brain 3D T1-weighted MRI for mean upper cord cross-sectional area (MUCCA) assessment; and (iii) in a sub-group of n=73 patients, phase-sensitive inversion-recovery at C2/3 and C3/4 for cord grey matter (GM) area assessment. Patients also underwent disability, 9-hole peg test (9HPT) and Timed 25-foot walking test (T25-FW) evaluation.
Results: Spinal cord lesion number/volume were not different between LOMS and AOMS. Also, we found no differences in MUCCA/cord GM area between LOMS/AOMS and their respective HC groups, nor between LOMS and AOMS. However, when looking at patients with longer DD (≥5 years), LOMS showed lower C3/4 GM area than AOMS (p=0.017). In LOMS, a higher cord lesions number correlated with higher T25-FW (r=0.70, p=0.04), while a higher cord lesion volume with higher disability (r=0.51, p=0.02) and T25-FW (r=0.58, p=0.007).
Conclusion: While lesion damage is comparable between LOMS and AOMS, cord GM atrophy seems to become more severe in LOMS vs AOMS as DD increases.
Disclosure: GG, NT, PV, FE have nothing to disclose. PP received speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon and Sanofi. He received research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). MF received compensation for consulting services or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events

for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM. MAR received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche, and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva, she receives research support from the MS Society of Canada, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM.

EPO-094 | Identifying new candidate biomarkers through proteomic analysis of cerebrospinal fluid in multiple sclerosis

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Background and aims: Multiple Sclerosis (MS) is a chronic disease recognized as a complex disorder influenced by various factors, where the interplay between genetic predispositions and environmental elements contributes to disease onset. Recognizing these differences may help anticipate how the disease will evolve and elucidate the distinct ways MS patients respond to various treatments. Key biomarkers play a role in enhancing patient diagnosis, treatment strategies, and prognostic evaluations. These biomarkers, (e.g., cytokines, chemokines, RNAs), highlight the diverse contributions of the immune system to the pathophysiology and progression of MS. Unfortunately, none of them demonstrate specificity for MS
Methods: Here we define a proteomics MS signature by using mass spectrometry in cerebrospinal fluid (CSF) of MS patients (n = 15) compared to not affected controls (NC) (n = 12).
Results: A total of 964 proteins were identified. Among these, 72 were exclusively found in MS patients, while 46 proteins were differentially expressed between NC and MS. MS patients exhibit unique proteins, such as proteolytic enzymes, cell adhesion factors, and those linked to stress and immune activity. Moreover, an upregulation of IGFBP-2 and a downregulation of IGF-2 was found. This imbalance could impair the neuroprotective effects of IGF-1, contributing to neurodegeneration. Machine learning was employed to assess which of the proteomic collection of identified proteins could be used to better classify MS compared to NC. It identified proteins effective in distinguishing MS from NC (Figure).

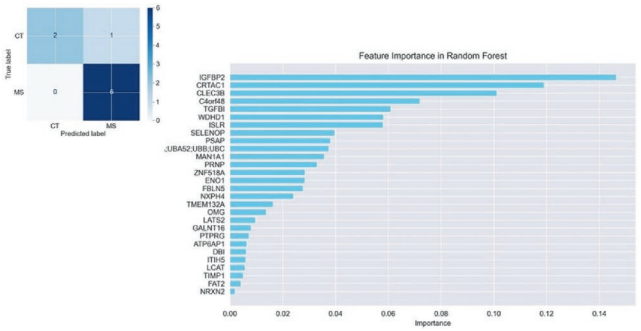

FIGURE 1 Putative candidate markers from CSF proteomic analyses

Conclusion: The putative proteomic biomarkers here identified, provide valuable information for MS management. IGFBP2 was validated as promising MS biomarkers in CSF.
Disclosure: Nothing to disclose.

EPO-095 | Efficacy and safety of Ofatumumab in the first year of clinical practice: A multicenter study

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Background and aims: The main goal was to analyze the efficacy and safety in MS patients treated with ofatumumab in real-world clinical practice.
Methods: Retrospective multicentre cohort study included patients treated with Ofatumumab using data from the EMCAM (Multiple Sclerosis Study group of Madrid) cohort. We described the clinical and demographic characteristic of the patients and analyzed the effectiveness and safety in the first year of treatment.
Results: A total of 285 patients were included. The clinical and demographic characteristics are shown in table 1. 15.1% of patients switched to ofatumumab due to relapse, 31.2% due to radiological activity and 18.7% for both reasons. 35% switched for other reasons such as safety concerns or adverse events (AE). 9 patients have discontinued treatment three by personal choice, two due to radiological disease activity, two due to relapse, one for both reasons and one for safety reasons. After one year of treatment with ofatumumab, the ARR decreased significantly to 0.02 and the mean of gadolinium-enhancing lesions decreased to 0.04. EDSS remained stable at one year 2,2 (0-8). Baseline IgG

and IgM levels were 10.12 (4.33-17.2) and 1.17 (0.11-5.37) G/L respectively. After twelve months IgG levels had decreased to 9.9 (4-17.7) and IgM to 0.86 (0.14-4.58) G/L. Adverse events were reported by 26.7% of patients after the first dose, with 67.7% of these experiencing mild flu-like symptoms. Three patients experienced herpes simplex during treatment.

Clinical-demographic characteristics	N= 285
Demographic characteristics	
Mean age at ofatumumab initiation (years)	41.4 (15-66)
Sex (woman/men)	178/107
Clinical features	
Baseline EDSS	2.2 (0-8)
Naive patients	78 (27,4%)
Baseline annualized relapse rate (ARR)	0.54
Baseline gadolinium-enhancing lesions (mean)	0.57
% of switchers	44%
Patients previously treated with high or very high efficacy modifying therapies (%)	55,9%

FIGURE 1 Clinical and demographic characteristics

Conclusion: Ofatumumab was well-tolerated, with no severe adverse events. After one year, significant reductions in ARR and Gd+ lesions were observed, supporting its efficacy and safety in treating relapsing multiple sclerosis.
Disclosure: none of the co-authors have any conflict of interest. This work has not been funded.

EPO-096 | McDonald criteria application by German neurologists suggests a need for further training

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Background and aims: McDonald criteria (MC) are a globally accepted standard for the diagnosis of multiple sclerosis (MS). Misdiagnosis of MS is a common problem that has significant clinical consequences for patients. Misapplication of MC is a potential source of MS misdiagnosis. Recent research has identified elements of the criteria that are frequently misunderstood by neurologists in the US. The aim of this study was to assess application of MC by neurologists in Germany.
Methods: A previously developed survey instrument was modified and distributed to neurology residents and specialists (general neurology, not MS-subspecialists).
Results: 68 neurologists (42 neurology residents (NR) and 26 neurology specialists (NS) completed the survey. We found frequent misapplication of MC. Symptoms atypical for MS were mistaken as typical by 31% of participants. Understanding of MRI dissemination in space criteria was poor. Periventricular and juxtacortical lesions were incorrectly identified by 46% and 55%, respectively. Most participants accepted purely anamnestic reports of previous neurological symptoms without objective clinical evidence as sufficient to prove dissemination in time.
Conclusion: Training and continuing education on MS diagnostic criteria needs to be improved, especially concurrent with dissemination of future iterations of MC.
Disclosure: Nothing to disclose.

EPO-097 | Characterizing functional and structural imaging features of cognitive phenotypes in multiple sclerosis

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Background and aims: This study aims at identifying distinct cognitive phenotypes in a large cohort of MS patients and characterize their clinical, structural MRI and resting state (RS) functional connectivity (FC) features.
Methods: We enrolled 369 right-handed MS patients and 168 age-and sex-matched healthy controls (HC). Participants underwent neurological and neuropsychological evaluation using the Rao Brief Repeatable Battery of Neuropsychological tests. 3.0T MRI was used to derive atrophy measures and RS FC in seven cognitive networks. Latent Profile Analysis on cognitive Z-scores identified MS cognitive phenotypes.
Results: Four cognitive phenotypes were detected: preserved cognition (PC) [n=67 (18.2%)], mild single domain-verbal fluency involvement (MSD-VF) [n=37 (10.0%)], mild single domain-attention (MSD-A) involvement [n=197 (53.4%)], and severe-multidomain (SMD) involvement [n=68 (18.4%)]. SMD had worse clinical and atrophy features compared to the remaining phenotypes (p=range <0.001-0.04). PC patients had similar RS FC to HC, while MSD-VF patients presented with increased RS FC of the executive control (ECN) (p=0.03) and language (p=0.02) network compared to SMD patients. Conversely, SMD patients had significantly decreased default-mode network (DMN) RS FC compared to other phenotypes (p=0.01-0.04). Finally, we observed significant quadratic trends (corresponding to increased RS FC in MSD-VF followed by decreased RS FC in MSD-A and SMD) for DMN (p=0.005), ECN (p=0.005) and language (p<0.001) networks.
Conclusion: While PC patients exhibited normal RS FC, SMD patients presented widespread structural abnormalities and severe DMN RS FC decrease. Observed functional changes may represent a continuum from compensation in the earlier MS stages to a complete breakdown when impairment becomes severe.
Disclosure: Disclosures. KJ was funded by MSIF and ECTRIMS in the form of MSIF-ECTRIMS McDonald Fellowship. PV, DM and AM have nothing to disclose. PP received speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb,

Genzyme, Horizon and Sanofi. He received research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). MF received compensation for consulting services or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM. MAR received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche, and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva, she receives research support from the MS Society of Canada, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM.

EPO-098 | Cognitive impairment and serum neurofilament level predict disease progression in pediatric multiple sclerosis

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Background and aims: To identify predictors of disease progression in pediatric multiple sclerosis (POMS).
Methods: Thirty-five POMS patients (median age: 15; 13.0-16.0), under treatment with disease-modifying therapies (DMTs) were followed up for 18 months and underwent physical disability (via expanded disability status scale - EDSS) and cognitive performance (via Symbol Digit modalities test - SDMT) assessments, and MRI. Serum neurofilament light chain (sNfl) and glial fibrillary acidic protein (GFAP) levels were measured at baseline and at the end of follow-up. Radiological progression was defined as an increase in T2 and/or Gd-positive lesions; clinical progression was defined as an EDSS increase of >=0.5 points.
Results: At baseline, mean EDSS score was 2.0, median SDMT was 44.0, median sNfl and GFAP levels were 18.1 pg/mL and 103.63 pg/mL, respectively. At follow-up, 37.1% experienced clinical progression, and 62.8% radiological progression. 63% showed cognitive improvement. As for biomarkers, 68% experienced a reduction in sNfl levels; GFAP levels remained stable. 54% of patients switched to high-efficacy therapy (HETs). A statistically significant association was found between lower SDMT scores and higher sNfl levels; between radiological progression and lower SDMT scores; between clinical progression and lower baseline EDSS scores. A trend of association was found between radiological progression and higher baseline sNfl levels. Cerebellar involvement and frequent relapses were significatively associated with switching to HETs.

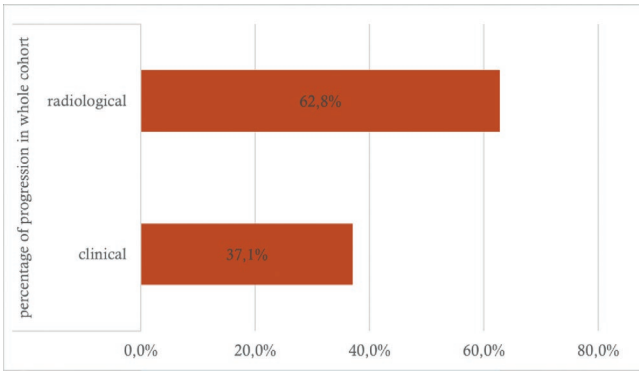

FIGURE 1 Disease progression.

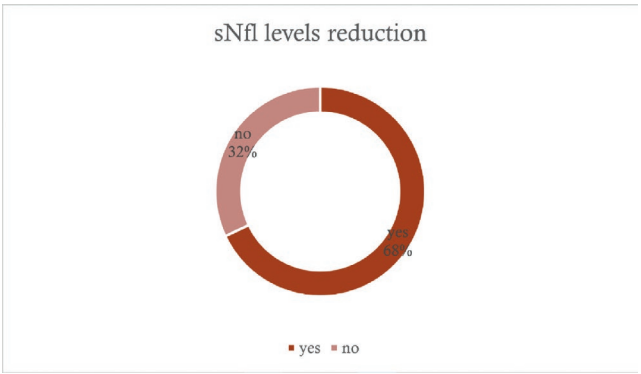

FIGURE 2 sNfl levels reduction.

Conclusion: Cognitive impairment and elevated sNfl levels at disease onset predict disease progression. This confirms the need for early cognitive and neurodegeneration assessments to inform targeted therapies.
Disclosure: Nothing to disclose.

EPO-099 | Ocrelizumab virtually eliminates new cortical lesions in people with multiple sclerosis

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Background and aims: Cortical lesions (CLs) are a common finding in multiple sclerosis (MS) but data regarding the impact of treatment on their evolution are lacking. This study evaluates CLs status and new CLs formation in a cohort of patients treated with ocrelizumab (OCR), their correlation with neurological disability and with white matter lesions (WMLs) accrual.

Methods: 92 relapsing-remitting MS patients [62(67%) women, mean(SD) age 39(9.9) years, median(IQR) baseline EDSS 2.5(2)] underwent clinical, neuropsychological assessment and brain 3T-MRI at baseline and two years after OCR start. CLs were manually segmented using Artificial Intelligence-Driven Imaging Reconstruction (AIDIR) sequences.
Results: At baseline, 22 patients (24%) had no CLs, 31 (34%) had 1 CL, 17 (19%) had 2 CLs, and 22 (24%) had>=3 CLs. Higher CLs number was associated with higher disease duration (r=0.2, p=0.06), lower SDMT (r=-0.22, p=0.07) and lower total brain volume (r=-0.32, p=0.002). 17 patients (19%) experienced WMLs accrual and 16 patients (17%) disability progression over follow-up, but none of them developed new CLs. We observed the formation of only one CL at follow-up in a female patient (29 years-old, disease duration 2.9 years). This patient maintained NEDA-3 status, showed improved physical disability (EDSS 3.5 to 2.5) and no cognitive decline despite baseline SDMT impairment (z score -1.4 to -0.21).
Conclusion: In a cohort of patients treated with OCR only one new CL in a patient without concurrent WMLs accrual was detected. These data support OCR efficacy in minimizing lesion accrual and suggest distinct mechanisms underlying CLs and WMLs development in MS.
Disclosure: This study was partially supported by a grant from Roche

EPO-100 | Abstract withdrawn

EPO-101 | Lesion location and functional connections reveal cognitive impairment networks in multiple sclerosis

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Background and aims: Cognitive impairment, fatigue, and depression are common in multiple sclerosis (MS) and may result from white matter (WM) lesion disruption of regional functional connectivity. We explored whether WM lesions functionally connected to specific brain regions contribute to these MS-related manifestations.
Methods: A total of 596 MS patients underwent 3T brain MRI acquisition, neurologic assessment, and neuropsychological evaluation using the Brief Repeatable Battery, Modified Fatigue Impact Scale (MFIS), and Montgomery-Asberg Depression Rating Scale (MADRS). Voxel-wise lesion probability maps were compared between MS patients' groups based on cognition, fatigue, or depression. WM lesion distributions were linked to a brain functional connectivity atlas to map lesion network associations. Lesion network maps were then compared among MS patients' subgroups ($p<0.05$, family-wise error-corrected).
Results: One hundred twenty-six (27.2%) MS patients were cognitively-impaired. These patients had significantly more widespread WM lesions, more functionally connected to bilateral hippocampi, thalami, cerebellum, and temporo-occipital cortices compared to cognitively preserved patients. Lesion networks were similar for impaired processing speed/attention. Verbal memory deficits were linked to WM lesions connected to hippocampi, parahippocampi, left lingual gyrus, and right cerebellum, while verbal fluency deficits involved connections to thalami and cerebellum. Visual memory deficits corresponded only to widespread WM lesion distribution. No significant lesion distribution or network differences were found for patients with fatigue (MFIS score>38, 184/493 [37.3%]) or depression (MADRS score>9, 192/495 [38.8%]).
Conclusion: Regional WM lesions disrupting connections to hippocampus, thalamus, cerebellum, and temporo-occipital cortices contribute to cognitive impairment. Lesion network map may clarify mechanisms underlying cognitive deficits in MS.
Disclosure: PP received speaker honoraria from Roche, Biogen, Novartis, Merck, Bristol Myers Squibb, Genzyme, Horizon and Sanofi. He received research support from Italian Ministry of Health and Fondazione Italiana Sclerosi Multipla (FISM). AF, PV, DM, FE have nothing to disclose. MM reports grants and personal fees from Sanofi Genzyme, Merck Serono, Roche, Biogen, Amgen and Novartis. MAR received consulting fees from Biogen, Bristol Myers Squibb, Eli Lilly, Janssen, Roche, and speaker honoraria from AstraZaneca, Biogen, Bristol Myers Squibb, Bromatech, Celgene, Genzyme, Horizon Therapeutics Italy, Merck Serono SpA, Novartis, Roche, Sanofi and Teva, she receives research support from the MS Society of Canada, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM. MF received compensation for consulting services or speaking activities from Alexion, Almirall, Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi Takeda, and TEVA; Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and FISM.

EPO-102 | Increased health utilisation before an MS diagnosis: Evidence from routine healthcare data in Wales

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Background and aims: Using an algorithm to identify people with Multiple Sclerosis (pwMS) in routine healthcare data we

determined if there was any evidence of an MS prodrome by looking at healthcare utilisation in Wales in those before the age of 16 (pre-16) and before the diagnosis of MS (pre-Dx) was made.
Methods: Using the Secure Anonymised Information Linkage (SAIL) Databank of 4.6 Million people in Wales, we identified inpatient admissions (top 10), GP attendances (top 10) and prescriptions (top 20) in pwMS and separate propensity matched controls (by gender and year of birth) pre-16 and also pre-Dx. We identified entries unique to MS, excluding MS/demyelinating codes, and assessed whether entries common to both groups were significantly different
Results: Pre-16 (N=313), admissions unique to MS included constipation (4.8%) and dental caries (3.5%); there was no significant difference in the 6/10 ICD-10 codes shared between pwMS/control cohorts. Pre-Dx (N=5,309), sensory symptoms (4.3%), paraesthesia (3.8%), headaches (3.7%) and urinary tract infections (3.6%) were unique to pwMS with the remainder 4/10 not being different between pwMS/control cohorts. For GP attendances (pwMS N=4798 pre-16, N=9648 pre-Dx), there were higher rates of attendances but no unique causes for attendance. In pwMS versus controls pre-16, they had more respiratory infections (pwMS 14.2%, p<0.001), consistent with this pre-16 they had higher rates of penicillin use. Pre-Dx they had more vaccinations and used more antibiotics, paracetamol, anti-inflammatories, hydrocortisone and PPI inhibitors.
Conclusion: pwMS have higher healthcare utilisation pre-16 and pre-Dx. This requires further study but does imply a MS prodrome.
Disclosure: None of the authors have anything to disclose related to this abstract.

EPO-103 | Relationship between neutrophil to lymphocyte ratio and neurofilament light-chain levels in patients with MS

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Background and aims: The pathogenesis of Multiple Sclerosis (MS) is unclear wherein the balance between peripheral and intrathecal immune systems may affect both relapsing activity and disease progression. Neutrophilic to lymphocyte ratio (NLR) has been proposed as possible surrogate biomarker for neuroinflammation. On the other hand, the prognostic value of cerebrospinal fluid (CSF) neurofilament light-chain levels gained increasing interest as marker of neurodegeneration. Aims of this study are to evaluate the relationship between NLR, cerebrospinal NfL and relapse activity in patients with MS.
Methods: individuals who underwent diagnostic work-up through lumbar puncture (LP) and with a definite diagnosis of MS were included. We obtained NLR and CSF-NfL for each patient. The Spearman's coefficient was employed to estimate the relationship between NLR and CSF-NfL. Finally, NLR and CSF-NfL were compared between pwMS with or without at least one relapse within 3 months preceding LP by using Mann and Whitney test.
Results: a total of 40 pwMS (age: 40.6 ± 13.6 years; female n=27, 67.5%; mean EDSS 2.4 ± 2) were included. Seventeen pwMS (42.5%) had at least one relapse before LP. A significant direct correlation was found between NLR and CSF-NfL (r=0.35; p=0.028; Fig. 1). CSF-NfL were higher in pwMS with a relapse before LP (p=0.024; Fig. 2) while NLR was similar between groups (p=0.57; Fig. 3).

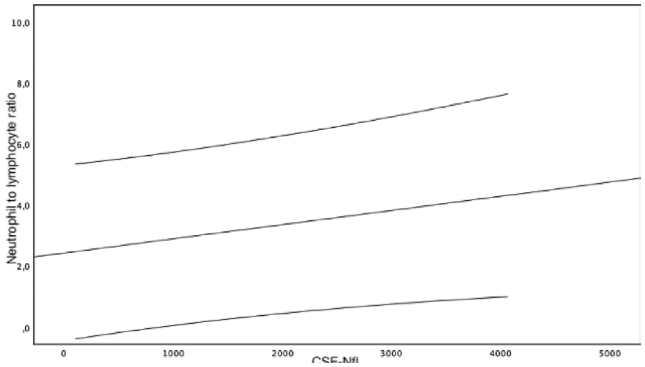

FIGURE 1 Scatterplot showing the linear correlation between NLR and CSF-NfL.

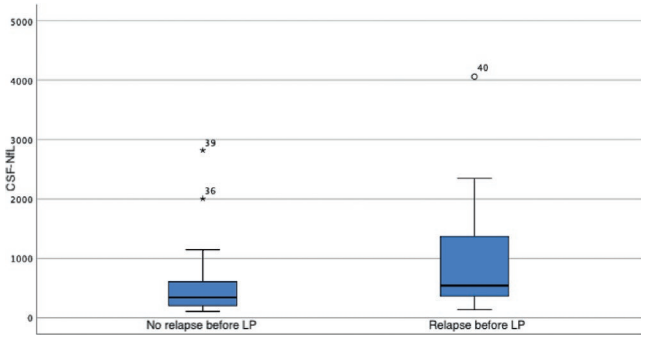

FIGURE 2 Box-plots showing the comparison of CSF-NfL levels in patients with or without MS relapses before lumbar puncture.

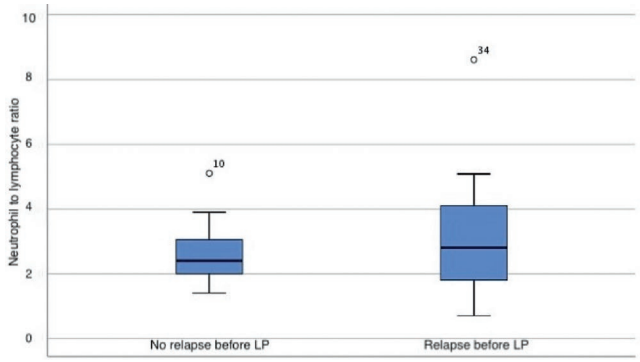

FIGURE 3 Box-plots showing the comparison of NLR in patients with or without MS relapses before lumbar puncture

Conclusion: Despite it did not change with relapse activity in pwMS, our results suggest a possible role of NLR as a simple and inexpensive surrogate biomarker of axonal damage.
Disclosure: Nothing to disclose.

EPO-104 | Inter-eye difference of ganglion cell layer alone in identifying optic neuritis in multiple sclerosis

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Background and aims: The 2024 McDonald criteria for diagnosing multiple sclerosis (MS) include optic nerve involvement as a fifth region for establishing dissemination in space. Optic neuritis (ON) can be detected through optical coherence tomography (OCT) using an inter-eye absolute or percentage difference (IEAD, IEPD) in ganglion cell-inner plexiform layer (GCIPL) thickness.
Methods: This cross-sectional retrospective study included people with MS (pwMS) who underwent an OCT scan. Diagnostic accuracy was assessed using ROC analysis.
Results: A total of 241 pwMS (mean age 34.7 years (SD 9.7), 70.1% female) were included. GCL IEAD (AUC 0.88, cut-off ≥0.04mm3 or ≥1.4µm, 80.0% sensitivity, 86.5% specificity) and IEPD (AUC 0.89, cut-off ≥4%, 79.0% sensitivity, 87.2% specificity) demonstrated excellent diagnostic accuracy for unilateral ON, showing non-inferiority to the established GCIPL IEAD/IEPD. An improvement in diagnostic performance of both models was observed in a subanalysis of pwMS with subclinical ON (AUC 0.95, sensitivity 93.8%, specificity 87.2%).
Conclusion: GCL IEAD and IEPD provide strong diagnostic accuracy for identifying unilateral ON and can be effectively used as an alternative to GCIPL IEAD/IEPD to facilitate implementation in clinical routine.
Disclosure: All authors declare no conflict of interest relevant to this study.

Muscle and Neuromuscular Junction Disorder 1

EPO-105 | Increased prevalence of extrathymic neoplasm in myasthenia gravis patients a population-based matched case-control study

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Background and aims: Myasthenia gravis (MG) is known to be associated with thymic neoplasms. However, an increased prevalence of extrathymic neoplasms has also been reported. This study aims to evaluate the rates of malignancy in MG patients, while also accounting for risk factors such as co-morbidities and immunomodulatory treatments.
Methods: We conducted a case–control study using Clalit health services (CHS) database, applying innovative machine learning (ML) algorithm developed by our group to avoid diagnosis misclassification. We included MG patients aged 18 and older, along with a sex- and age-matched control group in a 1:3 ratio. We compared the prevalence and hazard ratios of extrathymic neoplasms between the groups.
Results: 1,558 patients with a high probability of MG according to our ML model, were included in our cohort, alongside a control group of 4,674 non-myasthenic individuals. MG patients had higher prevalence of malignancy prior to the MG diagnosis with OR of 1.85 ($P < 0.001$), and higher incidence of malignancy after the MG diagnosis with HR of 1.64 ($P < 0.001$). Mean time between MG diagnosis and malignancy was 3.89 years (IQR, 1.19-8.83). The most prevalent extrathymic neoplasms after MG diagnosis were, lung, digestive, Skin cancer, and hematologic cancers. Age and male sex were associated with increased risk for developing cancer, while the present of tymoma and treatments were not.
Conclusion: Male and older MG patients have a higher prevalence of solid and hematologic neoplasms compared to non-myasthenic controls. Our ML model provided an accurate and reliable assessment of the MG population.
Disclosure: Nothing to disclose.

EPO-106 | Rituximab in the treatment of acetylcholine receptor antibody-positive – Myasthenia Gravis: A single center study

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Background and aims: Rituximab, a monoclonal antibody targeting CD20 B cells, has a well-established role in myasthenia gravis (MG) with muscle-specific kinase receptor (MuSK) antibodies. However, its efficacy and optimal timing in acetylcholine receptor antibody-positive (AChR-Ab+) MG remain contentious.
Methods: This single-center, observational study evaluated 26 AChR-Ab+ MG patients who received rituximab as the sole non-steroidal immunosuppressant for at least one therapeutic cycle and were observed for a minimum of 3 months.
Results: Patients aged 25–85 years (mean age at first infusion: 61.6). Among the cohort 12 (46%) had very late-onset MG (≥65 years), 16 (64%) were newly diagnosed (<2 years from diagnosis), 4 (15%) had thymoma-associated MG, and 6 (23%) had refractory MG. Dosing regimens included four weekly doses of 500 mg (16 patients, 62%), two doses of 500 mg two weeks apart (6 patients, 23%), and a single 500 mg dose (4 patients, 15%). At six months, 11 patients (42%) achieved pharmacologic remission, including those with refractory ocular and dysphagia symptoms. Additionally, 3 (11.5%) showed minimal manifestations, 8 (31%) demonstrated clinical improvement, and 1 (4%) remained unchanged. AChR-Ab titers decreased by 35% (data for 10 patients). Corticosteroid intake was reduced by 36%, and none required rescue therapy. At twelve months, 15 (58%) maintained their clinical status. No data available for the rest.
Conclusion: Rituximab demonstrated a favorable safety profile with no adverse events, even on very late-onset MG. It achieved sustained pharmacologic remission and a significant steroid-sparing effect, benefiting refractory MG patients and those with newly diagnosed or chronic subtypes.
Disclosure: Nothing to disclose.

EPO-107 | Higher risk of fractures in myasthenia gravis patients versus general population–national healthcare database study

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Background and aims: Methods NFZ is a mandatory health insurance in Poland. MG is the only indication for reimbursement of pyridostygmine bromide and ambenonium chloride. Aim: to determine incidence of fractures in myasthenia gravis as compared with control population (ConP).
Methods: MG patients receiving reimbursed pyridostigmine or ambenonium dispensed between 1.01.2013-31.12.2023 were identified. A control group matched for age and gender was randomly assigned. All fractures diagnosed in 2023 by ICD-10 codes were analyzed by localization, compared between MG and ConP.
Results: There were 10,300 MG patients in 2023; F (61%), mean age 62 years, median age 66 years. Patients with MG had 158,8% higher chance for osteoporotic fracture ($p<0.001$, $R2=0.104$). Independent risk factors for osteoporotic fractures were: age, female sex, MG, adrenal insufficiency, diabetes, cataract, using steroids >180 days. MG patients had 32% higher chance for other than osteoporotic fracture ($p<0.01$, $R2=0.025$) with independent risk factors: age, female sex, MG, adrenal insufficiency, cataract. MG patients had 127.9% higher chance for spine fractures ($p<0.001$, $R2=0.043$). MG patients treated with glucocorticosteroids (GCS) >180 days had 149.9% higher risk of having spine fractures than MG patients not treated with GCS ($p<0.001$, $R2=0.05$), with MG, age and female gender being an independent risk factors. MG patients treated with GCS >180 days had in general 58.6% higher risk of having any nonosteoporotic fracture than MG patients not treated with GCS ($p<0.01$, $R2=0.017$), MG, age and female gender were an independent risk factors.
Conclusion: MG patients have higher risk of fractures in comparison with general population.
Disclosure: Nothing to disclose.

EPO-108 | Burden of remaining symptoms and fluctuations of generalized myasthenia gravis on patients' daily lives – BEYOND study

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Background and aims: Generalised myasthenia gravis (gMG) is a rare autoimmune disorder affecting the neuromuscular junction with varying clinical manifestations that disrupt patients' daily lives; an estimated 30% of patients with gMG experience remaining symptoms despite treatment. The study objective is to describe how these remaining symptoms and their fluctuations may affect a person's daily activities while living with gMG.
Methods: A Delphi panel was conducted with adult patients with gMG (n=18 from France, Germany, Italy, the UK and Sweden), aiming to reach consensus regarding the burden of symptoms across key domains, following completion of two questionnaire rounds.
Results: Interim results from the first Delphi panel round (n=18) are summarised here. Respondents highlighted the impact of remaining symptoms in five key domains: daily activities, social life, mental and personal well-being, work and education, and future plans. Participants noted still requiring adaptations for personal hygiene (e.g. shower stool) and support with completing household chores (e.g., cooking, cleaning). Fluctuations, described as the variation in the intensity and predictability of remaining symptoms, significantly affected patients' daily lives, with participants highlighting the need to adapt their daily routines and future plans.
Conclusion: This study is the first to investigate the specific impact of remaining symptoms of gMG on patients' daily lives and how fluctuations may further aggravate this impact. These interim results demonstrate the burden of remaining symptoms and their fluctuations for patients; minimising these would likely improve patients' daily lives. Full study results will be presented at the 2025 EAN congress.
Disclosure: This study was sponsored by J&J Innovative Medicine. FS: public speaking honoraria from Alexion, argenx, Biogen, Genpharm, Medpharma, Madison Pharma, Neopharm Israel, Sanofi, Zai Lab; compensation for Advisory boards or consultation fees from Alexion, Amgen, argenx, AstraZeneca, Alexis, Biogen, Dianthus, J&J, Lexeo, Novartis, Reata, Roche, Sandoz, Sanofi, Takeda, UCB, Zai Lab; PI in clinical trials for

Alexion, argenx, Dianthus, Immunovant, Lediant, Novartis, Prilenia, Remgen, Sanofi. SL: speaker or consultancy honoraria or financial research support (paid to her institution) from Alexion, argenx, Biogen, Hormosan, HUMA, J&J, Merck, UCB and Roche. MBU: honoraria for consulting services from Alexion, J&J, Merck, UCB Pharma and UCB S.A.; speaking fees from Alexion, UCB Pharma and UCB S.A.; consulting services to Argenx. DS: honoraria for consulting services from Novartis Pharma AG and J&J. CC: Employee of Myaware which received speaker honoraria for her services from UCB, Argenx and J&J. GR, MM, WN, CG: Employees of J&J; may hold stock or stock options in J&J. DB, SP, CC: Employees of Adelphi Values PROVE, which received funding from J&J for the conduct of the study and for abstract development.

EPO-109 | Oral cladribine capsules for generalised myasthenia gravis: design of the actively-recruiting phase 3 myclad study

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Background and aims: Myasthenia Gravis (MG) is an autoantibody-mediated disorder of neuromuscular junction transmission, characterised by fluctuating muscle weakness. Cladribine is an immune reconstitution therapy (IRT) that selectively targets B and T cells and has shown preliminary efficacy in a pilot study of participants with generalised MG (gMG). We present the design of MyClad, a Phase 3 trial evaluating efficacy and safety of oral cladribine capsules (CladC) versus placebo in gMG.

Methods: MyClad is a 3-year Phase 3 trial aiming to recruit 240 participants with gMG Class II–IVa, irrespective of autoantibody serotype. In the first double-blind placebo-controlled period (24 weeks), participants will be randomised 1:1:1 to two short courses of placebo or low- or high-dose CladC (Figure). In the following blinded extension period (24 weeks), placebo recipients will be re-randomized to low- or high-dose CladC. During this period and a third double-blind follow-up period of 96 weeks, participants may be retreated with CladC if clinically needed. The primary endpoint is change from baseline (CFB) to Week 24 in MG-Activities of Daily Living (MG-ADL) score for each CladC dose versus placebo. Secondary endpoints include CFB to Week 24 in Quantitative MG (QMG), MG Composite and MG 15-Item Quality of Life Scale revised scores, proportions of MG-ADL and QMG responders, time from CladC full dose to retreatment or rescue treatment, safety and CladC pharmacokinetics.

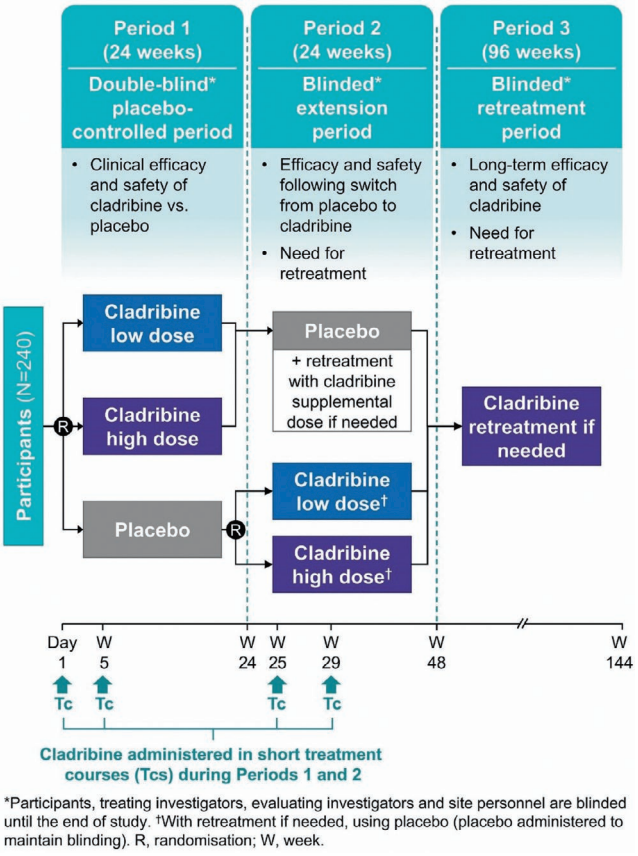

FIGURE 1 MyClad study design.

Results: Some participants have been recruited; enrolment is ongoing.

Conclusion: MyClad aims to establish efficacy, duration of effect and safety of IRT to target B and T cell-mediated autoimmunity with CladC in gMG.

Disclosure: The MyClad study (Clinicaltrials.gov: NCT06463587) is sponsored by Merck Healthcare KGaA, Darmstadt, Germany, an affiliate of Merck KGaA, Darmstadt, Germany. AN, SG, CLB, AJ, NA and DJ are employees of Merck KGaA or its affiliates. Other authors or their institutions have multiple financial and/or non-financial relationships with research organisations or pharmaceutical companies; further information will be included in the presentation.

EPO-110 | Myasthenia gravis medication related to pregnancy, a registry-based cohort study

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Background and aims: The unpredictable disease course of myasthenia gravis (MG) during pregnancy influences medication needs. Both medications and MG-autoantibodies transferred from mother to child could potentially harm the foetus. Medication-use patterns in relation to pregnancy are unknown in MG but should be mapped to disentangle the effect of maternal disease from in-utero medication-exposure. Our aim was to determine medication use related to MG-pregnancies, and to distinguish periods with stable and unstable disease.
Methods: We included all MG-pregnancies resulting in birth in Norway 2010-2020 and Sweden 2008–2019 using nationwide health- and population registries. MG-pregnancies were identified by a maternal MG-diagnosis from specialist care, or multiple pyridostigmine-purchases. Medication-use was assessed through filled prescription records from one year before pregnancy to six months postpartum. Next, MG-pregnancies will be grouped based on similar medication-use patterns by group-based trajectory modelling, a machine-learning method, and described through clinical parameters, such as hospitalizations.
Results: We identified 321 MG-pregnancies of 225 women from a background population of 1,962,396 pregnancies. In preliminary analyses, 37% used pyridostigmine before pregnancy, 34% during, and 29% after pregnancy. Prednisolone and azathioprine were used in 10% and 7% of pregnancies, respectively. No pregnancies were exposed to methotrexate, mycophenolate mofetil, or cyclophosphamide.
Conclusion: Most parturients with MG had not used any MG-medications before, during, or after pregnancy, indicating mild and stable MG. In the next step, to be presented at the congress, we will describe medication-use trajectories in MG-pregnancies. Assuming that add-on therapy in pregnancy is a sign of disease-worsening, these trajectories will describe disease severity in pregnancy.
Disclosure: JLVL has received financial support from UCB. NEG has received financial support from Grifols, UCB, Argenx, Janssen, Johnson&Johnson, Merck, Roche, Alexion, Immunovant, Huma, Denka, Amgen, and Dianthus. MHB has received speaker honoraria and/or consultancy honoraria from Teva, Eisai, AbbVie, Pfizer, Novartis, Lundbeck, Angelini Pharma, Jazz pharmaceuticals, and Lilly during the last five years, none in relation to the topic in the abstract. JMC declare no conflicts of interest. CEC, KF and JMC reports participation in research projects funded by pharmaceutical companies, all with funds paid to their institution (no personal fees) and with no relation to the work reported in this paper.

EPO-111 | Fatigue assessed by neuro-QoL in phase 3 vivacity-MG3 trial of nipocalimab vs placebo in generalized myasthenia gravis

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Background and aims: Generalized myasthenia gravis (gMG) is an autoantibody-mediated disease, with muscle weakness, considerable fatigue and associated impacts. Fatigue often correlates with gMG disease severity(1) emphasising need to manage both effectively. In Vivacity-MG3 (NCT04951622), nipocalimab+standard-of-care (SOC) demonstrated improved and sustained efficacy vs placebo+SOC. We evaluated changes in Neuro-QoL-Fatigue, patient-reported assessment of fatigue and its associated impact, and disease-severity measures between Vivacity-MG3 arms.

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Reference

Methods: Mean changes-from-baseline (CFB) in Neuro-QoL-Fatigue total score over 24weeks(W) were compared using mixed-model-repeated-measures. Proportion of patients achieving meaningful-within-person-improvement (MWPI) of 6.7-points from baseline at 24W were examined using Chi-square test statistics. Logistic regression models evaluated likelihood of sustaining MWPI for >=8,12,16, or 20W. Mean CFB at 24W was evaluated by stratifying patients based on baseline disease-severity scores observed above median on Myasthenia-Gravis-Activities-of-Daily-Living (MG-ADL) and Quantitative-Myasthenia-Gravis (QMG) scales (severe disease defined as MG-ADL >9 and QMG >15).
Results: LS-mean (95% CI) difference in CFB on Neuro-QoL-Fatigue was greater (p=0.001) with nipocalimab+SOC (-7.4[-11.94, -2.93]) by 4W and numerically higher at 24W (-4.3[-9.16, 0.62]) vs placebo+SOC. At 24W, 6.2% more patients on nipocalimab+SOC (42/67) achieved MWPI than placebo+SOC (35/62) (p>0.05). Nipocalimab+SOC-treated patients were approximately twice more likely to sustain MWPI for >=8,12,16, 20W (p<0.05). Among those with severe disease at baseline, mean improvement was numerically greater at 24W with nipocalimab+SOC vs placebo+SOC (difference=-9.0; 95% CI=-22.0, 4.1).
Conclusion: Nipocalimab+SOC-treated patients showed improvement on Neuro-QoL-Fatigue as-early-as W4. Nipocalimab+SOC-treated patients were also significantly more likely to sustain MWPI over time. Patients with more severe disease at baseline showed numerically greater improvements with nipocalimab+SOC than placebo+SOC.
Disclosure: This study was sponsored by Johnson & Johnson. John Vissing: Received consultant fees for serving on advisory

boards for Alexion Pharmaceuticals Inc., Argenx BV, Dianthus Therapeutics, Horizon Therapeutics (now Amgen Inc.), Janssen, Regeneron, Roche, and UCB Pharma SA. Kavita Gandhi, Sheryl Pease, Nida Imran, Maria Ait-Tihyaty, Ibrahim Turkoz, Charlotte Gary, Zia Chaudhry, and Sindhu Ramchandren: Employees of Johnson & Johnson, may hold stocks/stock options in Johnson & Johnson. Geoffroy Coteur: Owner of IPATH Solutions and received consultant fees from Johnson & Johnson.

EPO-112 | Herding-like behaviour in myasthenia gravis treatment decisions: exploring underlying mechanisms

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Background and aims: Herding-like behaviour occurs when physicians follow colleagues' recommendations instead of making independent decisions. It can lead to suboptimal outcomes in dynamic contexts, such as adopting new treatments for generalized myasthenia gravis (gMG). This study aimed to assess herding-like behavior and associated factors among neurologists managing gMG.

Methods: An electronic survey study was conducted with the Spanish Society of Neurology. Neurologists provided demographic, professional, and behavioural characteristics/traits. Herding-like behaviour was assessed using a simulated case scenario: 42-year-old woman with gMG stable for 3 years on pyridostigmine and azathioprine. Three months earlier, she experienced transient lower-extremity weakness, resolved spontaneously within 2-3 weeks. Her neurological examination remained unchanged (MG-ADL=0), with normal blood tests and no new medications. Seeking a second opinion, she was advised by a neuromuscular specialist to switch to ravulizumab. Agreeing with this recommendation, contrary to established guidelines, was classified as herding. Relationships between herding-like behaviour and neurologists' characteristics were assessed using Chi-square and Mann-Whitney-U tests.

Results: 149 neurologists participated (mean age [SD]: 39.0±9.4 years, 54.4% male, median experience managing gMG [IQR]: 7 [3-15] years; 32.2% fully dedicated to gMG; median gMG patients attended/month: 10 [5-20]). Herding-like behaviour was present in 38.9% (n=58/149). Neurologists with herding were older, not specialized in gMG, and more experienced (all $p<0.01$). Those without herding worked at reference hospitals, had specific gMG consultations, treated more patients, participated in clinical trials, and attended neuromuscular congresses ($p<0.05$).

Conclusion: Herding-like behaviour was observed in over one-third of neurologists. Addressing its impact and promoting specific interventions may enhance clinical decision-making and patient care.

Disclosure: GGG has received compensation for consulting services from CSL Behring, Biogen, Alter, Takeda, Akcea, Lupin Neuroscience, Roche, Alexion, and Argenx; congresses support from Alter, Esteve, Sanofi-Genzyme, Pfizer, and UCB Pharma; has scientific relation with Lilly, Alexion, Genzyme, Takeda, Biogen, Pfizer, and Alter; books with Exeltis, Alter, Esteve, Andrómaco, and Bristol-Myers; and has received grants and awards from Lilly, UCB Pharma, and CSL Behring. RGB, ES, PDA, and JM are employees of Roche Pharma Spain. JS has received travel/congress support and compensation for consulting services from Roche, Biogen, UCB, and Argenx. AA has received speaking honoraria, consultation services compensation, or travel support for congress and scientific meetings attendance from Almirall, Bayer, Biogen, BMS, Janssen, Merck, Novartis, Roche, Sanofi, and Teva. LQ received speaker honoraria from Merck, Sanofi, Roche, Biogen, Grifols and CSL Behring; provided expert testimony for Grifols, Johnson & Johnson, Annexon Pharmaceuticals, Sanofi, Novartis, Takeda, and CSL-Behring; and received research funds from Roche, UCB, and Grifols. ECV has received speaking and advisory boards honoraria from UCB Pharma, Alexion, Argenx, and J&J. The rest of the authors declare no conflict of interest for this work.

EPO-113 | Psychometric evaluation of resistance to change questionnaire: reluctance to adopt new treatments in myasthenia gravis

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Background and aims: Resistance to change is a well-recognized phenomenon in healthcare, impacting innovative treatments' adoption. Limited research has examined the validity of tools designed to assess this behaviour in the evolving therapeutic landscape of generalized myasthenia gravis (gMG). This study aimed to evaluate the dimensionality and item characteristics of the Resistance to Change questionnaire among neurologists treating gMG patients.

Methods: An electronic survey study was conducted with the Spanish Society of Neurology. Resistance to adopting gMG-selective therapies was assessed using a 34-item self-administered questionnaire evaluating resistance trait, openness to change, perceived usefulness, ease of use, value, peer influence, self-efficacy, and organizational support. A non-parametric item response theory approach (Mokken analysis) was used to examine the questionnaire's dimensional structure, with scalability coefficients and reliability assessed via Cronbach's alpha.

Results: A total of 149 neurologists were included (mean age [SD]: 39.0±9.4 years, 54.4% male, median experience managing gMG [IQR]: 7 [3-15] years). The questionnaire showed good internal reliability for the overall scale (0.88; 95% CI: 0.84 to 0.90) and its dimensions (range: 0.84 to 0.94). The Mokken analysis suggested two dimensions. First dimension included nine initial items (resistance trait and openness to change) and showed a scalability of 0.67 (strong scale). The second dimension comprised the rest of items and showed a scalability of 0.39 (weak scale).

Conclusion: The Resistance to Change questionnaire showed good internal reliability and a dimensional structure with a strong component related to resistance new gMG treatments introduction among neurologists. This tool may help identify and assess barriers to adopting novel medical interventions.

Disclosure: GGG has received compensation for consulting services from CSL Behring, Biogen, Alter, Takeda, Akcea, Lupin Neuroscience, Roche, Alexion, and Argenx; congresses support from Alter, Esteve, Sanofi-Genzyme, Pfizer, and UCB Pharma; has scientific relation with Lilly, Alexion, Genzyme, Takeda, Biogen, Pfizer, and Alter; books with Exeltis, Alter, Esteve, Andrómaco, and Bristol-Myers; and has received grants and awards from Lilly, UCB Pharma, and CSL Behring. RGB, ES, PDA, and JM are employees of Roche Pharma Spain. JS has received travel/congress support and compensation for consulting services from Roche, Biogen, UCB, and Argenx. AA has received speaking honoraria, consultation services compensation, or travel support for congress and scientific meetings attendance from Almirall, Bayer, Biogen, BMS, Janssen, Merck, Novartis, Roche, Sanofi, and Teva. LQ received speaker honoraria from Merck, Sanofi, Roche, Biogen, Grifols and CSL Behring; provided expert testimony for Grifols, Johnson & Johnson, Annexon Pharmaceuticals, Sanofi, Novartis, Takeda, and CSL-Behring; and received research funds from Roche, UCB, and Grifols. ECV has received speaking and advisory boards honoraria from UCB Pharma, Alexion, Argenx, and J&J. JB has collaborated in this study through a research contract between the UPV/EHU and Roche Farma Spain. The rest of the authors declare no conflict of interest for this work.

EPO-114 | Extended therapeutic experience with efgartigimod in myasthenia gravis: A multicenter study

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Background and aims: Efgartigimod has shown effectiveness in treating seropositive generalized myasthenia gravis (SP gMG). This extended study evaluated the efficacy and safety outcomes.

Methods: A multicenter study of 51 SP gMG patients (26 females, 25 males), assessed the impact of efgartigimod on MG-ADL scale, response patterns, steroid sparing, and safety.

Results: The cohort (mean age 58.9 years, range 19–87) had a median disease duration of 4 years (range 0.6–39). Patients were followed for a median of 8 months (range 2–29), receiving a median of 3 treatment cycles (range 1–13). After the first cycle, 78.6% showed ≥2-point MG-ADL improvement (median 7 to 2; $p = 0.0001$), 33.3% achieved minimal symptom expression. Among 33 patients followed >1 year, MG-ADL scores improved (median 6 to 2; $p < 0.0001$). Treatment was continued by 45.5% of patients, 24.2% did not need retreatment and treatment changed in 27.3% due to insufficient efficacy and in 3.0% for insurance reasons. In 29 evaluable patients, response patterns between cycles were: improvement with intermittent worsening to baseline (58.6%), improvement with less severe worsening (24.1%), and sustained improvement (17.2%). Of 31 prednisone users (mean dose 30.0 ± 14.6 mg), 58% had dose reductions (16.6 ± 22.01 mg; $p = 0.001$). Efgartigimod was well tolerated, with no treatment-related serious adverse events.

Conclusion: Efgartigimod demonstrated significant clinical benefits in SP gMG, including symptom reduction, steroid-sparing effects, and was safe. Treatment regimens were personalized, depending on response patterns ranging from single cycles to continuous maintenance of treatment cycles.

Disclosure: Nothing to disclose

EPO-115 | Molecular and ultrastructural basis of the neuromuscular junction defect in PURA syndrome

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Background and aims: PURA-related neurodevelopmental disorder is an ultrarare congenital genetic condition caused by pathogenic autosomal dominant variants in the PURA gene. Although the disease is primarily classified as a central developmental disorder, some phenotypic features such as positive effect of salbutamol/pyridostigmine bromide on muscle weakness indicate an endplate defect. The aim of this study is to decipher the structural and molecular basis of the endplate involvement in PURA syndrome.
Methods: We performed myopathological, ultrastructural, proteomic, and qPCR studies on the muscle biopsy from a 3-months-old patient carrying the pathogenic (c.159del; p.(Leu-54Cysfs*)) PURA variant. In addition, proteomic signature of extracellular vesicles and thrombospondin-4 (marker protein of neuromuscular junction function) level were examined in sera derived from 8 PURA-patients.
Results: Electron microscopy revealed structural endplate alterations consistent with perturbed synaptic transmission. Those include rarefication of postsynaptic clefts and vesicular alterations within endothelial capillary cells and the myofibres. Proteomics demonstrated dysregulation of structural proteins similar to those seen in congenital myopathies where treatment with endplate stimulators is frequently successful. Therefore, we suspect a defect in the vesicular transport of proteins from muscle to endplate. Further investigations, such as vesicle proteomics, thrombospondin-4 measurement, are currently being performed to better understand the molecular mechanisms of the disease.
Conclusion: In individuals with PURA Syndrome, the functional deficit observed at the neuromuscular junction may be attributable to aberrant vesicle transport.
Disclosure: Nothing to disclose.

EPO-116 | Safety profile of Duchenne muscular dystrophy gene therapy

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Background and aims: Delandistrogene moxeparvovec is a gene therapy available for ambulatory patients aged four through five years for whom there is no other therapeutic option of pathogenetic therapy in the Russian Federation at the expense of the charity foundation “Circle of Goodness” in May 2024.
Methods: 22 patients received gene therapy at the National Research Medical Center for Children's Health, Moscow, from July 2024 to December 2024. 29 weeks. We analyzed the types and timing of serious adverse events, its treatment and outcomes.
Results: 4 patients developed SAE. 2 patients developed acute liver injury with increased GGT and total bilirubin at 6-8 weeks after gene therapy. Both patients required pulse therapy with methylprednisolone, followed by oral prednisone with its gradual withdrawal. Another 2 patients developed immune - mediated myositis in the 4 week after gene therapy. The first patient started treatment with methylprednisolone pulse therapy followed by oral prednisone with its gradual withdrawal and IVIG on the fourth day of symptoms development. The motor decline were restored within four weeks to their level before treatment. The second patient started receiving therapy for myositis after 10th day of the onset of clinical symptoms. He required the use of invasive ventilation, methylprednisolone pulse therapy, IVIG, followed by oral prednisone and tacrolimus with full recovery in 10 weeks after starting treatment.
Conclusion: Our experience is useful for determining key periods of development of SAE after Delandistrogen moxeparvovec. Also we offer therapeutic options for complications.
Disclosure: Sofiya Popovich HONORARIA Novartis, PTC, Roche, Janssen, Astrazeneca Lyudmila Kuzenkova HONORARIA Novartis, PTC, Roche, Janssen, Astrazeneca Evgeniya Uvakina Tatyana Podkletnova HONORARIA PTC, Roche Oxana Globa HONORARIA Novartis.

EPO-117 | Implementation of FEES and the standardised FEES scores in the diagnosis of dysphagia in SMA - DYS-SMA trial

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Background and aims: Spinal muscular atrophy (SMA) is an autosomal recessive neuromuscular disease characterised by progressive degeneration of the 2nd motor neurons of the motor anterior horn. The clinical characteristics of SMA are mainly characterised by progressive muscle weakness and atrophy. The

bulbar symptoms, including dysphagia, pose a major therapeutic challenge with the frequent need for artificial feeding and a high risk of pulmonary complications. The aim of the DYS-SMA study (ClinTrials RegNo. NCT04773470; Investigator Initiated Trial supported by Roche Pharma AG) was to implement the Flexible Endoscopic Evaluation of Swallowing (FEES) and standardised FEES scores in the descriptive evaluation of swallowing pathomechanisms in patients with SMA type 1-3 treated at the University Hospital Giessen.
Methods: In the prospective, interventional, open, explorative and diagnostic study, 40 SMA patients were included in the study after detailed medical consultation. The study-related interventions were the clinical dysphagia screening and the FEES at two points in time (at visit 1 (T1) and 4 months after visit 1 (T2).
Results: The initial clinical assessment revealed dysphagia in 38.5% of SMA patients (n=15). After the subsequent initial FEES, the number of confirmed diagnoses of dysphagia increased to 84.6% (n=33). In our trial, most severe dysphagic symptoms are found in SMA type 1 and most frequent in SMA type 2. SMA type 3 shows only mild dysphagia.
Conclusion: The trial results indicate that FEES is a valid and very easy to implement imaging instrument for the diagnosis of dysphagia in SMA. Clinical assessments are insufficient to adequately diagnose dysphagia in SMA.
Disclosure: The trial was financially supported by Roche Pharma AG.

EPO-118 | Usefulness of repetitive nerve stimulation of the hypoglossal nerve in patients with Myasthenia Gravis

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Background and aims: Most repetitive nerve stimulation (RNS) protocols for diagnosing Myasthenia Gravis (MG) do not assess muscles with bulbar functions. Objectives: To describe a new, non-invasive RNS technique of the hypoglossal nerve and recorded in the submental complex muscles (SMC). The study also aimed to determine the technique's overall sensitivity, particularly in predominantly bulbar forms.
Methods: This observational, retrospective study included 102 individuals who underwent RNS for suspected myasthenic syndrome. Of these, 25 with a definitive MG diagnosis were selected and grouped according to their initial MGFA classification. RNS was preferably performed on five nerves: hypoglossal, accessory, radial, facial, and ulnar.
Results: Among the 25 diagnosed patients, 18 underwent both RNS and SFEMG, while 7 underwent RNS alone. The trapezius muscle demonstrated the highest overall sensitivity (48%) and in ocular forms (33%). The SMC had the second-highest overall sensitivity (40%) and was the most sensitive for detecting bulbar forms (80%), followed by the trapezius (56%). In one patient with mild bulbar symptoms (MGFA IIb), the SMC was the only muscle assessed that showed a decrement.
Conclusion: Despite limitations due to its retrospective nature and nerve selection bias, this study revealed that the SMC was the most sensitive muscle in bulbar forms, underscoring its usefulness in evaluating patients with suspected myasthenic syndrome. Particularly in bulbar-dominant MG, the SMC may be the only muscle showing abnormalities. Thus, this technique should be considered for inclusion in protocols for assessing myasthenic patients.
Disclosure: Nothing to disclose.

EPO-119 | Gender differences in myasthenia gravis: A retrospective cohort study

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Background and aims: Myasthenia gravis (MG) is an autoimmune disorder causing fluctuating muscle weakness. Early-onset MG predominantly affects females, while late-onset MG is more common in males. Generalized MG is more frequent in women, and ocular MG is more common in men. Other gender differences lack clear evidence. This study evaluates gender-related differences in a single-center MG cohort.
Methods: This retrospective study analyzed electronic health records, including age at diagnosis, clinical presentation, antibody status, electrophysiological studies, comorbidities, and treatment use. Statistical analysis was conducted using chi-square and Mann-Whitney U tests.
Results: Among 96 MG patients (55.2% female), 25% had ocular and 75% generalized MG. Half were early-onset and half late-onset. Anti-acetylcholine receptor antibodies were present in 71.9% of cases, 3 had anti-MuSK antibodies, and 27.1% were seronegative. Generalized MG was more frequent in women ($p<0.001$), while ocular MG was more common in men ($p<0.001$). Men with ocular MG more often presented with isolated ptosis ($p=0.020$). IVIG use was significantly higher in women with generalized MG ($p=0.027$), though there were no gender differences in exacerbations or MGFA Post-Intervention Status. Other variables, including age of onset, thymus pathology, antibody status, nerve stimulation abnormalities, treatment use (pyridostigmine, corticosteroids, immunosuppressants), and mortality, showed no significant gender differences.
Conclusion: Our findings confirm gender differences in MG subtypes. The higher IVIG use in women, despite similar disease severity, may reflect a gender-related perception of disease burden, warranting further study.
Disclosure: Nothing to disclose.

EPO-120 | **Abstract withdrawn**

EPO-121 | Longitudinal changes in [18F]FDG PET brain metabolism as a prognostic marker in autoimmune encephalitis

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Background and aims: Recent advancements in autoimmune encephalitis (AE) have enhanced diagnosis and management, but predicting long-term outcomes remains challenging. This study aimed to evaluate longitudinal changes in brain [18F]FDG PET patterns in AE patients to identify specific regional metabolic variations and predict clinical outcomes.
Methods: This retrospective study involved 22 AE patients who underwent brain [18F]FDG PET at baseline (BS) and after treatment (follow-up, FU). PET scans were analyzed voxel-wise using paired t-tests to compare metabolic activity between BS and FU. Significant clusters with at least 100 voxels and p<0.05 were identified. Volume of interest (VOI) values were correlated with clinical outcomes using partial Spearman's tests, and a general linear regression model (GLM) assessed the prognostic significance of VOI values.
Results: Three VOIs showed significant metabolic differences: VOI-A (relatively hypermetabolic) included the caudate-thalamus-parahippocampal region, right amygdala, and anterior cingulate cortex; VOI-B1 and VOI-B2 (relatively hypometabolic) corresponding to the right fusiform gyrus, precuneus and temporo-parietal cortex, respectively. Key findings include: i) lower metabolism in VOI-B1 at BS correlated with higher CASE scores at FU (p=0.014); ii) relapsing patients had lower VOI-B1 values at BS (p=0.026). At FU, higher metabolism in VOI-A (p=0.021) was noted in patients with mRS>2 at BS, alongside lower metabolism in VOI-B1 and VOI-B2 (p=0.036 and p=0.043). Lower metabolism in VOI-B1 at BS predicted relapse (p=0.011) and higher CASE scores at FU (p=0.021). Lower metabolism in VOI-B2 at FU predicted mRS>2 (p=0.028).

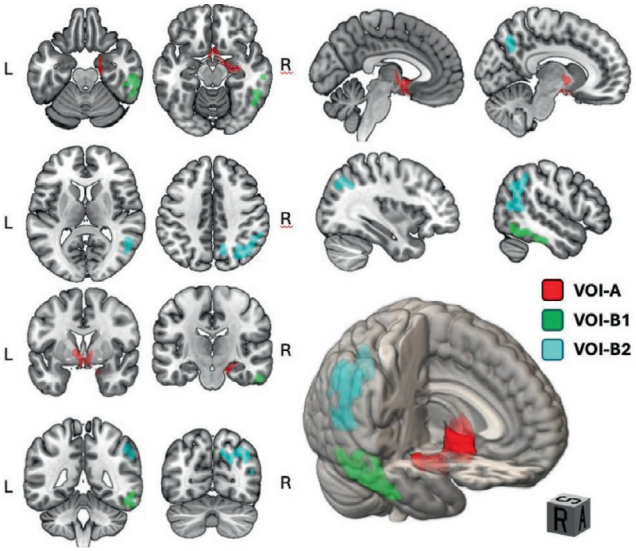
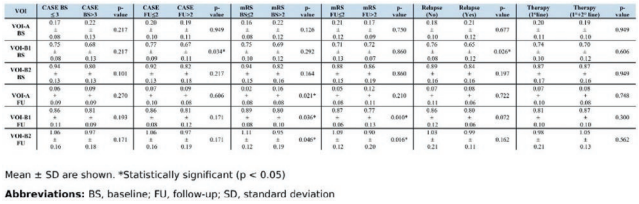


FIGURE 1 Relative hypermetabolic (VOI-A) and hypometabolic (VOI-B1 and B2) regions in BS compared to FU



Mean ± SD are shown. *Statistically significant (p < 0.05)
Abbreviations: BS, baseline; FU, follow-up; SD, standard deviation

FIGURE 2 Comparison between VOIs and clinical outcomes

TABLE 1 Backwards general linear regression model.

Predictors	Estimate	p-value	SE	VIF	R^2	AIC	BIC
Predictors at BS timepoint							
Backwards linear regression for CASE FU>2							
Age	0.01	0.586	0.02	1.67	0.33	82.5	89.1
CASE BS	0.11	0.408	0.13	1.56			
VOI-B1 BS	-7.74	**0.021***	3.05	1.30			
VOI-A BS	-2.70	0.384	3.02	1.12			
Backwards linear regression for relapse (no=0; yes=1)							
CASE BS	0.05	0.175	0.04	1.18	0.39	30.4	35.9
VOI-B1 BS	-3.46	**0.011***	1.22	2.15			
VOI-B2 BS	1.57	0.09	0.87	2.27			
Backwards linear regression for therapy (1°line=0; 1°+2°line therapy=1)							
Age	-0.02	**0.002***	0.005	1.05	0.41	30.2	35.6
VOI-A BS	-0.54	0.579	0.96	1.18			
VOI-B2 BS	0.31	0.625	0.62	1.18			
Predictors at FU timepoint							
Backwards linear regression for mRS FU>2							
VOI-A FU	0.80	0.475	1.10	1.14	0.32	29.1	33.3
VOI-B2 FU	-1.38	**0.028***	0.58	1.14			
Backwards linear regression for therapy (1°line=0; 1°+2°line therapy=1)							
Age	-0.02	**<0.001***	0.004	1.00	0.50	24.5	28.9
VOI-B1 FU	1.75	**0.046***	0.82	1.00			

*Statistically significant (p < 0.05)

Conclusion: Quantitative brain [18F]FDG PET analysis can provide prognostic information in AE, identifying hypometabolism in specific regions as a prognostic marker.
Disclosure: Nothing to disclose.

EPO-122 | Stepwise connectivity from the disease epicenter aligns with ALS-related gene expression in C9orf72 ALS patients

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Background and aims: Stepwise functional connectivity (SFC) detects whole-brain functional couplings of a selected region of interest at increasing topological distances. This study applied SFC to test the hypothesis that stepwise architecture propagating from the disease epicenter would be related with patterns of gene expression in patients with amyotrophic lateral sclerosis (ALS) carrying C9orf72 repeat expansion.
Methods: Thirty patients with C9orf72-ALS and 35 age-matched healthy controls underwent brain MRI on a 3T scanner. The region of interest was defined as the peak of atrophy observed using voxel-based morphometry in C9orf72-ALS patients. We tested the correlation between SFC architecture propagating from the disease epicenter in healthy conditions and the expression pattern of the major causative genes in ALS, as obtained from the Allen Human Brain Atlas.
Results: The disease epicenter was identified in the right frontal superior cortex in C9orf72-ALS patients. Significant correlations were identified between SFC topological distance from the right frontal superior cortex and TARDBP expression ($r=0.262$, $p=0.017$). Similar results were obtained analyzing the correlation between SFC maps and C9orf72 expression ($r=0.260$, $p=0.018$).
Conclusion: This study provides insights into the relationship between the topology of target functional networks in ALS patients with C9orf72 expansion and the transcriptomic patterns of ALS-related genes. Specifically, this study suggests that higher gene expression in regions more proximal to the disease epicenter might shape pathological spreading along the SFC architecture in C9orf72-ALS patients.
Disclosure: Funding. ERC (StG-2016_714388_NeuroTRACK); Foundation Research on Alzheimer Disease. Co-funding by the Next Generation EU [DM 1557 11.10.2022]. Disclosures: MF consulting fees from Alexion, Almirall, Biogen, Merck, Novartis, Roche, Sanofi; speaking fees from Bayer, Biogen, Celgene, Chiesi Italia SpA, Eli Lilly, Genzyme, Janssen, Merck-Serono, Neopharmed Gentili, Novartis, Novo Nordisk, Roche, Sanofi, Takeda, and TEVA; participation in Advisory Boards for Alexion, Biogen, Bristol-Myers Squibb, Merck, Novartis, Roche, Sanofi, Sanofi-Aventis, Sanofi-Genzyme, Takeda; scientific direction of educational events for Biogen, Merck, Roche, Celgene, Bristol-Myers Squibb, Lilly, Novartis, Sanofi-Genzyme; he receives research support from Biogen Idec, Merck-Serono, Novartis, Roche, the Italian Ministry of Health, the Italian Ministry of University and Research, and Fondazione Italiana Sclerosi Multipla. F. Agosta is Associate Editor of NeuroImage: Clinical, has received speaker honoraria from Biogen Idec, Roche, Eli Lilly and GE Healthcare, and receives or has received research supports from the Italian Ministry of Health, the Italian Ministry of University and Research, AriSLA (Fondazione Italiana di Ricerca per la SLA), the European Research Council, the EU Joint Programme – Neurodegenerative Disease Research (JPND), and Foundation Research on Alzheimer Disease (France).

EPO-123 | Altered hypothalamic functional connectivity in amyotrophic lateral sclerosis

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Background and aims: Hypermetabolism is a newly identified clinical feature of amyotrophic lateral sclerosis (ALS), associated with shorter survival. In ALS cases compared to healthy controls (HC), hypothalamic volume reduction and white matter (WM) alterations between hypothalamus, orbitofrontal and insular regions have been reported. These changes suggest a relationship between patients' hypermetabolic state and hypothalamic dysfunction. However, the hypothalamic functional connectivity and its association with clinical severity and WM connectivity in ALS remain unclear.
Methods: Seventy-one ALS patients and thirty-nine HC underwent structural and resting-state functional MRI. In each subject, the bilateral hypothalamus was manually segmented, and a seed-based resting-state functional connectivity (RS-FC) analysis was performed between this region and the rest of the brain. Hypothalamic RS-FC was then compared among groups. Furthermore, in ALS, the relationship between RS-FC significant changes, ALSFRS scores-defined by ALS Functional Rating Scale (ALSFRS)- and the WM tract integrity-assessed through tract-based spatial statistics- were investigated.
Results: Compared to HC, ALS patients exhibited increased hypothalamic RS-FC with the caudate nuclei bilaterally. Additionally, in patients, greater disease severity and decreased

WM integrity of the genu of corpus callosum correlated with increased RS-FC between hypothalamus, caudate nucleus and orbitofrontal cortex bilaterally.

Conclusion: Our findings support hypothalamic alterations in ALS. These changes may be related to the hypermetabolic clinical feature in these patients, but further studies are needed to verify this association and its impact on patients' survival. The early detection of the hypothalamic changes in ALS could be useful for prognostic stratification and for monitoring the effect of interventions.

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EPO-124 | Insights from multi-shell diffusion and functional MRI analysis in trigeminal neuralgia

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Background and aims: This study aimed to investigate microstructural alterations in gray matter (GM) and white matter (WM) in Trigeminal Neuralgia (TN) patients. Additionally, it explored the neural correlates of pain in TN patients during an observation functional MRI (fMRI) task.

Methods: Thirteen TN patients and 29 controls were enrolled and underwent multi-shell diffusion brain MRI and an fMRI task. TN patients were re-evaluated 3-months post-Gamma Knife radiosurgery (GKRS). Fractional anisotropy (FA), and Intra-Cellular Volume Fraction (ICVF) maps were computed using the NODDI model. Then, tract-based spatial statistics (TBSS) and GM-based spatial statistics (GBSS) were performed to estimate WM and GM damage between groups. fMRI task required patients to observe facial gestures during daily activities or specific movements that triggered pain. Brain activity was analysed between baseline and 3-months follow-up.

Results: TBSS showed reduced FA in the brainstem and decreased ICVF along the anterior thalamic radiation and near the periaqueductal grey in TN patients. GBSS revealed lower ICVF in the temporal lobe and higher ICVF in subcortical regions, insula and temporal pole, suggesting GM microstructural alterations. At 3-months ICVF increased in TN patients in precentral gyri, insula and temporal pole. At baseline, TN patients showed widespread brain activation, which decreased and shifted post-GKRS, reflecting changes in pain processing.

Conclusion: WM involvement suggests alterations beyond sensory and motor pathways, while microstructural GM changes may reflect persistent nociceptive stimuli. Moreover, these findings enhance our understanding of TN's neural mechanisms and GKRS's effect on brain function.

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EPO-125 | Role of brain MRI in PFBC (Primary Familial Brain Calcification): Results from a single-center Italian cohort

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Background and aims: PFBC (Primary Familial Brain Calcification) is a rare genetic neurodegenerative disorder characterized by bilateral calcium deposition in basal ganglia, featuring movement disorders, psychiatric or cognitive disturbances. Correlations between genetic, clinical and radiological data are scarce. CT scan is the gold standard technique to image brain calcification, whereas the role of MRI is currently limited and no clear correlations between genetic PFBC subtypes, clinical phenotypes and radiological features are known.
Methods: 45 PFBC subjects and 67 matched healthy controls from the ERN-RND Center of Padua University underwent 3T brain MRI (T1, FLAIR, SWI sequences, FreeSurfer cortical thickness analysis), genetic testing (NGS Illumina NextSeq), clinical and neuropsychological evaluations.
Results: FLAIR and SWI sequences proved sensitive in identifying brain calcifications. White matter involvement and leukopathy in both cerebrum and cerebellum were significantly associated with cognitive impairment (OR 5.7, p=0.02; mean MoCA 21 vs 26, p=0.004). The presence of dentate nuclei calcifications was a significant predictor of a genetic diagnosis (OR 7.3, p=0.03) and of behavioral-psychiatric symptoms (91% vs 56%, p=0.04). All MYORG mutation carriers (n=5) showed punctate calcifications in the brainstem in a region approximately corresponding to hypoglossal nerve nucleus, possibly contributing to dysarthria, a typical feature of this genetic subtype. Cortical thickness reduction was observed in the left premotor cortex in PFBC ($p<0.05$), whereas no alterations were documented in asymptomatic PFBC subjects compared to HC. Cerebellar atrophy was demonstrated in MYORG subjects.

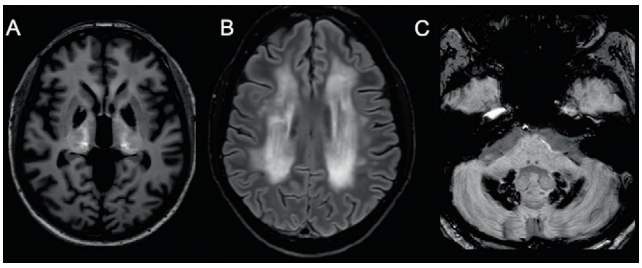

FIGURE 1 Brain MRI in PFBC. A: T1 sequence: basal ganglia calcifications in PFBC. B: FLAIR sequence: extensive leukoencephalopathy in a PDGFB mutation carrier. C: SWI sequence: dentate nuclei and brainstem calcifications in a MYORG mutation carrier.

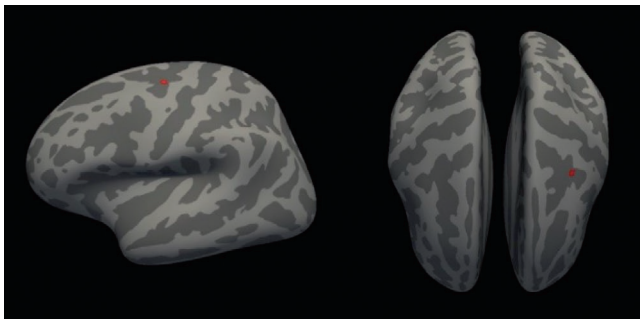

FIGURE 2 Cortical Thickness analysis results: in red the area (left premotor cortex) with significant atrophy in PFBC vs healthy controls.

Conclusion: Beside CT scan, brain MRI may be a useful tool to diagnose PFBC with potentially relevant prognostic correlates.
Disclosure: Nothing to disclose.

EPO-126 | Glymphatic dysfunction as an indicator of disease burden and a potential biomarker in anti-NMDAR encephalitis

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Background and aims: Glymphatic dysfunction is closely associated with the progression of neuroinflammation, indicating a potential mechanism underlying anti-N-methyl-D-aspartate receptor (anti-NMDAR) encephalitis. To date, no studies have reported about glymphatic dysfunction in anti-NMDAR encephalitis. The use of the diffusion tensor imaging analysis along the perivascular space (DTI-ALPS) index, free water in white matter (FW-WM) and perivascular space volume fraction (PVSVF) represent a noninvasive but conventional method for evaluating glymphatic function and disease severity. This study aimed to explore the utility of these biomarkers for evaluating glymphatic dysfunction in patients with anti-NMDAR encephalitis and establish their effectiveness in differentiating patients from healthy controls.
Methods: In the present study, we enrolled 20 patients with anti-NMDAR encephalitis and 18 age- and sex-matched healthy controls (HCs). Glymphatic function was assessed using DTI-ALPS index, FW-WM, and PVSVF. All participants underwent follow-up 3 months after discharge. Correlation analyses between magnetic resonance imaging (MRI) indices of glymphatic function and clinical factors were performed.

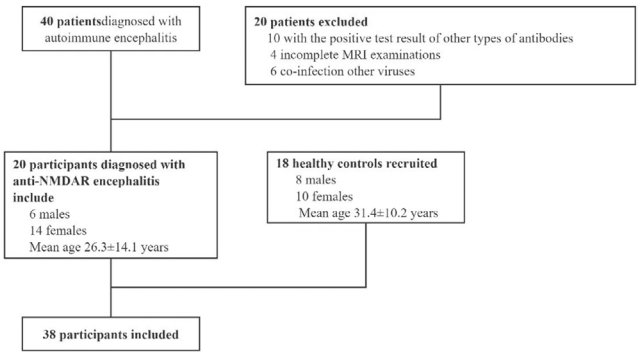

FIGURE 1 Patient selection flowchart.

Results: Patients with anti-NMDAR encephalitis demonstrated a significantly lower DTI-ALPS index and higher FW-WM and PVSVF values than HCs. Similar findings were observed in patients with negative conventional structural MRI findings. Significant correlations were identified between the MRI indices and clinical factors, including the Clinical Assessment Scale for Auto-immune Encephalitis score, the number of clinical symptoms, and other related clinical factors.

TABLE 1 Demographics and clinical characteristics of patients with anti-NMDAR encephalitis.

	Patients (n = 20)	Healthy control (n = 18)	P-value
Age (mean ± SD)	26.3±14.1	31.4±10.2	0.127
Gender (male/female)	6/14	8/12	0.168
symptoms-n (%)			
Seizure	12(60.0)	-	-
Psychiatric symptoms	14(70.0)	-	-
Disorders of consciousness	12(60.0)	-	-
Movement disorder	11(55.0)	-	-
Dysphasia	12(60.0)	-	-
Autonomic Dysfunction	13(65.0)	-	-
Cognitive Impairment	19(95.0)	-	-
Increased CSF-WBC (≥ 5 *10^6L) -n (%)	**10(50.0)**	**-**	**-**
Increased CSF protein level (≥ 45 mg/dL)-n (%)	**5(25.0)**	**-**	**-**
Anti-NMDAR antibody in CSF-n (%)		**-**	**-**
Low antibody titer (1:3.2-1:10)	7(35.0)	-	-
High antibody titer (1:32-1:100)	13(65.0)	-	-
Anti-NMDAR antibody in serum-n (%)		-	-
Negative	7(35.0)	-	-
Positive	13(65.0)	-	-
Abnormal brain MRI (%)	**9(45.0)**	**-**	**-**
EEG (%)		-	-
Mild to moderate abnormality	4(20.0)	-	-
Severe abnormality	8(40.0)	-	-
Normal	8(40.0)	-	-
CASE (mean ± SD)	**12.1 ± 9.2**	**-**	**-**
mRS (mean ± SD)	**3.4 ±1.8**	**-**	**-**

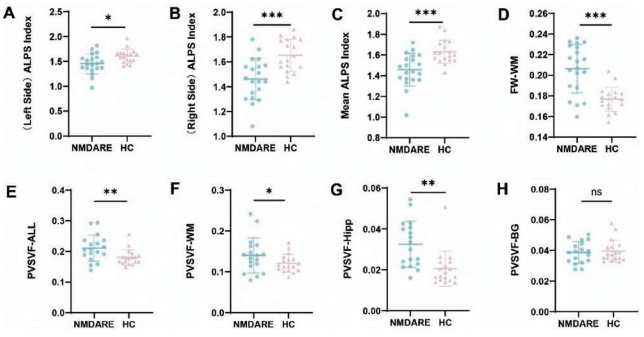

FIGURE 2 Comparisons of MRI indices between anti-NMDAR encephalitis patients and HCs.

Conclusion: Our study revealed glymphatic dysfunction in patients with anti-NMDAR encephalitis using MRI indices. PVSVF, DTI-ALPS index, and FW-WM are effective in distinguishing patients from HCs, offering deeper insights into disease progression beyond traditional MRI findings.
Disclosure: Nothing to disclose.

EPO-127 | Brain microstructural damage in multiple sclerosis using T1W/T2W ratio: An Italian neuroimaging network initiative study

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Background and aims: This study assessed T1w/T2w ratios from MRI scans as a potential marker for myelin content in multiple sclerosis (MS) using a large, multicenter cohort from the Italian Neuroimaging Network Initiative (INNI).
Methods: This cross-sectional study included 272 healthy controls (HC) and 918 MS patients from the INNI repository. MRI data, including sagittal 3D T1-weighted and axial 2D T2-weighted images, were collected. T1w/T2w ratios were calculated using a pipeline based on Ganzetti et al. that involved intensity bias correction, calibration, and histogram normalization. Tissue segmentation masks were overlaid to obtain the ratio values. Z-scores for MS were calculated by fitting linear mixed models on HC data. The study also explored associations between T1w/T2w ratios in various brain regions and disease duration and Expanded Disability Status Scale (EDSS) scores.
Results: Compared to HC, the T1w/T2w ratio was lower in white matter (WM) lesions of all MS phenotypes, in relapsing-remitting MS (RRMS) normal appearing WM (NAWM), and in the cortex for both RRMS and secondary progressive MS (all $p<0.001$). The ratio was higher in the thalamus, caudate, putamen, pallidum, and hippocampus of MS patients (all $p<0.046$). In relapse-onset MS, lower T1w/T2w ratios were observed in WM lesions, NAWM, and the cortex at EDSS <3.0 (all $p\leq0.003$). Higher ratios were noted in the thalamus, caudate, and putamen at EDSS≥4.0 (all $p\leq0.05$). Longer disease duration and higher EDSS correlated with changes in T1w/T2w ratios across brain regions.
Conclusion: The T1w/T2w ratio may serve as a clinically relevant marker of demyelination, neurodegeneration, and iron accumulation in MS.

Disclosure: Funding. Supported by Fondazione Italiana Sclerosi Multipla (FISM2023/S/1) and financed or co-financed with the '5 per mille' public funding. Disclosures. Nothing to disclose.

EPO-128 | Handwriting difficulties in Parkinson's disease: technological assessment and resting-state fMRI correlates

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Background and aims: Handwriting is a complex activity requiring cognitive and motor abilities, often impaired in people with Parkinson's Disease (pwPD). Proper handwriting assessment is essential to develop and evaluate the effect of rehabilitation protocols. To assess handwriting alterations in pwPD compared to healthy controls (HC) and to identify the functional neural correlates of handwriting changes through using resting-state fMRI functional connectivity (RS-FC) analysis.
Methods: Forty pwPD and 30 age- and sex-matched HC underwent handwriting and hand dexterity assessments, neuropsychological evaluation, and RS-fMRI. A tablet-based handwriting assessment included four tasks: Systematic Screening for Handwriting Difficulties-SOS test (copying a text), funnel test (coloring a shape), closed loop task (drawing specific symbols), and repetitive cursive loop task (writing repeated symbols). SOS test was executed also on paper. RS-fMRI analysis used MELODIC to identify RS-FC differences, and correlations with clinical variables significantly differing between groups were assessed.
Results: Compared to HC, pwPD showed smaller word size, slower drawing speed, and poorer performance in the handwriting tasks on tablet. SOS test on paper confirmed slower writing speed, smaller size, and lower writing quality in pwPD. RS-FC analysis revealed decreased connectivity in the basal ganglia, cerebellum, ventral default mode, and visual networks, alongside increased RS-FC in the salience and executive control networks. Correlations showed that smaller writing amplitude and poorer handwriting quality were associated with altered RS-FC in motor and cognitive networks.
Conclusion: PwPD exhibited handwriting impairments that were correlated to RS-FC changes in motor and cognitive networks, highlighting the neurological basis of handwriting difficulties in pwPD.
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EPO-129 | Structural connectivity between thalamic nuclei and hippocampus in temporal lobe epilepsy

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Background and aims: Hippocampal sclerosis (HS) is the most prevalent structural alteration in temporal lobe epilepsy (TLE), while thalamic atrophy is frequently observed in cases with extratemporal manifestations. This study aimed to investigate differences in the structural connectivity of individual thalamic nuclei between TLE patients and healthy controls.
Methods: Thirty-six TLE patients who underwent pre-surgical magnetic resonance imaging (MRI) and 18 healthy controls were enrolled in this study. Patients were subdivided into TLE with HS (TLE-HS) and MRI-negative TLE (TLE-MRneg). Probabilistic tractography and whole-brain segmentation, including the thalamus, were performed to determine the number of streamlines per voxel between the thalamic nuclei and hippocampus. Connectivity strength and volume of regions were correlated with clinical data.
Results: The volume of the entire thalamus ipsilateral to seizure onset was significantly decreased in TLE-HS compared to controls (Mann-Whitney-U test: pFDR <0.01) with the anterior thalamic nuclei (ANT) as important contributor. Furthermore, decreased ipsilateral connectivity strength between the

hippocampus and ANT was detected in TLE-HS (pFDR < 0.01) compared to TLE-MRneg and controls which correlated negatively with the duration of epilepsy (ρ = -0.512, p = 0.025) and positively with seizure frequency (ρ = 0.603, p = 0.006). Moreover, ANT volume correlated negatively with epilepsy duration in TLE-HS (ρ = -0.471, p = 0.042).

Conclusion: ANT showed atrophy and decreased connectivity in TLE-HS, which correlated with epilepsy duration and seizure frequency. Network analyses may enhance the understanding of seizure origin and propagation, and provide the promising potential to improve the selection of ideal DBS candidates and targets.

Disclosure: Nothing to disclose.

EPO-130 | Imaging blood-brain barrier dysfunction in drug-resistant epilepsy: a multi-center feasibility study

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Background and aims: Dysfunction of the blood-brain barrier (BBBD) has been linked to various neurological disorders, including epilepsy. This study aims to utilize dynamic contrast-enhanced MRI (DCE-MRI) to identify and compare brain regions with BBBD in patients with epilepsy (PWE) and healthy individuals.

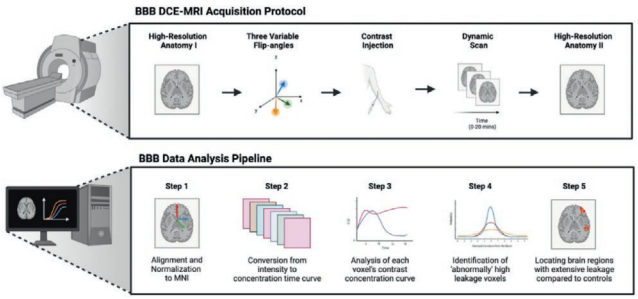

FIGURE 1 BBBD analysis uses DCE-MRI to capture brain images pre- and post-contrast, followed by alignment, curve conversion, voxel analysis, and identification of abnormal leakage regions.

Methods: We scanned 50 drug-resistant epilepsy (DRE) patients and 58 control participants from four global specialized epilepsy centers using dynamic contrast-enhanced MRI (DCE-MRI). The presence and extent of BBBD were analyzed and compared between PWE and healthy controls.

Results: Both greater brain volume and higher number of brain regions with BBBD were significantly present in PWE compared to healthy controls (p < 10-7). No differences in total brain volume with BBBD were observed in patients diagnosed with either focal seizures or generalized epilepsy, despite variations in the affected regions. Overall brain volume with BBBD did not differ in PWE with MRI-visible lesions compared with non-lesional cases. BBBD was observed in brain regions suspected to be related to the onset of seizures in 82% of patients (n = 39) and was typically identified in, adjacent to, and/or in the same hemisphere as the suspected epileptogenic lesion (n = 10).

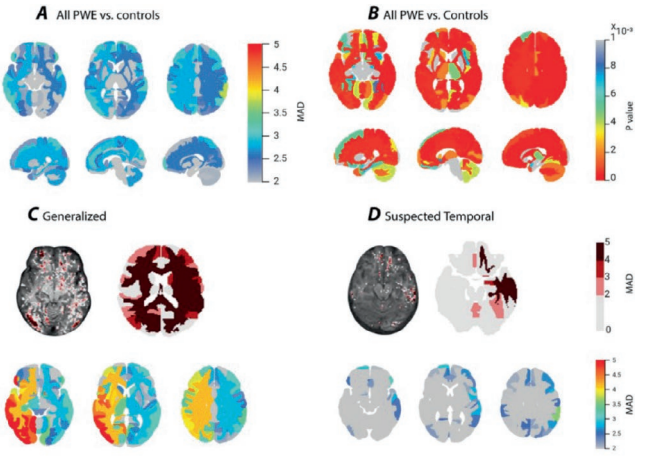

FIGURE 2 Imaging patients with epilepsy reveals a correlation between blood-brain barrier dysfunction and seizure onset zone diagnosis.

Conclusion: These findings are consistent with pre-clinical studies that highlight the role of BBBD in the development of DRE and identify microvascular stabilization as a potential therapeutic strategy.

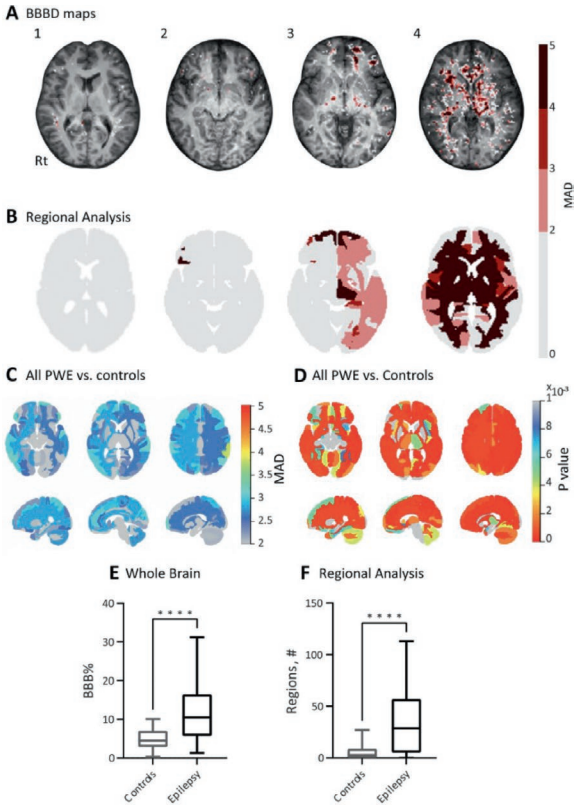

FIGURE 3 DCE-MRI reveals persistent BBBD in epileptic patients.

Disclosure: Nothing to disclose.

EPO-131 | Longitudinal evolution of Neuromelanin-MRI signal in the substantia nigra in Parkinson's disease

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Background and aims: Neuromelanin-sensitive MRI (NM-MRI) of the substantia nigra (SN) is increasingly utilized in Parkinson's disease (PD) research, showing reduced signal intensity and volume loss in patients. Although group differences are well established, the temporal evolution within individuals is less studied. To investigate, we analyzed NM-MRI scans from the Parkinson's Progression Markers Initiative (PPMI) database (www.ppmi-info.org).
Methods: We processed longitudinal NM-MRIs from 382 participants (168 PD patients, 214 prodromal). Scans from each visit were rigidly aligned and averaged. We used an Attention U-Net model to automate segmentation of the SN and a reference region in the crus cerebri, and calculated the contrast ratio (CR), contrast-to-noise ratio (CNR), and volume. Analyses were conducted with and without thresholding.
Results: 114 PD patients exhibited a reduced CR, while 54 showed increases between the first and last scans (1.4 years mean duration). A weaker trend was observed in the prodromal group (126 decreased vs. 88 increased). No significant changes were detected in CNR nor volume across thresholds (0, 1.5, 3.0), with these measures displaying more variability. With a linear curve fit, we estimated a CR loss of 2% per year in the patients ($p=10^{-6}$) and 0.7% in the prodromal cohort ($p=0.044$).

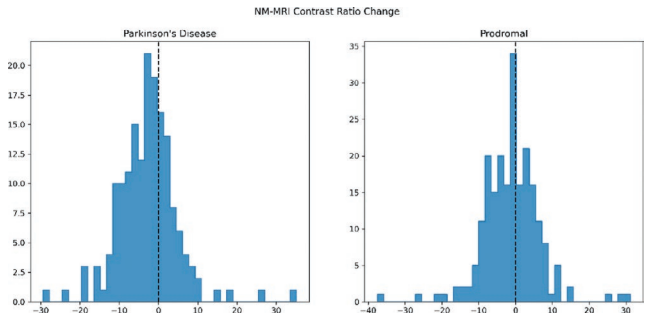

FIGURE 1 Percent change in CR between first and last measurements in prodromal and diagnosed Parkinson's disease.

Conclusion: The CR of the SN to crus cerebri offers a greater longitudinal stability than CNR and volume, and may prove useful for monitoring individual neurodegeneration on a relatively short timescale. The higher rate of CR loss in PD patients supports an accelerated neurodegeneration post-diagnosis than in the prodromal stage.
Disclosure: Nothing to declare

EPO-132 | 7T 3D-MR spectroscopic imaging reveals tissue- and lesion-specific oxidative stress in multiple sclerosis

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Background and aims: Oxidative stress is pivotal in Multiple Sclerosis (MS) pathogenesis, yet its in vivo mechanisms remain underexplored. Glutathione (GSH), the primary antioxidant countering oxidative stress, is difficult to measure due to low concentration and imaging limitations. Utilizing advanced 7T spectroscopy, we examined lesion- and tissue-specific oxidative stress, highlighting GSH's potential as a biomarker to enhance MS diagnostics and therapy.
Methods: This study included 18 MS patients (8F/10M, 47 ±11 years) and 12 controls (6F/6M, 31 ±7 years). Lesions were categorized as subcortical, juxtacortical, leukocortical, and intracortical using MP2RAGE and FLAIR. Segmented lesion masks were dilated and subtracted from WM/GM CSI masks, while control masks were derived directly. GSH and metabolites were quantified via Echo-less 3D MRSI and expressed as tCr ratios. Student's t-tests compared lesions to tissue types, and Pearson correlations assessed metabolite relationships for each lesion type with p-values adjusted for multiple comparisons.

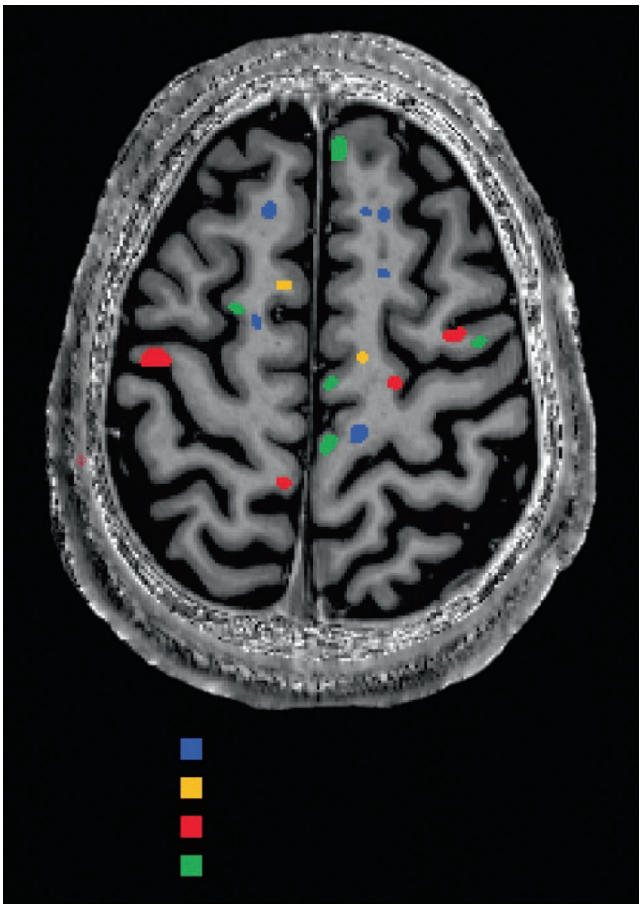

FIGURE 1 Segmentation and categorization of lesions. Color-coded regions represent subcortical (blue), juxtacortical (yellow), leukocortical (red), and intracortical (green) lesions on MP2RAGE.

Results: GSH/tCr was higher and Ins/tCr lower in all cortex-proximal lesions than surrounding tissue. Glu/tCr was elevated in subcortical lesions but lower in other types. Juxtacortical lesions showed positive correlations between tCho/tCr and GSH/tCr, and NAA/tCr and Ins/tCr. Glu/tCr positively correlated with NAA/tCr in leukocortical and intracortical lesions.

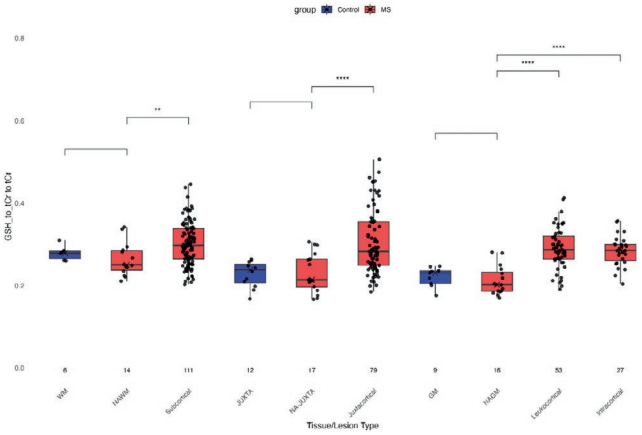

FIGURE 2 GSH/tCr ratios across tissue and lesion types. Significantly elevated GSH/tCr levels in lesions (red) compared to healthy tissues (blue) and normal appearing tissue (red), highlighting oxidative stress patterns. (**p < 0.01; ****p < 0.0001)

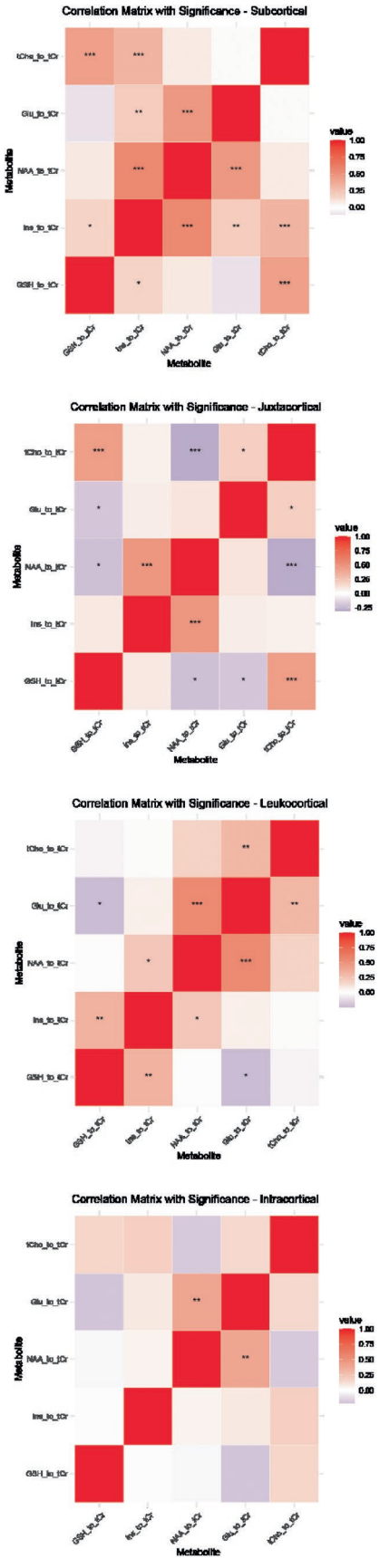

FIGURE 3 Correlation matrices with significance for tCho/tCr, Glu/tCr, NAA/tCr, Ins/tCr, and GSH/tCr ratios across subcortical, juxtacortical, leukocortical, and intracortical lesions. Significant correlations are marked (*p < 0.05, **p < 0.01, ***p < 0.001).

Conclusion: These findings are the first to reveal metabolic alterations and correlations, including altered GSH levels in cortex-proximal lesions, utilizing advanced 7T 3D echo-less MRSI, providing unprecedented spatial insights into oxidative stress mechanisms in MS.

Disclosure: This research was funded in whole, or in part, by the Austrian Science Fund (FWF):[10.55776/DFH50].

EPO-133 | H/M ratio cut-offs from standardized MIBG scintigraphy for diagnosing Parkinson's disease and related disorders

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Background and aims: ^{123}I-Metaiodobenzylguanidine (MIBG) myocardial scintigraphy, included in the global diagnostic criteria for Parkinson's disease (PD), previously relied on non-standardized data. This study evaluates the diagnostic accuracy of standardized analysis for distinguishing PD from related disorders. We also aim to establish optimal heart-to-mediastinum (H/M) ratio cut-offs for PD diagnosis using standardized methods.

Methods: We enrolled 268 parkinsonism patients (122 males, median age 71 years [Inter-quartile range: IQR 61–77], median disease duration 2 years [IQR 1–6]), diagnosed based on international standard criteria. ^{123}I-MIBG myocardial scintigraphy was performed, and H/M ratios were calculated using standardized protocols.

Results: Among 268 patients, 202 had PD and 66 had non-PD (Multiple system atrophy 24, Progressive supranuclear palsy 34, Corticobasal syndrome 8). H/M ratios in PD were lower in both early (median 1.90 [IQR 1.65–2.34]) and late phases (median 1.60 [IQR 1.36–2.08]) vs. non-PD (early: 2.90 [IQR 2.34–3.32]; late: 3.13 [IQR 2.29–3.57]) ($p < 0.001$, respectively; Kruskal-Wallis test). Receiver operating characteristic (ROC) analysis identified early-phase cut-off 2.24 (specificity 0.81, sensitivity 0.70, AUC 0.81) and late-phase cut-off 1.90 (specificity 0.81, sensitivity 0.70, AUC 0.83).

Conclusion: Our standardized analysis demonstrated a lower sensitivity for PD diagnosis compared to conventional methods. This finding is likely due to the predominance of early-stage PD in our cohort, where minimal cardiac sympathetic nerve damage is expected due to early Lewy pathology. Future studies should focus on cases with a relatively longer disease duration.

Disclosure: Nothing to disclose.

EPO-134 | Cerebral amyloid angiopathy prevalence in Alzheimer's disease according to different Boston criteria versions

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Background and aims: Cerebral amyloid angiopathy (CAA) commonly coexist with Alzheimer's disease (AD), exacerbating cognitive deterioration and complicating treatment strategies. Boston 2.0 criteria have shown increased sensitivity for CAA diagnosis, but few studies have explored the impact of their application in AD patients. The aim of our study was to assess the prevalence of CAA in a cohort of typical AD patients, according to the different versions of the Boston criteria.

Methods: A retrospective cohort of 108 consecutive AD patients, diagnosed using the Albert/McKhann criteria with biomarker support, was analyzed. Patients were included if an adequate MRI scan was available to assess hemorrhagic and non-hemorrhagic [centrum semiovale perivascular spaces (csPVS); and multispot white matter (WMH) hyperintensities pattern] CAA radiological biomarkers.

Results: The prevalence of CAA (possible and probable) rose from 35% to 79% using the Boston v2.0 criteria. The prevalence of probable CAA increased from 19% to 21% and 32%, with v1.0, v1.5 and v2.0 criteria respectively. Transitioning from v1.5 to v2.0 criteria, the reclassification was due to the presence of severe csPVS in 8 (13.3%) cases, WMH multisport pattern in 35 (57.4%) cases and both markers in 18 (29.5%) cases.

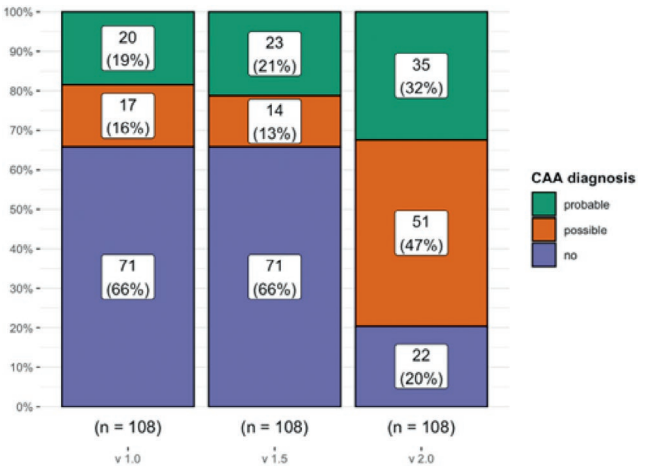

FIGURE 1 CAA prevalence in our population using the different versions of Boston criteria.

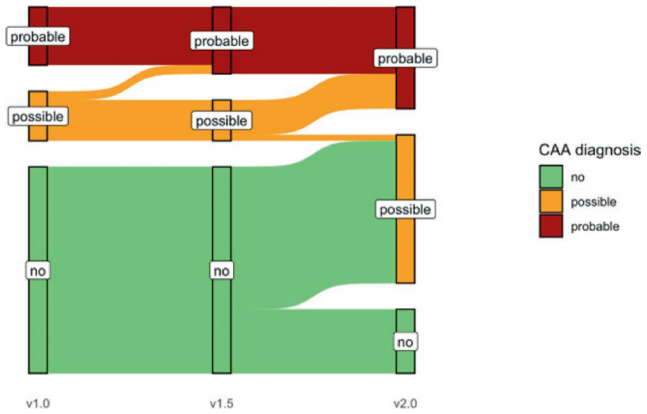

FIGURE 2 Sankey diagram showing the change in the diagnosis transition between different versions of Boston criteria.

Conclusion: The Boston 2.0 criteria significantly increased the prevalence of CAA diagnosis in AD patients, but the clinical significance regarding prognosis and treatment decisions deserve further studies, as their specificity in non-hemorrhagic patients remains uncertain. A careful interpretation of neuroradiologica data is essential to tailor the therapeutic choices to the patient, especially in relation to the use of anticoagulants and anti-amyloid immunotherapy.
Disclosure: Nothing to disclose.

Neuropathies

EPO-135 | Oligoclonal bands in blood and cerebrospinal fluid of patients with immune-mediated neuropathies

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Background and aims: Albuminocytological dissociation is usually seen in patients with Guillain Barre syndrome (GBS) and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Data on immunoglobulin oligoclonal bands (OCBs) are scarce. The aim was to analyze the presence of OCBs in cerebrospinal fluid (CSF) and serum of patients with GBS and CIDP.
Methods: During a ten-year old period, 344 patients were primarily diagnosed with GBS among whom 213 (62%) had OCB analysis - 64% males, age 53±16 years, GBS disability scale (GDS) at nadir 3.4±1.1. During the same period, 169 patients were diagnosed with CIDP among whom 125 (74%) had OCB analysis - 72% males, age at onset 56±15 years, duration 18±27 months, mean INCAT 3.6±2.1.
Results: Eighteen (8%) GBS patients had CSF OCBs - two had only CSF bands (one later developed CIDP and one connective tissue disease (CTD)), one had CSF bands and a smaller number of serum bands (diagnosed with Lyme disease), and 15 patients had parallel bands (two had CTD, two systemic vasculitis, one Hodgkin lymphoma, one monoclonal gammopathy, and one Lyme disease). Thirteen (10%) CIDP patients had OCB - five only CSF bands (one previously had meningoencephalitis and one was diagnosed with multiple sclerosis), one CSF bands and a smaller number of serum bands (with Sjogren's syndrome), and seven parallel bands (two had CTD and four paraprotein). Seven CIDP patients had parallel monoclonal bands due to paraprotein.
Conclusion: CSF oligoclonal bands are not common in immune-mediated neuropathies and if found, further analysis should be performed to seek for other diseases.
Disclosure: Nothing to disclose.

EPO-136 | Neuroleukemeiosis presenting similar to AIDP

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Background and aims: Neuroleukemeiosis, a rare condition where leukemic cells infiltrate peripheral nerves. We present a case which mimicked Acute Inflammatory Demyelinating Polyneuropathy (AIDP).
Methods: Case presentation of a 33-year-old male diagnosed with Acute Myeloid Leukemia (AML) in May 2024, undergoing chemotherapy with cytarabine, daunorubicin, and midostaurin. In July 2024, he developed left facial nerve palsy following a diarrheal illness, progressing to severe neurological symptoms, including shoulder and back pain, ascending paraesthesia, bilateral lower facial weakness, diplopia, bulbar dysfunction, paraparesis of upper limbs and asymmetrical lower limb weakness. Neurological examination revealed multiple cranial nerve palsies, including bilateral lower facial nerve palsy, right oculomotor nerve palsy with pupillary involvement, bulbar speech, tongue immobility, and global areflexia. Motor deficits showed severe upper limb paralysis and asymmetrical lower limb weakness. Sensory impairments included diminished vibration and proprioception.
Results: Initial cerebrospinal fluid (CSF) analysis on day 7 showed normal findings, while nerve conduction studies on day 14 confirmed non-length-dependent acquired demyelinating polyneuropathy. MRI of the lumbosacral spine revealed cauda equina thickening and enhancement, MR brain imaging ruled out cranial nerve enhancement or leptomeningeal pathology. Despite five days of intravenous immunoglobulin (IVIG) therapy, symptoms worsened. Repeat CSF flow cytometry confirmed leukemic infiltration (99% CD33-positive cells). Oncological treatment escalated but unfortunately patient didn't survive.

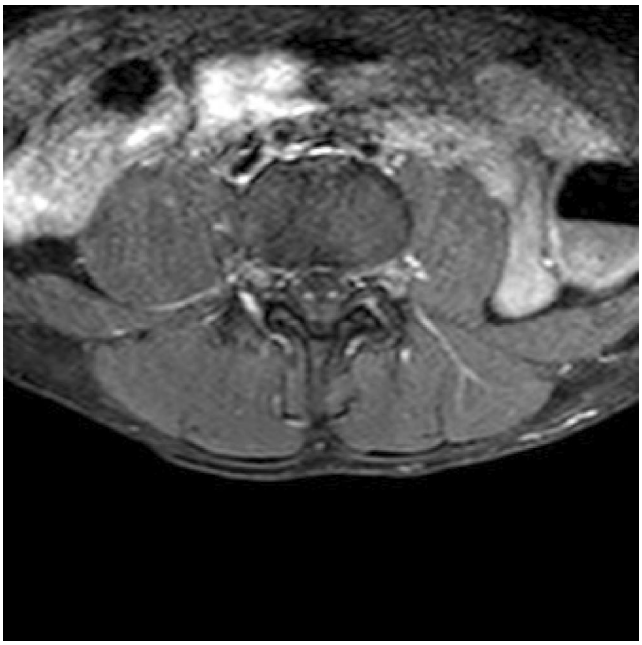

FIGURE 1 Enhanced thickened lumbosacral nerve roots on MR lumbosacral spine scan with GAD.

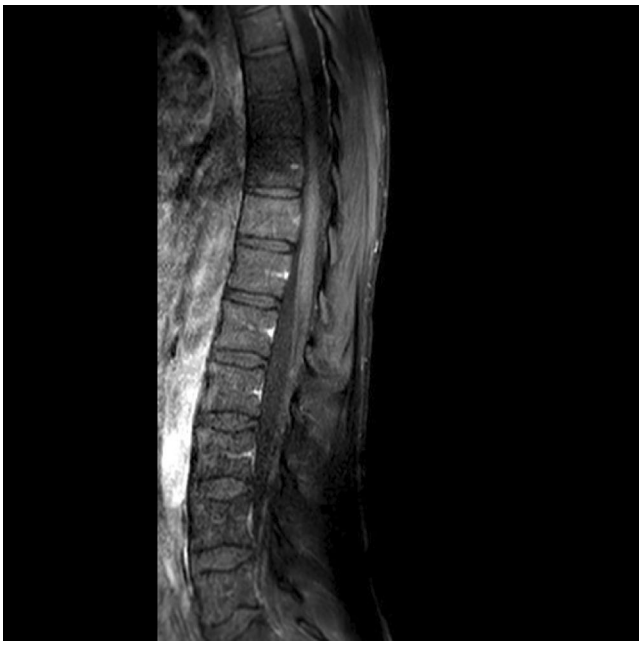

FIGURE 2 Thickened enhancing cauda equina nerve roots on MR lumbosacral spine scan with contrast.

Conclusion: This case highlights the rarity of neuroleukemeiosis and its potential to mimic AIDP. Key differentiators include asymmetrical weakness, worsening clinical state despite treatment, and imaging findings. Prompt recognition and diagnostic differentiation are crucial for appropriate management.
Disclosure: nothing to disclose.

EPO-137 | Rapidly progressive treatment refractory CIDP neuropathy, think of Paranodal neuropathy

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Background and aims: Paranodal neuropathies are a group of inflammatory neuropathies that are due to antibodies targeting nodal and paranodal antibodies in peripheral nerves. They share several clinical features to AIDP and CIDP, but with additional autonomic and systemic features. Here we present a case of neurofascin 155 IgG4 paranodal neuropathy
Methods: Case presentation of a 57years old female who over a 4-month period started having pins and needles in hands and feet, that ascended upwards, associated with ataxia, loss of dexterity in upper limbs and weakness in lower limbs requiring a use of wheelchair, significant loss of weight and constipation. Bedside examination showed bilateral subclinical facial muscle weakness, neck flexion weakness, and symmetrical proximal and distal weakness in 4 limbs, associated with global areflexia, impaired vibration up to iliac spine and impaired proprioception up to knees.
Results: Investigation supported a demyelinating inflammatory polyneuropathy, which included sural sparing pattern, significant reduced conduction velocity and prolonged distal motor and f waves. Lumbar puncture showed elevated CSF protein with normal white cells. Given the additional autonomic and systemic features plus facial weakness and significantly raised protein, paranodal antibodies panel sent and showed positive IgG4 for NF155.

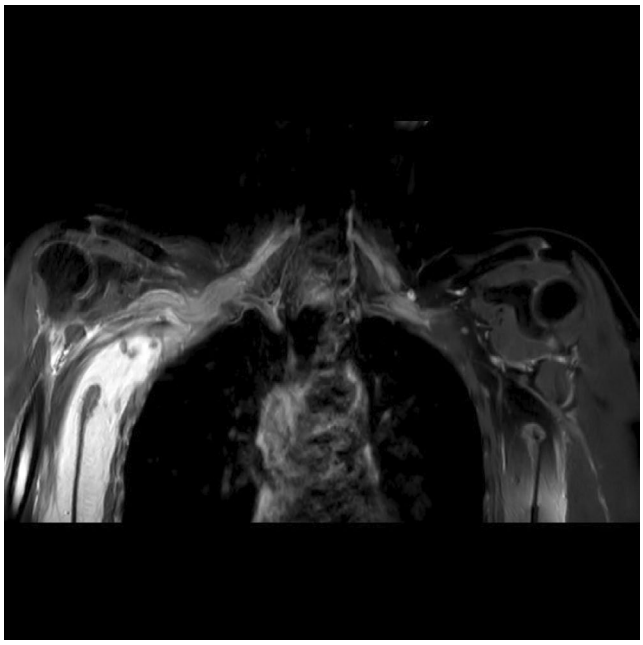

FIGURE 1 Brachial plexus with contrast showing avid enhancement and thickening of brachial plexus.

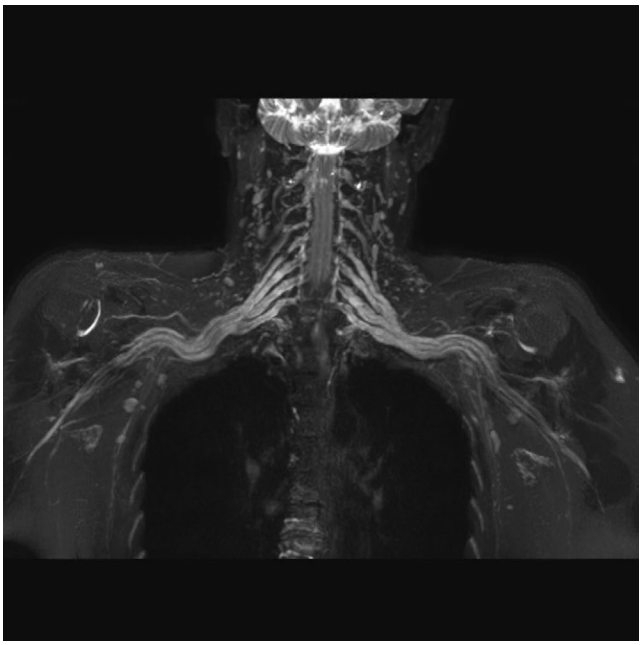

FIGURE 2 Coronal reconstructed MIP MPR MRi scan showing thickening of brachial plexus.

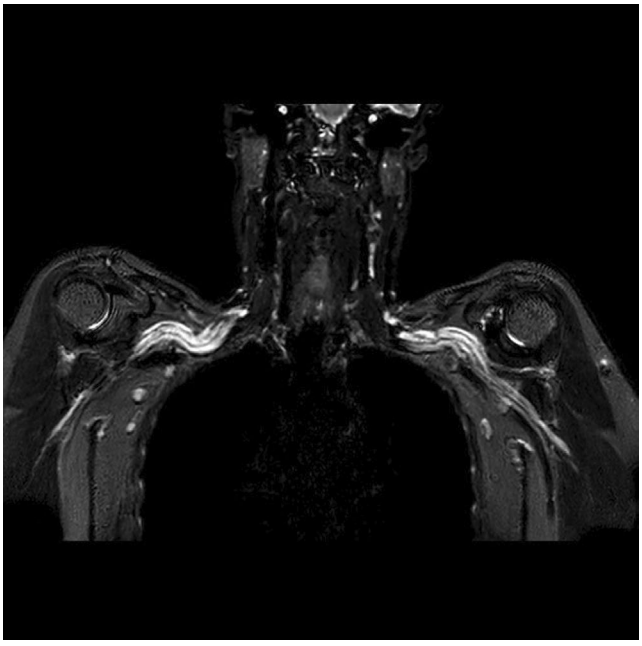

FIGURE 3 High signal of brachial plexus on STIR sequence.

Conclusion: Rapidly progressive symmetrical "CIDP" polyneuropathy with cranial, autonomic and systemic features with suboptimal response to IvIg should raise suspicion of paranodal neuropathies which respond better to B cell depleting therapy (Rituximab) and plasma exchange.
Disclosure: nothing to disclose.

EPO-138 | A case of ANCA-associated vasculitis mimicking lumbar disc herniation

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Background and aims: ANCA-associated vasculitides are autoimmune disorders characterized by small-vessel inflammation, often leading to systemic manifestations and peripheral neuropathy. Although vasculitic neuropathy typically presents as mononeuritis multiplex, asymmetric sensorimotor polyneuropathy can also occur.
Methods: A 50-year-old male presented with severe right lower extremity pain and foot drop. Lumbar disc herniation was initially suspected, and a discectomy was performed, but symptoms persisted. Within a month, he developed night sweats, weight loss, and progressive limb weakness. Physical examination revealed maculopapular erythematous lesions in the pretibial region. Laboratory tests, including C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and proteinase 3 (PR3)-ANCA, were performed. Imaging studies, such as cranial and spinal magnetic resonance imaging (MRI), and cerebrospinal fluid (CSF) analysis were conducted. Electromyography (EMG) was performed, and a sural nerve biopsy was taken for confirmation.
Results: Laboratory tests showed elevated CRP and ESR with positive PR3-ANCA. MRI and CSF analysis were unremarkable. EMG revealed axonal polyneuropathy affecting motor and sensory fibers. Sural nerve biopsy confirmed vasculitis. The patient initially received 1g intravenous steroid therapy but showed no significant clinical improvement. Subsequently, treatment with intravenous immunoglobulin (IVIg) and cyclophosphamide led to a marked reduction in inflammatory markers and significant relief of neuropathic pain.

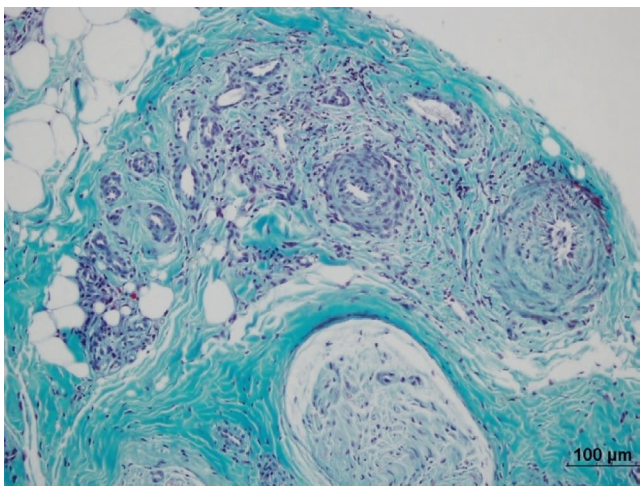

FIGURE 1 The sural nerve biopsy stained with modified Gomori's trichrome (MGT) shows perivascular inflammation.

Conclusion: This case highlights the need to consider vasculitis in the differential diagnosis of acute-subacute neuropathies. Early recognition and immunosuppressive therapy are essential to prevent irreversible nerve damage.
Disclosure: Nothing to disclose.

EPO-140 | Immunoglobulin vs efgartigimod: Indirect comparisons in chronic inflammatory demyelinating polyneuropathy (CIDP)

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Background and aims: As no relevant head-to-head randomized control trials (RCTs) have been published in CIDP, matching-adjusted indirect comparisons (MAIC) were conducted to evaluate the efficacy of Panzyga® intravenous immunoglobulin (IVIg) maintenance therapy versus efgartigimod subcutaneous neonatal Fc receptor (FcRn) inhibiting therapy in patients with CIDP.
Methods: Individual patient data (IPD) from the 1.0g/kg arm (N=69) and 2.0g/kg arm (N=36) IVIg phase 3 ProCID trial (NCT02638207) were respectively weighted to match aggregate baseline characteristics of patients from Stage A of subcutaneous efgartigimod PH20 phase 2 trial ADHERE (N=322; NCT04281472). ProCID patients who achieved confirmed Evidence of Clinical Improvement (ECI) were weighted (in both arms respectively) to match patients in the efgartigimod arm at the start of ADHERE Stage B (N=111). Based on clinically important baseline characteristics (age and sex), patients were matched. Weighted estimates from ProCID were compared (unanchored MAIC) against reported estimates in ADHERE for various clinical outcomes.
Results: A MAIC compared outcomes between ProCID patients and those in ADHERE's Stage A treatment period: Confirmed ECI (treatment responders), change from baseline in adjusted Inflammatory Neuropathy Cause and Treatment (aINCAT) score, Inflammatory Rasch built Overall Disability Scale (I-RODS) score, grip strength (dominant and non-dominant hands), and Medical Research Council (MRC) sum score. Another MAIC assessed deterioration following confirmed ECI in both ProCID treatment arms with efgartigimod patients in ADHERE Stage B respectively. Detailed results will be presented at the conference.
Conclusion: Although head-to-head RCTs are the reference, MAICs represent valuable comparative evidence for evaluating the growing treatment options for CIDP.
Disclosure: David R Cornblath (Consultant: Annexon Biosciences, Avilar Therapeutics, Boehringer Ingelheim, Dianthus Therapeutics, Grifols S.A., Hansa Medical AB, Johnson & Johnson, Nuvig Pharma, Octapharma AG, Pfizer, Inc; Data Safety Monitoring Board: Avidity Bio, Passage Bio, Sanofi, Vertex; Technology Licensing: Worldwide Clinical Trials, Inc., Beijing 3E-Regenacy Pharmaceuticals Co., Ltd., Passage Bio, CMIC, MedImmune Ltd., Fundacion GELTAMO, RWS Life Sciences; Scientific Advisory Board: Algotherapeutics, Nervosave) Jason C. Wilson (employee: Numerus Ltd, service provider: Octapharma AG) Mathurin Baquié (employee: Octapharma AG) Christoph Wissmann (employee: Octapharma AG) Elisabeth Clodi (employee: Octapharma PPG)

EPO-141 | The effects of efgartigimod therapy on autoimmune nodopathy

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Background and aims: Autoimmune nodopathy is a polyneuropathy characterized by IgG antibodies targeting the nodoparanodal region. Efgartigimod, an FcRn inhibitor lowering IgG and pathological autoantibodies, offers potential treatment. This study assessed efgartigimod's efficacy and safety in autoimmune nodopathy.
Methods: Three patients with autoimmune nodopathy (identified nodo-paranodal antibodies: NF155, CNTN1, NF186, Caspr1; IgG subtypes determined) participated in this open-label pilot study. Disease severity was assessed using aINCAT, MRC sum score, and I-RODS scores. Efgartigimod (10 mg/kg) was administered in four weekly infusions. Weekly clinical evaluations were conducted during and after treatment.
Results: Treatment was well-tolerated. Patient 1 (anti-NF186 IgG3) showed significant improvement after three doses, with sustained benefit but relapse after three weeks. Patient 2 (anti-NF155 IgG4) showed moderate improvement after four doses, with sustained benefit. Patient 3 (anti-NF155 IgG1/IgG4) showed improvement with efgartigimod and prior steroid treatment, with sustained benefit. Response varied based on antibody target and subtype.
Conclusion: Efgartigimod showed efficacy and safety in treating autoimmune nodopathy, suggesting a promising novel therapy. However, response variability highlights the need for further investigation into the influence of specific antibody targets and subclasses.
Disclosure: There are no disclosures to report.

EPO-142 | Multifocal predominant motor neuropathy in tangier disease: A case report

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Background and aims: Tangier Disease (TD) is a rare genetic disorder caused by mutations in the ABCA1 gene, resulting in low HDL levels and cholesterol buildup. Peripheral neuropathy occurs in about 50% of cases with heterogeneous clinical and electrophysiological patterns, from multifocal neuropathy, syringomyelia-like neuropathy, and, less commonly, distal symmetric polyneuropathy.
Methods: Case report.
Results: A 49-year-old male was referred to neurology appointment due to two months of paraesthesia and progressive loss of dexterity in his right upper limb. His medical history included smoking, excessive alcohol use, hypertension, type 2 diabetes, psoriasis and bilateral hip arthroplasty at age 35. Since 47, he has been monitored for extremely low HDL cholesterol (HDL <3 mg/dL) and severe hypertriglyceridemia (644 mg/dL), unresponsive to fenofibrate. Follow-up revealed hepatosplenomegaly and

pancytopenia. At 48, he had a myocardial infarction. There was no family history of lipid abnormalities or early-onset vascular disease. Neurological examination revealed weakness grade 3/5 in right wrist extension and 4/5 in fingers abduction and dysesthesia in the right median nerve distribution. Nerve conduction studies suggested an acquired demyelinating predominantly motor neuropathy with motor conduction blocks and temporal dispersion in the median and fibular nerves bilaterally and right ulnar nerve at non-compressible sites, and absent right median nerve SNAP. Genetic testing identified a ABCA1 gene variant (c.164A>G p.(His55Arg)) of uncertain significance, raising suspicion of Tangier disease.

Conclusion: Tangier Disease should be considered in patients with demyelinating multifocal motor or sensory-motor neuropathy and severe lipid abnormalities. This case highlights the importance of a multidisciplinary approach, for accurate diagnosis and management.

Disclosure: Nothing to disclose.

EPO-143 | When to consider CANVAS: A tertiary center's perspective on diagnostic clues

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Background and aims: Cerebellar Ataxia with neuropathy and bilateral vestibular areflexia syndrome (CANVAS) is a recently described syndrome that has become the focus of growing current interest, frequently cited as the most common cause of recessive genetic ataxia worldwide. The typical features are chronic progressive gait unsteadiness, eye movement abnormalities, including loss of vestibulo-ocular reflex (VOR), and polyneuropathy. Our goal was to characterize the clinical and paraclinical findings in 17 genetically confirmed CANVAS patients.

Methods: We retrospectively included patients tested for CANVAS in our tertiary center. Data retrieved from patients' records including demografic, symptoms, neurological assessment as well as EMG and neuro-ophtalmological evaluation and brain MRI findings were further analyzed.

Results: From a total of 38 patients tested for CANVAS, 17 were positive. Our CANVAS patients present a mean age of 66.76 years-old (SD 6.33). Most have experienced imbalance for about a decade, with this symptom being universal followed by oscillopsia. Downbeat nystagmus was present in 82% of patients and horizontal VOR was severely impaired in 75 % of patients. About 94% present the diagnostic triad, while the remaining did not have vestibular areflexia. All patients had abnormal SNAPs, which were absent in 82% of our sample. CMAPs were universally preserved. Clinical polyneuropathy was reported in 82% of the patients. Cerebellar atrophy was visible in 50% of patients.

Conclusion: Our results globally align with the literature. Clinical assessment alone may be sufficient to strongly suspect of CANVAS for an up-to-date clinician.

Disclosure: Nothing to disclose.

EPO-144 | Effect of efgartigimod PH20 SC on lower limb function in chronic inflammatory demyelinating polyneuropathy in ADHERE

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Background and aims: In the ADHERE trial (NCT04281472), subcutaneous (SC) efgartigimod PH20 (coformulated with recombinant human hyaluronidase PH20), a neonatal Fc inhibitor, reduced relapse risk and improved disability scores in chronic inflammatory demyelinating polyneuropathy (CIDP). This post hoc analysis explores the effect of efgartigimod PH20 SC on lower limb function.

Methods: Participants had active CIDP and were off treatment or on standard treatments (withdrawn during ≤12-week run-in). Participants received weekly efgartigimod PH20 SC 1000 mg (stage A). Responders were randomised (1:1) to weekly efgartigimod PH20 SC 1000 mg or placebo for ≤48 weeks (stage B). Outcomes included changes from run-in baseline (after participants withdrew prior treatments) to stage B last assessment in adjusted Inflammatory Neuropathy Cause and Treatment (aINCAT) leg score, selected Inflammatory Rasch-Built Overall Disability Scale (I-RODS) individual items, and Timed Up and Go (TUG) test.

Results: 322 participants entered stage A; 221 were randomised and treated in stage B (efgartigimod PH20 SC: 111, placebo: 110).

Tables 1 and 2, respectively, report participants who improved to an INCAT leg score of 0 or 1, and ≥1 points in I-RODS individual items at stage B last assessment. At stage B last assessment, mean (SE) TUG test completion time (seconds) in efgartigimod-treated participants decreased by −2.6 (0.66) from 16.5 (1.32) at run-in baseline, while in placebo-treated participants it decreased by −1.4 (1.48) from 19.9 (3.33).

TABLE 1 Percentage of participants who had an INCAT leg score of ≥2 at run-in baseline and improved to a score of 0 or 1.

	Stage B Efgartigimod PH20 SC (n=97)		Stage B Placebo (n=94)	
	Stage B Baseline	Stage B Last assessment	Stage B Baseline	Stage B Last assessment
Participants who improved to an INCAT leg score of 0 or 1/evaluable participants (%)	17/51 (33.3)	18/51 (35.3)	16/57 (28.1)	17/56 (30.4)

INCAT, Inflammatory Neuropathy Cause and Treatment (INCAT) Disability Score; PH20, recombinant human hyaluronidase PH20; SC, subcutaneous.

TABLE 2 Percentage of participants who had a score of 0 or 1 in selected individual I-RODS items at run-in baseline and improved ≥1 points.

	Stage B Efgartigimod PH20 SC (n=97)		Stage B Placebo (n=94)	
	Stage B Baseline	Stage B Last assessment	Stage B Baseline	Stage B Last assessment
Participants with a ≥1 score improvement/evaluable participants (%)				
Run	16/94 (17.0)	21/94 (22.3)	11/92 (12.0)	5/90 (5.6)
Walk outdoors	23/83 (27.7)	27/83 (32.5)	20/80 (25.0)	16/78 (20.5)
Walk one flight of stairs	21/83 (25.3)	25/83 (30.1)	20/83 (24.1)	15/81 (18.5)
Walk avoiding obstacles	16/72 (22.2)	19/72 (26.4)	24/73 (32.9)	14/71 (19.7)

I-RODS, Inflammatory Rasch-Built Overall Disability Scale; PH20, recombinant human hyaluronidase PH20; SC, subcutaneous.

Conclusion: Numerically more efgartigimod PH20 SC–treated participants with CIDP in ADHERE stage B experienced improvements from run-in baseline in lower limb function compared with placebo-treated participants.

Disclosure: As the disclosures of all the authors included in this abstract exceed 1500 characters, disclosures will be provided to the congress so they can be accurately reflected in the Congress Abstract book.

EPO-145 | Microvascular decompression for hyperactive dysfunction syndrome: A single-centre experience

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Background and aims: Hyperactive dysfunction syndromes (HDS) arise from vascular compression at the root entry/exit zone of cranial nerves. Commonly encountered neuropathies include trigeminal neuralgia (TN) in its classical (CTN), secondary (STN), or idiopathic (ITN) forms, hemifacial spasm (HFS), and glossopharyngeal neuralgia (GPN). Microvascular decompression (MVD) addresses the root cause of HDS and is considered an effective surgical treatment.

Methods: We retrospectively analyzed medical and surgical records of 1378 patients with HDS who underwent MVD at our center between 2014 and 2024.

Results: Between January 2014 and December 2024, 3624 patients with HDS were evaluated, of whom 1378 underwent MVD. Among operated patients TN was manifested in 1199 (87%), HFS in 83 (6%) and GPN in 17 (1.2%). Combined HDS was observed in 79 (5.7%) patients. The mean age of symptom onset was 47.8 years for CTN, 45.3 for STN, 37.4 for ITN, 47.3 for HFS, and 53.2 for GPN. Female predominance was observed across all HDS types, with ITN showing the highest female ratio. Right-sided involvement was most frequent with ITN having the highest bilateral occurrence. Transient postoperative complications occurred in 21%, predominantly CSF leaks (13%) and facial paralysis (2%). No perioperative deaths were reported. Recurrence was observed in 5.8% over follow-ups ranging from 1 month to 10 years.

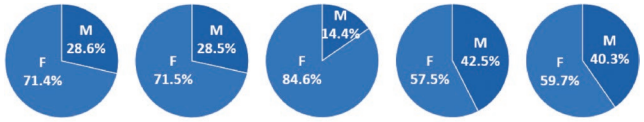

Figure 1. Gender of patients by neuropathy

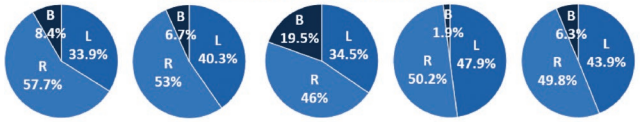

Figure 2. Affected side by neuropathy

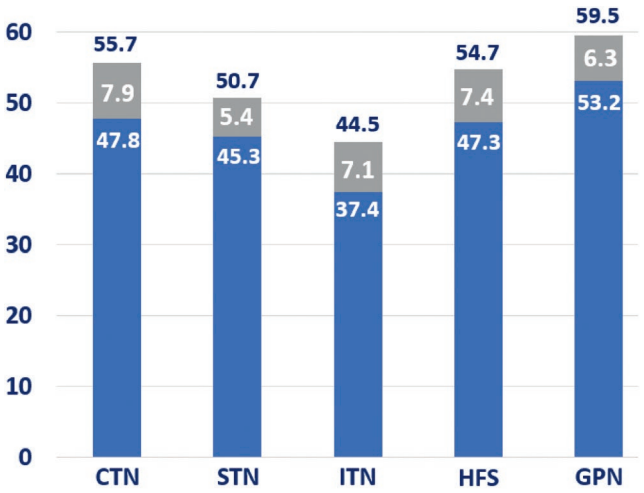

Figure 3. Age of onset, years of symptoms, and age at the time of surgery

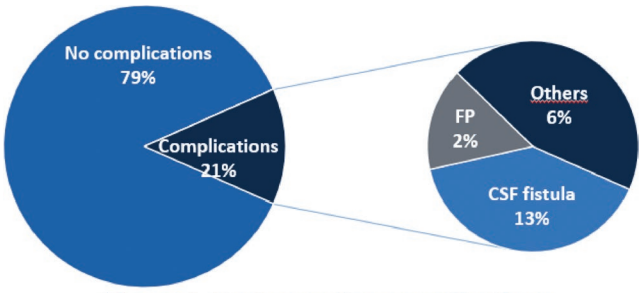

Figure 4. Postoperative complications

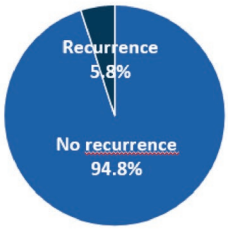

Figure 5. Symptoms recurrence rate

Conclusion: MVD is a safe and effective surgical treatment for HDS, offering significant symptom relief with minimal complications. This series, among the largest reported in Latin America, demonstrates outcomes consistent with international standards.

Disclosure: Nothing to disclose.

EPO-146 | Developing a blood-based biomarker targeting alpha-synuclein fragments for the early diagnosis of PD

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Background and aims: Developing a sensitive immunoassay that detects alpha-synuclein fragments cleaved by calpain I in peripheral blood for the early diagnosis of Parkinson's Disease (PD). It has been previously established that these fragments contribute to the formation of aggregates, which are associated with the early onset of the disease.

Methods: An antibody was generated to specifically target alpha-synuclein fragments cleaved by calpain I. A competitive ELISA was developed to analyze serum samples from clinical PD cohorts with a mean age of 64.2 years. These cohorts exhibited hypokinesia, postural instability, muscle rigidity, and tremor, having been diagnosed for one and a half years. Additionally, the SH-SY5Y neuroblastoma cell model was used to bridge brain pathology to peripheral biomakers and further validate the immunoassay.

Results: The developed antibody demonstrated specificity for α-synuclein fragments. A competitive ELISA was developed and validated for measurements in serum, it can significantly distinguish between healthy and PD serum samples. Moreover, alpha -synuclein fragments were detected in the supernatant of apoptotic SH-SY5Y cells.

Conclusions: Alpha-Synuclein fragments cleaved by calpain I represent key early drivers of PD pathology. This blood-based biomarker holds promise for early diagnosis and may provide crucial insights into patient eligibility for targeted therapeutic interventions in PD.

Disclosure: I work and own shares at Nordic Bioscience.

EPO-147 | Polyradiculoneuropathies associated with immune checkpoint inhibitors: Are we facing a new nosological entity?

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Background and aims: Immune checkpoint inhibitors (ICIs) are increasingly used to treat advanced cancers. While they enhance survival, ICIs can cause immune-related adverse events (irAEs) affecting the peripheral nervous system, notably acute inflammatory demyelinating polyneuropathy (AIDP) and chronic inflammatory demyelinating polyneuropathy (CIDP). Early diagnosis is challenging, leading to potential misclassification and suboptimal management.

Methods: A 48-year-old woman with melanoma, undergoing pembrolizumab therapy, developed progressive lower limb weakness, sensory disturbances, and areflexia after two cycles of treatment. Neurological evaluation suggested AIDP, and she was treated with intravenous immunoglobulin (IVIg), leading to initial improvement. However, 100 days later, the patient experienced a relapse with widespread weakness in all limbs, prompting a re-evaluation and reclassification of her condition as acute-onset CIDP (A-CIDP). This case highlights the difficulty in distinguishing between AIDP and A-CIDP, especially when considering the nuances of ICI-related neuropathies.

Table 1. The electrodiagnostic study performed at baseline and at different follow-up times in the A-CIDP patient

	Day of admission			Day 60			Day 100			Day 140		
	Lat (ms)	Amp (uV/mv)	CV (m/s)	Lat (ms)	Amp (uV/mv)	CV (m/s)	Lat (ms)	Amp (uV/mv)	CV (m/s)	Lat (ms)	Amp (uV/mv)	CV (m/s)
SENSORY												
R SURAL	2.7	7.8	50	2.6	7.8	59	2.7	11.4	43	2.5	10.4	44
L ULNAR	2	7.7	47.4	2.1	15.2	40	2.4	9.4	35	2	9.3	41
MOTOR												
R PERONEAL												
Ankle	3.8	9.9		2.5	8.1		3.6	8.0		2.9	5.6	
Fib Head	9.6	5.9	42	8.7	7.9	48	8.8	5.4	37	9.6	3.8	40.5
Pop fossa	11.0	5.7	45	10	7.7	58	10.5	4.5	38	11.7	3.7	45
F wave	NR			50			NR			55		
L TIBIAL												
AH	4.5	14.2		3.7	14.5		5	13.5		2.9	11	
Pop fossa	13	6.7	41	10	9.9	50	14.7	7.6	34	10	8	48
F wave	NR			52			NR			57		
R MEDIAN												
Wrist	2.7	11.9		2.2	10.9		3.7	11.9		2.8	11.7	
Elbow	6.6	11.5	52	6.2	10.2	56	7.7	6.4	44	6.9	7.8	53.3
L ULNAR												
Wrist	2.8	11.5		2.1	11.3		2.7	9		2	7.4	
B. elbow	5.6	6.5	43	5.7	8.9	50.6	6.2	4.5	38	4.7	5.8	46
A. elbow	7.7	5.5	40	7.9	7.7	53.4	9.1	2.9	42	8	5	39
F wave	51			29			NR			30		

**Sensory nerve conduction studies: latency represents the peak latency, and amplitude is measured in microvolts. Motor nerve conduction studies: latency represents the onset latency, and the amplitude is measured in millivolts.*

A., above; AH, abductor hallucis; Amp, amplitude; B., below; CV, conduction velocity; Fib, fibular; L, left; Lat, latency; Pop, popliteal; NR, no responses; R, right; S, superficial.

Results: A review identified 51 AIDP and 10 CIDP cases linked to ICI therapy. Symptoms included weakness, paresthesia, and gait instability, with NCS often showing demyelination. Most improved with steroids and/or IVIg, though some AIDP cases progressed to A-CIDP, suggesting potential misdiagnosis in ICI-induced neuropathies.

Conclusion: This case underscores the diagnostic challenges of ICI-related neuropathies, particularly A-CIDP, which may mimic AIDP. The immune dysregulation induced by ICIs often leads to atypical, aggressive presentations. Early cessation of ICIs and timely immunosuppressive therapy are crucial to prevent lasting disability. Recognizing A-CIDP enables better outcomes through personalized treatment and proactive monitoring.
Disclosure: Nothing to disclose.

EPO-148 | Femoral Nerve Injury causes – Retrospective study

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Background and aims: According literature, femoral nerve mononeuropathy is iatrogenic in 60% of cases. It is considered a rare condition, and its incidence may be underestimated. Electroneuromyography (ENMG) is frequently used in this clinical context. This study aims to determine the main risk factors, etiologies, and clinical course of this mononeuropathy in patients referred for electrophysiological evaluation.
Methods: Patients diagnosed with femoral mononeuropathy from the ENMG database between January 2020-July 2024, were included.
Results: 12 patients were included (58.3% male; median age of 61 years), referred for ENMG due to suspected femoral mononeuropathy. All had unilateral symptoms. Three main etiological mechanisms were identified: peri-surgical stretching, with four cases associated with hip prosthesis procedures and four cases with intra-abdominal surgeries; compressive, with three cases due to retroperitoneal hematoma in hospitalized patients on low molecular weight heparin (LMWH) anticoagulation; and direct trauma, with one case caused by a stab injury. Follow-up data were available for 75% of cases, of which 88.8% underwent physiotherapy. Despite symptomatic improvement, 66.6% of patients continued to experience symptoms. One case achieved complete recovery.
Conclusion: Medical-surgical iatrogenesis is the most common cause of femoral nerve mononeuropathy, accounting for 91.6% of cases in this cohort, with surgical causes being the most frequent. This highlights the importance of surgical awareness to minimize its occurrence. The presence of symptoms consistent with femoral nerve injury in patients on anticoagulation, particularly LMWH, should raise suspicion of retroperitoneal hematoma. Early diagnosis could allow timely suspension of anticoagulation (when possible), which may significantly impact prognosis.
Disclosure: Nothing to disclose.

EPO-149 | A Delphi panel to identify optimal outcome measures in chronic inflammatory demyelinating polyneuropathy (CIDP)

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Background and aims: CIDP is a rare, heterogenous, autoimmune polyradiculoneuropathy causing disability. Current clinical outcome assessments (COAs) may not capture all relevant aspects of the disease experience.
Methods: A multi-stakeholder modified Delphi study is ongoing to identify optimal COAs for CIDP, involving 18 health care providers (HCPs) and 18 patients from nine European countries. Preliminary results from the first-round survey from 13 HCPs and 10 patients are presented; full results are anticipated in 2025.
Results: Preliminary first-round results from 13 HCPs highlighted mobility, gait/balance, muscle/grip strength, functional independence, pain, mood, and fatigue as key domains for assessment. Ten patients recognised these as important, together with quality of life (QoL), sleep, and cognition. Pain management was prioritised by most patients (n=9/10) and was also deemed highly important by HCPs (n=11/13). Additionally, HCPs (n=10/13) noted time constraints and subjectivity as barriers to pain assessment, while patients (n=5/10) noted that pain relief could ameliorate other outcomes such as fatigue. HCPs (n=8/13) noted the visual analogue scale is frequently or always used in clinical practice, while patients (n=6/10) raised concerns regarding the use of scales to quantify the extent of their pain highlighting the need for more adapted assessment tools.
Conclusion: Given the clinical heterogeneity of CIDP, identifying a core set of COAs is essential. Preliminary findings suggest that beyond current outcomes valued by clinicians, several other elements are of relevance to patients. Multi-stakeholder alignment is needed to refine and optimise existing tools to reflect the full impact of CIDP on patients' lives from both HCP-and patient-centric perspectives.
Disclosure: The study was funded by Johnson and Johnson Innovative Medicine, which provided Adelphi Values PROVE with funding for the review; GMB, CG, and MM are Johnson and Johnson employees and may hold stock or stock options. YAR has received speaker/consultancy honoraria from LFB, Polyneuron, Argenx, Takeda, Grifols, Janssen, Sanofi, Dianthus, has received educational sponsorships from LFB and CSL Behring and has obtained research grants from LFB. EN-O has received speaker/consultancy honoraria from Argenx, Takeda, CSL Behring, Dianthus, Janssen, Kedrion, LFB, Roche and has received a research grant from Takeda. CF is a GBS/CIDP Foundation International employee.

EPO-150 | HyperCPKemia in Guillain–Barré syndrome: A cohort study

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Background and aims: Elevated creatine kinase (CK) levels have been observed in some Guillain-Barré syndrome (GBS) patients, particularly those with the acute motor axonal neuropathy (AMAN) subtype. This may indicate muscle damage and could be a marker of disease severity in specific GBS subtypes. Further research is needed to comprehend the implications fully.
Methods: We prospectively enrolled 106 patients with AIDP, AMAN, AMSAN, and unclassified groups whose serum CK levels were measured during their stay in the hospital between April 2022 and December 2024. Patients were classified into four different subtypes of GBS, based on nerve conduction studies, and further sub-classified into normal CK (serum CK ≤26-140 U/L) and CK elevation (serum CK ≥140 U/L) groups, respectively. The clinical features were compared among these groups.
Results: Out of 106 patients, 39 (36.8%), 55 (51.8%), and 12 (11.3%) were of AIDP, AMAN, AMSAN, and unclassified subtypes, respectively. Clinical characteristics were similar among normal CK (n=63) and CK elevation (n=43) groups. In our study, patients in the CK elevation group had autonomic dysfunctions. Among the two groups, the frequency of CK elevation was significantly higher ($p \leq 0.05$) in the AMAN subtype of GBS as evaluated by MRC sum (23.4 ± 13.6 & 32.3 ± 12.6) from admission to discharge, respectively.
Conclusion: CK elevation in AMAN subtype of GBS was associated with autonomic dysfunctions, potentially indicating disease severity in specific subtypes. Therefore, increased CK levels within the first four weeks of symptom onset may be a marker for axonal degeneration and poor prognosis in GBS.
Disclosure: Nothing to disclose.

EPO-151 | Pan-neurofascin nodo-paranodopathy presenting as fulminant Guillain-Barré Syndrome – case report and literature review

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Background and aims: Autoimmune nodo-paranodopathy (AINP) associated with pan-neurofascin antibodies (Ab-PanNF) is a rare subtype of autoimmune neuropathy that can present as a severe, prolonged, and sometimes fatal illness. However, timely recognition and appropriate treatment can lead to full or near-complete recovery, often with a monophasic course. Rituximab (RTX) is emerging as the most effective treatment, capable of inducing remission.
Methods: We present a single case report and a literature review on pan-neurofascin nodo-paranodopathy.
Results: We describe a patient initially diagnosed with Guillain-Barré Syndrome (GBS) who experienced partial recovery before worsening abruptly, developing tetraplegia, lower cranial nerve involvement, and dysautonomia. A diagnosis of AINP with Ab-PanNF was established, leading to RTX initiation and remarkable improvement. Our literature review summarizes 35 reported cases, highlighting key features of this novel entity and identifying red flags that should prompt early Ab-PanNF testing. These include age >60 years, rapidly progressive and severe GBS-like presentation, fulminant relapse after initial improvement, prolonged mechanical ventilation, and refractoriness to standard therapies.
Conclusion: Early recognition of AINP by neurologists and intensive care physicians is crucial, as prompt antibody-depleting therapy can dramatically alter patient outcomes.
Disclosure: Nothing to disclose.

EPO-152 | Radiation induced vasculopathy leading to ischemic lumbar radiculopathy

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Background and aims: Delayed effects of radiation can be manifold. A case of radiation induced vasculopathy leading to ischemic radiculopathy is presented here. Objective: Radiation related vasculopathy and radiculo plexopathy are rare. The latency period between radiation exposure and the onset of symptoms ranged from 6 months to 44 years. The incidence of radiation-induced lumbosacral plexopathy following pelvic radiotherapy ranged from 0.3% to 1.3%.
Methods: Case Report.
Results: 74-year-old lady had a year history of claudication symptoms in right leg. Right leg pain with walking was mentioned. While driving, she had to stop her car as sudden onset severed sharp pain appeared at the groin radiating to knee along the anterior thigh. Since then pins and needles sensation started from her right sole to the leg. She had right vulvar cancer treated with radiation 22 years earlier. Her right lower limb arterial pulses were not palpable including right femoral artery. Left side was normal. Right ankle jerk was absent. ABPI was 0.61. NCS were normal. EMG suggested the right L5/S1 radiculopathy. MRI of LS spine was unremarkable. MRA revealed moderate to severe stenosis of right common femoral artery while other vessels were patent.
Conclusion: A sudden onset intense groin pain limiting her functioning was followed by sensory symptoms in the distal lower limb. Patient had ischemic one lower limb symptoms. Primary cause of vasculopathy is linked to radiotherapy she received years ago. Spinal roots ischemia is suggested by sudden development of radiculopathy symptoms. It is a case of radiation vasculopathy leading to ischemic radiculopathy.
Disclosure: "Nothing to disclose."

EPO-153 | Comparative analysis of paranodal antibody assays in autoimmune nodopathies: Accuracy and inter-laboratory agreement

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Background and aims: Autoimmune nodopathies (AN) are a subgroup of neuropathies that harbour antibodies targeting paranodal/nodal proteins (PNAbs): NF155, NF186, CNTN1 and CASPR1. However, laboratory strategies for their detection are not standardized. We aimed to evaluate the performances of PNAbs detection assays in two expert Neuroimmunology Centres.
Methods: A cohort of chronic inflammatory demyelinating polyneuropathy (CIDP) patients (n=45), pathological controls (n=34, 6 immune-mediated neuropathies, 12 non-immune-mediated neuropathies, 16 normal pressure hydrocephalus), and healthy controls (n=10) were tested using a commercial CBA (CCBA) or in-house assays: CBA on living cells (LCBA) and ELISA. PNAbs positivity required confirmation by both in-house tests at either Centre. CIDP patients with PNAbs were considered AN and "true positives." We assessed analytic performances using sensitivity, specificity and accuracy, and inter-laboratory agreement using Fleiss' Kappa test with 95% confidence intervals (CI).
Results: In-house assays detected PNAbs in 21 AN patients (NF155 = 11, PanNF =1, CNTN1 = 6, CASPR1 = 3), with an overall accuracy of 99.6% (sensitivity: 99.6%; specificity: 100%), with substantial agreement between Centres (Fleiss' kappa: 0.668, 95% CI: 0.528 – 0.778). CCBA demonstrated comparable performance (accuracy: 98.4%; sensitivity: 92.8%; specificity: 98.8%). ELISA showed the lowest accuracy (95.5%; sensitivity: 97.6%; specificity: 95.4%). Substantial overall inter-laboratory agreement for PNAbs (Fleiss' kappa: 0.735, 95% CI: 0.635 – 0.817) was observed, with only 3/89 (3.4%) discordant samples. CCBA showed the highest agreement (0.914), while ELISA the lowest (0.712).
Conclusion: PNAbs assays have overall good performances and reproducibility. CCBAs represent a reliable alternative to in-house assays for their detection.
Disclosure: Nothing to disclose.

EPO-154 | GBS at the Norfolk and Norwich Hospital (NNUH): A retrospective study regarding our practice and adherence to guidelines

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Background and aims: Guillain-Barre Syndrome (GBS) is an autoimmune polyradiculoneuritis causing ascending paralysis, sensory impairment and potential bulbar and autonomic dysfunction. Diagnosis is clinical and supported by CSF analysis and NCS/EMG. In the UK, the incidence is estimated at around 2/100,000/year, with 3-7% mortality. National guidelines enforce early IVIg/PLEX treatment and close FVC monitoring. Our study aims to evaluate our department's performance in diagnosing and treating the condition according to the guidelines and identify areas requiring improvement.
Methods: A retrospective analysis was conducted on GBS patients admitted to NNUH (January 2019 - July 2023). Data analysed included demographic details, Hughs score, CSF analysis, NCS/EMG and FVC.
Results: Thirty-nine GBS patients were identified (M:F = 2:1, average age 59). 66% presented with typical ascending paralysis. Other presentations included ataxia, ophthalmoplegia, and bulbar palsy. Average Hughs score was 2.8 - 4. IVIg were administered to 80% of patients (100% of patient requiring it due to Hughs > 2). Albuminocytologic dissociation was detected in 48.7% cases. Supportive NCS/EMG were found in 49% patients. 23% patients required ITU admission (FVC<1.5). Incidence was 0.89/100.000/year with 10% mortality.
Conclusion: NNUH showed very good guideline compliance regarding investigations, monitoring and escalation of GBS patients. All eligible cases received prompt immunotherapy and ventilatory support in ITU. CSF analysis and NCS/EMG were performed to support the diagnosis, reflecting good clinical practice. Our study showed lower incidence and higher mortality in our catchment area compared to the national average, suggesting underdiagnosis of milder cases which did not reach hospital attention.
Disclosure: Nothing to disclose.

EPO-155 | Electrophysiological evaluation of peripheral nerve injuries after the february 6 earthquake in Turkey

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Background and aims: The February 6, 2023, earthquake in Turkey caused over 50,000 deaths and more than 100,000 injuries. This study aims to evaluate the peripheral nerve, plexus, and root injuries of earthquake-affected patients in terms of EMG findings.
Methods: The clinical and EMG findings of patients trapped under rubble and admitted to three different centers after the earthquake were retrospectively evaluated.
Results: Among the 47 patients examined in the EMG laboratory, 19 were male and 28 were female. The average age of the patients undergoing EMG was 29.5 years, with the youngest being 6 years old and the oldest 69 years old. Seventeen of the patients were under the age of 18. Upper extremity injuries were

found in 12 patients, lower extremity injuries in 34 patients, and both upper and lower extremity injuries in 1 patient. The average duration of being trapped under rubble was 29.5 hours. EMG examinations revealed peripheral nerve injury in 37 patients, plexus injury in 8 patients, root injury in 1 patient, and both plexus and peripheral nerve injury in 1 patient. The most common peripheral nerve injury was found in the peroneal nerve at a rate of 46%, followed by sciatic and tibial nerve injuries.
Conclusion: Severe peripheral nerve injuries were identified in earthquake survivors, causing significant disability. Long-term follow-up is necessary to assess nerve regeneration and the effectiveness of physiotherapy.
Disclosure: Nothing to disclose.

EPO-156 | Intraepineurial FF as a novel biomarker in TTR amyloidosis patients and asymptomatic carriers using MR neurography

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Background and aims: Transthyretin familial amyloid polyneuropathy (ATTRv-PN) is a rare and progressive neurodegenerative disorder characterized by axonal neuropathy. Early detection of disease onset and progression is crucial for timely therapeutic intervention. Intra-epineurial fat fraction (FF) could reflect lipid droplets in amyloid deposits or epineurial fatty-rich replacement due to nerve fibers loss. This study investigates the utility of quantitative magnetic resonance imaging (qMRI) biomarkers, particularly intra-epineurial FF, in differentiating ATTRv-PN from asymptomatic carriers (ATTRv-C) and healthy controls (HC).
Methods: 53 patients with TTR mutations, (31 symptomatic ATTRv-PN, 22 ATTRv-C), and 24 HC were included and imaged, Sciatic and tibial nerves were segmented on anatomical sequences. qMRI parameters including FF, MTR (Magnetization transfer ratio) and volume were computed from the sciatic and tibial masks to quantify nerve morphology, structural integrity, and intraepineurial fat fraction-like. Correlations between qMRI metrics, clinical and electrophysiological parameters were calculated.

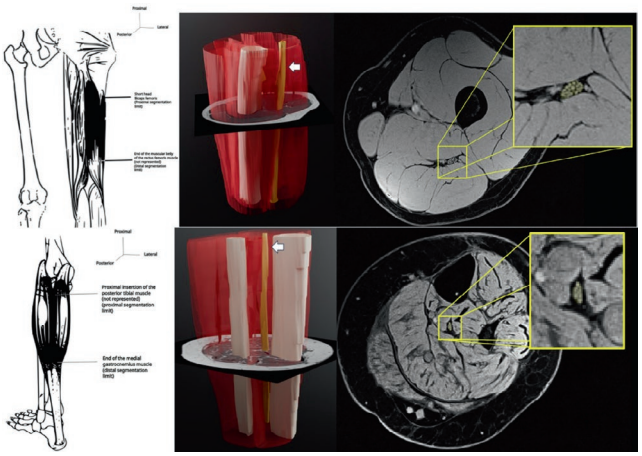

FIGURE 1 Anatomical Landmarks for segmentation limits are shown in the left column. Sciatic nerve (upper row) and tibial nerve (lower row) are marked by a white arrow (3D reconstruction, central column) and marked in yellow (right column).

Results: Symptomatic ATTRv-PN patients exhibited significantly higher intra-epineurial FF in both sciatic (median value 32.4% IQR [24.4-38.1]) and tibial nerves (median value 13.7%, IQR [9.97-20.7]) compared to controls (sciatic median value 22.3%, IQR [16.6-28.5]; tibial median value 9.74%, IQR [6.36-12.5] respectively) ($p<0.05$). Intra-epineurial FF values were positively correlated in both uni- and multivariate analysis with clinical and electrophysiological scores. ATTRv-C also showed increased FF compared to controls ($p<0.05$). Additionally, MTR and nerve volumes exhibited less pronounced differences across groups.

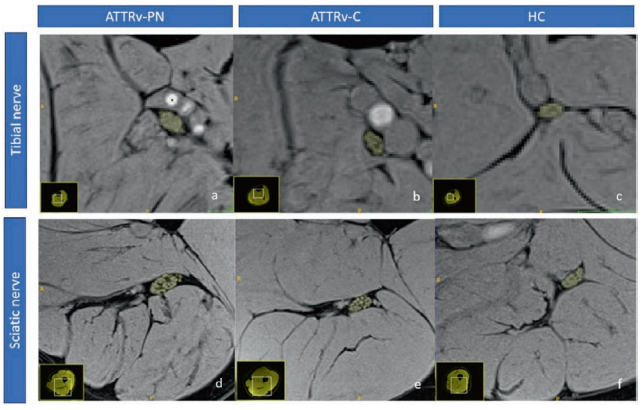

FIGURE 2 Enlarged views of nerve ROIs. Tibial nerve ROI in a symptomatic ATTRv-PN patient (a); ATTRv-C patient (b) and healthy control (c); Sciatic nerve ROI in an ATTRv-PN patient (d); ATTRv-C patient (e) and healthy control (f).

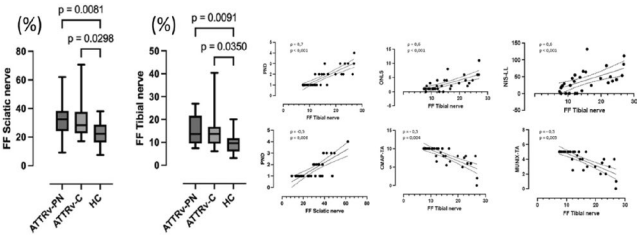

FIGURE 3 represents Intra-Epineurial FF differences between ATTRv-PN, ATTRv-C and HC, and correlations with clinical and electrophysiological scores

Conclusion: These results suggest that intra-epineurial FF is a promising qMRI biomarker for identifying early changes in ATTRv-PN, with potential for broader application in other axonal neuropathies.
Disclosure: Nothing to disclose.

EPO-157 | Diagnostic comparison of nerve ultrasound in immune-mediated neuropathies

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Background and aims: Chronic immune-mediated neuropathies represent a diverse group of peripheral nerve disorders with variable clinical phenotype and course, as well as response to treatment. Recognizing rare forms like anti-myelin-associated-glycoprotein (MAG) neuropathy from chronic inflammatory demyelinating polyneuropathy (CIDP) would improve patient management and treatment strategy.
Methods: 4 CIDP and 4 anti-MAG neuropathy patients were selected for detailed nerve ultrasound analysis, performed by single trained expert in nerve ultrasound. All patients were previously clinically evaluated, as well as other relevant data as treatment, duration of the disease and age at onset were documented.
Results: 8 male patients were enrolled - 4 CIDP and 4 anti-MAG neuropathy patients. For patient base line demographic and treatment data, see Table Nr 1. At the time of enrolment, the median age was 62 years (range 50-79 years). The median age at onset for CIDP patients was 59 years, for anti-MAG neuropathy patients – 52 years. Detailed nerve ultrasound results are represented in Table Nr 2.

TABLE 1 Patient demographic data and characteristics.

Case	Age at enrollment in this study	Diagnosis	Age at onset	Treatment	Treatment response
1	58	CIDP	50	SCIg	Ig responder
2	76	CIDP	68	SCIg	Ig responder
3	59	CIDP	50	SCIg	Ig responder
4	79	CIDP	69	none/remission	Ig responder
5	74	anti-MAG	64	none	Ig non responder
6	65	anti-MAG	56	Rituximab, PLE	Ig non - responder
7	51	anti-MAG	47	Rituximab, IVIG	Ig non-responder
8	50	anti-MAG	48	Rituximab	Ig non-responder

SCIg - subcutaneous immunoglobulins
IVIG - intravenous immunoglobulins
PLEX - plasma exchange procedure

TABLE 2 Comparison of ultrasound findings in CIDP and Anti-MAG antibody neuropathy.

Case	Type of immune-mediated neuropathy	UPSS				NUP			Morphology of nerve and nerve fascicle	
		UPS A	UPS B	UPS C	UPSS total	BUS (Step1)	Step2	Step3	HC	Distinctive regional fascicle enlargement
1	CIDP	2	1	1	4	2	1	0	0	no
2	CIDP	5	1	1	7	3	1	1	1	yes
3	CIDP	3	0	0	3	0	1	1	0	no
4	CIDP	4	2	1	7	3	2	2	1	no
5	Anti - MAG	11	2	3	16	4	2	2	2	no
6	Anti - MAG	4	0	1	5	1	2	1	0	no
7	Anti - MAG	8	1	1	10	1	1	1	1	no
8	Anti - MAG	4	0	0	4	0	2	1	1	no

CIDP - Chronic inflammatory demyelinating polyradiculoneuropathy, Anti- MAG - Anti-Myelin Associated Glycoprotein Peripheral Neuropathy, UPSS - Ultrasound Pattern Sum Score, BUS - Bochum ultrasound score, NUP - Neuropathy Ultrasound Protocol, HS - Homogeneity score

Conclusion: High resolution nerve ultrasound can be used as a complementary diagnostic tool to nerve conduction studies and serological findings to differentiate between hereditary, immune - mediates and axonal polyneuropathies. Our small case study coincides with and complements the limited number of publications on the usefulness of nerve ultrasound for differentiation between CIDP and anti - MAG antibody polyneuropathy. Anti - MAG antibody neuropathy shows more homogenous nerve enlargement, tends to affect distal nerves more while in CIDP there are more noticeable fascicular changes with or without nerve enlargement.
Disclosure: Nothing to disclose.

EPO-158 | Immunoadsorption versus plasma exchange in Guillain-Barre syndrome: A meta-analysis and systematic review

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East Avenue Medical Center

Background and aims: Guillain-Barre Syndrome is a debilitating neurological disease with an incidence of 1.1 - 1.8 per 100,000. Autoantibodies affecting peripheral nerve membranes play an important role in understanding the pathophysiology and treatment of it. Treatment options for its cure continue to unfold and evolve. Different clinical trials resulted in increased interest in therapeutic apheresis for treatment of severe and refractory disease. Conflicting results of immunoadsorption compared to plasma exchange in the management of Guillain-Barre Syndrome led us to synthesize available evidence from published studies.
Methods: Review Manager software was used for this review and classified the outcomes into primary (curative effect) and secondary (safety profile and relapse rate). Quality assessment and statistical data analysis were conducted using the said software.

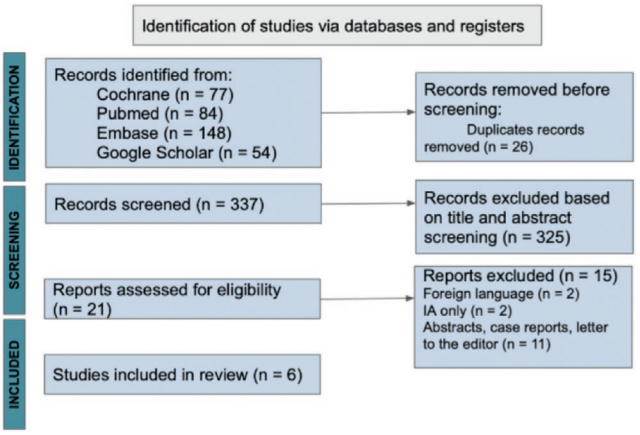

FIGURE 1 Flowchart of the systematic literature search on four electronic databases according to the PRISMA guidelines.

Results: The odds of achieving at least one grade disability and functional improvement was similar for patients treated with immunoadsorption and plasma exchange (OR: 0.77; 95% CI: 0.34 - 1.74; p = 0.53). Reduced risk of complications for patients treated with immunoadsorption group as compared to plasma exchange group (RR: 0.69; 95% CI: 0.43 - 1.11; p = 0.13) was noted. Increased risk of relapse for patients who underwent immunoadsorption (RR: 1.70; 95% CI: 0.96 - 3.00; p = 0.07).

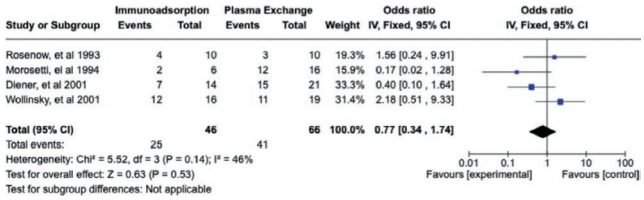

FIGURE 2 A forest plot showing analysis of patients that had achieved at least 1 score reduction in the Hughes scale 4 weeks or functional improvement after GBS treatment.

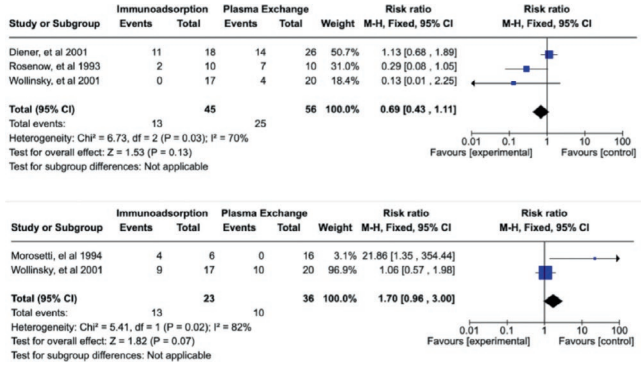

FIGURE 3 A forest plot showing analysis of patients that had complications after the GBS treatment and that had relapse or lack of clinical improvement after the GBS treatment.

Conclusion: Immunoadsorption is at least as effective as plasma exchange in the treatment of Guillain-Barre Syndrome based on its curative effect by lowering its disability and improving functional score. Immunoadsorption showed reduced complications but relapse rates were higher compared to plasma exchange.
Disclosure: Nothing to disclose.

EPO-159 | Romberg test in the 21st century: Differences in sway patterns in patients with vestibular and proprioceptive disorders

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Background and aims: The Romberg Test (RT) is a traditional bedside test for static balance, but its nonspecific original description has cast doubt over its diagnostic utility. The development of variants, designed to improve the assessment of vestibular causes of imbalance, has expanded the scope of balance evaluation. These, combined with advanced assessment techniques, have intensified the debate regarding the diagnostic utility of the RT. This study aims to evaluate whether there are specific patterns of sway during the RT and its variants that differentiate individuals with vestibular and proprioceptive deficits.
Methods: We assessed 6 healthy individuals and 18 patients whose main complaint was imbalance. Patients were divided into three groups: unilateral vestibular loss, bilateral vestibular loss, isolated peripheral neuropathy. Participants underwent clinical history collection, physical examination, and ancillary tests such as vestibular function testing as appropriate. Each participant performed four stance tasks, recorded using the SwayStar.
Results: Greater sway in the stance task on foam surface were more indicative of the presence of vestibulopathy compared to neuropathy. Conversely, patients with peripheral neuropathy exhibited greater imbalance in tasks on firm ground compared to tasks on foam surface. Patients with bilateral vestibular loss swayed more than the unilateral vestibular loss group, but both groups behave similarly and thus differed from the neuropathy group.
Conclusion: This study identified distinct patterns of postural sway associated with vestibulopathy and neuropathy during stance tasks, providing clear differentiation between these conditions. These findings underscore the potential of targeted stance tasks to enhance diagnostic accuracy in clinical practice.
Disclosure: Nothing to disclose.

EPO-160 | Fluid biomarkers in Charcot-Marie-Tooth disease

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Background and aims: Objective, responsive biomarkers are required to assess disease progression and inform clinical trials in Charcot-Marie-Tooth disease (CMT), the most common inherited neuropathy. Peripherin and periaxin, biomarkers of peripheral nerve axonal damage and acute demyelination, respectively, have recently been validated in the inflammatory neuropathies Guillain-Barré syndrome (GBS) and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Here, we evaluate whether peripherin and periaxin are elevated in CMT, and their potential utility for longitudinal monitoring alongside neurofilament light chain (NfL) and existing outcome measures.
Methods: We measured serum peripherin, periaxin, and NfL in patients with CMT1A (n=12), CMT2A (n=8) and CMTX (n=8), and compared levels to healthy controls (HC, n=20).
Results: Peripherin was higher in CMT1A, CMT2A, and CMTX compared to HC (all $p<0.05$). NfL was higher in all neuropathy groups versus HC (all $p<0.001$). Periaxin was elevated in two out of eight CMT2A patients, two out of eight CMTX patients, and below detection limit in CMT1A. Strong correlations were observed between peripherin and clinical tests: stair climb test CMT1A (rho = -0.912, p=0.0006) and 6-minute walk test in CMTX (rho = -1, p=0.0167).
Conclusion: Fluid biomarkers show promise in CMT. We aim to selectively measure periaxin in patients with clinical evidence of disease progression, where elevated levels may indicate active demyelination. Larger cohorts are being tested to assess the individual and combined contributions of all three biomarkers to clinical evaluation.
Disclosure: Nothing to disclose.

EPO-161 | Fluid biomarkers in chronic inflammatory neuropathies: comparative analysis and evaluation of diagnostic utility

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Background and aims: Objective, responsive biomarkers are required to assess disease progression and inform clinical trials in the inflammatory neuropathies. Peripherin and periaxin, biomarkers of peripheral axonal damage and demyelination, respectively, have recently been validated in Guillain-Barré syndrome (GBS) and chronic inflammatory demyelinating polyradiculoneuropathy (CIDP). Here, we evaluate their potential clinical utility in chronic immune-mediated neuropathies, alongside neurofilament light chain (NfL) and existing outcome measures.
Methods: Clinical data were retrospectively analysed. Peripherin and NfL were measured in samples from patients with multifocal motor neuropathy (MMN, n=11), POEMS syndrome (n=14), anti-MAG neuropathy (n=14), multiple sclerosis (MS, n=20), and healthy controls (HC, n=20).
Results: Peripherin levels were higher in MMN and POEMS compared to HC ($p=0.01$). NfL was higher in MMN vs HC ($p=0.0053$), and the peripherin/NfL ratio was higher in MMN compared to MS ($p=0.029$). In three POEMS patients with longitudinal data, peripherin closely mirrored VEGF levels over time.
Conclusion: Fluid biomarkers show potential in the inflammatory neuropathies. Work is underway to measure peripherin, periaxin, and NfL in larger, deeply phenotyped patient cohorts. We will compare MMN levels to lower motor neuron-predominant motor neurone disease, and evaluate correlation with paraprotein levels, antibody titres (GM1, GQ1b, MAG), VEGF, and existing outcome measures.
Disclosure: Nothing to disclose.

EPO-162 | Comprehensive evaluation of outcomes after nerve transfers for brachial plexus injuries

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Background and aims: Nerve transfers are a key surgical strategy for managing brachial plexus injuries (BPIs). This study provides a comprehensive assessment of their clinical, neurophysiological, and patient-reported outcomes.
Methods: We analyzed 34 nerve transfers in 21 patients treated over an 11-year period. Evaluations included muscle strength grading (MRC), functional capacity (Mallet scores), disability impact (DASH), and electrophysiological data to monitor synkinesis and voluntary activation. Additional metrics included pain levels and quality of life assessments.
Results: Of the nerve transfers, 58.8% achieved M3 or greater muscle strength, and 14.7% reached M4 or higher. Synkinesis-free recovery occurred in 29.4% of cases. A significant correlation was observed between early reinnervation (≤6 months) and better muscle strength ($Rs=0.528$). Patient-reported outcomes showed an inverse relationship between improved strength and disability ($Rs = -0.510$). Early surgical intervention emerged as the most critical factor for success.

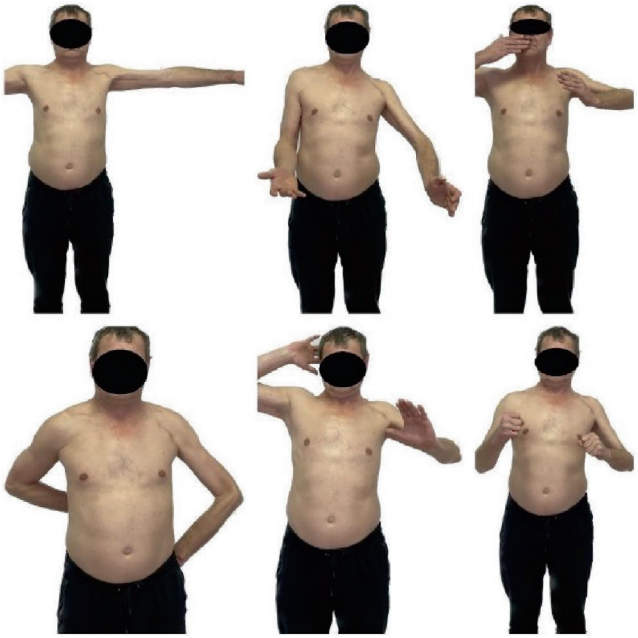

FIGURE 1 Mallet scale.

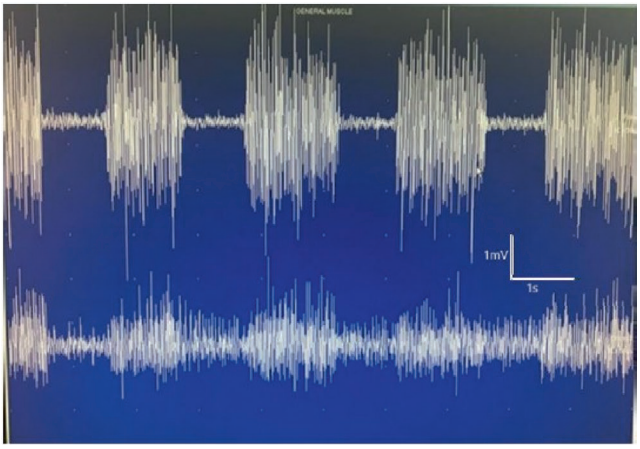

FIGURE 2 Early reinnervation changes in needle EMG.

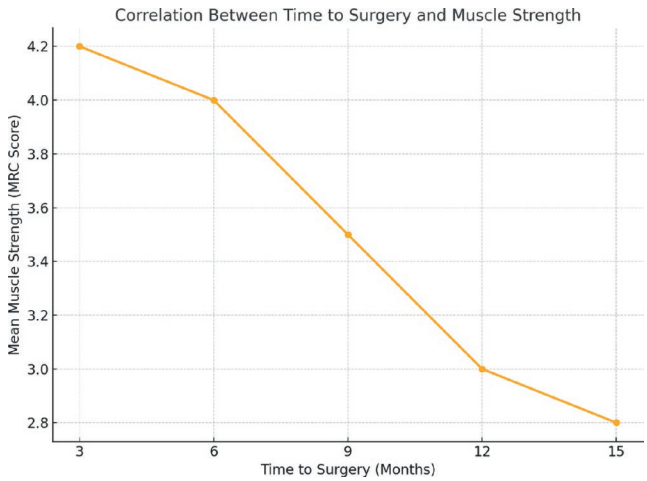

FIGURE 3 Correlation between muscle strength and time to surgery.

Conclusion: Nerve transfers significantly improve functional outcomes in BPI patients. Early intervention is essential for maximizing neuroplasticity and reducing long-term disability. This study highlights the multifactorial nature of recovery, emphasizing the need for personalized, multidisciplinary care approaches.
Disclosure: Nothing to disclose.

EPO-163 | Brachial neuritis in hepatitis E: Pleomorphic presentations in three cases

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Background and aims: Brachial neuritis (BN), also known as neuralgic amyotrophy, is a rare condition with an annual incidence of 1 in 1000. Its aetiology is multifactorial, often without specific risk factors. Hepatitis E virus (HEV) has been identified as a potential trigger, with immune-mediated mechanisms implicated in its pathophysiology.
Methods: We present three cases of HEV-associated BN, highlighting their clinical variability and outcomes.
Results: Case 1: A 54-year-old male presented with bilateral shoulder pain followed by profound bilateral upper limb weakness after acute HEV infection. ALT was >2000 U/L, and MRI revealed patchy denervation oedema in selected muscle groups, supported by EMG findings. Corticosteroid treatment led to partial recovery over one year. Case 2: A 65-year-old male developed acute interscapular pain followed by orthopnoea but no weakness. HEV serology was positive (mildly raised ALT). CXR showed bilateral raised hemidiaphragms. EMG revealed bi-diaphragmatic denervation (confirmed on videofluoroscopy). The patient remains on home non-invasive ventilation. Case 3: A 65-year-old female presented with bilateral sequential shoulder pain followed by right scapular winging and bilateral upper limb weakness. HEV serology was positive (raised ALT), MRI showed denervation oedema, but early EMG findings were normal. Corticosteroids resulted in gradual recovery.
Conclusion: These cases highlight the pleomorphic presentations of HEV-associated BN, ranging from diaphragmatic weakness to scapular winging or profound arm weakness, with variable recovery. Routine HEV testing is crucial in BN presentations. While corticosteroid therapy has been controversial, it has alleviated pain in these cases. Further research is needed to understand long-term outcomes.
Disclosure: All authors declare no conflicts of interest related to this study. This work was conducted independently and received no specific funding or sponsorship.

EPO-164 | Reactivity to HNK-1 glycans and complement activation in anti-MAG antibody-associated neuropathy

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Background and aims: Complement activation is hypothesized to play a significant role in the pathophysiology of anti-myelin-associated glycoprotein antibody-associated neuropathy (MAGN), but its exact contribution remains unclear. This study investigated the relationship between IgM antibody reactivity to human natural killer-1 (HNK-1) carbohydrate, complement activation, and disease severity in MAGN. The inhibitory effects of classical complement pathway inhibitors were also evaluated.
Methods: Serum samples from 43 patients with MAGN (median age: 69 years) and 33 patients with chronic inflammatory demyelinating polyneuropathy (CIDP) (median age: 71 years) were analyzed. IgM antibody reactivity and complement C3c deposition were quantified using biotinylated synthetic HNK-1 glycans immobilized on streptavidin-coated plates. Correlations with clinical parameters were assessed, and the inhibitory effects of C1 inhibitor, anti-C1q antibody, and C1s inhibitor were evaluated.
Results: All MAGN patient sera showed reactivity to HNK-1 carbohydrate, absent in CIDP sera. A strong correlation was identified between HNK-1 reactivity and complement C3c deposition ($rs = 0.66$, $p < 0.0001$), suggesting a role for complement activation in MAGN. Complement activation correlated with ataxia scores ($rs = 0.33$, $p = 0.02$) but not with other parameters. In vitro, complement activation was dose-dependently inhibited by C1 inhibitor, anti-C1q antibody, and C1s inhibitor.
Conclusion: The study highlights complement activation's potential role in MAGN pathophysiology and the utility of synthetic HNK-1 glycans for studying this mechanism. While complement inhibitors demonstrated in vitro efficacy, further preclinical and clinical studies are required to evaluate their therapeutic potential.
Disclosure: Nothing to disclose.

Sleep-wake Disorders

EPO-165 | A Fragile Slumber: Understanding sleep in long-COVID Syndrome: a cross-sectional study

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Background and aims: Approximately 25% of people with COVID-19 experience residual or new symptoms even one month after infection, while 10% continue to have symptoms after 12 months. These patients are often referred to as sufferers of Long-COVID syndrome (LCs), of whom a significant proportion experiences sleep-related disorders. Our aim was to establish the prevalence of sleep disorders in patients with LCs, and secondly to examine the associations of sleep quality with other parameters.
Methods: A cross-sectional study was performed in the outpatient clinic of the Neurology Clinic Nicosia General Hospital from September 2022 to April 2024. All patients met the WHO definition (2021) for LCs.
Results: The sample consisted of 39 women and 12 men (N=51, mean age: 54.1 years ± 11.9). The mean PSQI index score was 9.2 ± 5.3 (0-18), and 40 (78.4%) patients exhibited poor sleep quality. The PSQI score demonstrated a significant correlation with the following study parameters, in decreasing order: number of symptoms ($r=0.675$, $p<0.001$), fatigue ($r=0.604$, $p<0.001$), stress ($r=0.546$, $p<0.001$), anxiety ($r=0.523$, $p<0.001$) and depression ($r=0.521$, $p<0.001$). The multivariate analysis of associations of sleep quality revealed that the only statistically significant association of sleep quality was with fatigue ($b = 0.85 \pm 0.35$, $beta = 0.33$, $p = 0.02$).
Conclusion: A high proportion of patients diagnosed with LCs experience poor sleep quality. The analysis revealed that fatigue, the psychological state of patients, and the number of physical symptoms of LCs collectively accounted for up to 49.6% of the variability in the sleep quality index.
Disclosure: Nothing to disclose.

EPO-166 | Sleep microstructure: Cyclic alternating pattern analysis in patients with Parkinson's disease and cognitive impairment

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Background and aims: Sleep microstructure evaluates the subtle changes of graphoelements which constitute sleep electroencephalogram, specifically the cycling alternating pattern (CAP) considers the relationship between periodic activity (A-phases) and background rhythm (B-phases). CAP takes into account sequences of transient electrocortical events distinct from

background activity and recurring at up to 1 minute intervals. A-phases are part of an arousals hierarchy that arrange the sleeping brain to the flexibility around the referential state: the non-CAP slow wave sleep; establishing CAP as a marker of sleep instability and preservation. In people with neurodegenerative disorders, sleep macrostructure prevents to appraise the subtle variations of graphoelements, whereas different studies displayed a significant reduction of CAP indexes in Alzheimer's disease, REM sleep behaviour disorder and Parkinson's disease(PD). This study analyzes CAP in PD patients with cognitive impairment, evaluating the correlation with neurodegeneration progression.

Methods: 16 PD patients with mild cognitive impairment (PDMCI) and 16 with PD dementia (PDD), diagnosed according to Movement Disorder Society's clinical, cognitive and functional criteria, have been recruited. Patients underwent an in-lab full-night polysomnography for sleep macrostructure and microstructure scoring.

Results: REM sleep percentage (%TST_R), CAP-rate and A-phases indexes decreased in PDD patients, with mayor statistical significance for A3-phases and CAP-rate in N1-stage.

Conclusion: A logistic binomial regression model, combining %TST_R and CAP-rate_N1, has been used to predict accurately patients as PDMCI and PDD. Despite the small sample, sleep microstructure seems to add information about neurodegeneration progression in PD cognitive decline. CAP-rate could be an economical and non-invasive neurophysiologic marker of neurodegeneration.

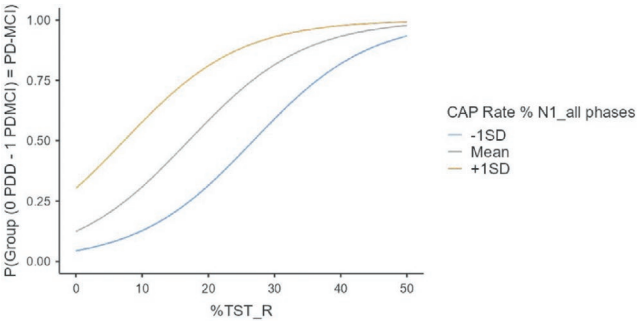

FIGURE 1 Curve estimated via binomial regression logit model. On the x-axis, the percentage of REM sleep, while the CAP-rate_N1 allows to find the best fit of the standard deviations. The dependent variable on the ordinate axis goes from PDD=0 to PDMCI=1.

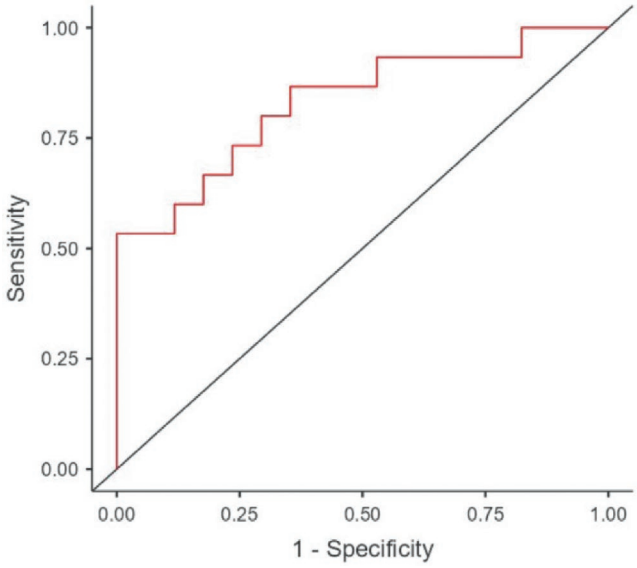

FIGURE 2 ROC curve of the prediction model.

Disclosure: Nothing to disclose.

EPO-167 | New associations between chronic insomnia and medication overuse headache (MOH)

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Background and aims: In our previous study we found that chronic insomnia was one of the most significant factors associated with medication overuse headache (MOH). This study aimed to analyze use of painkillers and clinical features of headaches in patients with MOH suffering from chronic insomnia compared with patients with MOH without insomnia in age- and gender-matched patient groups.

Methods: A prospective case-control study was done at the International Headache Center "Europe-Asia" between March 2021 and December 2023. The study included 171 patients with MOH (mean age 43.3 years, 81.9% women) and 173 patients without MOH (mean age 41.4 years, 74.6% women).

Results: Among patients with MOH, 103 patients (60.2%) had chronic insomnia (mean age 46.1, 86.1% females) and 68 patients (39.8%) did not suffer from insomnia (mean age 39.0, 84.2% females). NSAIDs were used by 85% of patients with MOH and chronic insomnia and 87% of patients with MOH without insomnia. We found for the first time that nocturnal headaches (74.8%, p=0.04, OR 2,0; 95% CI 1.01-3.8), use of analgesics at night (66%, p=0.005, OR 2.5, 95% CI 1.3-4.6) and taking ≥2 doses of painkillers per day (66%, p=0.008, OR 2,3; 95% CI 1,2-4,3) were significantly associated with chronic insomnia. Patients with chronic tension-type headache suffered from chronic insomnia more frequent (40.8%, p=0.03, OR 2.1; 95% CI 1.1-4.6).

Conclusion: Our findings stress the necessity of early treatment of chronic insomnia, early withdrawal of analgesics, especially with the tendency to their night use and night headaches.

Disclosure: Nothing to disclose.

EPO-168 | Sleep hygiene in epilepsy: Coffee-to-go or coffee-to-seize?

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Background and aims: Sleep and epilepsy share a well-established bidirectional relationship. Caffeine, as a stimulant, is one of the key points of sleep hygiene, having an impact on sleep structure. Sleep disruption may lead to poor control of seizures in adults with epilepsy (AWE). We aimed to identify the potential effects of caffeine on sleep and epilepsy parameters in AWE and its implications for disease management.
Methods: AWE from a tertiary sleep and epilepsy center were divided into two groups: Non-Coffee consumers (NCC), Coffee Consumers (CC). CC were divided into Non-late (NLCC) and Late Coffee (LCC) Consumers (after 17:00). Sleep quality and excessive daytime sleepiness were assessed using validated Armenian version of Pittsburgh Sleep Quality Index and Epworth Sleepiness Scale respectively. Mann-Whitney U and Chi-square tests were used for statistics.
Results: Sample: n=175, mean age 35.4±13.7(18-71), females-47.4%(83). Of them, 85.7%(150) were CC, with LCC comprising 65.1%(97) of the latter. The results of the performed analyses to see whether patients in CC group differ from those from NCC are presented in Tables 1 and 2. We found significant links to leg movement and periodic leg movement indices, and for arousal index. Finally, we found important association between higher seizure frequency and CC. Table 3 shows results for NLCC vs LCC.

Sleep Disorder/Parameter	Non-Coffee Consumers	Coffee Consumers	P
Insomnia (%)	34.8	48	**<0.05**
Excessive daytime sleepiness (%)	21.7	41.3	0.07
Snoring (%)	30.4	44.7	>0.05
Repetitive leg movements in sleep (%)	13	32.7	**<0.05**
Being on Antiseizure Medication (%)	72	74.7	>0.05
Poor sleep quality (by PSQI) (%)	63.6	62.3	>0.05
Restless legs syndrome (%)	8	22.7	0.07
Obstructive sleep apnea (%)	15.4	38.7	>0.05
Excessive daytime sleepiness (by ESS, score cutoff >10) (%)	26.1	16.4	>0.05
Periodic Leg Movements in Sleep (PLMI cutoff ≥ 15/h)	0	17.3	**<0.05**

PSQI - Pittsburgh Sleep Quality Index, ESS - Epworth Sleepiness Scale, PLMI – Periodic Leg Movements Index.

FIGURE 1 Chi squared analysis of caffeine consumers vs non-consumers in epilepsy patients.

Parameter	Non-Coffee Consumers	Coffee Consumers	P
Age	32.5	35.9	>0.05
Duration of epilepsy (years)	8.6	11.1	>0.05
Body Mass Index (kg/m^2)	23.9	24	>0.05
Average sleep duration (h)	8.7	7.4	**<0.01**
Yearly Seizure Frequency (n)	17	38.6	**<0.05**
Monthly Seizure Frequency (n)	2	4	**<0.05**
PSG parameters			
Total Sleep Time (mins)	402.4	436	>0.05
Oxygen Desaturation Index (/h)	5.4	7.6	>0.05
Apnea-Hypopnea Index (/h)	4.6	7.2	>0.05
NREM %	88.2	85.6	>0.05
REM %	11.8	13.95	>0.05
Leg Movement Index (/h)	4.3	13.9	**<0.01**
Periodic Leg Movement Index (/h)	0.3	6.3	**<0.01**
Arousal Index (/h)	18.2	27.2	**0.01**

NREM - Non-Rapid Eye Movement Sleep, REM - Rapid Eye Movement Sleep.

FIGURE 2 Comparison of means related to polysomnographic parameters and seizure frequency depending on coffee consumption.

Parameter	Non-Late Coffee Consumers	Late Coffee Consumers	P
Age	36.6	35.4	>0.05
Duration of epilepsy (years)	11.7	10.7	>0.05
Body Mass Index (kg/m^2)	23.7	24.1	>0.05
Average sleep duration (h)	6.9	7	>0.05
Yearly Seizure Frequency (n)	19.7	49.1	**<0.05**
Monthly Seizure Frequency (n)	2.2	5	**<0.05**
PSG parameters			
Total Sleep Time (mins)	429.9	439.4	>0.05
Oxygen Desaturation Index (/h)	6	8.5	>0.05
Apnea-Hypopnea Index (/h)	5.6	8	>0.05
NREM %	84.3	86.4	>0.05
REM %	14.9	13.4	>0.05
Leg Movement Index (/h)	11.7	15.1	**<0.05**
Periodic Leg Movement Index (/h)	5.3	6.9	**<0.05**
Arousal Index (/h)	26.8	27.4	>0.05

NREM- Non-Rapid Eye Movement Sleep, REM- Rapid Eye Movement Sleep.

FIGURE 3 Comparison of means for late coffee consumers in epilepsy.

Conclusion: Our results show that coffee may be a potential threat as an exacerbating factor for seizures in AWE, with evening consumption leading to worse outcomes. Sleep hygiene education is an important component of health management for epilepsy patients with impact on seizure frequency and sleep quality.
Disclosure: Nothing to disclose.

EPO-169 | Screening of sleep-wake disturbances in acute ischemic stroke: The bernese sleep health questionnaire

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Background and aims: Sleep-wake disturbances (SWD) are common in ischemic stroke and often persist, worsening outcomes when multiple SWD co-occur. However, comprehensive SWD screening in acute stroke is often time-consuming and impractical. This study assessed SWD prevalence in acute ischemic stroke patients using the new Bernese Sleep Health Questionnaire (BSHQ).
Methods: We enrolled all patients with acute ischemic stroke from the monocentric observational Risk of Atrial Fibrillation In Stroke patients with Sleep disordered breathing study, who completed the BSHQ between July 2022 and November 2024. The BSHQ, a 16-item self-reported questionnaire designed to screen for a wide range of SWDs, was administered to clinically stable patients within 72 hours of stroke onset at the Stroke Unit of the University Hospital Bern (Inselspital). The BSHQ assesses symptoms related to sleep-disordered breathing (SDB), insomnia, excessive daytime sleepiness (EDS), fatigue, restless legs syndrome (RLS), and parasomnias.
Results: A total of 369 patients (146 women, 39.6%; mean age: 69.8 years) completed the BSHQ. An elevated risk for SDB, according to a NoSAS-Score of ≥8, was found in 66.7%. Insomnia

symptoms were reported by 15.4% at least three times per week, while 8.7% experienced RLS symptoms at least once weekly. EDS and fatigue symptoms (≥1x/week) were present in 30.6% and 35.8% of patients, respectively. Signs of parasomnias (≥1x/week) were identified in 4.3% of patients.

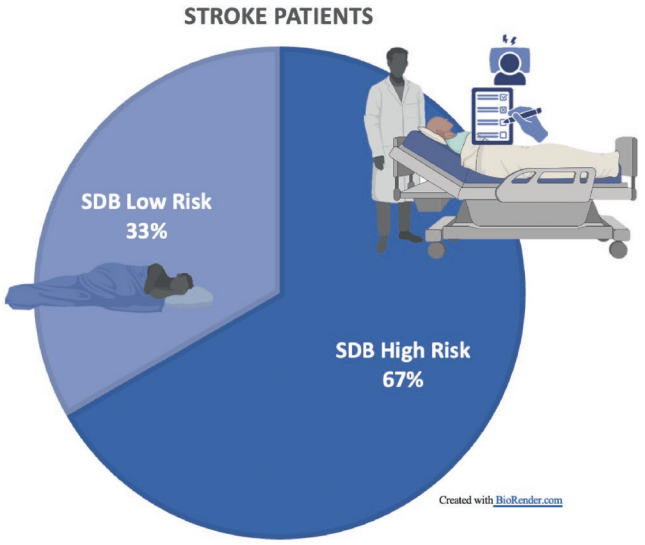

FIGURE 1 An elevated risk for SDB, according to a NoSAS-Score of ≥8, was found in 66.7% of patients.

Conclusion: The BSHQ revealed high rates of SWD in acute ischemic stroke patients, aligning with prior evidence. The BSHQ may serve as an effective screening tool for SWD in stroke patients, further validation studies are ongoing.
Disclosure: Nothing to disclose.

EPO-170 | Stress in adult DoA: A web-based survey

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Background and aims: Disorders of Arousal (DoA) are NREM parasomnias, encompassing three main clinical entities: sleepwalking (SW), confusional arousals (CA), and sleep terrors (ST). Clinical evidence suggests a bidirectional relationship between stress and DoA, wherein stress exacerbates parasomnia episodes, and the episodes themselves may contribute to psychological stress, impacting quality of life. The aim of our study was to evaluate the prevalence of these three DoA entities and their relationship with subjective perception of distress within a university population.
Methods: A web-based survey was conducted among students aged 18 to 35 at Bicocca University of Milan between May and June 2023. The survey collected data on sociodemographic characteristics and lifestyle habits, along with responses to two validated Italian questionnaires: the Arousal Disorder Questionnaire (ADQ), used to assess the occurrence of DoA (1), and the General Health Questionnaire (GHQ-12), a widely utilized tool for measuring current psychological distress (2).
Results: A total of 1,039 students completed the survey (259 males, 780 females), with a median age of 23.0years (IQR: 21.0–25.0). The prevalence of SW, ST, and CA was 2.7%, 3.0%, and 5.9%, respectively. The overall GHQ score was 6.0 (IQR: 5.0 - 8.0). Comparing subjects with or without DoA, perceived distress was significantly higher in individuals with ST (p=0.0359) and CA (p=0.0034), whereas no significant differences were observed for SW.
Conclusion: These findings align with prevalence rates reported in broader adult populations and confirm an association between DoA and stress, claiming for new targeted therapeutic strategies.
Disclosure: Nothing to disclose.

EPO-171 | ECS improves depression and sleep regulation through modulation of the microbial-gut-brain axis

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Background and aims: Electroconvulsive therapy (ECT) has shown potential to alleviate depressive symptoms, but its impact on the gut-brain axis and microbiome is underexplored. This study investigates how ECT regulates depressive behaviors and the composition of the gut microbiota via the microbiota-gut-brain axis.
Methods: Chronic Unpredictable Mild Stress (CUMS) was used to induce depression in rats, which were divided into control, depression, and ECT treatment groups. Depressive behaviors were assessed by body weight, the open field test, sugar and water consumption, and the forced swimming test. Brain and intestinal histology, microcirculatory blood flow, and inflammatory factors (TNFα, IL1β, IL6) in intestinal tissues were measured by HE staining, immunofluorescence, and ELISA. Intestinal microbiota composition was analyzed via metagenomic sequencing. ANOVA and Kruskal-Wallis tests were used for data analysis (P<0.05 considered significant).
Results: ECT treatment significantly improved depressive behaviors (P<0.01), reducing immobility time in the forced swimming and hanging tail tests (P<0.05). Histology revealed reduced intestinal inflammation (P<0.05), and immunofluorescence showed increased c-Fos expression (P<0.05). ECT also significantly decreased TNFα, IL1β, and IL6 levels (P<0.01). Metagenomic sequencing revealed increased intestinal microbiota diversity, with a significant restoration of Bacteroidota and Verrucomicrobiota abundance (P<0.05).

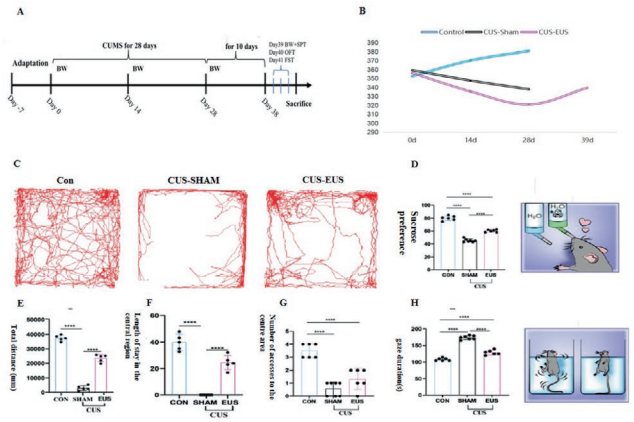

FIGURE 1

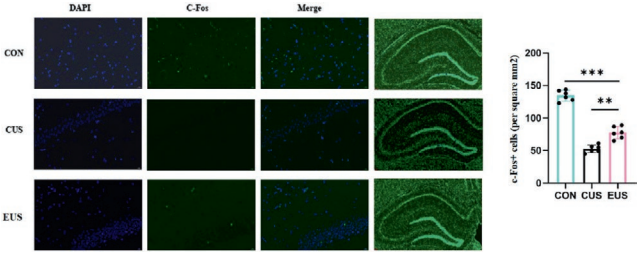

FIGURE 2

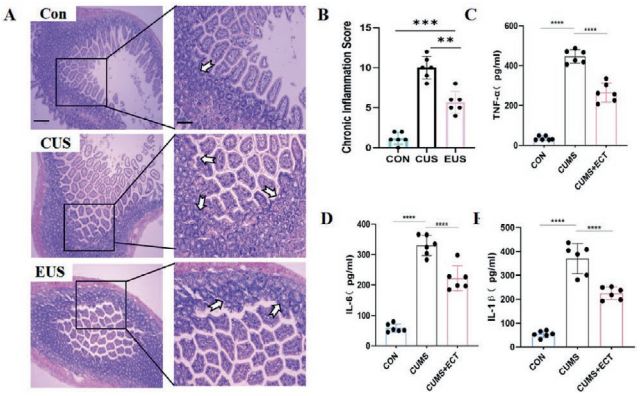

FIGURE 3

Conclusion: ECT alleviates depressive symptoms and improves sleep quality by regulating the gut microbiota and enhancing the function of the brain-gut axis.
Disclosure: Nothing to disclose.

EPO-172 | Sleep in functional motor disorders: A case-control polysomnographic study

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Background and aims: Sleep problems are frequent in functional motor disorders (FMD). Surprisingly, objective correlates of impaired sleep and its relationship to other comorbidities have been understudied, and no polysomnographic study is available. We aimed to map the polysomnographic parameters in the context of self-reported sleep and mood symptoms and search for comorbid sleep disorders in FMD and healthy controls.
Methods: Thirty-seven patients (mean age (SD), 48.2(10.6) years) with clinically definite FMD and 37 controls (48.6(11.2) years) underwent structured medical and sleep history assessment, neurological examination, and polysomnography and completed questionnaires for sleep quality, sleepiness, depression, and anxiety.
Results: In FMD, specific sleep disorders were identified in our cohort, with 32% having restless legs syndrome, 38% clinically significant obstructive sleep apnea, and 8% periodic limb movements in sleep. FMD patients reported worse sleep quality ($p<0.001$), higher sleepiness ($p<0.001$), depression ($p<0.001$), and anxiety ($p<0.001$), and had longer REM sleep latencies ($p<0.001$). Furthermore, statistical trends for longer sleep latencies ($p=0.030$), worse sleep efficiency ($p=0.012$), and higher wake and REM sleep ratios ($p=0.013$, resp. $p=0.027$) were found in FMD. In FMD, subjective sleep quality positively correlated with depression (rho=0.54; $p<0.002$) and anxiety (rho=0.61; $p<0.001$), and subjective sleepiness correlated with depression (rho=0.42; $p=0.010$). Self-reported measures did not correlate with any polysomnographic parameters.
Conclusion: Polysomnography detected sleep structure changes in FMD. Sleep abnormalities, including impairments in REM sleep, should be considered in the management of FMD. Future studies should further explore the role of REM sleep disturbances in the pathophysiology of FMD.
Disclosure: This work was supported by the Czech Ministry of Health Project AZV NU20-04-0332, the project National Institute for Neurological Research (Programme EXCELES, ID Project No. LX22NPO5107) – Funded by the European Union – Next Generation EU; Charles University: Cooperation Program in Neuroscience; General University Hospital in Prague and Ministry of Health of the Czech Republic project MH CZ-DRO-VFN64165. Nothing to disclose.

EPO-174 | Impulsivity and impulse control disorders in restless legs syndrome

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Background and aims: This study aims to examine impulsivity and prevalence of Impulse Control Disorders (ICDs) in patients with Restless Legs Syndrome (RLS), while also exploring differences in impulsivity subtypes independent of ICD presence.
Methods: A total of 19 RLS patients and 19 controls were enrolled in the study. The frequency and severity of ICDs were assessed using the modified Minnesota Impulsive Disorders Interview (mMIDI), while disease severity was measured with the International Restless Legs Syndrome Study Group Rating Scale (IRLSRS). Impulsivity was evaluated using the Barratt Impulsiveness Scale-11 (BIS-11) and the Go/NoGo task, which assess attentional and motor impulsivity.
Results: The results revealed a higher prevalence of ICDs among RLS/WED patients. Notably, compulsive eating disorder was observed in 45% of RLS patients, compared to just 5% in the control group ($p=0.005$). All patients with ICDs were receiving dopaminergic treatment, suggesting a potential link between DA therapy and ICD development. Furthermore, RLS patients exhibited significantly higher attentional impulsivity than controls ($p=0.047$), which correlated with symptom severity ($r=0.574$, $p<0.001$). However, no significant differences were found in motor impulsivity.
Conclusion: RLS patients exhibited heightened attentional impulsivity, which correlated with symptom severity, while motor impulsivity remained unaffected. Additionally, compulsive eating disorder emerged as a significant concern among RLS patients. Notably, all RLS patients with ICDs were undergoing dopaminergic treatment, highlighting the need for further research to explore this association and its potential connection to attentional impulsivity.
Disclosure: Nothing to disclose.

EPO-175 | iSPHYNCS: The internationalization and new approaches of the swiss primary hypersomnolence and narcolepsy cohort study

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Background and aims: The international Swiss Primary Hypersomnolence and Narcolepsy Cohort Study (iSPHYNCS) aims to provide new data to improve diagnostics and the management of primary central disorders of hypersomnolence (CDH). The three main specific aims of iSPHYNCS are 1) discovery of new biomarkers, 2) assessment of treatment adherence, and 3) patient-related outcomes, to set the ground for personalized patient treatment.
Methods: The study is ongoing at 10 study sites in Switzerland, Germany, the Netherlands and Italy, and plans to prospectively include 500 CDH patients and 60 healthy controls (HC) by the end of 2026. The multi-modal approach includes questionnaires, clinical assessments, video-polysomnography, the Multiple Sleep Latency Test (MSLT), vigilance tests, actigraphy, long-term activity monitoring with Fitbit, immunological studies, quantitative hypocretin measurements, proteomics, gut microbiomics, and genetics/epigenetics. AI-powered analyses, including unsupervised clustering, are used for data-driven patient phenotyping.
Results: 281 participants, including 10 children, have been recruited. The study population comprises 71 individuals with narcolepsy type I (NT1), 171 individuals of the "narcoleptic borderland" (NBL), such as narcolepsy type 2, idiopathic hypersomnia and insufficient sleep syndrome, as well as 39 HC. Initial analyses reveal notable differences among NT1, NBL, and HC groups across various domains, including questionnaire

responses, neuropsychiatric profiles, gut microbiome, polysomnographic, Fitbit and vigilance data.

TABLE 1 Description of the iSPHYNCS Population.

Characteristic	Overall, N = 281[1]	Healthy controls, N = 39[1]	Narcolepsy Type 1, N = 71[1]	Narcolepsy borderland, N = 171[1]	p-value[2]
Age	26 (21, 33)	30 (24, 34)	25 (20, 33)	25 (21, 33)	0.14
Gender (Female)	68 %	59 %	62 %	73 %	0.10
BMI	23.6 (21.1, 27.2)	22.7 (21.2, 25.8)	23.8 (21.9, 28.7)	23.7 (20.7, 27.2)	0.14
HLA positive	39 %	16 %	98 %	23 %	<0.001
Hypocretin < 110	38 %	NA	95 %	0 %	<0.001
ESS	14 (10, 17)	4 (2, 5)	16 (14, 19)	14 (12, 17)	<0.001
FSS	4.8 (3.3, 5.9)	1.8 (1.5, 2.1)	5.0 (3.4, 5.8)	5.4 (4.3, 6.2)	<0.001
SNS	24 (4, 36)	25 (21, 34)	-27 (-53, -6)	32 (22, 39)	<0.001
Cataplexy-like events	27 %	0 %	91 %	6.0 %	<0.001
Disturbed nighttime sleep	35 %	5.4 %	59 %	32 %	<0.001
Sleep drunkenness	52 %	14 %	38 %	67 %	<0.001
Sleep duration weekdays	7.8 (7.0, 8.5)	7.0 (7.0, 7.5)	7.5 (6.5, 8.0)	8.0 (7.0, 9.0)	<0.001
Sleep duration weekends	9.0 (8.0, 10.0)	8.0 (7.5, 8.5)	8.5 (7.5, 10.0)	9.5 (8.5, 11.0)	<0.001
Delay of diagnosis (years)	6 (4, 11)	NA (NA, NA)	7 (5, 12)	6 (3, 10)	0.026

[1] Median (IQR); %

[2] Kruskal-Wallis rank sum test; Pearson's Chi-squared test; Fisher's exact test

Conclusion: Following an initial three-year phase in Switzerland, the internationalization of iSPHYNCS was successfully launched in 2023. Preliminary results suggest novel and promising clinical, biological, and digital markers of CDH. Proteomics and genetics/epigenetics analyses are currently being explored.

Disclosure: The authors declare no conflict of interest. The study is supported by the Swiss National Science Foundation (SNF 320030_185362; SNF 32003B_215721).

EPO-176 | Diencephalic–mesencephalic junction dysplasia, a congenital malformation that may cause hypersomnolence: a case report

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Background and aims: Diencephalic-mesencephalic junction dysplasia (DMJD) is a rare, congenital malformation. It leads to caudal expansion of the diencephalon and a short-thick midbrain. Few cases of DMJD have been described in adults. We present a case of type B DMJD in a patient with hypersomnia and explore the potential causal relationship between both.

Methods: A 48-year-old male with a history of hypersomnolence for at least 8 years, which led to two traffic accidents. Initially his hypersomnolence was interpreted due to OSAS and morbidly obesity. Despite treatment with CPAP and bariatric surgery he continued to experience somnolence. A multiple sleep latency test (MSLT) showed daytime hypersomnolence without SOREMs. He had an HLA haplotype of HLA-DRB115, DQA01:02, DQB1*06:02 and normal cerebrospinal fluid hypocretin levels. Brain MRI revealed type B DMJD with the characteristic butterfly sign.

Results: Only three adult cases of type B DMJD are reported in the literature. One patient clinically presented with frontotemporal dementia (FTD) another with involuntary movements and the third patient had headaches. Among the secondary causes of daytime hypersomnolence, structural lesions affecting the hypothalamus-mesencephalon have been reported. After excluding other causes of hypersomnolence, and considering that this patient presents hypersomnolence associated with obesity we hypothesize that DMJD may be the cause of the patient's clinical presentation.

Conclusion: We highlight the importance of considering structural causes in patients with hypersomnolance and we present the first case reported in the literature of DMJD associated with hypersomnolence. Further studies are needed to establish a clearer association between both.

Disclosure: Nothing to disclose.

EPO-177 | Clinical decision support systems for oxygen-enriched PAP therapy in obstructive sleep Apnea

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Background and aims: Obstructive Sleep Apnea (OSA) treatment often uses positive airway pressure (PAP) devices, but manual titration poses challenges like patient discomfort and inaccurate SpO2 monitoring. This study evaluates a Clinical Decision Support System (CDSS) with Markov decision processes (MDP) to enhance PAP and oxygen titration, focusing on oxygenation and pCO2 control.

Methods: A single-center observational study included 14 adults (mean age: 63±8 years, BMI: 41±8 kg/m^2) with OSA-induced hypoxemia. PAP titration was guided by SpO2 and pCO2 metrics during a one-night protocol. Manual CPAP/BiPAP adjustments and oxygen supplementation were used to optimize SpO2 (>89%) and reduce apnea events. A paired t-test assessed changes in AHI and SpO2, while Pearson correlation coefficients evaluated the relationship between pCO2 and IPAP during BiPAP therapy. MDPs modeled treatment state transitions to predict optimal adjustments.

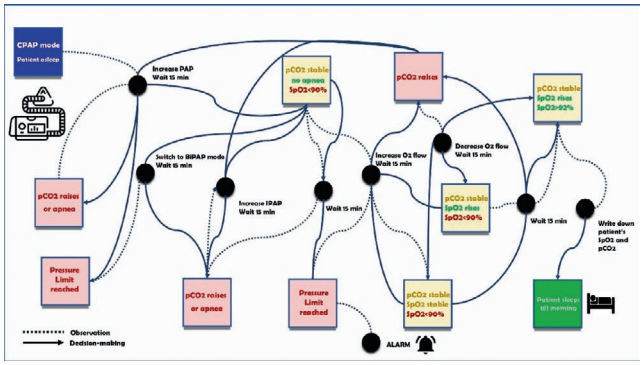

FIGURE 1 Expert knowledge-based clinical decision support framework for PAP and oxygen titration using Markov decision processes.

Results: The intervention significantly reduced the AHI (mean of delta AHI 48.9±31.9 events/hour ($p<0.0001$). Mean SpO2 increased by 9%±6.0% ($p<0.0003$). Transitioning from CPAP to

BiPAP (N = 7) significantly reduced pCO2 ($p<0.05$ for each intervention) in 5 patients, with a strong negative correlation to increased IPAP (mean correlation coefficient: -0.71±0.06). Markov model simulations supported effective decision-making in oxygen titration and demonstrated stable patient respiratory states.

Patient	Initial Hypercapnia	SpO_2 >88%		Pearson Correlation Coefficient for pCO_2			
		Before	After	CPAP (PAP)	p value	BiPAP (IPAP)	p value
1	<55 mmHg	No	Yes	0.79	<0.0001	-0.69	0.001
2	>55 mmHg	Yes	Yes	0.2	0.56	-0.6	0.007
3	>55 mmHg	No	No	0.4	0.04	-0.63	0.09
4	<55 mmHg	No	Yes	0.65	0.0006	-0.78	<0.0001
5	>55 mmHg	No	No	0.19	0.34	-0.72	0.04
6	<55 mmHg	No	No	0.79	0.007	0.33	0.67
7	<55 mmHg	No	Yes	0.27	0.33	-0.77	0.006

FIGURE 2 Pearson correlation coefficients of pCO2 comparing the PAP modes.

Conclusion: The integration of MDPs into CDSS frameworks for PAP and oxygen titration has shown potential for improving OSA treatment outcomes. By facilitating precise adjustments to therapy, the system enhances SpO2 levels and reduces AHI, particularly in hypercapnic patients. Future work should focus on refining algorithms with larger datasets to achieve personalized respiratory care.
Disclosure: Nothing to disclose.

EPO-178 | Brief intervention to discontinue inappropriate z-hypnotic use among older adults: A randomised controlled trial

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Background and aims: Recommendation from healthcare guidelines suggest avoiding long-term use of z-hypnotics in older adults. Yet, inappropriate use (prolonged use at high doses) is common. We tested a brief intervention (BI) for discontinuing inappropriate z-hypnotics use in older adults.
Methods: Triple-blind two-arm randomised controlled trial comparing BI conducted by trained GPs to business-as-usual (BAU) at baseline and six-week follow-up. Intention-to-treat (ITT) and per-protocol (PP) analyses were performed, employing t-test/Fisher's exact test. The pre-defined primary outcome was the proportion of participants without inappropriate z-hypnotic use (≥four weeks, ≥three times per week). Secondary outcomes included sleep complaints, pain levels, and cognition.
Results: Both study arms reduced inappropriate use and improved usage pattern (figure). No difference was found in the ITT analysis of BI and BAU at six-week follow-up (Fisher's exact test p-value = 0.51, proportions no inappropriate use BAU = 71% and BI = 57%). There were no significant differences between the BI and BAU groups in cognitive function (BI: mean = 18.12, SD = 2.15; BAU: mean = 17.61, SD = 2.89; t(31.3) = 0.59, p = 0.56), global sleep assessment (BI: mean = 6.90, SD = 3.40; BAU: mean = 7.56, SD = 4.19; t(28.458) = 0.51, p = 0.61), or pain levels (BI: mean = 1.67, SD = 1.96; BAU: mean = 1.75, SD = 2.05; t(31.64) = 0.12, p = 0.90). The PP analysis showed similar results.

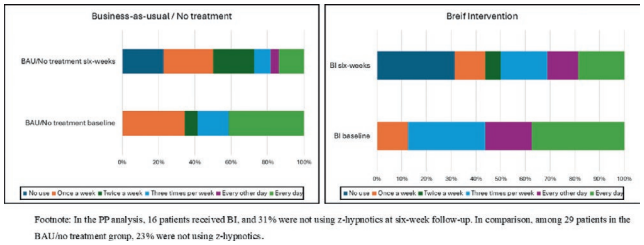

FIGURE 1 Z- hypnotics frequency use in BI and BAU/no treatment group (per protocol analysis).

Conclusion: Although many patients reduced their use of z-hypnotics, there was no significant difference in inappropriate use between the BI and BAU groups.
Disclosure: Disclosure: CL has participated on an advisory board and received payment for lectures arranged by Abbvie Pharma AS, Novartis AS, and Roche AS, Norway. He has also received research sponsorship from Abbvie pharma. All other authors declare that they have no conflicts of interest. CT registration: NCT06032715 (registered 17th Aug 2023).

EPO-179 | Efficacy and safety of daridorexant in women with insomnia disorder during menopausal transition: A subgroup analysis

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Background and aims: Insomnia is common, burdensome, and under-researched in women undergoing the menopausal transition. This is the first evaluation of the efficacy and safety of daridorexant (a novel insomnia treatment), specifically in an age group representative of the menopausal transition, enrolled in the phase 3 study NCT03545191.
Methods: In this randomized, double-blind study, 930 patients with insomnia disorder received daridorexant 25 mg, 50 mg or placebo for 3 months. Subgroup analyses were performed among the 117 women aged 47-55 years (25 mg n=43; 50 mg n=35; placebo n=39). Efficacy endpoints included change from

baseline in polysomnography-measured wake after sleep onset (WASO) and latency to persistent sleep (LPS), self-reported total sleep time (sTST) and insomnia-related daytime impairment (Insomnia Daytime Symptoms and Impacts Questionnaire [IDSIQ]).

Results: At Month 3, daridorexant 50 mg vs placebo decreased WASO and LPS by a least-squares mean (LSM) of 13.8 min (95% CI -29.0, 1.4) and 14.7 min (-30.0, 0.6) respectively, increased sTST by a LSM of 21.8 min (-3.9, 47.4) and decreased (improved) IDSIQ total score by an LSM of -4.1 (-14.4, 6.3) (Figure). These results were generally consistent with those of the overall study population. The incidence of somnolence/fatigue was low in both daridorexant groups and comparable to placebo. Comparable improvements in morning sleepiness (visual analogue scale score) were observed across groups.

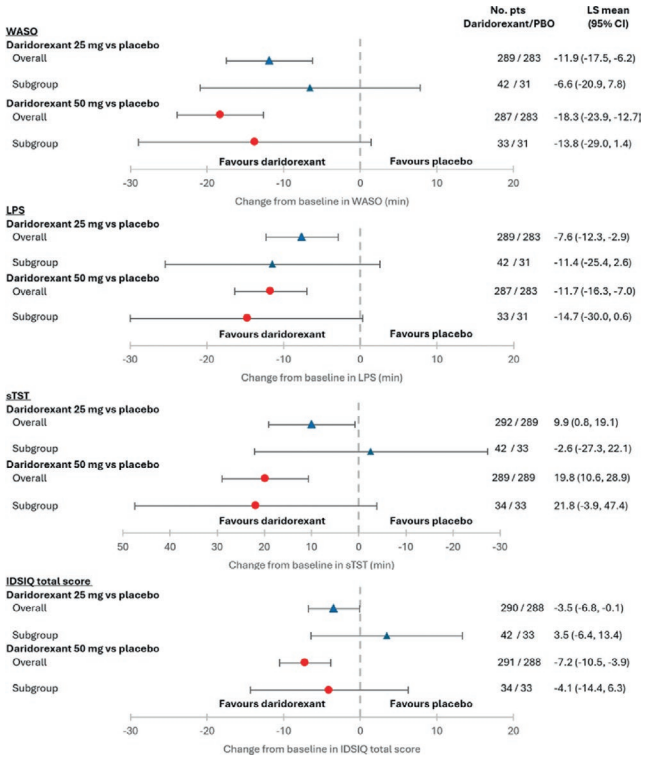

FIGURE 1 Change from baseline to Month 3 in efficacy endpoints.

Conclusion: These post-hoc exploratory analyses suggest that daridorexant 50 mg improves sleep outcomes and daytime functioning and is well tolerated in women aged 47-55 years with insomnia disorder.

Disclosure: Schaedel Z has received speaker and advisory fees from Theramex, Besins, Idorsia, Astellas and Bayer. Bassetti C served as consultant for IDORSIA 2017-2023. Bertisch SM has received consulting fees from Idorsia and Elemind. Cassel P has received honoraria for consultations and presentations and travel expense compensations from Idorsia, Dr. Pfleger Arzneimittel GmbH and from mementor Deutschland GmbH. Palacios S has no conflicts of interest to disclose. Palmay C has received speaking and moderating engagements/ Honoraria from Pfizer, Merck, Allergan, Bayer, GSK, Galderma, Valeant, Lundbeck, AZ, Bausch Health, Lundbeck, Sunovion, Nuvopharm, Novartis, Lupin, Abbvie, Aspen, Moderna, Sunpharma, Searchlight, Moderna, Sanofi, Seqirus, Idorsia. She has received consulting fees from Dr. Ho Medical, MDBriefcase, The Rounds, Eisai, Sunovion, CCRN. PeerVoice, CCRN Board Director, CTC, Abbvie. She has contributed to Lawrence Park Magazine, CTC Primary Care Podcast, Co-editor Primary Care Updates. Silvestri R has received honoraria for consultancies and presentations from Idorsia. Stute P has no conflicts of interest to disclose. Trémollieres F has received expert and/or conference fees from Astellas, Bayer, Besins Healthcare France and Theramex. Bakker T, Briasoulis O, Pain S are employees of Idorsia Pharmaceuticals Ltd.

Sunday, June 22 2025

Ageing and Dementia 1

EPO-180 | CSF synaptic biomarkers negatively correlate with disease duration: New insights into Alzheimer's disease synaptopathy

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Background and aims: Synaptic dysfunction is an early event in Alzheimer's disease (AD). This study explores the relationship between cerebrospinal fluid (CSF) synaptic biomarkers (neurogranin, SNAP-25, and CAP2) and biomarkers of neurodegeneration, glial cell activation, and inflammation in vivo.

Methods: We selected 60 AD patients based on an A+T+N+ CSF biomarker profile. We analyzed demographic variables, cognitive status (MMSE score), disease duration, and CSF biomarkers levels using SIMOA, Luminex, and standard ELISA in AD patients and 40 age- and sex-matched controls (HC). Correlations were assessed through Spearman's partial correlation, adjusting for age and sex. Network analysis, collinearity diagnostic measures and backward multivariable linear regression were performed.

Results: AD patients exhibited significantly higher CSF levels of synaptic ($p<0.001$) and inflammatory markers ($p<0.01$) compared to HC. CAP2 showed the strongest positive correlation with inflammatory and neurodegeneration markers, but no correlation with biomarkers of amyloidosis. All synaptic biomarkers negatively correlated with disease duration, with CAP2 being the most negatively correlated. Network analysis revealed different relationships between synaptic, neuronal, glial, and inflammatory markers, with neurogranin being the most related to mild inflammatory changes.

Conclusion: Higher CSF synaptic and inflammatory biomarkers suggest a compensatory synaptic response to initial AD

pathology and its link to inflammatory alterations. The negative correlation with disease duration indicates that AD progression sees these compensatory mechanisms overwhelmed, lowering CSF synaptic biomarkers levels. The lack of correlation with amyloidosis biomarkers suggests that synaptopathy is less driven by beta-amyloid accumulation. These findings support the potential of a CSF synaptic biomarker panel for AD staging.
Disclosure: Nothing to disclose.

EPO-181 | Comparative analysis of serum NfL measurements: Agreement between SiMoA and ella platforms in ATTR polyneuropathy

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Background and aims: Neurofilament light chains (NfL) are neuron-axonal proteins whose serum concentrations serve as biomarkers for neurological diseases. Due to their low serum levels, precise detection methods are critical. This study aimed to scrutinize the comparability of two techniques: Single Molecule Assay (SiMoA) and Ella automated immunoassay, analyzing serum NfL levels in ATTR polyneuropathy patients and carriers.
Methods: A cohort of 55 ATTRv patients and 55 carriers were recruited. We compared the two detection methods using Bland–Altman plots and Passing-Bablock regression.
Results: The mean age of participants was 60 years (25-75th percentile 47-72), with 41 females. The median serum NfL concentration measured by Ella (28.4 pg/mL, 25-75th percentile 9.6-69.8) was significantly higher ($p < 0.001$) than that measured by SiMoA (8.9 pg/mL, 25-75th percentile 5.7-17.2). The Spearman correlation showed a strong positive correlation ($r = 0.8$, $p < 0.001$) between the results of the two methods. The t-value was 5.2 and $p < 0.001$. Bland-Altman analysis showed a mean bias of 15.5 pg/mL (LOA: -41.1 pg/mL to 72.0 pg/mL), indicating that Ella overestimated values by 15%. Passing-Bablock regression showed a linear relationship between the two datasets ($p = 0.44$) and a slope of 1.72, confirming that Ella measurements were generally higher.

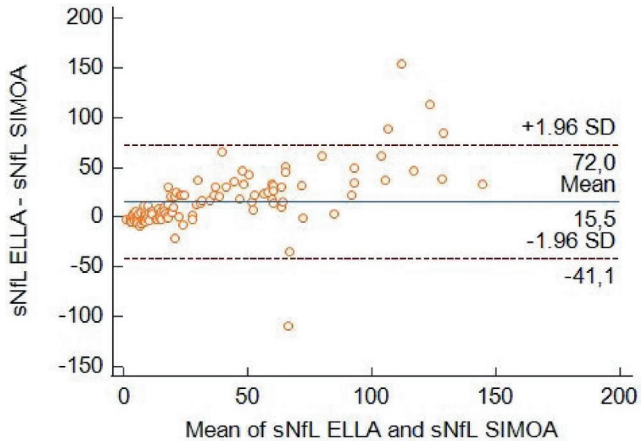

FIGURE 1 The Bland-Altman plot shows the differences between the two methods, with the median line representing the mean difference and the limits of agreement (+/- 1.96 SD) marking where 95% of differences fall. Random variation and no trends suggest potential ag.

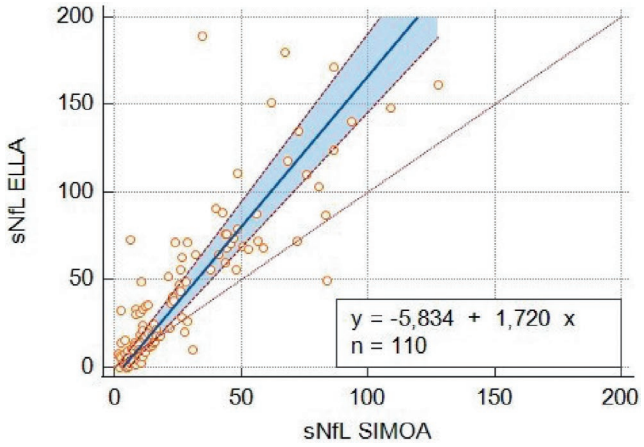

FIGURE 2 The Passing-Bablok regression plot shows a linear relationship between the two datasets, suggesting no significant proportional bias. The regression slope of 1.72 indicates that Ella measurements are generally higher than those with SIMOA.

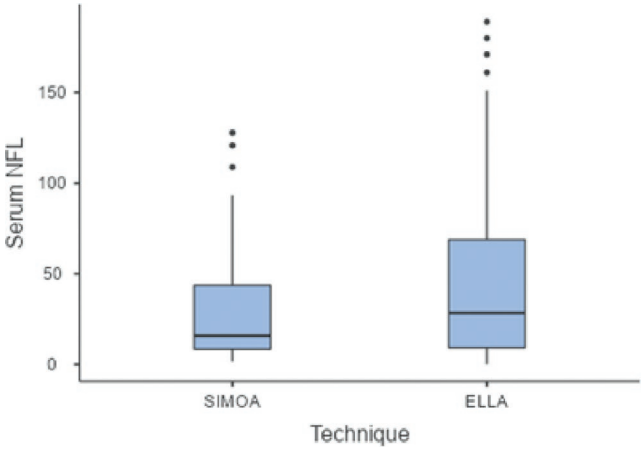

FIGURE 3 The Paired T-test plot shows a statistically significant difference between the means of the two measurement methods, considering the data variability.

Conclusion: Our findings underscore that both platforms are effective in measuring serum NfL, but Ella consistently yields higher values, especially at higher concentrations. Future studies should focus on standardizing conversion factors to reconcile discrepancies between the two methods.
Disclosure: Nothing to disclose.

EPO-182 | Serotonergic receptor maps overlap with cortical metabolism changes and CSF NPTX2 in prodromal Alzheimer's disease

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Background and aims: Alzheimer's disease (AD) is characterized by progressive cognitive decline, often beginning with Mild Cognitive Impairment (MCI). Early molecular changes and neurodegeneration interact with diffuse projection systems, including dopaminergic, noradrenergic, and serotonergic pathways. Understanding these interactions may enhance knowledge of the disease pathology.
Methods: This study assessed baseline [18F]FDG-PET metabolism and its relationship with monoaminergic receptor maps and cerebrospinal fluid (CSF) biomarkers in 49 MCI-AD patients. We compared [18F]FDG-PET scans to 40 matched healthy controls, analyzing spatial correlations between hypometabolism and neurotransmitter receptor/transporter distributions. Fisher's Z-transformed correlations were used in linear models with distinct CSF biomarkers associated with AD pathology (Aβ42/Aβ40, pTau181, t-Tau, NPTX2, neurogranin), and NFL, controlling for demographic and cognitive variables.
Results: Patients exhibited significant hypometabolism in bilateral temporo-parietal regions. Negative correlations emerged between hypometabolism and receptor distributions for 5-HT1A ($r=-0.36$, $p<0.001$), D1 ($r=-0.15$, $p=0.03$), and mGluR5 ($r=-0.14$, $p=0.02$), indicating that reduced glucose uptake in MCI-AD was strongest in areas with normally high receptor densities. This suggests that these regions, which typically have abundant receptors, are particularly affected by metabolic decline. CSF NPTX2 levels correlated with the co-localization of hypometabolism and 5-HT1A ($\beta=0.003$, $p=0.038$) with no significant associations for other CSF markers.
Conclusion: Our findings highlight the role of synaptic dysfunction in AD progression, particularly affecting serotonergic cortical targets while relatively sparing noradrenergic pathways. CSF NPTX2 may serve as a biomarker for disease staging and monoaminergic vulnerability. Further research into synaptopathy and projection system deterioration may enhance understanding of early AD pathology.
Disclosure: Nothing to disclose.

EPO-183 | Improving MRI-based ML models predicting AD progression in SCD patients with segmentation of early-affected structures

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Background and aims: Alzheimer's disease (AD) is a devastating neurodegenerative disorder with increasing prevalence worldwide. Anti-amyloid therapies should be administered early, before disabling symptoms develop. Therefore, concept of subjective cognitive decline (SCD) was developed. MRI-based evaluation of neurodegeneration holds promise for predicting clinical progression, but subtle early changes and the number of brain regions assessed necessitate multivariate analysis, such as machine learning (ML) methods. In this study, we aimed to compare performance of models based on standard segmentation (FreeSurfer 6.0) and on adding detailed segmentation of structures affected early in AD - basal forebrain nuclei and medial temporal lobe subfields, obtained using in-house segmentation pipeline.
Methods: Using data from Czech Brain Aging Study (n=93), we trained random forest regressor models on two datasets, using SCD data only: "standard model" using volumetric MRI features (FreeSurfer 6.0) and an "enriched model", including segmentation-derived features by custom protocol. SCD patients were categorized based on their clinical trajectory and biomarker status as biomarker-positive progressors or biomarker-negative nonprogressors. Model performance was evaluated using regression and classification metrics with area under receiver operating characteristic curve (ROC-AUC) and compared using DeLong and paired t-tests.
Results: The "enriched model" had higher ROC-AUC (0.83 vs. 0.77) and reduced root mean squared error (0.427 vs. 0.436) compared to the "standard model", though results lacked statistical significance.

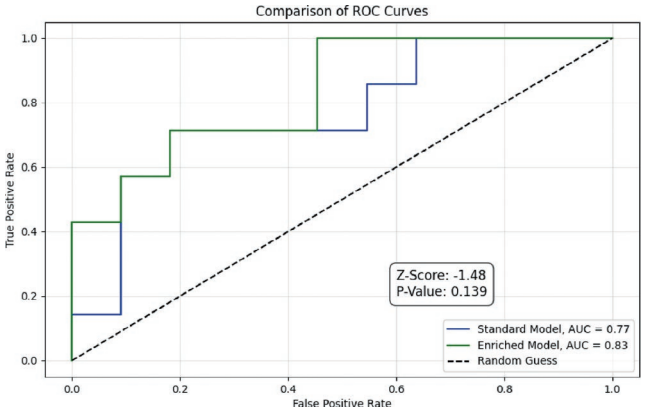

FIGURE 1 Comparing ROC AUC of "standard model" and "enriched model" using DeLong test

Conclusion: Using detailed MRI segmentation protocols including structures affected early in the course of AD may have positive effect on ML model performance in predicting AD progression. Larger datasets and extended follow-ups are needed to validate clinical applicability.
Disclosure: Nothing to disclose.

EPO-184 | Abstract withdrawn

EPO-185 | Efficacy and safety of sodium oligomannate and acetylcholinesterase inhibitors in Alzheimer's disease

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Faculty of Medicine, Cairo University, Cairo, Egypt

Background and aims: Alzheimer's disease (AD) is a prevalent neurodegenerative disorder. While current treatments like acetylcholinesterase inhibitors (AChEls) offer symptomatic relief, they do not halt disease progression. Sodium oligomannate (GV-971) has emerged as a potential therapeutic agent with promising effects in preclinical studies. This meta-analysis evaluates the efficacy and safety of sodium oligomannate, alone or in combination with AChEls, compared to donepezil or placebo in treating AD.
Methods: We systematically searched online databases for randomized controlled trials (RCTs) investigating GV-971 in AD patients. Data from seven RCTs involving 1,352 participants were pooled and analyzed using RevMan 5.4.1, with outcomes including cognitive function, daily living activities, neuropsychiatric symptoms, and safety profiles.

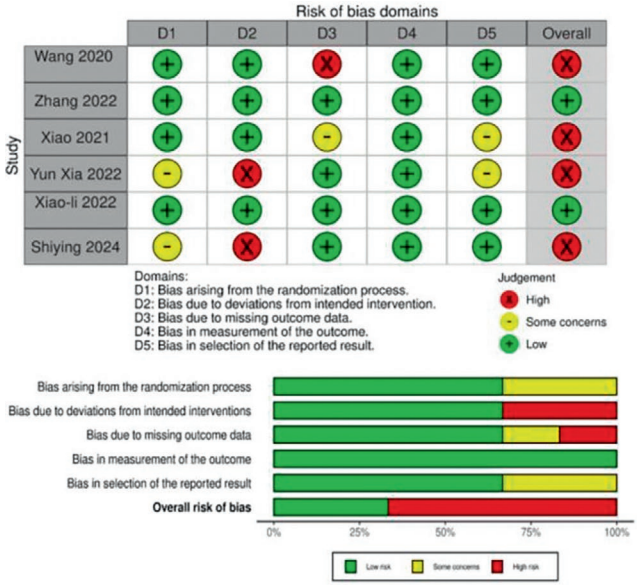

FIGURE 2 Risk of bias according to ROB-2.
We assessed the risk of bias in the included studies using the Rob 2 tool, which is a Cochrane-approved instrument for evaluating the quality of randomized controlled trials. This tool included five domains: bias from randomization process, allocation concealment, integrity of the intervention, bias of missing data, and bias missing outcome data, measurement outcomes and selection of the reported results. Four included studies showed a high risk of bias using RoB-2 except Zhang 2022 and Xiao-li 2022. The details of the RoB-2 assessment are shown in Figure 2.

Results: Sodium oligomannate significantly improved cognitive function compared to placebo (MD = -2.96, 95% Cl -5.30 to -0.62, p=0.01) and donepezil (MD = -5.67, 95% CI -9.17 to -2.17, p=0.002) on the ADAS- Cog12 scale. When combined with AChEls, GV-971 also demonstrated superior efficacy over AChels alone (MD = -3.25, 95% Cl -5.27 to -1.23, p=0.002). However, secondary outcomes such as ADCS-ADL and NPI showed mixed results, and no significant differences were observed in the MMSE scores. Safety analysis indicated no significant increase in adverse events compared to placebo.

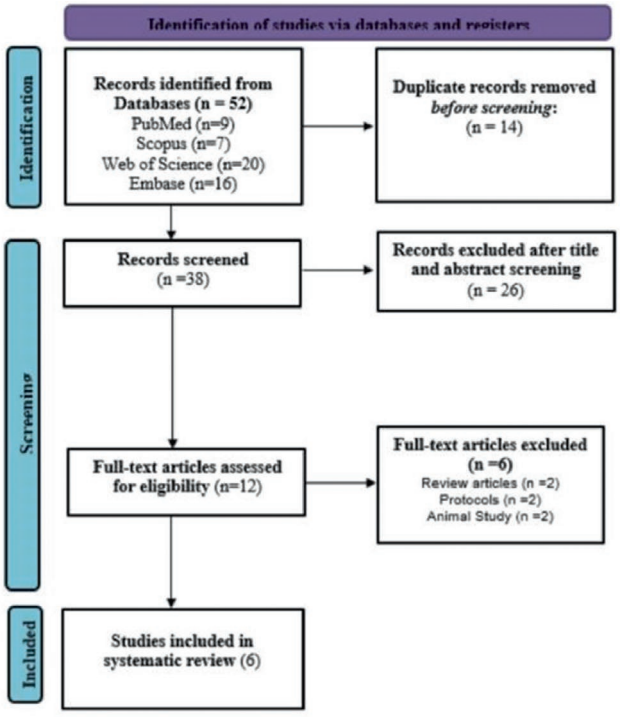

Figure 1. PRISMA flow diagram

Our search retrieved 38 unique articles. Following the abstract screening, only 12 studies were eligible for full-text screening. Finally, six randomized clinical trials (RCTs) were included in this review with 1252 patients.

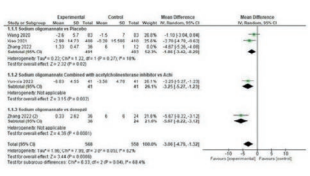

Fig.S-1 Forest plot showing the sensitivity analysis of ADAS-COG12

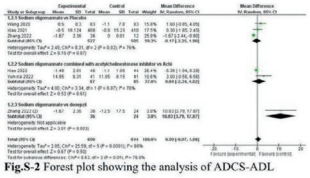

Fig.S-2 Forest plot showing the analysis of ADCS-ADL

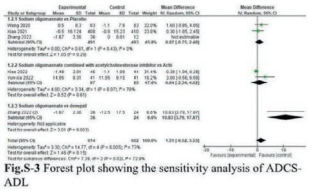

Fig.S-3 Forest plot showing the sensitivity analysis of ADCS-ADL

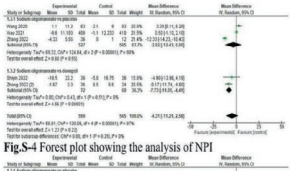

Fig.S-4 Forest plot showing the analysis of NPI

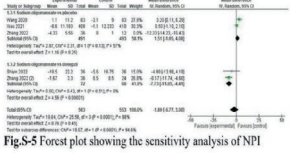

Fig.S-5 Forest plot showing the sensitivity analysis of NPI

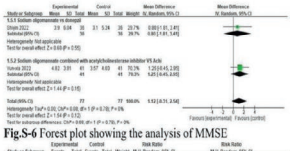

Fig.S-6 Forest plot showing the analysis of MMSE

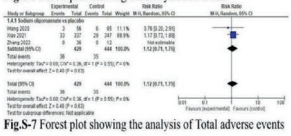

Fig.S-7 Forest plot showing the analysis of Total adverse events

FIGURE 3 Sodium oligomannate significantly improved cognitive function compared to placebo (MD = -2.96, 95% Cl -5.30 to -0.62, p=0.01) and donepezil (MD = -5.67, 95% CI -9.17 to -2.17, p=0.002) on the ADAS- Cog12 scale. When combined with AChEls, GV-971 also d.

Conclusion: Sodium oligomannate shows promise in enhancing cognitive function in AD, particularly when compared to donepezil or placebo. While its safety profile is comparable to placebo, larger, well-designed RCTs are necessary to validate these findings and explore the long-term benefits of GV-971, especially in combination therapies.

Disclosure: Nothing to disclose.

EPO-186 | Mini-linguistic state examination: The French-Canadian version of an international test for degenerative aphasias

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[1]Department of Neurology, DMU Neurosciences, National Reference Center for « Rare or Early Onset Dementias », Pitié-Salpêtrière University Hospital, Assistance Publique Hôpitaux de Paris (AP-HP), Paris, France; [2]Clinique Interdisciplinaire de Mémoire, Département des Sciences Neurologiques de l'hôpital universitaire- CHU de Québec, Québec (QC), Canada

Background and aims: There is need for rapid internationally applicable tests assessing language in neurodegenerative conditions to allow for homogenized diagnosis/classification of primary progressive aphasias (PPA), monitoring language decline, and providing endpoints in clinical/therapy trials. Such a tool, the 'Mini-Linguistic State Examination' (MLSE) is currently developed within a worldwide network (22 countries). Our Paris-Québec collaboration aimed at developing a French/Canadian version (fc-MLSE), validating it with healthy controls, and applying it to patients.

Methods: The fc-MLSE was adapted from the English version. Stimuli were selected to have similar linguistic complexity. Like the English version, the fc-MLSE included 11 sub-tests assessing 5 linguistic domains (motor-speech, phonology, semantics, syntax, verbal working-memory), providing a total-score and 5 sub-scores. It was applied to 182 controls to generate normative scores, and to 36 PPA patients (nonfluent/agrammatic [nfav-PPA, n=8], logopenic [lv-PPA, n=20], semantic [sv-PPA, n=8]), and 6 Alzheimer's disease (AD) patients.

Results: Testing-durations were ~8/~12 (controls/patients). Inter-rater consistency was 92%. There were no ceiling effects in controls, and sub-score results led to stratifications according to age-ranges and educational levels. The fc-MLSE distinguished PPA and AD patients from controls. PPA had lower total-scores than AD patients. Sub-scores distinguished PPA variants, showing highest error-rates for motor-speech, verbal working-memory, and semantics in nfav-PPA, lv-PPA and sv-PPA, respectively.

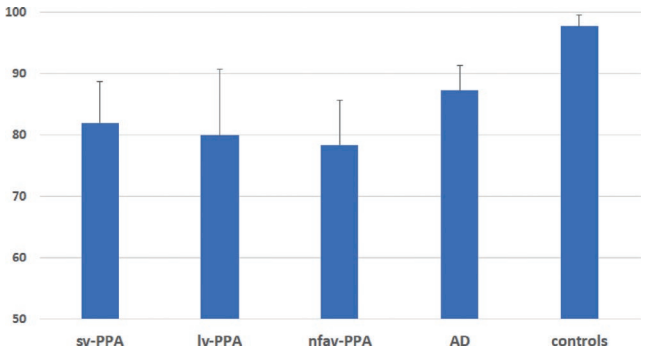

FIGURE 1 fc-MLSE total scores (/100) in patients with PPA variants and AD, and in healthy controls

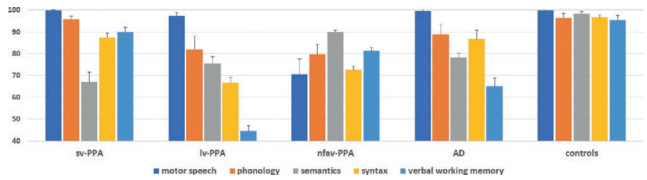

FIGURE 2 Response accuracy (%) of patients with PPA variants and AD, and in healthy controls in the five language domains of the fc-MLSE

Conclusion: The fc-MLSE is a rapid, examiner-consistent language test, validated with a large population of controls. It is suitable for classification of PPA variants, and will allow for follow-up and trial monitoring in neurodegenerative diseases affecting language. The international use of MLSE versions will improve consistency/uniformity of language assessments.
Disclosure: Nothing to disclose.

EPO-187 | Abstract withdrawn

EPO-188 | Distinguishing MCI and Alzheimer's disease: A machine learning framework using neuroimaging biomarkers

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[1]Health Science University Sultan Abdulhamid Han Research and Training Hospital, Department of Neurology, Istanbul, Turkey; [2]Bogazici University, Department of Computer Engineering, Istanbul, Turkey; [3]Health Science University Sultan Abdulhamid Han Research and Training Hospital, Department of Radiology, Istanbul, Turkey; [4]Health Science University Sultan Abdulhamid Han Research and Training Hospital, Department of Nuclear Medicine, Istanbul, Turkey; [5]Health Science University Sultan Abdulhamid Han Research and Training Hospital, Department of Psychology, Istanbul, Turkey

Background and aims: It is still unknown and unclear what precise characteristics set people with mild cognitive impairment (MCI) apart from those who develop Alzheimer's disease (AD). Our goal is to use machine learning techniques to identify neuroimaging biomarkers that can predict the likelihood of developing AD from MCI.
Methods: A custom and local dataset of 251 visits of 237 patients was created. The clinical relevance of the data was verified by statistical methods and shown to be clinically consistent. In addition to MRI volumetric and density measurements, cognitive tests such as MMSE, ACE-R and PET values were also included in the analysis, thus adopting a multimodal approach. We compared the statistical outcomes with the machine learning classification results. MRI measurements were extracted using FreeSurfer version 7.4.1.
Results: Forty-one statistically significant MRI features and 15 significant PET features were detected. In MRI volumetric evaluation, structures such as left and right caudate nucleus, left amygdala, corpus callosum posterior, left hippocampus and left nucleus accumbens were associated with the risk of conversion from MCI to AD. For 27 patients, vector similarity was used to analyze the risk of conversion from MCI to AD. Based on MRI measurements, we demonstrated that some patients may have a higher risk of progression to AD.
Conclusion: It is important that we can use such machine learning models, thanks to their neuroimaging value, to distinguish between MCI and AD, to predict diagnosis and to identify early stage patients who are the target of future treatment options.
Disclosure: This project was supported by TUBITAK.

EPO-189 | In vivo GABA imaging using CEST MRI to investigate the therapeutic effect of RF-EMF exposure in AD mice

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Background and aims: Radiofrequency–electromagnetic field(RF-EMF) are beneficial in treating Alzheimer's disease(AD), but the underlying neurophysiological mechanisms remain unclear. It has been proposed that EMF promotes GABAergic neurogenesis, and abnormal GABA levels are an important influence in AD. Therefore, in vivo GABA imaging is essential. As an essential branch of molecular imaging, chemical exchange saturation transfer(CEST) magnetic resonance imaging(MRI) can provide vital information for quantitative imaging.
Methods: The AD mice received RF-EMF treatment for 4weeks. The level of GABA was assessed by CEST MRI in vivo and ELISA in vitro. GABA Receptor expression was assessed by western blot. Aquaporin-4(AQP4) polarization and amyloid-β(Aβ) accumulation were quantified by the immunohistochemistry. Neuronal functional status was examined by Nissl staining. Spatial learning memory function was evaluated by the Morris water maze test.

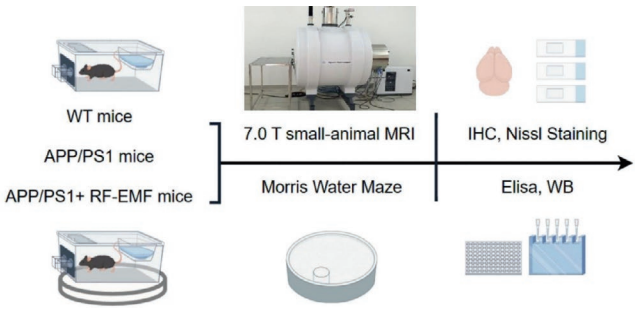

FIGURE 1 Study design

Results: 1. MRI results showed that RF-EMF could significantly increase the GABA signal in the hippocampus of AD mice. ELISA's results were consistent with the Variable Delay Multi Pulse(VDMP)-CEST results, and VDMP-CEST was more accurate in detecting changes in cortical GABA signals than Continuous Wave(CW)-CEST. Correlation analysis revealed that the correlation of GABA signals with GABA levels was more significant with VDMP-CEST than CW-CEST. 2. With the pathological validations, we found RF-EMF can elevate hippocampal GABA levels by polarizing AQP4, reducing Aβ accumulation and neuronal degeneration, improving cognitive impairment.

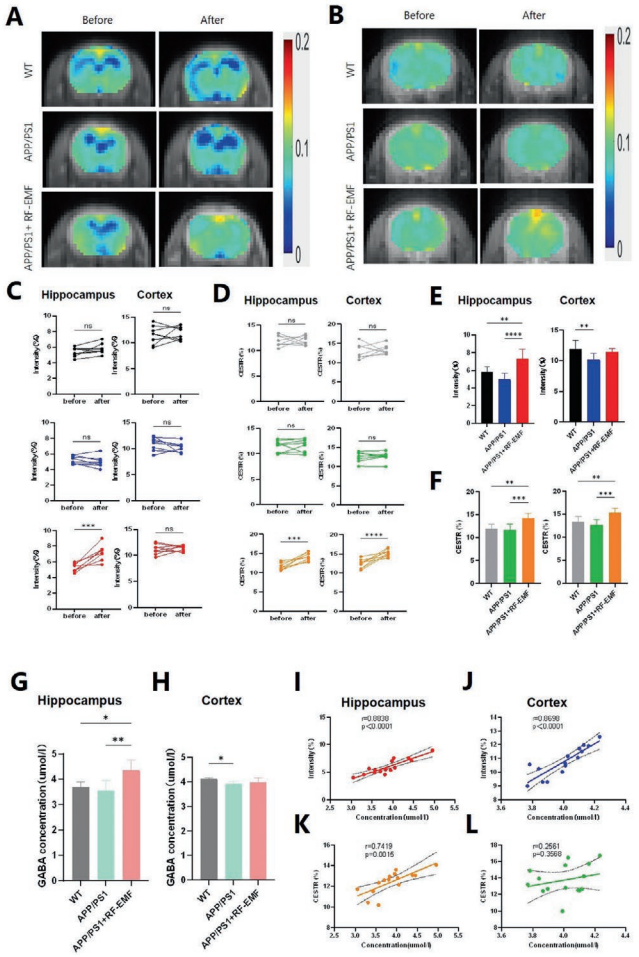

FIGURE 2 Results of CEST MRI and ELISA

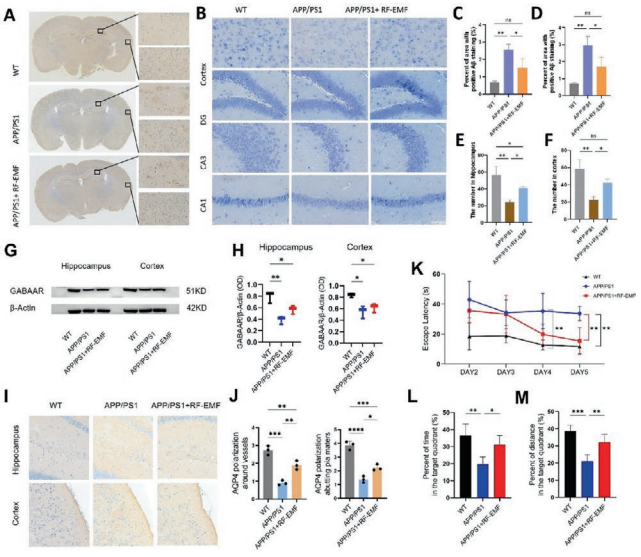

FIGURE 3 Pathological validations and Behavioral Testing of the Therapeutic Effect of RF-EMF on AD

Conclusion: 1. VDMP-CEST enables non-invasive in vivo GABA imaging 2. GABA levels in AD would be a specific and effective biomarker for monitoring the effect of RF-EMF treatment.

Disclosure: Nothing to disclose.

EPO-190 | Electroencephalographic patterns as diagnostic endpoints across the dementia spectrum

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Clouds of Care, Ghent, Belgium

Background and aims: As dementia represents several neurodegenerative disorders with distinct clinical and cognitive symptoms, a robust tool for accurate differentiation is necessary. This study investigates the potential of electroencephalography (EEG) to distinguish between dementia subtypes, using machine learning techniques.

Methods: Routine EEG data were analysed from 386 participants, clinically categorised into Alzheimer's disease (AD), non-Alzheimer's dementia (non-AD), mild cognitive impairment (MCI), subjective cognitive decline (SCD), healthy controls (HC), and non-cognitive symptomatic controls (SC). Spectral features (e.g., relative power, peak frequency, and aperiodic components) were extracted from the EEG recordings. Three machine learning models (random forest, gradient boosting, and linear support vector machine (SVM)) were trained for multiclass classification, using nested cross-validation with stratified 6-fold cross-validation to optimise hyperparameters and assess performance.

Results: AD subjects exhibited significantly increased low-frequency power and decreased high-frequency power with elevated alpha3/alpha1 and alpha3/alpha2 ratios (alpha1 = 8-9Hz, alpha2 = 9-11Hz, alpha3 = 11-13Hz) compared to controls and other subtypes. Non-AD subjects showed increased delta and theta power compared to controls, with higher theta peak frequency than HC, MCI, and SCD. MCI exhibited elevated delta power compared to controls but no differences with SCD, along with lower theta peak frequency than controls and higher delta and theta peak frequencies compared to SCD. Gradient Boosting showed the best generalization performance (AUROC: 0.875, F1-score: 0.608), outperforming Random Forest (AUROC: 0.860, F1-score: 0.560) and Linear SVM (AUROC: 0.781, F1-score: 0.391).

Conclusion: EEG shows potential as a non-invasive tool to distinguish between dementia-related conditions, aiding in diagnosis of this syndrome.

Disclosure: Julie Clarot, Emiel Vereycken, Nigel Colenbier, Velislava Zoteva are employees of Clouds of Care Caroline Neuray, Pieter van Mierlo are consultants and shareholders at Clouds of Care.

EPO-191 | Brexpiprazole for agitation in alzheimer's disease: A meta-analysis of randomized controlled trials

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Background and aims: Agitation in Alzheimer's disease (AD) requires effective and well-tolerated interventions. Recently, Brexpiprazole has emerged as a promising therapeutic avenue.

Methods: We systematically searched ClinicalTrials.gov, PubMed, Embase, and Cochrane Library for randomized controlled trials (RCT) comparing Brexpiprazole to placebo in patients with AD presenting with agitation. A random-effects model was employed to compute mean differences and risk ratios using R software 4.3.1. The results were reported following the PRISMA guideline.
Results: A total of 3 double-blind RCTs were included, comprising 1,028 patients with an average age of 74 years. Throughout a 12-week mean follow-up period, Brexpiprazole was associated with no changes in Clinical Global Impression-Severity of illness (MD -0.19; 95% CI -0.38 to 0.00; p=0.05) and Neuropsychiatric Inventory-Nursing Home scores (MD -1.51; 95% CI -3.63 to 0.62; p=0.16). However, there was a notable improvement in Cohen-Mansfield Agitation Inventory score (MD -3.04; 95% CI -5.04 to -1.04; p<0.01). Additionally, no difference was observed for the incidence of at least 1 treatment-emergent adverse events (TEAE) (RR 1.10; 95% CI 0.94 to 1.28; p=0.52), discontinuation due to TEAE (RR 1.50; 95% CI 0.81 to 2.78; p=0.20), dizziness (RR 1.04; 95% CI 0.52 to 2.11; p=0.86), extrapyramidal disorders (RR 2.60; 95% CI 0.44 to 15.40; p=0.99), and all-cause death (RR 1.51; 95% CI 0.25 to 8.94; p=0.48).

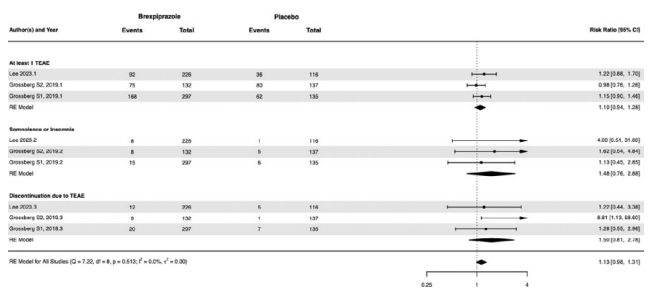

FIGURE 1 Adverse Events

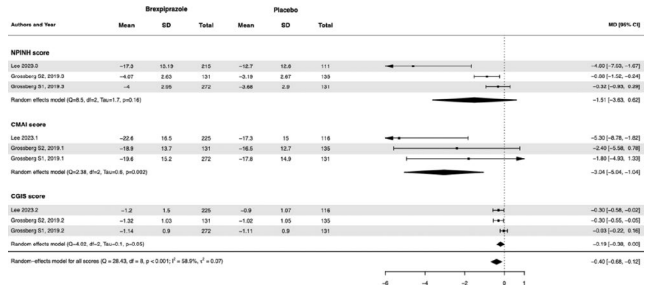

FIGURE 2 Agitation score change

Conclusion: In this systematic review and meta-analysis of 3 RCTs and 1,028 patients, Brexpiprazole was associated with a modestly favorable modulation in agitation score, concurrent with a positive safety profile.
Disclosure: Nothing to disclose.

EPO-192 | Tauopathy worsens with adiponectin deficiency and improves with adiporon treatment in mice with human tau mutation

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Background and aims: Tauopathy is characterized by the accumulation of hyperphosphorylated tau proteins in neurons. It is a pathological hallmark of Alzheimer's disease. Adiponectin (APN), an adipokine secreted from adipocytes, exerts anti-inflammatory effects and promotes hippocampal neurogenesis. However, whether APN contributes to tau-mediated neurodegeneration remains unknown. We aim to investigate the impact of APN deficiency on cognitive functions and neuropathologies in mice with tauopathy.
Methods: Cognitive functions of 9-month-old wildtype, APN knockout (APN-/-) mice, human tau P301S mutation transgenic (TauP301S) mice, and APN-deficient tau (TauP301S; APN-/-) mice were examined by the novel object recognition (NOR) test. Hyperphosphorylated tau accumulation, microgliosis, and neuronal loss in the brain were analyzed by immunofluorescent staining. The therapeutic effect of an APN receptor agonist, adipoRon, was assessed by treating 6-month-old TauP301S and TauP301S; APN-/- mice for three months.
Results: TauP301S; APN-/- mice spent significantly less time exploring the novel object than wildtype during the NOR test. The immunoreactivity of hyperphosphorylated tau (AT8) and microglia markers ionized calcium-binding adaptor molecule 1 (Iba1) in the brain of TauP301S; APN-/- mice were significantly elevated compared with other groups. TauP301S; APN-/- mice exhibited significantly fewer neuronal nuclei (NeuN) positive neurons than other groups. Importantly, chronic adipoRon treatment reduced AT8 immunoreactivity in TauP301S; APN-/- mice markedly compared with vehicle-treated TauP301S; APN-/- mice.
Conclusion: APN deficiency aggravates tauopathy, characterized by increased hyperphosphorylated tau accumulation, microgliosis, and neuronal loss, which are reversed by adipoRon treatment. Further experiments will be conducted to study the underlying mechanism of how adipoRon improves tauopathy.

Disclosure: This project is supported by Health & Medical Research Fund.

Autonomic Nervous System Diseases

EPO-193 | Craniocervical instability in patients with hypermobility syndrome: A surgical condition

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Background and aims: Craniocervical instability (CCI) is increasingly found to manifest from heritable connective

tissue disorders. Hypermobile Ehlers-Danlos Syndrome (hEDS) causes ligamentous laxity leading to an abnormal range of motion in joints, including the craniocervical junction. Symptoms of CCI often present as head and neck pain in addition to symptoms of autonomic dysfunction. We hypothesize that the hyper-rotation of the atlanto-axial joint and hyper-flexion of the atlanto-occipital joint causes repetitive stress on the sympathetic chain and transient mechanical compression and stretching of the venous system and surgical treatment improves symptoms for these patients.

Methods: A retrospective cohort study was performed on surgical patients diagnosed with hypermobile Ehlers-Danlos syndrome, neck/head pain and symptoms of autonomic dysfunction, and radiographic findings of CCI at the O-C1, C1-2 or O-C2 levels.

Results: Twelve patients underwent posterior cervical fusion at the level indicated for treatment (O-C1: n=3, C1-2: n=6, O-C2: n=3). Radiologic findings showed an average C1-2 angular displacement of 34 degrees in each direction. Clinical presentation included head and neck pain (100%), headaches (100%), dizziness (75%), POTS symptoms, (50%) vision disturbances (42%), brain fog (50%), vertigo (33.3%), tinnitus (42%), and gastrointestinal dysfunction (33.3). Post-operatively, patients had significant improvement in overall (p=0.01), head (p=0.01), and neck (p=0.003) pain on the VAS. Post-operatively, all 12 patients reported improvement in their neurological and autonomic symptoms (12.5 months mean follow up).

Conclusion: Our study demonstrates that fusion and stabilization of this junction leads to significant relief of patient's symptoms from CCI in the setting of hEDS.

Disclosure: Nothing to disclose.

EPO-194 | Early high-efficacy disease-modifying therapies may slow progression of autonomic dysfunction in people with MS

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Background and aims: The research aimed to explore changes and predictors of autonomic dysfunction (AD) in people with multiple sclerosis (pwMS) from disease onset over six years.

Methods: A total of 121 pwMS were recruited at disease onset. After six years, data were available for 75 participants. Subjective AD was assessed with the Composite Autonomic Symptom Score-31 (COMPASS-31) questionnaire at the start and end of follow-up. Objective tests of AD were performed at baseline and every two years, with results recorded using the Composite Autonomic Scoring Scale (CASS). Symptomatic dysautonomia was identified if COMPASS-31 score was greater than the cohort median (7.913) and if CASS score was greater than 0.

Results: There were no significant changes in COMPASS-31 and CASS results between the beginning and the end of follow-up. However, a significant decline was observed in the cardiovagal index (p=0.001) and the sudomotor index (p=0.036 and p=0.001, respectively) at Years 4 and 6 compared to baseline. The number of participants with symptomatic dysautonomia increased significantly from Year 0 to Year 6 (p=0.049). Multivariable logistic regression analysis revealed that experiencing a relapse during the six years increased the likelihood of symptomatic dysautonomia by 388.6% (Exp(B) 3.886, 95% C.I. 1.019-14.825, p=0.047). Conversely, transitioning to high-efficacy disease-modifying therapy (HET) reduced the probability of having a CASS score greater than 1 at Year 6 by 77.9% (Exp(B) 0.221, 95% C.I. 0.067-0.734, p=0.014).

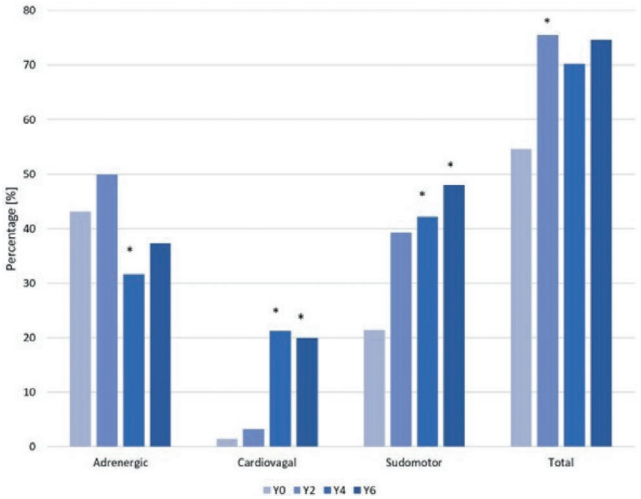

FIGURE 1 Distribution of pathological CASS and its indices during a six-year follow-up. *statistically significant results in comparison to baseline for the same index

TABLE 1 Results of the multivariable analysis identifying predictors of CASS>0 at year 6 visit.

	Multivariable logistic regression		
	Exp(B)	95% C.I. for Exp(B)	p value
Age (years)	1.021	0.959-1.088	0.508
Brainstem MRI lesions at baseline	1.619	0.959-1.088	0.502
Baseline T2 lesions >9	0.678	0.158-2.917	0.602
BS	0.630	0.155-2.555	0.518
TM	3.146	0.653-15.170	0.153
HET in six years	0.221	0.067-0.734	0.014

Conclusion: Cardiovagal and sudomotor dysfunction progresses alongside disease duration in MS. The early initiation of HET in pwMS may reduce the risk of developing AD.

Disclosure: Nothing to disclose.

EPO-195 | The involvement of sensory and autonomic peripheral nervous system in Hypermobility Spectrum Disorder

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Background and aims: Hypermobile Spectrum Disorder (HSD) patients often have a history of sensory and autonomic symptoms. The aim of this study is to assess the peripheral involvement of sensory and autonomic nervous system in HSD.
Methods: 31 HSD patients (M/F=3/28; 36±14years) and 38 SFN patients (M/F=8/30; 52±14years) were recruited. Both groups underwent assessment of symptoms and sensory and autonomic dysfunction trough the "Small-Fiber-Neuropathy-Symptoms-Inventory-Questionnaire" (SFN-SIQ), "Composite-Autonomic-Symptoms-Score" (COMPASS-31), Quantitative Sensory Testing(QST), cardiovascular reflexes, sympathetic skin response (SSR) and Dynamic Sweat Test(DST). Cutaneous sensory and autonomic innervation was analyzed on punch biopsies from leg, thigh and fingertip applying indirect Immunofluerescence procedures.
Results: HSD patients were younger, with earlier onset of symptoms then SFN patients. They complained of generalized pain with involvement of the perineal region in a third of the cases. In both groups, abnormal QST for each sensory modality was observed. Autonomic symptoms involving the cardiovascular, gastrointestinal and sudomotor domains were significantly more frequent in HSD than in SFN patients. Evidence of Postural Orthostatic Tachycardia Syndrome(PoTS) was observed in half of HSD. DST showed a non-length-dependent reduction of sweat output per individual gland in HSD compared with SFN patients. Morphological analysis revealed a greater loss of pilomotor and sudomotor nerve fibers, with a mild non-length-dependent loss of epidermal nerve fibers (ENF) in HSD compared to SFN patients.
Conclusion: Small fibers involvement in HSD compared to SFN patients presents with generalized pain, involving perineal region and autonomic symptoms mostly involving cardiovascular and gastrointestinal domains. Morphological picture underlying this condition is a greater loss of autonomic nerves and a mild non-length-dependent loss of ENF.
Disclosure: Nothing to disclose.

EPO-196 | Chiari malformation and small fiber neuropathy associated with a novel COL6A5 mutation

F. Masciarelli[1]; D. Dell'Aversana[1]; R. Iodice[1]; F. Vitale[1]; G. Caporaso[2]; R. Dubbioso[1]; L. Ruggiero[1]; V. Provitera[2]; S. Tozza[1]; L. Micale[3]; L. Santoro[1]; F. Manganelli[1]; M. Castori[3]; M. Nolano[1]
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Background and aims: We describe a patient and her daughter with Chiari Malformation type-I (CMI) and painful symptoms in which a COL6A5 gene mutation was found.
Methods: Patient and her daughter underwent Next-Generation-Sequencing with a gene panel for hereditary connective tissue disease. Variant detected was confirmed by Sanger sequencing. Patient underwent assessment of neurological symptoms and autonomic dysfunction trough the "Small-Fiber-Neuropathy-Symptoms-Inventory-Questionnaire" (SFN-SIQ), "Composite-Autonomic-Symptoms-Score" (COMPASS-31), cardiovascular reflexes, sympathetic skin response (SSR) and Dynamic Sweat Test (DST). Cutaneous sensory and autonomic innervation and Collagen VI presence in extracellular matrix were analyzed on punch biopsies from leg, thigh and fingertip applying indirect immunofluorescence procedures.
Results: Patient (57-year-old woman) and her daughter (33-years-old) had CMI. Both genetic analysis pointed out a heterozygous 5 bp-deletion COL6A5 variant, predicted to introduce a premature stop codon. They complained diffuse and chronic musculoskeletal and burning pain, itchy scalp, allodynia and autonomic symptoms involving cardiovascular, gastrointestinal and sudomotor domains. Patient autonomic assessment showed a Postural Orthostatic Tachycardia Syndrome (PoTS) and a non-length-dependent reduction of sweat gland density and sweat output per gland at DST. Morphological analysis revealed a severe loss of sensory and autonomic nerve fibers. Collagen VI staining was reduced in extracellular matrix compared to healthy subject.

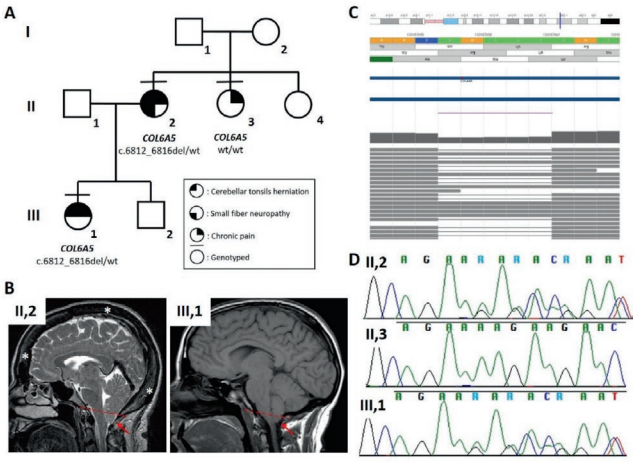

FIGURE 1 Family, radiological and molecular features of the family.

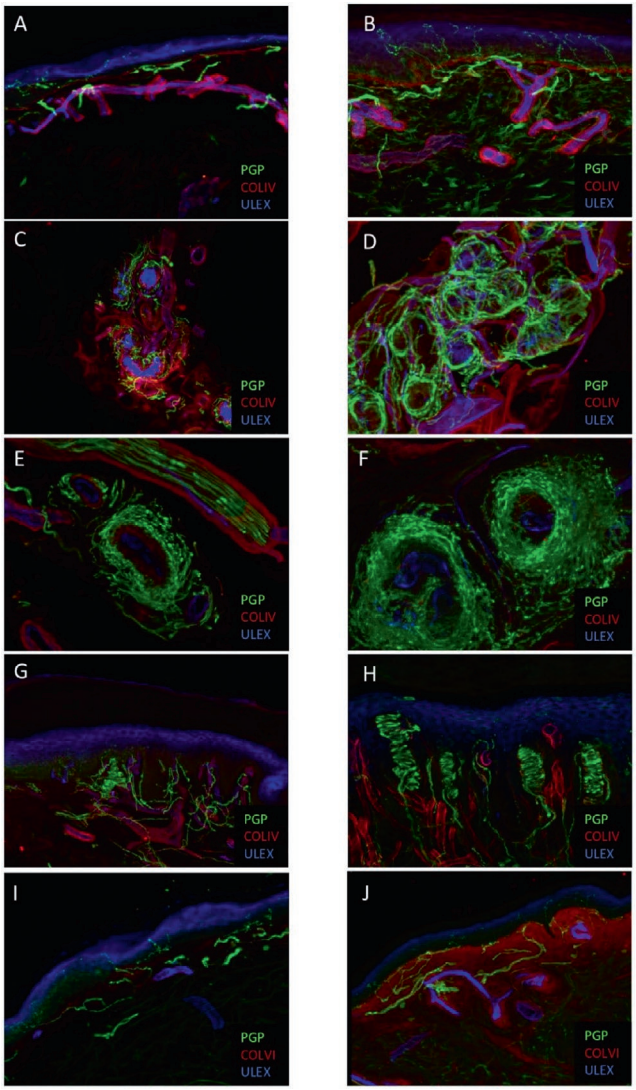

FIGURE 2 Digital confocal images showing epidermal and dermal denervation in our patient (A, C, E, G, I) compared to a healthy control (B, D, F, H, J)

Conclusion: Patient received a small fibers neuropathy (SFN) diagnosis. The reduced collagen VI expression in extracellular matrix could indicate the pathogenicity of this variant. Mutation in the same gene locus has been described associated to CMI or to chronic itch, suggesting that the variant we found is likely pathogenic for a syndrome that associate both SFN and CMI.
Disclosure: Nothing to disclose.

EPO-197 | Characterizing sudomotor dysfunction in multiple sclerosis: Insights from QSART, SUDOSCAN, and COMPASS-31

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[2]*Department of Neurology, University Hospital Center Zagreb, Zagreb, Croatia*

Background and aims: This study aimed to characterize sudomotor dysfunction in people with MS (pwMS) using the Quantitative Sudomotor Axon Reflex Test (QSART) and SUODSCAN.
Methods: Forty-one consecutive treatment naïve pwMS were enrolled within 5years from symptom onset. Symptoms of sudomotor dysfunction were evaluated with question 8 of the Composite Autonomic Symptom Score (COMPASS-31). The sudomotor function was assessed with QSART, a test that measures the axon-reflex-mediated evaporated sweat response, and SUDOSCAN, which measures the electrochemical skin conductance of hands and feet through reverse iontophoresis.
Results: Symptomatic hyperhidrosis was present in 15 (36.6%) pwMS. Pathological result of the QSART (sudomotor index (SI) >0) was found in 11 (26.8%) pwMS, while SUDOSCAN results were pathological in 5 (12.20%) pwMS. pwMS with symptomatic hyperhidrosis had higher values on SUDOSCAN leg (83.00±5.26 vs 78.92±6.22, p=0.039), while there was no difference in the QSART results. There was no correlation between the results of the QSART and SUDOSCAN. However, pwMS with hypohidrosis on the QSART had the lowest results on the SUDOSCAN (Figure 1a and 1b). In contrast, pwMS with persistent hyperhidrosis or persistent sweating on the QSART had higher values on the SUDOSCAN (Figure 1a and 1b). pwMS with lesions present on the brainstem and spinal cord MRI had lower volumes on QSART compared to pwMS without lesions on both locations (distal leg 0.92±0.611 vs 0.92±0.611.65±1.46, p=0.037).

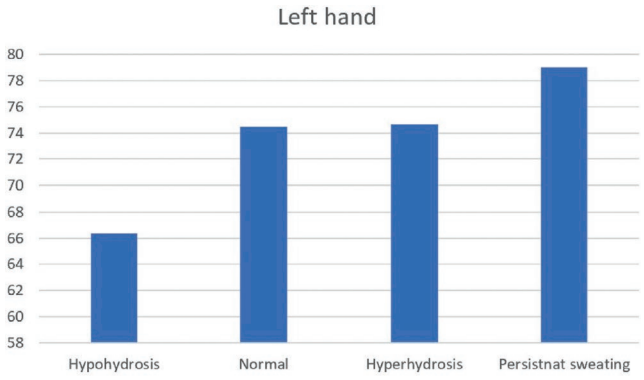

FIGURE 1 Results of SUDOSCAN based on QSART

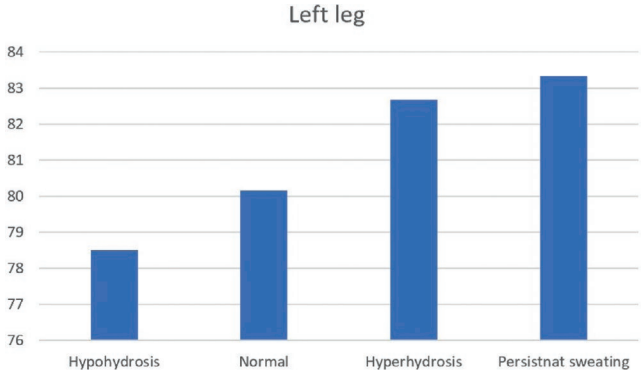

FIGURE 2 Results of SUDOSCAN based on QSART

Conclusion: pwMS frequently have sudomotor dysfunction measured with COMPASS-31, QSART, and SUDOSCAN. Detection of sudomotor problems in pwMS with different methodologies indicates differences in causes of sudomotor dysfunction in pwMS.

Disclosure: Funding: Croatian Science Foundation (IP-2019-10-8200) Financial & competing interest disclosure KJ: Nothing to disclose. IA, TG, BB, MH: Received consultation and/or speaker fees from Biogen, Merck, Novartis, Roche, Astra Zeneca, Amgen. MKS: Received consultation and/or speaker fees from Roche.

EPO-198 | Monocular dynamic pupillometry in healthy controls and patients with autonomic dysfunction: a technical validation study

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Background and aims: Pupillometry is widely used to determine pupil diameter for corneal refractive surgery. Monocular devices are non-invasive tools to assess pupillary parameters including ocular parasympathetic and sympathetic function. This study aims to generate normative pupillomotor autonomic values in healthy controls (HC) and to technically validate a handheld pupillometer.
Methods: 40 HC had monocular pupillometry using the PLR-4000®(NeurOptics). Twelve patients with autonomic disorders additionally underwent binocular pupillometry (Neuroptics DP2000). Pupillary parasympathetic and sympathetic function were assessed by responses to light stimulus and to 0.5% apraclonidine eye drops, respectively. 4 HC had repeat assessment at a second timepoint.
Results: In HC, mean light reflex ratio was 42 ± 5.7% and median response to apraclonidine was -5.0 (-8.8 – 2.8)%. Younger controls had larger mean resting pupils than older individuals (p=0.001, 95% CI = 0.4 – 1.4). There was no age-related difference in mean light response (p=0.355). Results of normal pupillary function, parasympathetic, sympathetic, or combined denervation were comparable as assessed by the two pupillometers. Intra-individual repeatability showed: median difference in resting pupil size 0.5mm (IQR 0.13 – 0.93mm), median light response difference 2 (1 – 4)%, median % difference in response to apraclonidine 8.4 (4.7 – 13.6)%.
Conclusion: The presented device provides accurate and reproducible assessments of pupillary parasympathetic and sympathetic function in healthy controls and patients with autonomic disorders. With normative data provided, it is a well-tolerated, easily accessible tool to quantitatively assess autonomic ocular innervation. Further studies are needed to investigate its clinical use for autonomic screening and monitoring disease progression.
Disclosure: LS is supported by the University of Basel, Switzerland, and the Freiwillige Akademische Gesellschaft Basel. GO, CB, SB, GC, FB report no disclosures. VI is supported by the National Institute for Health Research, University College London Hospitals Biomedical Research Centre and by the Autonomic Charitable Trust (ACT) (Lord Bagri) Research Award. VI has received honoraria from Theravance Biopharma not related to this work.

EPO-199 | Clinical validation of autonomic ocular function assessments using monocular dynamic pupillometry

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Background and aims: Pupillary function is frequently impaired in disorders affecting the autonomic nervous system. Dynamic pupillometry allows us to quantitatively evaluate ocular parasympathetic and sympathetic innervation. Monocular, handheld devices are easily accessible tools to assess various pupillary parameters. The aims of this study were to clinically validate the handheld pupillometer PLR-4000® (NeurOptics) in patients with autonomic dysfunction.
Methods: In this prospective study, 100 patients with autonomic failure and intermittent autonomic disorders underwent pupillometry from April – December 2024 using the PLR-4000® (NeurOptics). Pupillary parasympathetic and sympathetic function were assessed by responses to light stimulus and to 0.5% apraclonidine eye drops, respectively.
Results: In patients with neurodegenerative disorders (n=24), autonomic neuropathies (n=39), and autonomic ganglionopathies (n=9), pupillary abnormalities were very prevalent (52%, 45%, and 100%, respectively). In patients with alpha-synucleinopathies, sympathetic denervation was the most common abnormality (9/21; 43%). 3/6 patients with autoimmune autonomic ganglionopathy presented with pupillary fatigue. All patients with intermittent autonomic disorders (n=28) presented with normal pupillary function.
Conclusion: Monocular dynamic pupillometry robustly measures pupillary parasympathetic and sympathetic function in patients with autonomic disorders. It is an easily accessible and valuable tool to quantitatively assess autonomic ocular innervation in addition to cardiovascular autonomic function testing. Further studies are needed to investigate its use as a tool for early autonomic screening, monitoring disease progression and response to treatment in different disorders.
Disclosure: LS is supported by the University of Basel, Switzerland, and the Freiwillige Akademische Gesellschaft Basel. GO, CB, SB, GC, FB report no disclosures. VI is supported by the National Institute for Health Research, University

College London Hospitals Biomedical Research Centre and by the Autonomic Charitable Trust (ACT) (Lord Bagri) Research Award. VI has received honoraria from Theravance Biopharma not related to this work.

EPO-200 | Gastrointestinal motility and ANS function in children with inflammatory bowel disease and irritable bowel syndrome

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Background and aims: Electrogastrography (EGG) is a noninvasive method for the measurement of gastric myoelectrical activity that uses abdominal surface electrodes. This study aimed to investigate the differences in gastric motility measured with EGG and its correlation with standardized autonomic nervous system tests in children with inflammatory bowel disease (IBD), irritable bowel syndrome (IBS), and healthy children (HC).
Methods: Sixty-two children were enrolled: 18 in the IBD, 26 in the IBS, and 18 in the HC group. ANS symptoms were evaluated with the Composite Autonomic Symptom Score (COMPASS-31). COMPASS31 >7.913 was considered a clinically significant autonomic symptom burden. The severity and distribution of ANS function were quantitated using adrenergic, cardiovagal, and sudomotor indices of the Composite Autonomic Severity Scale (CASS). Gastric myoelectric activity was obtained from EGG in the preprandial and postprandial periods (standardized meal 300 kcal).
Results: There was no statistically significant difference in any of the EGG parameters between groups (all p>0.05). Autonomic symptom burden measured with COMPASS-31 score negatively correlated with postprandial PDF (r=-0.316, p=0.02). The gastrointestinal domain of the COMAPSS-31 did not correlate with PDF (p>0.05). However, the orthostatic intolerance domain of the COMAPSS-31 negatively correlated with postprandial PDF (r=-0.364, p=0.007). Children with clinically significant autonomic symptom burden had lower values of postprandial PDF (2.8 (IQR 0.19) vs 2.9 (IQR 0.23), p=0.016). CASS and its indices did not correlate with any of the EGG parameters.
Conclusion: These findings indicate that children with higher and clinically significant autonomic symptom burden postprandially have lower levels of gastric activity.
Disclosure: AMP: Nothing to disclose. PR: Nothing to disclose. MKS: Received consultation and/or speaker fees from Sanofi Genzyme, Roche. MH: Received consultation and/or speaker fees from Biogen, Merck, Novartis, Roche, Astra Zeneca, Amgen. IH: Received honoraria for lectures from Sandoz, BioGaia, Ewopharma, Oktalpharma, Hipp, Nutricia, Biocodex, Nestle, and GM Pharma.

EPO-201 | Ultrasound assessment of peripheral nerve size in Guillain-Barré syndrome: A systematic review and meta-analysis

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Background and aims: Guillain-Barré syndrome (GBS) is an acute autoimmune disorder characterized by progressive muscle weakness and paralysis due to peripheral nerve damage. Changes in nerve size may serve as important biomarkers of nerve involvement. Ultrasound (US) has emerged as a non-invasive tool for assessing peripheral nerve changes, including alterations in nerve size. This study aims to evaluate peripheral nerve size changes in patients with GBS using US.
Methods: A systematic literature search was conducted in PubMed, Scopus, Embase, and the Web of Science from inception until September 2024. Data extraction was performed using a standardized form.
Results: A total of 26 studies with 1,462 patients were identified, of which 18 were included in the analysis. Significant nerve size changes ($p < 0.05$) were observed across multiple anatomical regions, including the Cervical, Fibular, Median, Peroneal, Sural, Tibial, and Ulnar nerves. The most notable changes were found in the Tibial nerve at the popliteal region (MD 6.23, 95% CI 3.6 to 8.86), the Peroneal nerve (MD 2.09, 95% CI 1.31 to 2.88), and the Median nerve in the upper arm (MD 1.94, 95% CI 1.14 to 2.74) and forearm (MD 1.62, 95% CI 0.71 to 2.53).

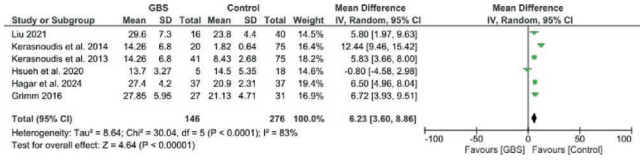

FIGURE 1 Mean difference (MD) in nerve size for the Tibial nerve at the popliteal region in patients with Guillain-Barré syndrome.

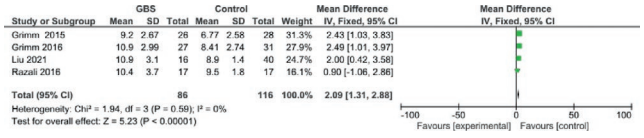

FIGURE 2 Mean difference (MD) in nerve size for the Peroneal nerve in patients with Guillain-Barré syndrome.

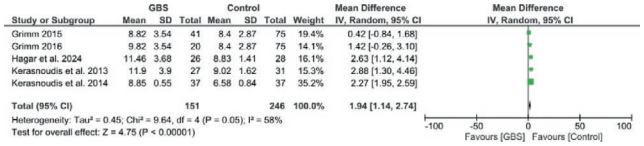

FIGURE 3 Mean difference (MD) in nerve size for the Median nerve in the upper arm and forearm regions in patients with Guillain-Barré syndrome.

Conclusion: US imaging reveals significant nerve size changes in multiple anatomical regions in GBS patients. These findings underscore the potential of US as a non-invasive tool for monitoring nerve alterations and disease progression in GBS.
Disclosure: Nothing to disclose.

EPO-202 | The therapeutic effect of transcranial alternating current stimulation on persistent postural perceptual dizziness

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Background and aims: Persistent postural perceptual dizziness (PPPD) is a disease with chronic vestibular dysfunction as its main manifestation. There is no standardized treatment for PPPD, but transcranial alternating current stimulation (tACS) is a non-invasive neuromodulation technique. Previous study using transcranial direct current stimulation (tDCS) at left dorsolateral prefrontal anode showed a significant reduction in DHI scores and some reduction in HAMD score; however, no study has studied the outcomes of tACS to PDDD. The aim of this study was to apply tACS for the treatment of PPPD and to investigate its therapeutic effect.
Methods: A total of 10 patients with PPPD were recruited in this study. The effect of tACS for PPPD was assessed by applying AC stimulation with a current size of 1.5 mA and a frequency of 10 Hz to five electrodes in the dorsolateral left prefrontal lobe of the subjects, and assessing the subjects' vertigo level, anxiety and depression status.

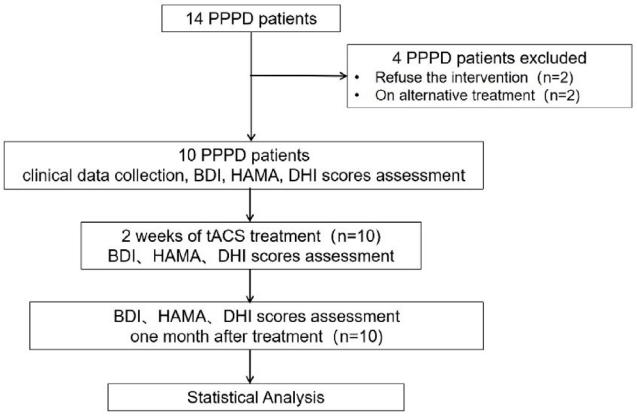

FIGURE 1 Study flowchart

Results: Three scales were significant compared among the three groups at the baseline level before tACS, after tACS, and after one month of tACS, indicating that they were statistically different before and after the treatment, proving that there was a significant improvement in vertigo level, depressive state and anxiety state in the PPPD patients included before and after tACS.

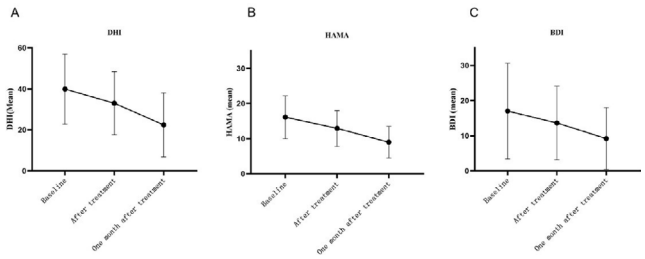

FIGURE 2 BDI, HAMA and DHI scores changes after treatment

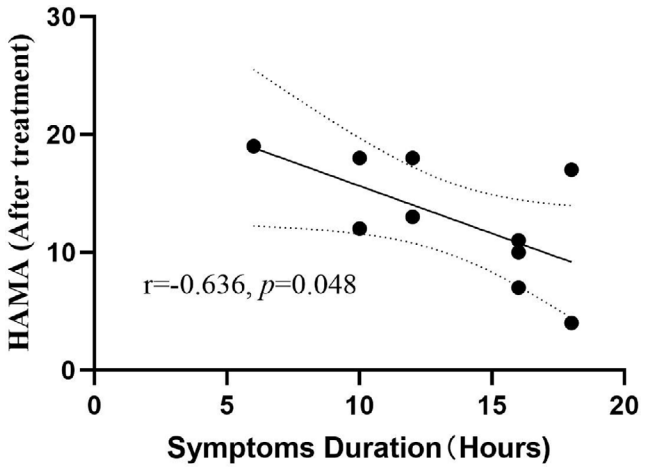

FIGURE 3 Correlation between HAMA and symptoms duration after treatment

Conclusion: This study supports the application of tACS in PPPD patients to improve their anxiety and depression symptoms. Meanwhile, the results of this study suggest that DLPFC is involved in the pathogenesis of PPPD and may be a target for further research.
Disclosure: Nothing to disclose.

EPO-203 | Delayed orthostatic tachycardia – is the time frame for postural orthostatic tachycardia syndrome arbitrary?

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Background and aims: Postural Orthostatic Tachycardia Syndrome (POTS) is defined as increase in heart rate by >30 bpm within 10 minutes of upright posture without significant orthostatic hypotension (OH). The basis of this time frame remains unclear. Patients who develop delayed orthostatic tachycardia (DOT) in the absence OH remain uncharacterized. The present study was aimed at defining the characteristics of the DOT group.
Methods: We reviewed clinical histories and laboratory tests performed in our laboratory for assessment of orthostatic intolerance (OI) in last 10 years. Laboratory tests included autonomic testing (sweat test, heart rate variability tests, and 45-minute upright tilt table test) and quantitative sensory testing.
Results: Among 974 patients who underwent laboratory tests most common referral symptoms were orthostatic palpitations/tachycardia (49.3%), syncope (18.7%) and light-headedness

(7.3%). Among this cohort, 419 (43.0%) had POTS, and 167/974 (17.1%) had DOT manifesting as onset/aggravation of presyncopal symptoms, with a mean HR increase by 49.7 bpm from baseline (Range: 40 BPM- 103 BPM) without OH, narrowing of pulse pressure, ($\bar{x}$ = 15.4, Range: 9.2 mm Hg- 24.8 mm Hg), and syncope (10.8%). Among the patients with delayed OI, 64.7% had small fiber/autonomic neuropathy.

FIGURE 1 A 45min upright TTT in a 35-year-old female with orthostatic symptoms shows delayed orthostatic tachycardia (green) without any significant orthostatic hypotension (red). The green triangles mark the start and ending of tilt test whereas the vertical line shows

Conclusion: A significant number of patients with OI have DOT on TTT without significant OH. Reduction in PP and small fiber/autonomic neuropathy in this group suggests that reduced cardiac output due to peripheral blood pooing causes DOT, which may be on the continuum of POTS and should be ruled out with appropriate testing protocols.
Disclosure: Nothing to disclose.

Cerebrovascular Diseases 2

EPO-204 | Tenecteplase administration after the usual treatment window in acute ischemic stroke: A meta-analysis

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Background and aims: Data regarding the efficacy and safety of tenecteplase (TNK) in patients with acute ischemic stroke (AIS) who present outside the standard treatment window are limited. This study aims to evaluate the role of TNK at a dose of 0.25 mg/kg, in treating AIS patients in an extended time window.

Methods: Searches were performed in PubMed, Scopus, Embase, and Cochrane CENTRAL to include randomized-controlled trials (RCTs) comparing TNK (0.25 mg/kg) to no thrombolysis in AIS patients presenting after 4.5 hours of symptom onset or wake-up AIS. The primary efficacy outcomes included a 3-month excellent functional outcome (mRS ⩽1), and a good functional outcome (mRS ⩽2). Secondary safety outcomes assessed included symptomatic intracranial hemorrhage (sICH), and 3-month all-cause death. A random-effects model was used to calculate summary estimates,

Results: 4 RCTs were included (n = 1632 patients) in the meta-analysis. The pooled analysis demonstrated a significantly improved excellent functional outcome on 90 days (OR = 1.38, 95% CI: 1.12 to 1.69) and good functional outcome (OR = 1.23, 95% CI: 1.01 to 1.50) with TNK administration compared to control. No statistically significant association was observed for the two groups regarding all-cause death (OR = 1.11, 95% CI: 0.82 to 1.50) and sICH (OR = 2.02, 95% CI: 0.93 to 4.38).

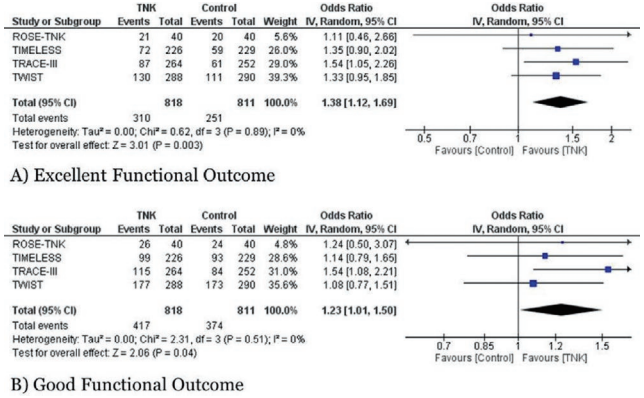

FIGURE 1 Forest plots for (A) Excellent functional outcome and (B) Good functional outcome.

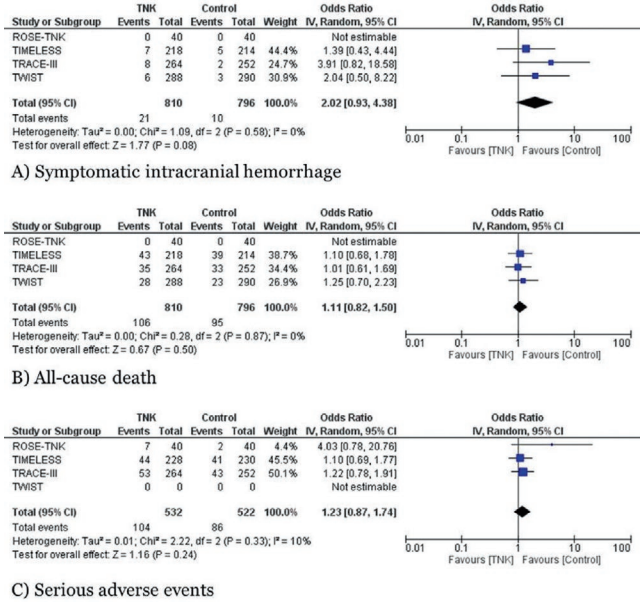

FIGURE 2 Forest plots for (A) Symptomatic intracranial hemorrhage, (B) All-cause death, and (C) Serious adverse events.

Conclusion: TNK administration outside the conventional treatment window in AIS patients leads to favorable neurological outcomes with a good safety profile.
Disclosure: Nothing to disclose.

EPO-205 | Recombinant human pro-urokinase vs. alteplase within 4.5 hours of acute ischemic stroke: A meta-analysis

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[1]Rawalpindi Medical University, Pakistan; [2]Dow Medical College, Pakistan; [3]Royal Brompton Hospital, London, UK; [4]Royal Wolverhampton NHS Trust. New Cross Hospital, Wolverhampton; [5]University Hospital Southampton NHS Foundation Trust; [6]Sheikh Shakhbout Medical City

Background and aims: Recombinant human pro-urokinase (rhPro-UK) has emerged as a potential alternative to alteplase for patients with acute ischemic stroke (AIS) presenting within 4.5 hours of symptom onset. This meta-analysis evaluates and compares the efficacy and safety of rhPro-UK with alteplase in this patient population.
Methods: A comprehensive search was conducted on PubMed, Cochrane and EMBASE to find eligible RCTs comparing rh-Pro-UK with r-tPA in AIS patients treated within 4.5 hours of symptom onset. A random-effects meta-analysis was conducted using RevMan Web.
Results: Three RCTs encompassing 2,289 patients (rhPro-UK: 1141; r-tPA: 1148) met the inclusion criteria. The pooled analysis demonstrated no significant difference between rhPro-UK and alteplase in achieving excellent functional outcome (mRS 0-1 at 90d: RR = 1.04, 95% CI = 0.98 to 1.10; P = 0.17) and good excellent functional outcome (mRS 0-2 at 90d: RR = 1.0, 95% CI = 0.96 to 1.05; P = 0.86). No statistically significant difference was observed for early neurological improvement (RR 1.05, 95% CI 0.96 to 1.15), symptomatic intracranial hemorrhage (RR = 0.52, 95% CI = 0.19 to 1.43), all-cause mortality (RR 1.10, 95% CI 0.64 to 1.91) and severe adverse events (RR = 0.92, 95% CI = 0.75 to 1.13).

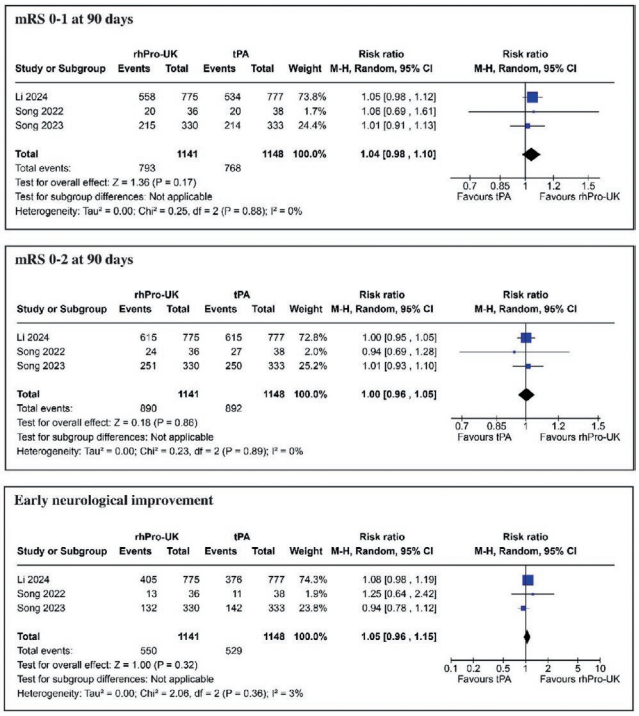

FIGURE 1 Forest plots for (A) Excellent Functional Outcome, (B) Good functional Outcome, and (C) Early Neurological Improvement.

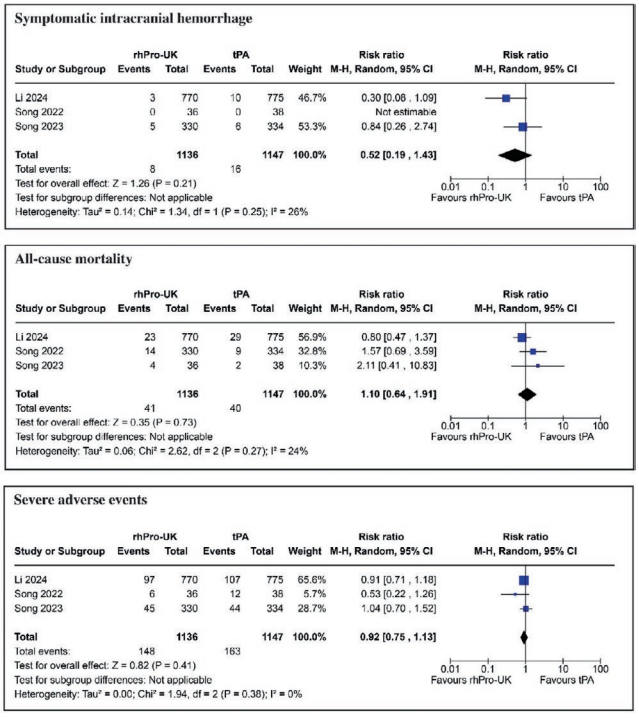

FIGURE 2 Forest plots for (A) Symptomatic intracranial hemorrhage (B) All-cause mortality, and (C) Serious adverse events.

Conclusion: This meta-analysis found no significant differences between rhPro-UK and alteplase in functional recovery, early neurological improvement, or safety outcomes, including symptomatic intracranial hemorrhage and all-cause mortality. rhPro-UK shows promise as a cost-effective alternative, but further large-scale RCTs are required to confirm its role in AIS management.

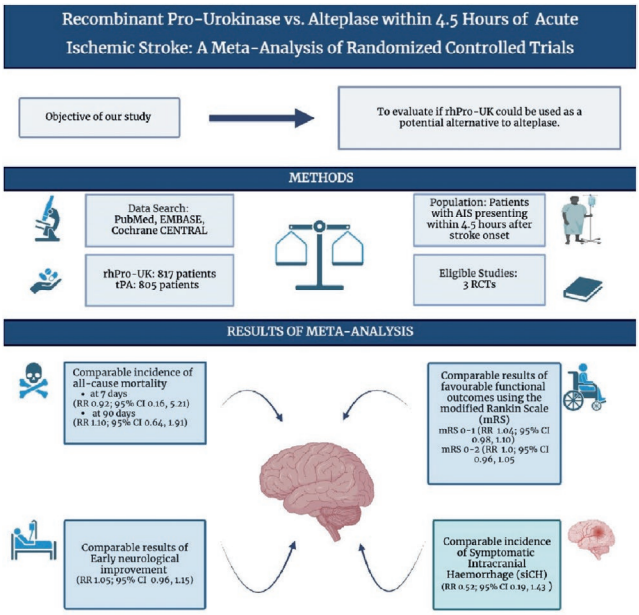

FIGURE 3 Graphical abstract

Disclosure: Nothing to disclose.

EPO-206 | Paracentral Acute Middle Maculopathy: a retinal stroke which strokeologists should know about

D. Damas[1]; S. Matos[1]; A. Jorge[1]; A. Martins[2]; G. Santo[1]; F. Silva[1]; J. Lemos[1]
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Background and aims: Paracentral acute middle maculopathy (PAMM) represents a unique subtype of retinal stroke that has been associated to vascular risk factors, including carotid disease and microvascular retinopathy. It typically causes sudden monocular vision loss with strikingly normal fundoscopic examination. Only when performing optical coherence tomography (OCT), will one confirm the presence of hyperreflective bands in the inner retina indicating ischemia.
Methods: Case reports.
Results: Case 1. A 56-year-old female with arterial hypertension presented with acute scotoma in the right eye, without other neurological symptoms. Best corrected visual acuity (BCVA) was 16/20 on the right eye and fundus examination was unremarkable. Perimetry showed a central scotoma in the right eye. OCT revealed hyperreflective band in the inner nuclear and outer plexiform layers, consistent with PAMM. Vascular investigation showed no significant findings, and was attributed to hypertensive microvascular disease. Secondary prevention was initiated. Follow-up showed perimetric improvement. Case 2. A 53-year-old male with arterial hypertension reported acute visual loss of right eye and left-sided weakness. BCVA was 30/20 on the right eye and fundus examination was grossly normal. OCT showed hyperreflective bands in the right macula, compatible with PAMM. Vascular imaging revealed narrowing and intramural thrombus of the right internal carotid artery, suggesting carotid dissection. Antiplatelet therapy and rehabilitation was initiated.
Conclusion: Acute monocular vision loss with a normal fundoscopic examination can still reflect a retinal stroke, from hypertensive microvasculopathy to imminent atherosclerotic retinal artery occlusion. The detection of hyperreflective bands on OCT confirms PAMM and should prompt exclusion of cerebrovascular disease.
Disclosure: Nothing to disclose.

EPO-207 | Multiscale neural signals in seizure prediction: A comprehensive literature review and meta-analysis

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[1]MME Foundation; [2]Newgiza University; [3]Badr University in Cairo; [4]Modern University for Technology and Information

Background and aims: Predicting epileptic seizures accurately remains a critical challenge in neuroscience, with profound implications for improving patient quality of life. This review and meta-analysis evaluates the effectiveness of multiscale neural signal analysis in enhancing seizure prediction accuracy.
Methods: A systematic search of PubMed, Embase, and Cochrane Library identified studies utilizing electroencephalography (EEG), magnetoencephalography (MEG), or intracranial EEG (iEEG) data for seizure prediction. Key metrics extracted included prediction accuracy, sample size, signal processing methods, and machine learning algorithms. Meta-analyses were performed using R to compute pooled effect sizes and confidence intervals.
Results: Thirty studies met inclusion criteria. Meta-analysis demonstrated that multiscale neural signal analysis improves seizure prediction accuracy by an average of 15% (95% CI: 12%–18%) compared to traditional methods. Techniques that integrated time and frequency domain features, such as wavelet transforms and Fourier analysis, showed superior performance. Deep learning approaches, particularly long short-term memory (LSTM) networks, achieved the highest predictive accuracy. Larger sample sizes ($n > 50$) and cross-validation methods were associated with more robust outcomes.
Conclusion: Multiscale neural signal analysis significantly enhances seizure prediction accuracy, outperforming traditional approaches. Combining advanced signal processing with machine learning techniques, particularly deep learning, offers substantial promise for developing reliable predictive models. However, methodological standardization is needed to improve reproducibility and comparability across studies. Future research should focus on integrating multiscale signal analysis with emerging technologies to further refine and optimize seizure prediction methods.
Disclosure: Nothing to disclose.

EPO-208 | The effect of early dysphagia screening on stroke unit mortality: insights from RES-Q registry

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Institute of Psychiatry and Neurology

Background and aims: Guidelines strongly recommend early dysphagia screening despite limited supporting evidence. We aimed to evaluate the effect of early dysphagia screening on hospital mortality in acute ischaemic stroke patients admitted to stroke units that perform dysphagia screening routinely.
Methods: We performed a retrospective analysis of patients with ischemic stroke admitted to 24 Polish stroke units from January 2022 to December 2024 and reported to the RES-Q registry. Patients were stratified by baseline stroke severity, with adjustment for age, sex, baseline NIHSS, reperfusion therapy, and congestive heart failure.
Results: Of 14 788 reported to the registry, 388 were excluded due to the lack of dysphagia screening (n=53) or missing data (n=333). We observed a significant difference in the distribution of hospital mortality, favoring screening at 4-24h after admission (388 of n=5437, 6.7%) over screening <4h (741 of n=7852, 9.4%) and screening >24h (106 of n=725, 14.6%). After stratification for stroke severity, we found that patients with baseline NIHSS 0-5 subjected to dysphagia screening ≤24h were less likely to die compared to those screened >24h (1.4% vs. 4.9%, p=0.001; aOR 0.32, 95% CI: 0.12-0.81). No such association was seen in patients with NIHSS 6-16 (7.6% vs. 9.8%, p=0.174) or with NIHSS >16 (28.2% vs. 24.1%, p=0.147).
Conclusion: In stroke units that have already implemented dysphagia screening into routine practice, screening performed ≤24 hours of admission appears to reduce hospital mortality compared to more delayed screening. This refers particularly to patients with minor ischemic strokes who are typically considered the low-risk population.
Disclosure: Nothing to disclose.

EPO-209 | Impact of sex and infarct volume on early functional outcomes after mechanical thrombectomy in acute ischemic stroke

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[1]Student Scientific Group in Cerebrovascular Diseases, Jagiellonian University Medical College. Krakow Poland; [2]Department of Neurology. Jagiellonian University Medical College, Krakow Poland; [3]Department of Neurology, University Hospital, Krakow, Poland

Background and aims: The influence of factors like sex on outcomes after mechanical thrombectomy (MT) in acute ischemic stroke (AIS) patients remains uncertain. This study analyses pre-MT computed tomography perfusion (CTP) imaging values and early neurological improvement (ENI), a 24-hour post-MT metric of outcome, to examine sex-based differences in early recovery.
Methods: We retrospectively analyzed 573 consecutive patients with AIS in anterior circulation who underwent successful MT (TICI>=2b) at University Hospital, Krakow (2019–2023). We collected demographic and clinical factors including CTP imaging followed by post-processing analysis with RAPID software. Early neurological improvement (ENI) was defined as a reduction of >=4 on the National Institutes of Health Stroke Scale (NIHSS) compared with the baseline score or an NIHSS <2 within 24 hours after MT. Early infarct volume (EIV) was calculated using CTP-derived cerebral blood flow<30% volume.
Results: In the multivariate regression analysis, older age (OR=0.982 [0.967-0.997]) and pre-stroke diabetes (OR=0.643 [0.422-0.978) decreased odds for ENI, whereas perfect recanalization (TICI>=2c) increased the odds for achieving ENI (OR=2.139 [1.403-3.260], p<0.001). Although sex itself was not associated with ENI, an interaction between sex and EIV was observed (p=0.043), with EIV impacting female odds for ENI more substantially (OR=0.841 [0.764-923 per 10ml, p<0.001) in comparison to males (OR=0.949 [0.887-1.017, p=0.139).

Table 1: Baseline characteristics of AIS patients with and without early neurological improvement (ENI)

	Patients without ENI (N=214)	Patients with ENI (N=359)	*P* value
Demographics			
Female, n (%)	117 (54.7)	181 (50.4)	0.324
Age, years, median [IQR]	75 [66-82]	71 [63-80]	0.008
Stroke risk factors			
Hypertension, n (%)	165 (77.1)	259 (72.1)	0.191
Diabetes Mellitus, n (%)	66 (30.8)	70 (19.5)	0.002
Hiperlipidemia, n (%)	46 (21.5)	77 (21.4)	0.989
Atrial fibrillation, n (%)	73 (34.1)	121 (33.7)	0.921
History of stroke/TIA, n (%)	33 (15.4)	36 (10)	0.055
Smoking, n (%)	30 (14)	92 (25.6)	0.001
Clinical characteristics			
Baseline NIHSS, median [IQR]	17 (14-20)	16 (12-20)	0.103
Time from LKW to puncture, median [IQR]	262 [187-314]	229 [160-305]	0.021
Intravenous thrombolysis, n (%)	103 (48.1)	205 (57.1)	0.037
Perfect recanalization, (mTICI≥2c), n (%)	148 (69.2)	294 (81.9)	0.001
Stroke localization			
ICA, n (%)	37 (17.3)	44 (12.3)	0.036
M1, n (%)	126 (58.9)	212 (59.1)	
M2, n (%)	30 (14)	79 (22)	
Tandem, n (%)	21 (9.8)	24 (6.7)	
Stroke-related complications			
Pneumonia, *n* (%)	69 (32.3)	53 (14.8)	<0.001
Urinary tract infection, *n* (%)	45 (21)	43 (12)	0.004
No hemorrhagic transformation, *n* (%)	143 (66.8)	283 (78.8)	0.001
Outcomes			
90 functional independency (mRS<3), n(%)	74 (34.6)	292 (81.3)	<0.001
Death after 90 days, n (%)	71 (33.2)	30 (8.4)	<0.001
Radiological examination			
Infarct (CBF<30%), ml, median [IQR]	15 [5-41]	8 [0-25]	<0.001
ASPECTS, median [IQR]	8 [6-9]	8 [7-9]	0.015
Penumbra, ml, median [IQR]	95.5 [56.75-135]	88 [55-122]	0.381

* TIA transient ischemic attack, LKW - last known well; CBF cerebral blood flow; NIHSS National Institutes of Health Stroke Scale

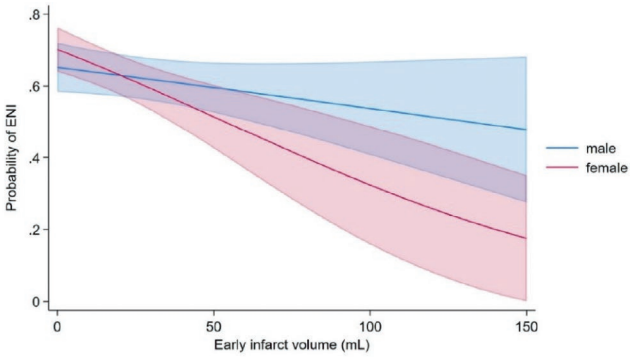

Figure 1: Regression analysis of early infarct volume (EIV) and probability of ENI (early neurological improvement) by patient sex

Table 2 . Multivariate regression results

	Adjusted OR for ENI (95% confidence interval)	Adjusted p-value
Age (per 1 year)	0.982 (0.967-0.997)	0.021
Diabetes	0.643 (0.422 – 0.978)	0.039
Smoking	1.561 (0.943-2.585)	0.083
Intravenous thrombolysis	1.404 (0.977-2.020)	0.067
Perfect TICI (≥2c)	2.139 (1.403-3.260)	<0.001
Early infarct volume in females (per 10mL)	**0.841 (0.764-923)**	**<0.001**
Early infarct volume in males (per 10mL)	**0.949 (0.887-1.017)**	**0.139**
Occlusion localization		
ICA	(reference)	
M1	1.443 (0.856-2.434)	0.168
M2	2.266 (1.190-4.311)	0.013
Tandem occlusion	1.139 (0.515-2.519)	0.749

Abbreviations: OR – odds ratio; ENI – early neurological improvement; TICI – thrombolysis in cerebral infarction; ICA – internal carotid artery; M1 – first segment of middle cerebral artery

Conclusion: This study illustrates that pre-procedural EIV in the female sex undergoing MT for anterior circulation AIS more significantly impacts early post-stroke outcomes. This may stem from sex-specific vulnerability to cerebral ischemia.
Disclosure: ERA-NET-NEURON/21/2020 BioStroke grant.

EPO-210 | Gender inequalities in stroke management in a comprehensive Italian hospital: A retrospective study on 9167 patients

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Background and aims: Several studies have demonstrated that risk factors and symptoms of stroke differ radically between the sexes. Furthermore, gender inequalities in stroke management have been widely described. The primary aim of this study was to analyze differences in stroke management between sexes. Moreover, we analyzed differences in in-hospital pathways and symptoms at onset of stroke by sex.
Methods: In this retrospective, cohort study, we consecutively enrolled adult patients admitted to the Emergency Department (ED) of an Italian comprehensive stroke center for suspected stroke from 2015 to 2022. Univariate comparisons were performed using Mann-Whitney, Kruskal-Wallis and χ2-tests, as appropriate. Binary and ordinal logistic regression models were used for the adjusted analyses.
Results: Overall, 9167 patients with suspected stroke were included in the study, of whom 4070 (44.4%) had a confirmed discharge diagnosis of Acute Ischemic Stroke (AIS). Considering the entire study population, we found that, in the adjusted analysis, male sex was an independent predictor of a lower likelihood of waiting ≥15 minutes in the ED (OR 0.694 95% CI (0.493-0.978);p=0.037) and of being classified as non-emergency code at triage (common OR 0.757 95% CI (0.580-0.988);p=0.040). Considering patients with a discharge diagnosis of AIS, we found that women were significantly older than men (p<0.001) and had higher median NIHSS at onset (p<0.001). No gender differences were found in the rate of revascularization treatments, hospitalization, and in-hospital mortality.
Conclusion: Although no differences were found in the rate of revascularization treatments administered, some sex inequalities in stroke management still persist and therefore require attention within in-hospital pathways.
Disclosure: Nothing to disclose.

EPO-211 | Positron emission tomography for diagnosing cerebrovascular disorders: a scoping review with practical suggestions

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Background and aims: Positron emission tomography (PET) has several potential applications in cerebrovascular pathology; however, it is poorly available as it requires radioactive tracers and has high costs. This scoping review aims to evaluate the current literature on the clinical applications of PET after stroke to lay the foundation for a framework of clinical use.
Methods: We conducted a scoping review according to the PRISMA statement. PubMed and Scopus databases were searched (on January 20th, 2024) for relevant articles. Study inclusion criteria were: observational design (cohort, cross-sectional, or case series studies with more than five patients), using PET with any technique, and reporting on clinical outcomes such as stroke recurrence, death, or clinical improvement. The Newcastle-Ottawa Scale (NOS) was used to assess the risk of bias.
Results: Out of 9866 initially included records, 13 articles were selected. Various PET tracers have been employed across studies, mostly including 18FDG, 15O, 11C PIB, 18F-florbetapir, and 18F-florbetaben. The most common cerebrovascular diseases included primary angiitis of the central nervous system (PACNS) detected using fluorodeoxyglucose (FDG)-PET and cerebral amyloid angiopathy (CAA) detected using amyloid tracer PET.
Conclusion: The use of cerebrovascular PET imaging tracers shows promise in assisting with diagnosis, though their current application remains restricted to experimental settings. Factors such as the use of different tracers and the evaluation of a limited number of patients hinder their diagnostic value. The most

promising applications of PET imaging are in diagnosing CAA and PACNS. However, standardized protocols are still required.
Disclosure: Nothing to disclose.

EPO-212 | Thrombophilia screening in young ischemic stroke patients

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Background and aims: Approximately 10-15% stroke patients are young adults aged between 18-50 years. Often, standard diagnostic work-up does not reveal stroke etiology. Thrombophilia testing is a common procedure although its clinical relevance remains unclear. Our aim was to assess routine thrombophilia testing and its clinical implications in young stroke.
Methods: A retrospective cohort study of ischemic stroke patients aged 18-50 years hospitalized at our tertiary stroke centre between January 2020 and December 2024 was performed. We determined baseline patients' characteristics, medical history, identified etiology and – if performed – results of the thrombophilia testing. Primary outcome was a positive thrombophilia screening. Association with age, gender, history of thromboembolism, patent foramen ovale (PFO) and cryptogenic stroke etiology was analysed.
Results: Out of 142 patients, 116 had a complete work-up and 68 were tested for thrombophilia. Any positive result was identified in 17 patients (25%, figure 1). There was no difference in age, gender, baseline neurologic deficit or cardiovascular risk factors (table 1). In only 4 patients (6%), positive thrombophilia screening results were deemed relevant or led to management change. In a multivariate logistic regression, positive thrombophilia screening was associated with lower odds of having a PFO-related stroke (OR 0.12 [0.22-0.66], p=0.02) while there was no association with other prespecified risk factors.

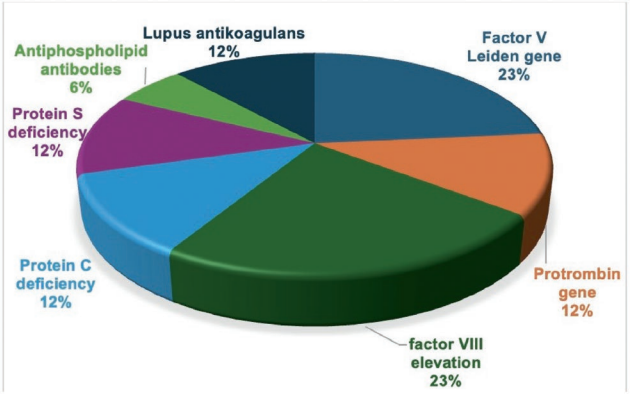

Figure 1: Distribution of positive test results

		Total	Tested	Negative screening	Positive screening	(p value)[1]
		N=116	N=68	N=51	N=17	
Age	median (IQR)	43.5 (37-47)	41.5 (34-46)	41 (34-46)	42 (38-44)	0.86
Gender male	n (%)	68 (58.6%)	34 (50%)	24 (47%)	10 (59%)	0.40
Baseline NIHSS	median (IQR)	4 (2-11)	4 (1-11)	3 (1-12)	7 (3-12)	0.23
Risk factors:						
Arterial hypertension	n (%)	40 (34.5%)	17 (25%)	12(24%)	5 (29%)	0.63
Hyperlipidemia	n (%)	74 (63.8%)	43 (63%)	30 (59%)	12 (71%)	0.39
Diabetes	n (%)	13 (11.2%)	5 (7%)	3(6%)	2 (12%)	0.42
Atrial fibrillation	n (%)	5 (4.3%)	0 (0%)	0 (0%)	0 (0%)	
History of stroke	n (%)	17 (14.7%)	8 (12%)	5 (10%)	3 (18%)	0.38
History of smoking	n (%)	52 (44.8%)	30 (44%)	21 (41%)	10 (59%)	0.21
Family history of stroke	n (%)	25 (22.9%)	18 (28%)	17 (35%)	2 (12%)	0.08
Hormonal contraception	n (% of female)	6 (12%)	6 (18%)	6 (19%)	0 (0%)	0.15
Hormonal treatment	n (%)	6 (6%)	5 (9%)	2 (5%)	3 (18%)	0.12
History of oncological diagnosis	n (%)	11 (9.5%)	8 (12%)	4 (8%)	3 (18%)	0.12
History of abortion	n (% of female)	2 (2%)	1 (3%)	1 (6%)	0 (0%)	0.5
History of VTE	n (%)	17 (15.0%)	15 (23%)	11 (22%)	4 (24%)	0.93
Prevalence of PFO	n (%)	31 (40%)	25 (45%)	23 (56%)	2 (14%)	0.007
Etiology –TOAST						0.30
1	n (%)	5 (4.3%)	2 (3%)	2 (4%)	0 (0%)	
2	n (%)	20 (17.2%)	6 (9%)	5 (10%)	1 (6%)	
3	n (%)	15 (12.9%)	7 (10%)	4 (8%)	3 (18%)	
4	n (%)	42 (36.2%)	32 (47%)	28 (51%)	5 (29%)	
5	n (%)	34 (29.3%)	21 (31%)	14 (27%)	8 (47%)	
Cryptogenic stroke etiology	n (%)	18 (15.5%)	17 (25%)	12 (24%)	6 (35%)	0.34
PFO-related stroke	n (%)	16 (13.8%)	13 (19%)	13 (25%)	0 (0%)	0.02

Table 1: Baseline characteristics in the total study group, tested patients a comparison of positive and negative screening results.
Abbreviations: NIHSS – National Institutes of Health Stroke Scale, VTE – venous thromboembolism, PFO – patent foramen ovale, IQR – interquartile range
1 – p value of positive vs negative screening using appropriate tests (Pearson's chi2 for binary and categorical variables, Wilcoxon rank-sum for continuous variables)

Conclusion: Routine thrombophilia screening in young stroke patients has low yield and its results are rarely clinically significant. There was high prevalence of cardiovascular risk factors in our young stroke cohort. Larger studies are necessary to assess testing for thrombophilia in different stroke subtypes.
Disclosure: Nothing to disclose.

EPO-213 | Pathological breathing patterns in unilateral lateral medullary infarction: a voxelwise lesion–behavior mapping study

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Background and aims: Acute unilateral lateral medullary infarction (ULMI) can damage the autonomic respiratory network and cause breathing disturbances in some patients. We aimed to find an association between lesion location/size and the occurrence of pathologic breathing patterns (PBP).
Methods: We prospectively followed 38 patients with ULMI (mean age 58±12 years, 30 (79%) men) hospitalized in our centre from 2015 to 2019. Polysomnography (PSG) and 1.5T MRI scans were performed in the acute phase. The presence of PBP such as tachypnea, moderate/severe ataxic breathing, and periodic breathing was documented from PSG. MRI lesions were mapped on the MNI-152 template using a computational algorithm and manual correction. All lesions were flipped to the right side and were blurred using a 3mm FWHM spatial filter. Subtraction analysis using voxelwise t-test was performed between patients with and without PBP (PBP vs non-PBP, respectively), identifying regions where the lesion burden differed significantly at p=0.05.
Results: PBP occurred in 25(66%) patients. The main lesion cluster was larger in PBP group compared to non-PBP group (2115 vs. 148 voxels). Subtraction analysis showed that PBP lesions more often affected a larger area of the rostral medulla, involving key autonomic, respiratory, and bulbar networks. An area in the inferior cerebellar peduncle (involved in vestibular

and somatosensory functions) was statistically more frequently affected in non-PBP group (Figure 1).

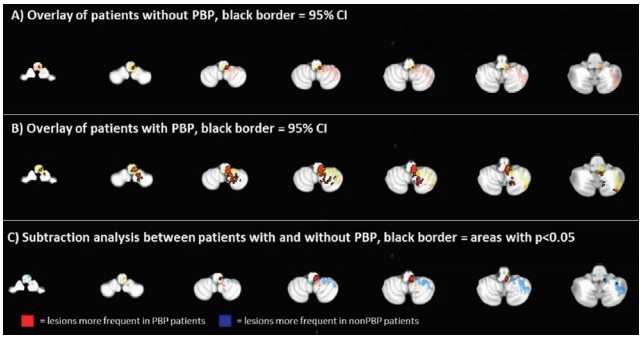

FIGURE 1 Overlay maps of lesions in patients with (A) and without (B) pathological breathing patterns (PBP). C) Subtraction analysis using a voxewise t-test between patients with and without PBP.

Conclusion: Our findings indicate that the presence of PBP in ULMI patients is associated with larger lesions in the medullary regions responsible for autonomic, respiratory, and bulbar functions.
Disclosure: There is nothing to declare.

EPO-214 | Stroke as a complication after transcatheter aortic valve implantation

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Background and aims: Stroke is one of the most concerning complications following transcatheter aortic valve implantation (TAVI). The aim of our study is to describe the characteristics of the event at our center and analyze factors potentially associated with stroke development.
Methods: We collected data from TAVIs performed at a tertiary university hospital between 2018-2024 and conducted a retrospective descriptive study. Additionally, we evaluated the association of stroke with patient characteristics and vascular risk factors using multivariate analysis.
Results: A total of 574 patients were included, 17 (3%) of whom experienced a cerebrovascular event. Of these, 10 (59%) were women, with an average age of 84 years. Atherosclerosis in the supra-aortic trunks was found by CT angiography in 53% of the cases. Binary logistic regression showed atrial fibrillation (AF) as the only risk factor with odds ratios of 11.68 (CI 95%: 2.123-64.259, p=0.005), observed in 58.8% of stroke patients versus 32% of non-stroke patients. The type of stroke was exclusively ischemic, 65% occurred within the first 24 hours and 35% between 24 and 48 hours after the procedure. Of the strokes, 76.5% were minor, and 23.5% were major. Only one patient was a candidate for fibrinolysis and one for mechanical thrombectomy. No patient died as a result of the cerebrovascular event.
Conclusion: Incidence of stroke was 3% in our series, generally presented as a minor stroke with no direct impact on mortality. Previous AF was the only risk factor.
Disclosure: Nothing to disclose.

EPO-215 | Discovery and validation of miRNAs in stroke: Profiling and bioinformatic target analysis

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Background and aims: MiRNAs and their target genes are recognized in the pathophysiology of ischemia.
Methods: Microarrays were performed with acute ischemic stroke vs control samples. Top non-coding regulators of ischemia (miR-18a-5p, miR-4467, miR-199a-5p and miR-3135b) was validated.
Results: Microarray data identified 146 up and 258 downregulated DE probes. Target prediction showed 67 up and 125 downregulated mRNAs mapped by multiMir R package. Targets of upregulated top miRNAs were most associated with BDNF, IL-2 signaling, FSH regulation of apoptosis, Axon guidance and TGF-beta regulation of EC matrix. Downregulated miRNAs were most associated with Axon guidance, Neuronal system and Signaling by NGF. ANKRD52, AGO1 were targeted by all types of DE miRNAs. Most susceptible to regulation by upregulated miRNAs: ANKRD12 and HIFIA and downregulated miRNAs: GNAI2 and GRIN. qRT-PCR analysis showed that miR-18a-5p was higher in stroke patients both at day l and 7 compared to control (p=0.001, p=0.009, respectively). MiR-199a-5p was higher in stroke group, and stayed higher at day? (p<0.001, p=0.002 respectively). MiR-4467 and miR-3135b were lower in stroke patients at day l compared to control (p<0.001, p<0.001, respectively). ROC curve showed diagnostic value for all studied miRNAs for acute stage of stroke (p<0.01).

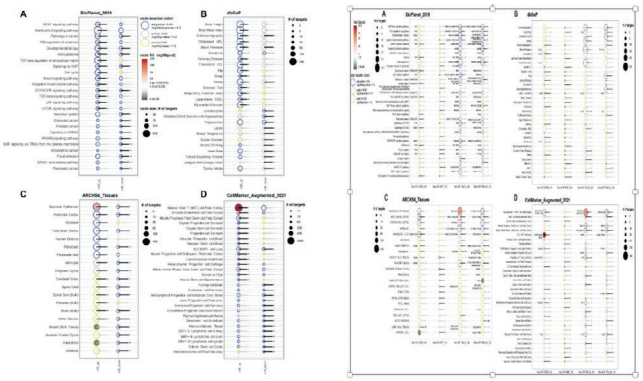

FIGURE 1

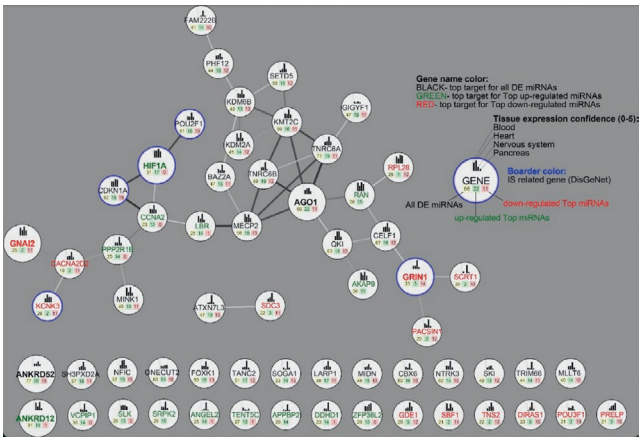

FIGURE 2

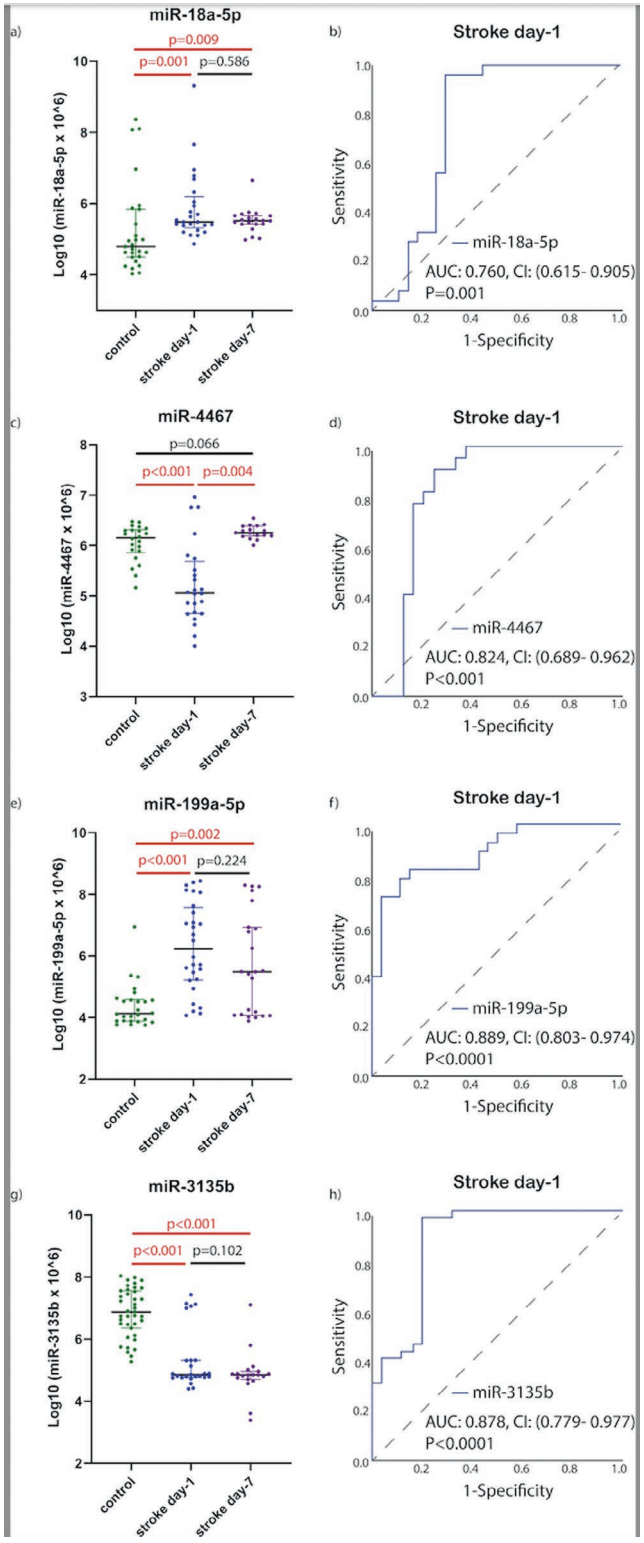

FIGURE 3

Conclusion: In our study microarray, validation and bioinformatic analysis results identified miR-18a-5p known to play a role in the pathophysiology of ischemia. Another promising biomarker of recovery from ischemia that was identified is miR-3135b. The measurement techniques for determining miRNA are developing and may in the near future enable the use of these biomarkers in clinical practice. OPUS; 2018/31/B/NZ7/01137.

Disclosure: No competing interest.

EPO-216 | Surgical material cardioembolic stroke as a complication of ablative thoracoscopy

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Background and aims: Perioperative cardioembolic stroke is severe complication of cardiac surgery. The particularity of this case lies in the thrombectomy's findings, where the extracted emboli consisted of exogenous surgical material. To our knowledge, no similar cases have been previously reported.
Methods: Description of a case report.
Results: A man in his late 70s, with a history of hypertension and refractory atrial fibrillation underwent thoracoscopic ablation. During the procedure, he experienced a rupture of the left superior pulmonary vein and left atrium, resulting in pericardial effusion, cardiac tamponade, and cardiogenic shock. An emergent pericardiocentesis followed by pericardiotomy to repair the atrial rupture were performed. A CT scan revealed acute infarction in the left hemisphere and left carotid artery thrombosis, and the patient was transferred to a Comprehensive Stroke Center in the area for mechanical thrombectomy. Recanalization (TICI 2b) was achieved with a single thrombectomy device pass. A thrombus which included textile/fibre-like material was obtained, and embolization of exogenous material during emergent pericardiotomy was suspected as the stroke cause. Despite optimal medical therapy, the patient passed away a few days later.

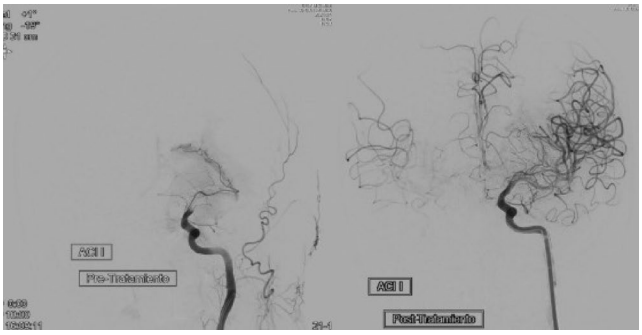

FIGURE 1 Left internal carotid arteriography pre-treatment and post-treatment

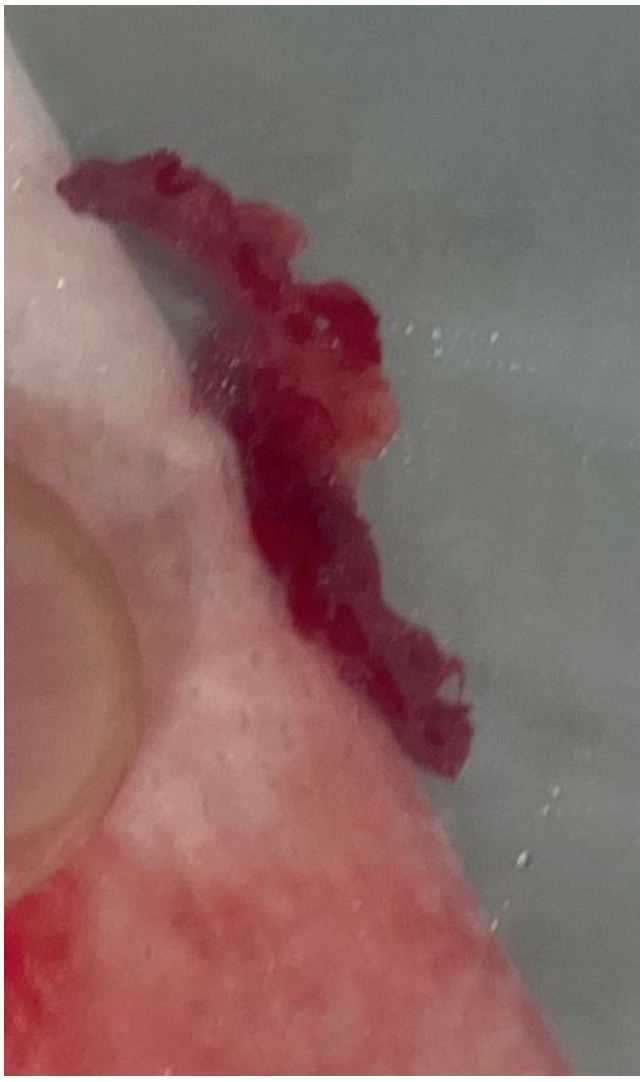

FIGURE 2 Extracted material consisting of a surgical gauze and hematic content

Conclusion: Perioperative stroke still occurs in 2.6% of patients undergoing cardiac surgery despite the application of prevention measures. Despite being uncommon, foreign-body cardioembolic stroke should be in the differential diagnosis, as it has previously been described.
Disclosure: Nothing to disclose.

EPO-217 | Locked-in syndrome due to severe case of varicella zoster virus vasculitis

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Background and aims: Varicella zoster virus (VZV) vasculitis is a rare but serious complication arising from the reactivation of the varicella zoster virus. This condition primarily affects the elderly and immunocompromised individuals, posing significant challenges in diagnosis and management. The virus can lead to vasculitis by directly invading blood vessel walls or triggering

an immune response that targets vascular structures. VZV vasculitis can have diverse clinical presentation, ranging from skin lesions and neurological deficits to systemic manifestations. Skin findings often include vesicular eruptions in a dermatomal distribution, resembling herpes zoster, while neurological involvement may lead to cerebrovascular accidents or encephalitis. The intricate interplay between viral factors and the host's immune response contributes to the complex pathogenesis of VZV vasculitis.
Methods: Case report.
Results: 69-year-old female patient with severe course of VZV-vasculitis first presented with headache, meningismus, undulating dysartria and general malaise but over next week progressed to locked-in syndrome due to vast ischemic damages in brainstem and cerebellar region, shown on images 1-3. Diagnosis was confirmed by radiological findings and presence of VZV IgG antibodies in cerebrospinal fluid. The patient was treated with intravenous acyclovir for 21 days, along with intravenous methylprednisolone, without remarkable positive effect.

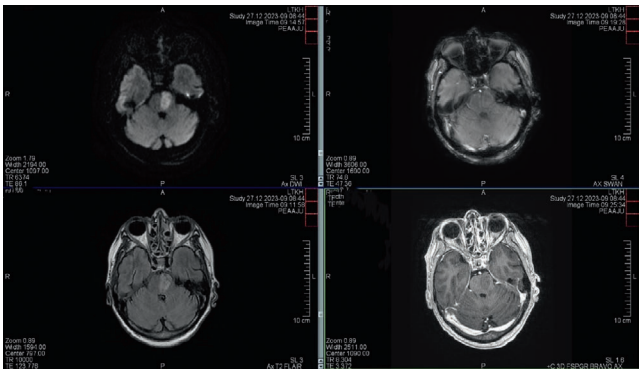

FIGURE 1 Second MRI scan showing ischemic lesion in the brainstem on the left.

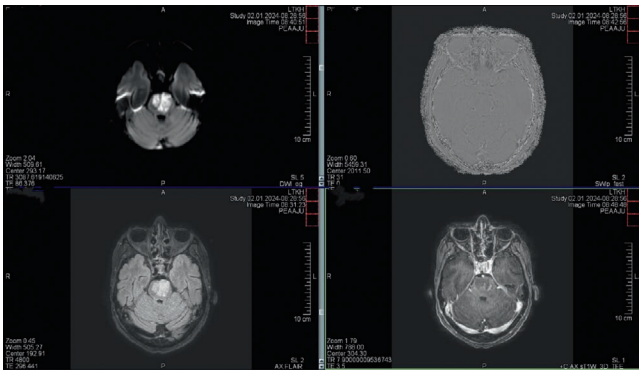

FIGURE 2 Third MRI scan showing ischemic lesion's progression in the brainstem.

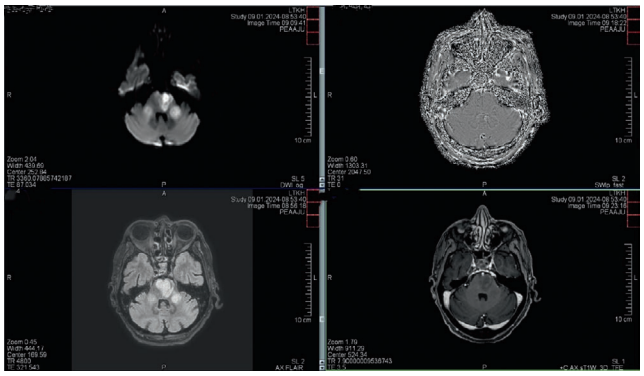

FIGURE 3 Fifth MRI scan showing ischemic lesions' dynamic in the brainstem and cerebellar peduncles.

Conclusion: Diagnosing VZV vasculitis requires multidisciplinary approach, combining clinical evaluation, imaging and laboratory analyses. Early recognition is crucial to initiate prompt antiviral and immunosuppressive therapy, aiming to mitigate the inflammatory response and prevent further vascular damage. This abstract emphasizes the need for awareness among clinicians, given the potential for severe morbidity and mortality associated with VZV vasculitis.
Disclosure: Nothing to disclose.

Neurological Manifestation of Systemic Diseases and Neurotoxicology

EPO-218 | Subacute cerebellar syndrome, gait disorder and nistagmus due to hypomagnesemia

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Background and aims: Hypomagnesemia is known to cause neurological symptoms such as tremor, tetany, and seizures, though it rarely presents as an acute cerebellar syndrome accompanied by oculomotor disturbances, with vertical nystagmus being the most frequently reported. We describe a case of pendular nystagmus and cerebellar ataxia in the context of severe hypomagnesemia.
Methods: A 62-year-old woman on long-term proton pump inhibitor therapy presented with abdominal pain, nausea, dizziness, and diplopia following a gastroenteritis episode and intensification of treatment. Three days later, she developed gait ataxia, lateropulsion, instability, and primary gaze nystagmus with changes in orientation and direction during ocular pursuit. Over subsequent days, appendicular cerebellar syndrome and limb myoclonus emerged.
Results: Initial brain MRI and MR angiography revealed no abnormalities. Laboratory tests highlighted significant

hypocalcemia (7.8 mg/dL) and hypomagnesemia (0.5 mg/dL). Magnesium replacement therapy was promptly initiated. Nystagmus resolved within hours, and ataxia improved over the following days. 5 months later, mild nystagmus during ocular pursuit and slight diplopia persisted, alongside a mildly unsteady but stable gait.

Conclusion: Severe hypomagnesemia can manifest as acute cerebellar ataxia, additional cerebellar symptoms and oculomotor abnormalities, particularly downbeat nystagmus. Pendular nystagmus is typically associated with demyelinating diseases, acquired brainstem lesions, cerebellar syndrome, genetic disorders, and metabolic conditions. This case underscores the importance of considering electrolyte imbalances in the differential diagnosis of acute cerebellar syndromes and highlights the potential for rapid neurological recovery with timely intervention. Further research is needed to elucidate the mechanisms underlying pendular nystagmus in hypomagnesemia.

Disclosure: Nothing to disclose.

EPO-219 | Neurological conditions after bariatric surgery, addressing more than complications

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Background and aims: Bariatric surgery (BS) as an obesity treatment has increased. Although reports suggest improvements in headaches and cognitive function post-op, neurological conditions may arise, often linked to nutritional deficits. This study aims to describe neurological conditions associated with BS.

Methods: Six-year retrospective study, descriptive analysis.

Results: We analysed 385 patients (83.9% female, mean age: 47.6 years (SD=11.2)). Comorbidities were mostly vascular risk factors. Procedures included gastric bypass (GB) (50.9%), sleeve (45.2%) and SADI-S (3.9%). Vitamin supplementation began 3.1 days (SD=4.2) post-op. Neurological complications occurred in 3.1% (all female, 11 (91.7%) post-GB) at median onset-time of 29.5 months (IQR=50-20.25) post-BS: 3 compressive mononeuropathies, 2 Wernicke's encephalopathies, 6 cognitive complaints (CC) and 1 Guillain-Barré syndrome (GBS). CC cases (median onset: 24 months (IQR=52-24) post-op) were referred to Neurology consultation, with 2 improving after initial observation. Brain-image showed subcortical atrophy in 1 case. CC were linked to B12-vitamin deficiency and psychopathology in 2 cases each. Previous headaches were reported in 23 patients (13 with neurological follow-up). In 19 migrainers, 8 reduced headache frequency post-op, 3 discontinuing prophylaxis. Three patients (2 with suspected obstructive sleep apnea and 1 with idiopathic intracranial hypertension) experienced complete resolution.

Conclusion: Our sample had a low rate of neurological complains, consistent with literature. Nearly 50% of migrainers improved post-BS, suggesting potential benefit. Although unclear, other factors than vitamin deficits, like hormonal changes, may link weight loss to cognitive impairment. Besides typical complications, we highlight the case of GBS, which could imply potential influence of BS on immune mediated responses.

Disclosure: Nothing to disclose.

EPO-220 | Evaluation of the role of omega-3 fatty acids in nicotine-induced neurotoxicity in pregnant Wistar rats and their pups

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Background and aims: This study investigated maternal and their pup neurobehaviour following nicotine exposure during gestational and postnatal periods and neuroprotective effect of Omega-3 fatty acids.

Methods: The study used thirty pregnant female Wistar rats for this study. Groups I and II were treated with 1ml/kg/day of normal saline for 42 days; III was treated with 4 mg/kg/day of nicotine for 42 days; IV-VI were co-administered nicotine 4 mg/kg and 100, 300, 600 mg/kg/day of Omega-3 fatty acids respectively for 42 days.

Results: The beam walk time of the mother rats in groups III and IV were significantly higher when compared with other groups. Similarly, the beam walks time of the pups of groups III and IV were significantly higher when compared with the pups of the mother rats in other groups. The brain dopamine and serotonin levels of mother rats in groups III, IV and V were significantly higher when compared with other groups. Also, the brain dopamine and serotonin levels of the pups in groups III and IV were significantly higher when compared with the pups in other groups. The reduced glutathione and catalase of mother and pup rats in groups III and IV were significantly lower when compared with other groups. Photomicrographs of cerebellum and hippocampus of the rats treated with nicotine showed scattered arrangement of pyramidal cells with vacuolated neurons. These alterations were significantly reversed with Omega-3 fatty acids following nicotine exposure.

Conclusion: Omega-3 fatty acids at 300 and 600mg/kg ameliorated nicotine-induced neurotoxicity in mother rats and their pups.

Disclosure: Nothing to disclose.

EPO-221 | Two sisters with facial paresis and low back pain – genetic Neurosarcoidosis?

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Background and aims: Sarcoidosis is a systemic immune-mediated disease characterized by granulomatous inflammation affecting multiple organs. Neurosarcoidosis (NS) affects 5-10% of patients with systemic sarcoidosis. The existence of familial forms suggests that genetic predisposition plays an important role in sarcoidosis pathogenesis.

Methods: Case report and literature review.

Results: Two sisters with no relevant personal medical history presented with similar symptoms, two years apart. TRS at 49 years developed severe low back pain (LBP), thoracic band-like hypoesthesia and fever lasting four weeks, followed by left facial paresis. ERS at 54 years presented right facial paresis, followed one month later by left facial paresis, distal paresthesia, abdominal band-like hyposthesia, gait imbalance, LBP, and urinary hesitation. Both

cases presented CSF with pleocytosis and hyperproteinorrachia with no evidence of infection, elevated serum ACE levels, chest CT scans with lymphadenopathies, and lymph node biopsy with non-necrotizing granulomas. The neuro axis MRI showed gadolinium enhancement of the left facial nerve in TRS, and along the roots of the cauda equina in ERS. Both patients improved with corticotherapy, supporting the diagnosis of NS.
Conclusion: The relevance of these cases lies in the identification of neurosarcoidosis in two sisters with a similar clinical presentation. Having a relative with sarcoidosis is a known risk factor, and both genetic and environmental factors appear to contribute to its pathophysiology. Furthermore, one of the patients presented with polyradiculopathy, an uncommon manifestation of neurosarcoidosis. Additional studies are needed to improve diagnosis and treatment, as well as to better understand the pathophysiology of this condition.
Disclosure: Nothing to disclose.

EPO-222 | Dementia in the patients with inflammatory arthritis: An analysis of data from national health insurance service

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Background and aims: We evaluated the risk of dementia between the patients of inflammatory arthritis and matched population, using data from National Health Insurance Service.
Methods: We defined the patients of ankylosing spondylitis, seropositive rheumatoid arthritis, and psoriatic arthritis and enteropathic spondyloarthropathy, using the combination of main diagnosis. Control group was defined by 1:5 propensity score matching in each disease.
Results: In a multivariate analysis including dementia risk factors (hypertension, diabetes, dyslipidemia, and depression), a diagnosis of rheumatoid arthritis with a positive serologic test was associated with a greater incidence of dementia with HR 1.10, 95% CI 1.02-1.20 (p=0.0159), the incidence of dementia was lower in the group that used biological agents than in the group that did not (HR 0.46, 95% CI 00.33-0.65, p<0.0001). Among biological agents, the group using non-TNF blocker had a significantly lower incidence of dementia (HR 0.37, 95% CI 0.21-0.65, p=0.0005).
Conclusion: In the case of rheumatoid arthritis with a positive serological test, this study also showed a high risk of developing dementia, similar to the results of other previous studies. Regarding changes according to the administration of biological agents, previous studies have shown that anti-TNF antagonists lower the risk of developing dementia, but this study also showed that the administration of biological agents lowers the risk of developing dementia, and anti-TNF antagonists Rather, in the case of non-anti-TNF antagonists, a statistically significant decrease was shown.
Disclosure: Nothing to disclose.

EPO-223 | Protecting the brain with cognitive reserve while healing hearts with coronary artery cardiac surgery

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Background and aims: Postoperative cognitive decline (POCD), can range in severity from mild cognitive impairment to dementia and delirium, is one of the most serious side effects after coronary artery bypass grafting (CABG). Significant POCD, which includes a decline in cognitive functions and social functioning, is common in CABG patients. Cognitive reserve (CR), a protective factor that acts as a buffer against the effects of neuropathology, aging, and/or trauma, may be able to mitigate these negative effects. It describes the distinct ways that people approach tasks, which may allow them to be more resilient than others.
Methods: Using extracorporeal circulation, we evaluated 101 patients both prior to and four months following cardiopulmonary bypass surgery. The evaluation comprised measures of depression, anxiety, CR, and cognitive functions. CR was estimated using functional score, occupation, age, educational attainment, and vocabulary measurements.
Results: Focusing on median split, each patient was assigned to either the high (n=50) or low CR (n=51) group. On post-surgery neuropsychological evaluation, patients with low CR were significantly more likely than those with high CR to exhibit post-surgical cognitive decline in attention, memory, visuospatial perception, and executive functions, according to the effect of chi-square tests.
Conclusion: Cognitive rehabilitation is essential due to severity of POCD and its impact on functioning, which are aspects of quality of life. CR may predict the neuropsychological effects of heart surgery, identify patients with low CR, and assist them in engaging in intervention programs that may slow cognitive aging, lower the risk of dementia, and improve their overall recovery following surgery.
Disclosure: Nothing to disclose.

EPO-224 | OverTTuRe study: Disease burden at diagnosis in ATTR amyloidosis patients with neurological impairment in Spain

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Background and aims: Amyloid Transthyretin (ATTR) amyloidosis is a debilitating and often misdiagnosed condition, characterized by the accumulation of transthyretin amyloid fibrils in various organs and tissues. The OverTTuRe study seeks to provide insights into the pre- and post-diagnosis journeys of ATTR patients (all phenotypes) - this communication focuses on the baseline data (up to diagnosis) of patients in Spain with

neurological impairment (peripheral neuropathy -PN- and mixed).

Methods: Observational, retrospective chart review in 11 hospitals across Spain. 107 ATTR-PN patients and 150 ATTR mixed patients with diagnosis from 2009 onwards were included (Figure 1).

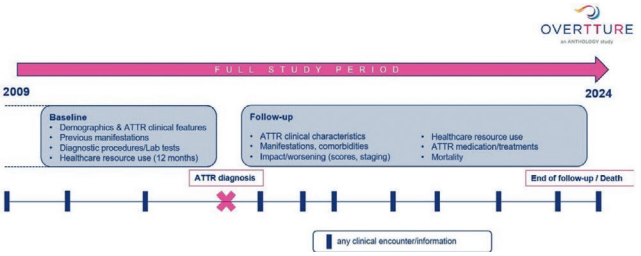

FIGURE 1 Study flowchart.

Results: At diagnosis, mean age (SD) was 66.1 (16.1) years, and 35.8% were female. 75.9% had ATTRv (hereditary), with Val50Met-late onset being the most predominant variant. 81.7% had a late onset (defined as age at diagnosis ≥ 50). From the first clinical manifestation associated with ATTR until diagnosis, the median time was 9.6 months (mean 44.9mos.), with notable differences between ATTR-PN (5.2mos.) and mixed (20.2mos.). The NIS mean score was 13.7, with most patients at FAP stage 1 (82.5%) and a PND score of 1 or 2 (88.2%). Healthcare resource utilization (HCRU) prior to diagnosis were generally greater in mixed patients. Baseline data are summarized in Table 1. A wide range of clinical manifestations were already present at diagnosis (Table 2).

TABLE 1 Baseline characteristics.

Baseline characteristics		ATTR all (PN + mixed) (N = 257)		ATTR-PN (N = 107)		ATTR mixed (N = 150)	
Age at diagnosis, years – mean (SD)		66.1 (16.1)		54.8 (14.9)		74.1 (11.4)	
< 50 years (early onset) - %		18.3%		39.3%		3.3%	
≥ 50 years (late onset) - %		81.7%		60.8%		96.7%	
Sex, female (%)		35.8%		46.7%		28.0%	
Family history of ATTR amyloidosis (confirmed) - %		53.7%		81.4%		31.2%	
Genotype - %	Hereditary	75.9%		100%		58.7%	
	Wild-type	19.5%		-		33.3%	
	Unknown/Unavailable	4.7%		-		8.0%	
Type of mutation – %	Val50Met – late onset	54.7%	N: 161	50.6%	N: 81	58.8%	N: 80
	Val50Met – early onset	14.3%		25.9%		2.5%	
	Val142Ile	10.6%		9.9%		11.3%	
	Other	20.4%		13.6%		27.4%	
Time from 1st manifestation to diagnosis, months	Mean (SD)	44.9 (68.4)	N: 152	29.8 (61.4)	N: 58	54.2 (71.1)	N: 94
	Median	9.7		5.2		20,2	
Biopsy-proven diagnosis - %		27.6%		26.2%		28.7%	
Neuropathy Impairment Score (NIS) – mean (SD)		13.7 (15.9)	N: 91	9.6 (13.3)	N: 56	20.2 (17.5)	N: 35
FAP Coutinho - %	Stage 0	6.3%	N: 160	5.2%	N: 77	7.2%	N: 83
	Stage 1	82.5%		88.3%		77.1%	
	Stage 2	10.0%		6.5%		13.3%	
	Stage 3	1.3%		-		2.4%	
PND score - %	Score 1	66.0%	N: 153	77.6%	N: 67	57.0%	N: 86
	Score 2	22.2%		14.9%		27.9%	
	Score 3A	4.6%		3.0%		5.8%	
	Score 3B	5.2%		4.5%		5.8%	
	Score 4	2.0%		-		3.5%	
NYHA stage - %	I	50.6%	N: 168	90.9%	N: 55	31.0%	N: 113
	II	41.1%		7.3%		57.5%	
	III	8.3%		1.8%		11.5%	
	IV	-		-		-	
HCRUs – 12 months prior to diagnosis							
≥ 1 visit to PC or specialist - %		87.7%	N: 220	88.5%	N: 99	87.4%	N: 121
PC visits, Total – mean (SD)		2.5 (5.2)		2.1 (4.0)		2.9 (6.0)	
PC, ATTR-related* - mean (SD)		0.4(1.2)		0.5 (1.2)		0.4 (1.2)	
Specialist, Total – mean (SD)		6.0 (6.7)		5.2 (5.6)		6.5 (7.5)	
Specialist, ATTR-related* - mean (SD)		3.7 (5.0)		4.2 (4.0)		3.3 (5.7)	
≥ 1 Hospitalisation - %		28.1%	N: 224	12.4%	N: 97	40.2%	N: 127
≥ 1 Hospitalisation, ATTR-related* - %		21.0%		8.3%		30.7%	
Hospitalisations, Total – mean (SD)		0.4 (0.6)		0.1 (0.4)		0.5 (0.7)	
Hospitalisations, ATTR-related* – mean (SD)		0.2 (0.4)		0.1 (0.3)		0.3 (0.5)	
Days hospitalised**, Total - mean (SD)		14.4 (17.5)	N: 56	10.5 (8.0)	N: 11	15.4 (19.1)	N: 45
Days hospitalised**, ATTR-related* – mean (SD)		14.0 (10.1)	N: 40	11.7 (9.0)	N: 7	14.5 (10.4)	N: 33

SD: standard deviation; FAP: Familial amyloid polyneuropathy; PND: Polyneuropathy Disability; NYHA: New York Heart Association; HCRU: Healthcare Resource Utilisation; PC: Primary Care
* ATTR-related: although ATTR diagnosis was not present, participating hospitals could determine relation to ATTR retrospectively.
** Among hospitalised patients

TABLE 2 Clinical manifestations at baseline.

Clinical manifestations	ATTR all (PN + mixed) (N = 244)		ATTR-PN (N = 110)		ATTR mixed (N = 134)	
Polyneuropathy	62.9%	N: 256	83.0%*	N: 106	48.7%	N: 150
Carpal tunnel syndrome	36.0%	N: 250	38.0%	N: 100	34.7%	N: 150
Autonomic neuropathy	25.6%	N: 250	33.7%	N: 101	20.1%	N: 149
Gait disorder	15.0%	N: 246	16.5%	N: 97	14.1%	N: 149
Cardiomyopathy	39.6%	N: 245	4.2%	N: 95	62.0%	N: 150
Heart Failure	24.6%	N: 244	1.0%	N: 96	39.9%	N: 148
Atrial fibrillation	23.5%	N: 243	1.0%	N: 95	37.8%	N: 148
Gastrointestinal dysfunction	27.3%	N: 256	36.8%	N: 106	20.7%	N: 150
Chronic kidney disease	12.3%	N: 243	3.2%	N: 95	18.3%	N: 148
Erectile dysfunction	22.1%	N: 253	22.3%	N: 103	22.0%	N: 150
Dyspnoea	33.6%	N: 244	8.3%	N: 96	50.0%	N: 148
Chronic pain	20.1%	N: 249	26.7%	N: 101	15.5%	N: 148
Edema	11.0%	N: 245	1.0%	N: 97	17.6%	N: 148
Hypotension	12.4%	N: 251	13.9%	N: 101	11.3%	N: 150
Hypertension	41.0%	N: 251	26.7%	N: 101	50.7%	N: 150

Note: clinical manifestations present in >10% of the analysis population have been included in this table.
*ATTR-PN patients without polyneuropathy at diagnosis had other dysautonomia symptoms and were therefore classified as "ATTR-PN" by investigators.

Conclusion: Our data underscore the substantial disease burden of the patients with ATTR-PN and ATTR-mixed amyloidosis already at diagnosis, partly due to a long and difficult diagnostic journey. These insights may help to establish improved recommendations for diagnostic procedures.

Disclosure: The OverTTure study is sponsored and funded by AstraZeneca.

EPO-225 | Lack of awareness of transthyretin amyloidosis with polyneuropathy and its impact on Spanish patients: ATENAS Study

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Background and aims: Transthyretin amyloidosis with polyneuropathy (ATTRv-PN) is a rare, hereditary, progressive and systemic disease that can highly impact patients' quality of life (QoL). However, studies addressing the patient's experience with ATTRv-PN are scarce.

Methods: The ATENAS Study is an observational and cross-sectional ongoing study describing the experiences of patients with ATTRv-PN, their caregivers and specialized clinicians. For this communication, 15 patients partook in semi-structured interviews. Interviews were recorded, and anonymized data were coded and analyzed thematically.

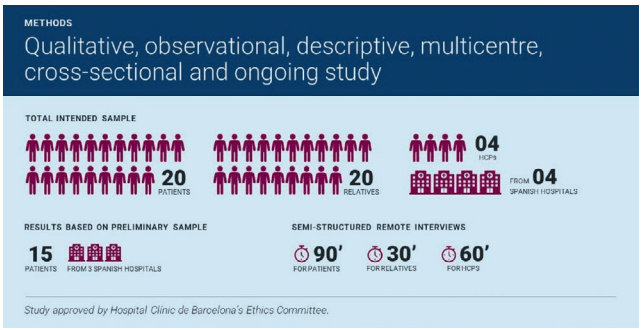

FIGURE 1 ATENAS study design

Results: Diagnostic delays from first symptoms' appearance until diagnosis –mean of 27 months for index patients and 9.5 months for patients with family history– were identified, reflecting lack of symptom and disease awareness among patients and healthcare professionals. The effect of ATTRv-PN on QoL divided patients into two groups. Group 1 presented many symptoms, with diarrhea and loss of mobility the most incapacitating and affecting QoL, and blindness the most feared in the future. Lack of early detection of symptoms worsened impact on QoL. Group 2 had fewer symptoms, with loss of feeling on the extremities and fatigue the most common. ATTRv-PN had been detected early, and patients reported good QoL. Polyneuropathy Disability (PND) score alone could not capture the severity of ATTRv-PN from patients' perspective since it was conditioned by the gravity of dysautonomia and patients' expectations according to their age.

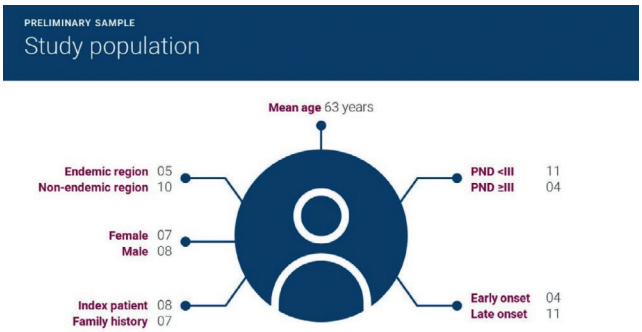

FIGURE 2 Description of the study population

Conclusion: Early detection and treatment of ATTRv-PN is crucial to delay the appearance of incapacitating symptoms and allow patients to live with good QoL. Increasing awareness of ATTRv-PN can be a step towards this goal.

Disclosure: This study has been sponsored and fully funded by AstraZeneca Farmacéutica Spain.

EPO-226 | Emotional and social impact of transthyretin amyloidosis with polyneuropathy on patients and caregivers: ATENAS Study

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Background and aims: Transthyretin amyloidosis with polyneuropathy (ATTRv-PN) is a rare, hereditary, and progressive disease caused by mutations in the transthyretin gene. Despite ATTRv-PN's impact on quality of life (QoL), very few studies have examined the lived experience of patients and families.
Methods: The ATENAS Study is an observational and cross-sectional ongoing study describing the experiences of patients with ATTRv-PN, their relatives and specialized clinicians. For this communication, 15 patients and 8 relatives partook in semi-structured recorded interviews. Data were anonymized, coded, and analyzed thematically.

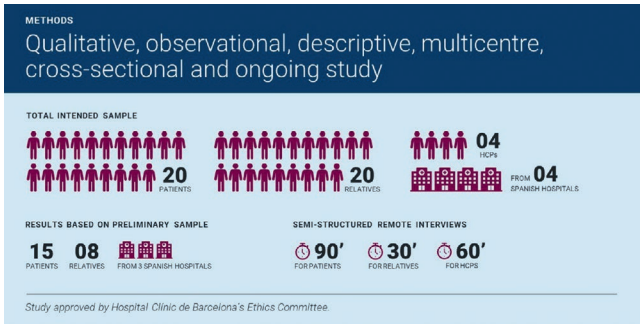

FIGURE 1 ATENAS study design

Results: Patients with severe symptoms faced distress, frustration and shame. Their social and work lives were significantly impacted. Their relatives endured considerable emotional challenges due to drastic lifestyle changes and high patient dependency, with loss of work opportunities and personal income, and high impact on their social lives. Patients with mild symptoms experienced fewer emotional, social and work impacts. Their relatives did not consider themselves caregivers and remained optimistic about the course of ATTRv-PN. Some patients and relatives thought ATTRv-PN would manifest similarly in their offspring. Some patients and relatives with severe symptoms hoped the disease would manifest differently (or not at all) in their offspring. All hoped future medical advances would allow their offspring to live with good QoL.

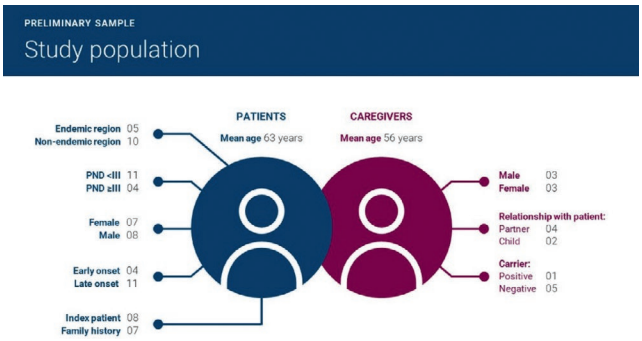

FIGURE 2 Description of the study population

Conclusion: Severe disabling symptoms impacted the emotional, social and work lives of patients and relatives, requiring psychological and emotional support. Multidisciplinary teams treating these patients should be aware of it to improve their QoL.
Disclosure: This study has been sponsored and fully funded by AstraZeneca Farmacéutica Spain.

EPO-227 | The Hidden Dangers of Nitrous Oxide: Minutes of laughter and source of severe neurological sequelae

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Background and aims: The rising use of nitrous oxide among young people, many of whom are unaware of its potential side effects, has become a growing epidemiological issue. This substance can cause significant neurological sequelae such as gait and sensory disturbances by cianocobalamine interference or depletion.
Methods: We describe the case of a 24-year-old male with a history of recreational drug abuse. He presented to the emergency department with a one-month history of fingertip paresthesia and mild gait disturbances, progressing over two weeks to severe instability and ataxia. The patient reported daily use of 6 nitrous oxide canisters (666 g each) for the past 18 months. Neurological examination revealed distal paresis in the upper limbs, distal and proximal weakness in the lower limbs, hyperactive patellar reflexes and hypoactive Achilles reflexes, absence of vibratory sensation in extremities and bilateral dysmetria in the upper limbs, worsened by visual deprivation. Gait examination showed widened base and lower limb weakness.
Results: Diagnostic workup revealed a normal cranial CT and in the bloodwork a vitamin B12 deficiency stands out. Cervical spine MRI showed hyperintensity in anterolateral and dorsal columns, typical of subacute combined degeneration.
Conclusion: This case highlights the importance of considering substance abuse, such as nitrous oxide, in the differential diagnosis of young patients with neurological symptoms like subacute sensory ataxia, paraparesis and polyneuropathy. Nitrous oxide is becoming increasingly popular, but its use can lead to permanent sequelae. Early diagnosis and rapid treatment are crucial to prevent them.
Disclosure: Nothing to disclose.

EPO-228 | Neurology practice among solid organ transplant candidates and recipients: The European academy of neurology survey

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Background and aims: Since neurological disorders can occur both before and after a solid organ transplant (SOT), the European Academy of Neurology (EAN) survey intended to provide a preliminary analysis of the extent and circumstances where neurologists are consulted in a transplantation setting.
Methods: A web-based survey was prepared and sent to all EAN members on behalf of the EAN Panel on Neurocritical care.
Results: A total of 176 neurologists completed the survey. Only 1 out of 5 neurologists see SOT candidates, mainly for neurological comorbidities, although they are not always involved in multidisciplinary meetings to establish transplant eligibility; neurologists are more often involved when a neurological complication occurs after a SOT (31.8% of respondents), mainly delirium (26.7%); less than 1 out of 10 received specific training on neurological issues in the transplantation setting during their residency; lastly, only a small number of neurologists are involved in research programs in the emerging field of brain-body interactions.
Conclusion: The survey clearly showed neurologists are seldom involved in SOT candidate evaluations even though a cognitive screening is recommended. Also, while post-SOT neurological complications for which neurologists are consulted can be life-threatening, only a minority of these professionals received specific training. The survey provided the basis for general guidelines to be agreed between the different associations/consortia of neurologists operating in this field.
Disclosure: - Authors have no conflicts of interest to declare relating to this study.

EPO-229 | When the Brainstem isn't to blame: A diagnostic challenge

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Background and aims: A clinical presentation suggestive of brainstem involvement often leads to the assumption of central

nervous system pathology. However, brain imaging might not reveal intracranial abnormalities, leading to a broader diagnostic process. We present a case report that highlights the importance of considering alternative causes for neurological symptoms suggestive of brainstem involvement.
Methods: We describe the clinical case of a patient with neurological symptoms indicative of brainstem involvement. He underwent multiple diagnostic tests, including brain MRI, chest CT, spine MRI, and biopsy for diagnosis confirmation.
Results: A 69-year-old man, with smoking habits, presented with sudden onset discoordination and weakness of the right lower limb. Neurological examination revealed Horner's syndrome of the left eye, dysphonia, ataxia and paresis of the right lower limb and ataxic gait. Brain MRI showed no abnormalities; however, chest CT revealed a mediastinal lesion extending into the vertebral canal from D1 to D4. Spine MRI confirmed spinal cord compression and invasion at this level. Biopsy identified the mass as a small cell lung cancer of the left apex (Pancoast tumour). Despite corticosteroid and radiotherapy treatment, the condition worsened, leading to paraparesis and urinary retention. The patient died 1 month after diagnosis.

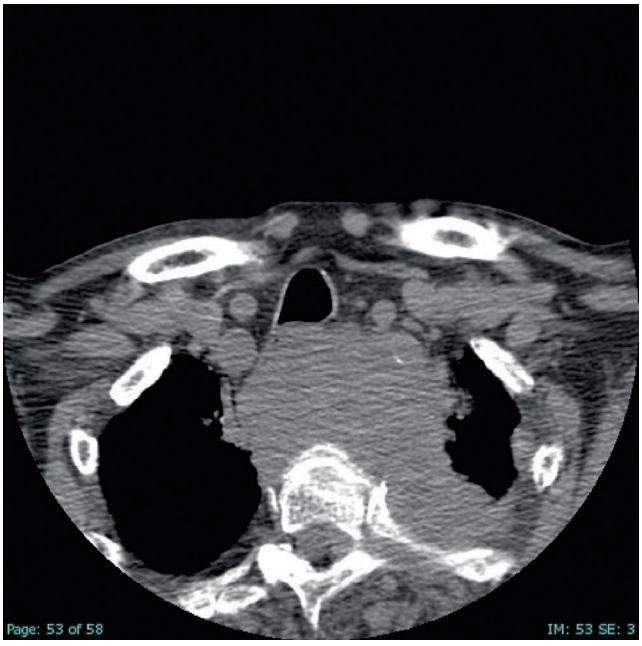

FIGURE 1 Chest CT showing a large solid mass with origin in the left pulmonary apex and invasion of the aorta and mediastinum.

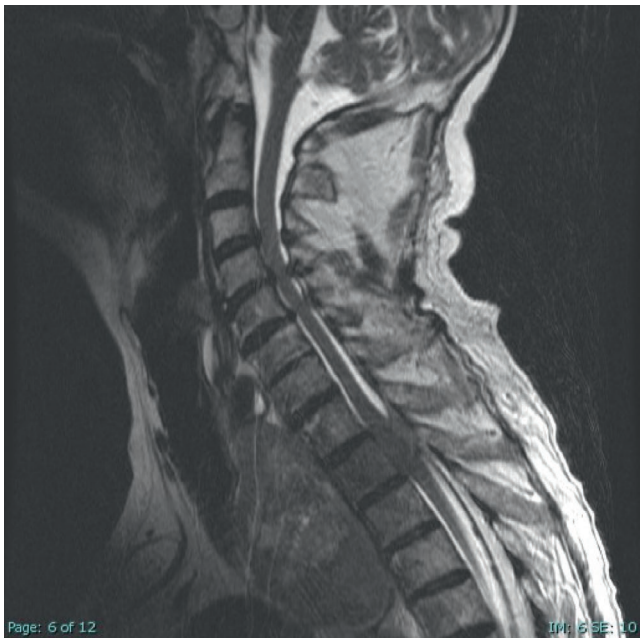

FIGURE 2 Spine MRI showing a large mass with signs of bone invasion of the vertebral bodies from D1 to D4, extension into the intraspinal region at these levels and compression of the spinal cord.

Conclusion: Pancoast tumors can present with neurological deficits mimicking brainstem syndromes due to compression of the spinal cord, recurrent laryngeal nerve, and sympathetic pathways, prompting a diagnostic challenge in distinguishing between central and peripheral causes of these symptoms. Early recognition and advanced imaging are crucial to avoid misdiagnosis and ensure appropriate treatment.
Disclosure: Nothing to disclose.

EPO-230 | Upper extremities neuropathy, industrial mercury intoxication: Immunopathology mechanisms

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Background and aims: Distinctive features of the clinical picture of chronic mercury intoxication are tremor, erethism (increased neuropsychic excitability and irritability) and pronounced vegetative disorders, sleep disorders, emotional and cognitive impairment, gingivitis. Neuropathy is a pathology of nervous system, in which the structure of one or a group of nerves is damaged. There is pain syndrome, weakness, numbness of limbs, tingling. As a result, function of nerve fibers is impaired, after which they cannot correctly transmit electrical impulses. Nerve damage in our cases were caused by industrial mercury intoxication. Depending on extent of damage, toxic mononeuropathies and polyneuropathies are distinguished.
Methods: Under our observation were 76 mercury induced neuropathy patients, men and women aging from 29 to 57 years old. We performed stabilography, a method for quantitatively studying characteristics of posture control, based on measuring the coordinates of pressure center in plane of support, carried out using a stabiloplatform.

Results: It was revealed that mercury intoxication neuropathy affects predominantly upper extremities. In neuropathies and polyneuropathies, clinical syndromes characterized by isolated or diffuse damage to peripheral nerve fibers, unit of damage is mainly fibers that make up various nerves, probability of damage to which depends on their length, caliber, antigen composition, metabolic intensity, etc.
Conclusion: Clinical manifestations of polyneuropathies, considered as widespread, symmetrical, usually distal and progressive nerve damage, vary widely, differing in the rate of progression, severity of symptoms, the ratio of sensory and motor disorders, and presence of irritation symptoms. Immunoglobulins IgA, IgM and IgG were increased in almost all patients.
Disclosure: Nothing to disclose.

EPO-231 | Cerebral venous thrombosis associated with Behcet's disease in 24 Morrocan patients

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Background and aims: Cerebral venous thrombosis (CVT) is the most common manifestation of vasculo-Behc¸et's disease and may be superficial and/or deep localization. The aim of our study was to evaluate the clinical and radiological features of CVT associated with Behc¸et's disease in our population and to compare findings with previous studies.
Methods: We report a retrospective study of 24 cases of CVT secondary to Behc¸et's disease, collected between 1999 and 2019. The diagnosis of Behc¸et's disease was made in all cases according to the 2014 International Study Group Criteria for Behc¸et diseases. Patients received antithrombotic treatment, combined with corticosteroids, in six cases of superficial CVT and with immunosuppressants in cases of deep CVT.
Results: The diencephalic-mesencephalic syndrome was found in 18 patients, whereas intracranial hypertension (71%) and headache (57%) were the most common presentations of superficial CVT. Unlike previous studies, magnetic resonance angiography and conventional angiography performed in our patients confirmed the predominance of deep venous thrombosis (18 cases), whereas superficial CVT was observed only in six cases.
Conclusion: Shortterm outcome was favorable, but sequelae of CVT were noted in 20 patients (75%). The outcome of patients was commonly mRS 02, however 70% of patients presenting with deep CVT at the beginning had a poor outcome (mRS 03) and we did not record any case of venous thrombosis relapse.
Disclosure: Nothing to disclose.

EPO-232 | Hyperglycemia-induced acute neurological syndromes: Insights from a portuguese retrospective study

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Background and aims: Uncontrolled hyperglycemia in patients with Diabetes Mellitus (DM) can present with various acute neurological symptoms, such as symptomatic seizures or movement disorders. We aim to characterize demographics, clinical presentation, laboratory, and imaging studies of patients with acute focal neurological manifestations associated with hyperglycemia.
Methods: Retrospective observational study including patients admitted to our Neurology department between January 2017 and August 2024 with acute neurological manifestations and a final causal diagnosis of hyperglycemia. Demographic, clinical, laboratory, and imaging data were collected and analyzed descriptively.
Results: Eight patients, all female with a mean age of 65 years, were included. Five had type 2 DM, two had type 1 DM, and one was newly diagnosed. The average disease duration was 20 years, with five patients exhibiting microvascular complications and one was newly diagnosed. Neurological manifestations included focal motor seizures (3), focal seizures with contralateral hemichorea-hemiballism syndrome (1), isolated hemichorea-hemiballism syndrome (2), central pontine myelinolysis (1), and acute diabetic neuropathy (1). Admission glucose levels exceeded 300 mg/dL in all cases, with a median HbA1c of 11.25%, indicating poor chronic glycemic control. MRI findings were typical in most cases, with specific patterns correlating to clinical presentations. Metabolic control led to neurological improvement in all patients.
Conclusion: Hyperglycemia remains a significant, underrecognized cause of neurological emergencies in Europe. Early recognition of diabetic causes in acute focal neurological syndromes, especially in emergency settings, is crucial for timely and effective treatment, emphasizing the central role of glycemic control in recovery.
Disclosure: Nothing to disclose.

Headache 2

EPO-233 | Potential genetic link of chronic migraine with detoxification and nitric oxide pathways

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Background and aims: Chronic migraine (CM) is a multifactorial condition, affecting up to 5% of individuals diagnosed with migraine. This suggests the existence of specific genetic factors

that contribute to its chronification. To explore this hypothesis, a comparative genetic study was conducted between CM patients and a healthy population control to identify genetic patterns and associations potentially associated with the chronic form of migraine.

Methods: Our study included 16 female CM patients. Population control data were derived from the European cohort of the 1000 Genomes Project. A targeted next-generation sequencing approach was performed using the PGRNseq-NDD panel, specifically designed to investigate 186 genes linked to inflammation, immune response, oxidative stress, neurodegeneration, metabolism and detoxification pathways.

Results: The analysis identified four single nucleotide polymorphisms (SNPs) with significantly different genotype distributions in the CM group compared to controls: rs34504481 in ARG1 ($p=0.049$), rs8192925 in CES2 ($p=0.044$), rs62359375 in MOCS2 ($p=0.035$), and rs548541129 in SLCO2B1 ($p=0.010$), (Fig. 1). These SNPs had not been previously reported in available genetic databases. Notably, the ARG1 gene is associated with increased nitric oxide production, while MOCS2, CES2, and SLCO2B1 are involved in xenobiotic and endogenous substance detoxification.

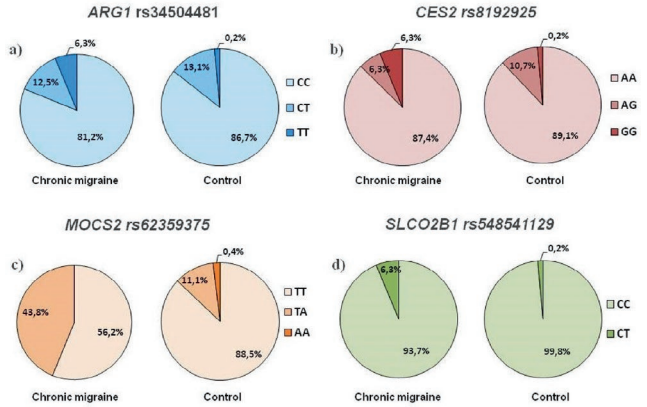

FIGURE 1 Distribution of genotypes in chronic migraine patients and population control from the 1000 Genomes Project for the following single nucleotide polymorphisms: a) rs34504481 ARG1, b) rs8192925 CES2, c) rs62359375 MOCS2, d) rs548541129 SLCO2B1

Conclusion: Thus, this study highlights a potential link between CM and genetic variations in ARG1, CES2, MOCS2 and SLCO2B1 genes. The findings suggest that mechanisms such as increased nitric oxide production and impaired detoxification processes may contribute to the development of chronic migraine.

Disclosure: This study was supported by the Kazan Federal University Strategic Academic Leadership Program (PRIORITY-2030).

EPO-234 | Study design of CORNERSTONE: A prospective observational study of atogepant effectiveness in routine clinical practice

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Background and aims: Atogepant is an oral calcitonin gene-related peptide receptor antagonist approved for the preventive treatment of migraine. The Prospective Observational Study of Atogepant Effectiveness in Routine Clinical Practice(CORNERSTONE) study is designed to document the patient's real-world experience and measure the effectiveness, tolerability, and safety of atogepant for the preventive treatment of migraine.

Methods: This multi-country, prospective, observational study will enroll adult patients with a minimum 1-year migraine diagnosis, who independently initiate atogepant per local standard of care prior to inclusion. The study includes a 28-day pre-atogepant retrospective recall period, 96-week treatment period, and 30-day follow-up and safety period (Figure 1). Monthly Headache Days occurring in the 28 days prior to each study visit will be estimated by patient recall, optionally aided by a headache diary. Patients on other preventive migraine medications must maintain a stable regimen for at least three months before enrollment, and prescribers must confirm that there are no plans to alter this regimen during the first 12 weeks after enrollment.

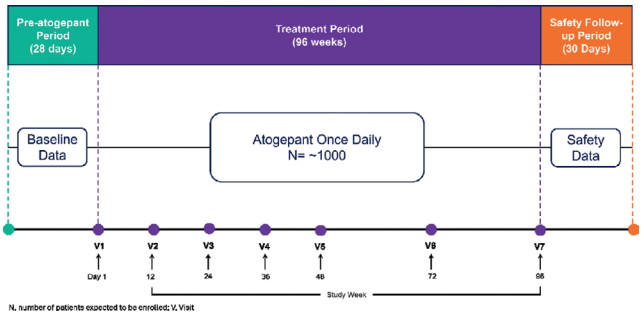

FIGURE 1 Study design

Results: The study aims to enroll 1000 patients from 100 sites in 15 countries to provide necessary precision. The primary endpoint of the study is the achievement of "much better" or "very much better" at Week 12, as assessed by Patient Global Impression of Change (PGIC), recorded via electronic patient-reported outcomes devices during clinical visits. Secondary endpoints include effectiveness and functional outcomes (Table 1). Adverse events and vitals will be monitored through the follow-up safety period.

TABLE 1 Secondary effectiveness and functional outcomes.

Abbr	Assessment	Schedule
MHD	Monthly Headache Days	RR (at least 50% reduction in monthly headache days) at Weeks 9–12, 21–24, 33–36, and 45–48 CFB in monthly headache days at Weeks 9–12, 21–24, 33–36, 45–48
HIT-6	Headache Impact Test-6	CFB of total score at Weeks 12, 24, 36, 48
MSQv2.1 RFR	Migraine Specific Quality of Life, Role Function Restrictive	CFB in domain score at Weeks 12, 24, 36, 48
MIBS-4	Migraine Interictal Burden Scale	CFB in score at Weeks 12, 24, 36, 48
PROMIS	Patient-Reported Outcomes Measurement Information System Cognitive Function – Abilities Subset – Short Form 6a Version 2.0	CFB in score at Weeks 12, 24, 36, 48
	Acute Medication Use Days	CFB in monthly medication use days at Weeks 9–12, 21–24, 33–36, 45–48
	Acute Prescription Medication Use Days	CFB in monthly prescription medication use days at Weeks 9–12, 21–24, 33–36, 45–48
PSSM	Patient Satisfaction with Study Medication	RR ("Satisfied" or "Extremely Satisfied") at Weeks 12, 24, 36, 48
PGIC	Patient Global Impression of Change	RR ("much better" or "very much better") at Weeks 24, 36, 48

CFB, change from baseline; RR, responder rate

Conclusion: CORNERSTONE will provide clinically meaningful insights into the real-world effectiveness of atogepant in routine clinical practice.

Disclosure: Elizabeth Leroux has received consultancy fees and/or speaker fees from Abbvie, Eli Lilly, Miravo, Lin Pharmaceutical, Lundbeck, Novartis, Paladin, Pfizer, and Teva. Andreas R. Gantenbein serves as consultant for, advisory board member of, or has received honoraria or research support from AbbVie, Allergan, Biomed, Curatis, Eli Lilly, Lundbeck, Neurolite, Novartis, Pfizer, and Teva. Karen Carr, Yingyi Liu, Brett Dabruzzo, Pranav Gandhi, and Sarah Caughlin are employees of AbbVie and may own AbbVie stock. Taoufik Alsaadi has received consultancy fees, speaker fees, and research grants from Novartis, Eli Lilly, GlaxoSmithKline, Lundbeck, Pfizer, Hikma and AbbVie. Cristina Tassorelli has participated in advisory boards for AbbVie, Dompé, Eli Lilly, Ipsen, Lundbeck, Medscape, Pfizer and Teva, and has lectured at symposia sponsored by AbbVie, Eli Lilly, Ipsen, Lundbeck, Pfizer and Teva. She is principal investigator or collaborator in clinical trials sponsored by AbbVie, Eli Lilly, Ipsen Lundbeck, Pfizer and Teva. She has received research grants from the European Commission, the Italian Ministry of Health, the Italian Ministry of University, the Migraine Research Foundation, and the Italian Multiple Sclerosis Foundation. Jennifer McVige has served as a speaker and/or received research support from Allergan (now AbbVie Inc.), Alder, Amgen/Novartis, Avanir, Biohaven, Eli Lilly, Lundbeck, and Teva.

EPO-235 | Effectiveness of anti-CGRP monoclonal antibodies in chronic migraine refractory to onabotulinumtoxinA: Re-MATe study

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Background and aims: Chronic migraine (CM) refractory to onabotulinumtoxin A (BoNT-A) treatment refers to a condition where patients experience persistent, frequent migraines despite toxin injections. This form of CM remains resistant to conventional therapy, making it more challenging to manage and requiring alternative treatment approaches. We aimed to evaluate the clinical efficacy and safety of monoclonal antibodies targeting calcitonin gene-related peptide (anti-CGRP) in reducing the symptoms and frequency of migraine in patients diagnosed with CM refractory to BoNT-A in clinical practice.

Methods: Re-MATE (Real-Migraine Antibodies Treatments Evidence) is an observational, retrospective study comparing the following variables at 3 and 6 months after initiating an anti-CGRP treatment: number of monthly migraine days, number of days using rescue medication, retention rate at 6 months, and side effects.

Results: Seventy patients were included, 57 (81%) women, with an average age of 50.1±1.3 years, previously treated for 12.7±2.4 months with BoNT-A. anti-CGRP treatment significantly reduced the number of headache days and the use of rescue medication days per month (16.6±0.9 and 15.9±0.8, respectively) at 3 months (5.20±0.64, t1,58=12.5, p=0.001 and 4.69±0.62, t1,58=11.46, p=0.001, respectively) and at 6 months (4.07±0.67, t1,53=11.12, p=0.001; 3.91±0.72, t1,53=10.28, p=0.001). Furthermore, 3 (15%) patients were migraine-free at 3 months and 5 (8%) at 6 months. Four (7%) patients reported side effects, and the adherence rate at 6 months was 91%.

Conclusion: Anti-CGRP treatment was effective in patients diagnosed with CM refractory to BoNT-A, showing high levels of compliance and safety at 6 months.

Disclosure: Nothing to disclose.

EPO-236 | Eptinezumab reduced disease burden in chronic migraine and medication-overuse headache: Secondary RESOLUTION trial data

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Background and aims: The RESOLUTION trial assessed the efficacy and safety of eptinezumab vs placebo when given in addition to patient education in chronic migraine (CM) and medication-overuse headache (MOH). The trial met its primary and all key secondary endpoints. Here we report the impact of eptinezumab vs placebo on multiple patient-reported outcomes (PROs) measuring headache-related burden and quality of life, migraine-related disability, and work productivity and activity impairment.

Methods: RESOLUTION (NCT05452239) included a 28-day screening (baseline) period and a 12-week double-blind, placebo-controlled period. Adults (18-75y) with CM and MOH (excluding opioid-overuse headache) were randomised (1:1) to IV

eptinezumab 100 mg or placebo, both with a Brief Educational Intervention about MOH prior to infusion. Secondary endpoints included several PROs assessing disease burden and health-related quality of life at Weeks 4 and 12.

Results: Of 608 participants randomised, 596 (98.0%) completed the placebo-controlled period. Baseline scores were indicative of moderate to severe disease burden. Eptinezumab treatment was associated with greater improvements compared to placebo at Week 4 across all PRO scores (Table; HIT-6, mMIDAS, WPAI:M, MSQ, EQ-5D-5L, HADS, and TSQM-9). Greater improvements with eptinezumab vs placebo were sustained at Week 12.

Table. Summary of patient-reported outcome scores.

	Treatment arm	Baseline, mean	CFB to Week 4, LS mean (SE)	CFB to Week 12, LS mean (SE)
HIT-6 total score[1]	Eptinezumab	66.4	-6.3 (0.55) ****	-7.1 (0.59) ****
	Placebo	66.5	-2.3 (0.55)	-3.6 (0.59)
mMIDAS total score[1]	Eptinezumab	33.1	-14.7 (1.48) ****	-13.8 (1.49) ***
	Placebo	29.9	-6.6 (1.48)	-8.8 (1.50)
WPAI:M domain score: Absenteeism[1]	Eptinezumab	19.2	-4.7 (2.04) *	-4.7 (2.34) ns
	Placebo	13.9	-0.1 (2.00)	-1.2 (2.32)
WPAI:M domain score: Presenteeism[1]	Eptinezumab	56.3	-20.3 (2.57) ****	-19.1 (2.60) **
	Placebo	57.7	-7.2 (2.50)	-10.1 (2.54)
WPAI:M domain score: Work productivity loss[1]	Eptinezumab	60.5	-20.7 (2.74) ****	-19.9 (2.79) ***
	Placebo	61.0	-7.0 (2.67)	-9.0 (2.73)
WPAI:M domain score: Activity impairment[1]	Eptinezumab	62.1	-20.7 (2.07) ****	-18.9 (2.07) ****
	Placebo	62.6	-8.2 (2.14)	-10.4 (2.08)
MSQ domain score: Role function-restrictive[2]	Eptinezumab	34.5	24.0 (1.90) ****	22.6 (1.87) ****
	Placebo	34.9	10.2 (1.90)	11.8 (1.88)
MSQ domain score: Role function-preventive[2]	Eptinezumab	52.3	18.6 (1.86) ****	18.0 (1.83) ****
	Placebo	51.3	7.9 (1.86)	10.2 (1.84)
MSQ domain score: Emotional function[2]	Eptinezumab	43.2	23.8 (2.14) ****	22.1 (2.19) ****
	Placebo	41.3	10.1 (2.15)	11.7 (2.19)
EQ-5D-5L VAS score[2]	Eptinezumab	65.3	5.1 (1.56) **	7.4 (1.53) ***
	Placebo	67.2	0.5 (1.57)	2.2 (1.54)
HADS-Depression subscale score[1]	Eptinezumab	6.6	-1.6 (0.29) ***	-1.8 (0.30) ****
	Placebo	6.1	-0.6 (0.30)	-0.6 (0.30)
HADS-Anxiety subscale score[1]	Eptinezumab	7.5	-1.3 (0.26) **	-1.4 (0.26) ***
	Placebo	6.8	-0.5 (0.26)	-0.4 (0.26)
			Week 4, LS mean (SE)	Week 12, LS mean (SE)
TSQM-9 domain score: Effectiveness[2]	Eptinezumab	–	58.2 (2.23) ****	58.0 (2.26) ****
	Placebo	–	39.0 (2.24)	40.9 (2.28)
TSQM-9 domain score: Convenience[2]	Eptinezumab	–	69.6 (1.74) ***	69.4 (1.79) ***
	Placebo	–	63.6 (1.74)	63.1 (1.80)
TSQM-9 domain score: Global satisfaction[2]	Eptinezumab	–	59.6 (2.09) ****	62.5 (2.14) ****
	Placebo	–	43.6 (2.10)	47.0 (2.15)

[1]Lower scores are better. [2]Higher scores are better.

*p<0.05, **p<0.01, ***p<0.001, and ****p<0.0001 vs placebo (not controlled for multiplicity).

CFB, change from baseline; HADS, Hospital Anxiety and Depression Scale; HIT-6, 6-item Headache Impact Test; LS, least-squares; mMIDAS, modified Migraine Disability Assessment; MSQ, Migraine-Specific Quality-of-life questionnaire (version 2.1); ns, not significant (vs placebo); TSQM-9, 9-item Treatment Satisfaction Questionnaire for Medicine; VAS, visual analogue scale; WPAI:M, Migraine-specific Work Productivity and Activity Impairment questionnaire.

Conclusion: Eptinezumab resulted in greater improvements than placebo across all patient-reported outcome measures at the first post-baseline timepoint (Week 4) in patients with CM and MOH also receiving patient education. Improvements in headache-related life impact, migraine-related disability, work productivity and activity impairment, and health-related quality of life continued to favour eptinezumab vs placebo at Week 12.

Disclosure: Trial sponsored by Lundbeck.

EPO-237 | IIH without papilledema in chronic migraineurs and revisiting of Friedman's diagnostic criteria

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Background and aims: The application of revised Friedman's criteria to diagnose IIH WOP will prevent many patients from proper diagnosis and treatment. Our prospective study aimed to compare the prevalence of IIH WOP in case of following Friedman's criteria and in case of novel proposed criteria (OP > 200 mmH2O and radiological finding ≤ two), also reporting the predictive radiological signs for IIH WOP.

Methods: Patients underwent ophthalmologic, neurological evaluation, MRI, and a lumbar puncture (LP) with opening pressure (OP) measurement. CSF withdrawal was performed in patients with CSF OP > 200 mmH20. IIHWOP was defined according to Friedman's criteria. The effect of CSF withdrawal was evaluated clinically after two months.

Results: One hundred and two consecutive CM patients were enrolled (95 F, age 32.34 ± 9.45, and BMI 29.04 ± 5.89) without papilledema. Eighteen patients (17.65%) had OP greater than 250 mmH2O, and 20 patients (19.61%) with OP ≥ 200 mmH2O and ≤ 250 mH2O. Prevalence of suggested IIH WOP was applied only in three patients (2.9%). In case of violation of these criteria (Absent 6th nerve palsy, ICP > 200 mmH2O, and ≥ two radiological signs), more five patients were added to IIH WOP (7.8%). After CSF withdrawal, 85% of cases with OP > 200 mm H2O improved.

Conclusion: The prevalence of IIH WOP with the novel proposed diagnostic criteria increased to 7.8 % in comparison to 2.9% in the case of revised Friedman's criteria. Bilateral TSS was the predictor for IIH WOP.

Disclosure: Nothing to disclose.

EPO-238 | Sudden severe headache in the emergency department

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Background and aims: There is limited data on patients arriving the emergency department (ED) with sudden onset severe headache (SOSH), a subgroup of headache that may indicate a subarachnoid haemorrhage (SAH). Having applied the gold standard to differentiate SAH from other aetiologies, we wanted to assess the prevalence and the final diagnoses of such patients.

Methods: The medical records of every awake and alert patient with SOSH admitted to Nordland Hospital 2008-2020 was scrutinized. Rehospitalisation or death associated with the headache was monitored until April 2022.

Results: A total of 588 patients, with mean age of 42.5 ± 17.9 years (61.6% female, 38.4% male), were identified, representing 0.4% of all the ED admissions. Half (49.7%) presented with thunderclap headache. Twenty percent (20.2%) were diagnosed with a secondary headache, of which half (9.9%) had an SAH, including 38 (6.5%) with an aneurysmal SAH. Most patients, 338 (57.5%),

received an unspecific headache diagnosis. No deaths or readmissions attributed overlooked SAH were recorded by the final review in 2022.

Conclusion: SOSH represents only a small proportion of hospital admissions. At least 2 in 10 will have a secondary headache, and 1 in 10 will have a subarachnoid haemorrhage, of which two-thirds are attributed to an aneurysmal rupture. The majority of patients are discharged with an unspecific headache diagnosis. Our data underscore the importance of thorough evaluation of SOSH to identify SAH, but also the need for improved diagnostics to differentiate between other acute headache aetiologies.

Disclosure: Nothing to disclose.

EPO-239 | Refractory chronic cluster headache: Exploring the potential of repetitive transcranial magnetic stimulation

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Background and aims: Chronic cluster headache (CCH) presents significant therapeutic challenges, particularly in refractory cases. Repetitive transcranial magnetic stimulation (rTMS) has emerged as a potential alternative, though evidence for its efficacy in CCH remains limited.

Methods: We conducted a randomized, double-blind, placebo-controlled, crossover pilot study to evaluate rTMS in patients with refractory CCH. Participants were randomized into two sequences: A (rTMS followed by sham) or B (sham followed by rTMS), each treatment period consisting of 10 consecutive working days, with a one-month washout period and a three-month follow-up. The primary outcome was change in number of attacks per week (APW). Secondary outcomes included treatment tolerability, side effects and changes in attack intensity, duration, and rescue medication use.

Results: Eight patients were enrolled (5 in sequence A, 3 in sequence B), with three completing the full study. No significant effectiveness was achieved after rTMS period, although two patients experienced complete remission after day 4 of treatment. However, symptoms recurred 7 days after last treatment session. Secondary outcomes remained unchanged. Side effects were mild and transient, occurring in two cases (tingling and nuisance). Three of five dropouts were attributed to logistical challenges, such as the time commitment required for daily visits and a lack of perceived benefit early in treatment. The remaining two were due to lack of efficacy.

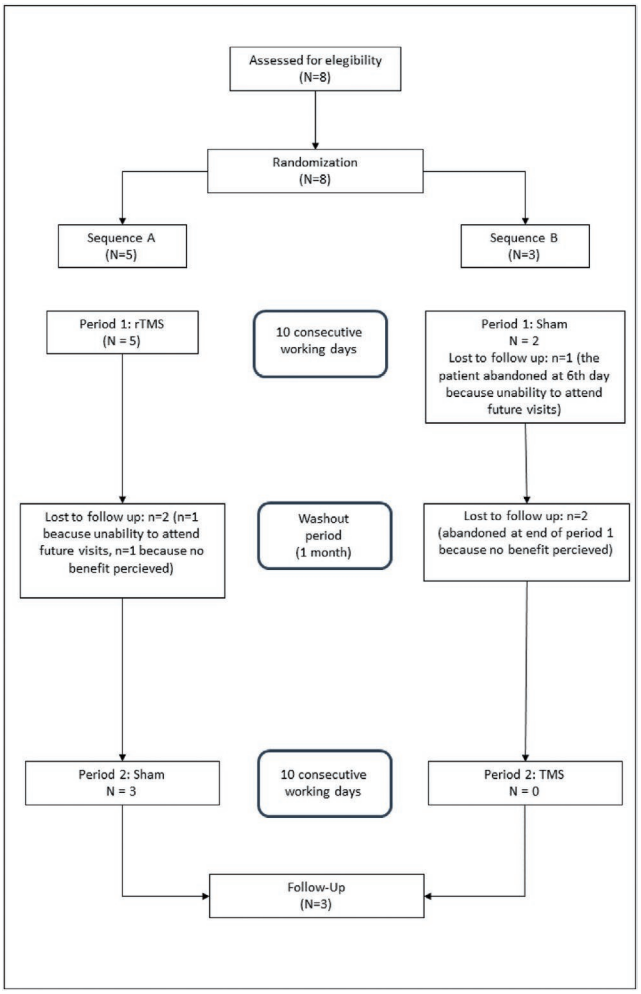

FIGURE 1 Flow diagram.

	Attacks per week (Mean (SD); Median)						
	Baseline	End of Period 1	Baseline 2	End of Period 2	Follow up		
					W2	W4	W12
Sequence A N=5 (rTMS -> Sham)	19.8 (10.1)	22 (14.5)	5.67 (1.02)*	4.67 (1.2)*	6 (0.57)*	7.33 (0.88)*	6.67 (1.2)*
Sequence B N=3 (Sham -> rTMS)	15.3 (2.9)	17.3 (7.3)**;12	0***	0***	0***		

*Results obtained from N=3 patients completing both sequences.

**Data includes the results of a patient who dropped out after the first week.

***There are no results due to patients withdrawing from the study.

Table 1. Outcome evaluations.

Conclusion: This pilot study suggests that rTMS may have some benefit in selected refractory CCH cases, but its effects appear short-lived. Maintaining treatment adherence is a key challenge and it depends on the protocol used.

Disclosure: Nothing to disclose.

EPO-240 | PACAP6-38 reduces nitroglycerin-induced central sensitization by modulating synaptic plasticity in the TNC of rats

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Background and aims: Chronic migraine (CM) is a common neurological disorder with complex mechanisms. Pituitary adenylate cyclase-activating peptide (PACAP) has been linked to migraine attacks, but targeting PACAP and its receptors shows varying therapeutic results. This study explores the effect of PACAP type I receptor (PAC1R) antagonist, PACAP6-38, on nitroglycerin (NTG)-induced central sensitization in CM.
Methods: CM was induced in Sprague-Dawley rats via repeated NTG injections. Mechanical and thermal thresholds were measured, and central sensitization was assessed by c-Fos expression. PACAP6-38 was injected into the trigeminal nucleus caudalis (TNC). Synaptic proteins, phospho-ERK1/2, p-CREB, BDNF, and synaptic structures were analyzed by western blotting, immunofluorescence, TEM, and Golgi-Cox staining.
Results: PACAP and PAC1R expression were elevated in the TNC following NTG injections. PACAP6-38 treatment alleviated nociceptive sensitization, inhibited c-Fos overexpression, restored synaptic structures, and reduced the ERK/CREB/BDNF pathway activation.
Conclusion: PACAP6-38 improves NTG-induced central sensitization by modulating synaptic plasticity in the TNC, likely through the ERK/CREB/BDNF pathway. This suggests that PACAP/PAC1R may be a novel target for migraine treatment.
Disclosure: Nothing to disclose.

EPO-241 | When two headaches collide: The importance of treating chronic migraine in cluster headache chronification

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Background and aims: The extreme severity of cluster headache (CH) symptoms usually overshadows migraine symptoms in the clinical settings, leading both patients and clinicians potentially to dismiss the significance of migraine symptoms. In this study, we explore the relationship between the two, and the predictors that may contribute to increased risk of CH chronification.
Methods: Data from successive new consultations of patients with CH referred to the Acute Service at King's College Hospital, London from 2018-2024, was collected (n=118). A generalised linear model using binomial distribution and logit link function was used to evaluate predictors of having chronic CH, taking episodic CH as reference and age, sex, age of cluster onset, years since the diagnosis, number of cluster preventives during the assessment, chronic migraine and number of abortive treatments used: triptans and oxygen.
Results: Our predictors significantly improved the model fit ($\chi = 20.79$, $Df = 7$, $P = 0.004$). When abortive treatments were included in the model, despite not being itself significant, chronic migraine became a significant predictor of chronification ($\beta = 1.92$, $P = 0.049$). Older age of onset ($\beta = 0.04$, $P = 0.042$) and number of cluster preventives ($\beta = 0.74$, $P < 0.006$) were predictors of chronification. The remaining variables were not significant.
Conclusion: Patients with both CH and CM who take acute treatments daily may have a higher likelihood of progressing to chronic cluster headache. This highlights the importance of not only treating cluster headache preventively but also addressing the underlying chronic migraine condition, which can play a pivotal role in chronification.
Disclosure: Nothing to disclose.

EPO-242 | Retinal changes in optical coherence tomography in migraine

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Background and aims: Migraine affects approximately 15% of the global population and significantly impairs quality of life. Structural and vascular retinal changes, including reductions in the retinal nerve fiber layer (RNFL) and ganglion cell layer (GCL), as well as enlargement of the foveal avascular zone (FAZ), have been associated with migraine. This study evaluates retinal alterations in migraine patients, examines longitudinal changes, and investigates associations with migraine subtypes and prophylactic therapies.
Methods: In this prospective study, 40 participants (20 migraine patients, 20 age- and sex-matched controls) underwent ophthalmological examinations, optical coherence tomography (OCT), and OCT angiography (OCT-A) at baseline, 6 months, and 12 months. Migraine patients were classified into episodic (25%) and chronic (75%) subtypes. Retinal layer thickness (RNFL and GCL) and vascular parameters including vessel density in the superficial, intermediate, and deep capillary plexuses and FAZ area, were assessed.
Results: Preliminary analysis of 40 participants (20 migraine patients, 20 controls) revealed no significant differences in RNFL or GCL thickness. However, the FAZ was significantly larger in migraine patients, particularly in the left eye ($p < 0.01$). Vessel density in the intermediate and deep capillary plexuses was also significantly reduced in the left eye, with a non-significant trend in the right eye.
Conclusion: These initial findings indicate migraine-associated retinal vascular changes, characterized by FAZ enlargement and reduced vessel density, predominantly in the left eye. Further analyses, planned as part of this ongoing study, aim to validate these results, stratify by migraine subtypes (e.g. with and without aura) and assess possible associations with prophylactic therapies.
Disclosure: MD, SK, AK, PN, JI, RJ, EA, AA, PJ, and RG declare no conflicts of interest. TK and VK have received travel grants from AbbVie, Ipsen, and Merz (unrelated to the submitted work). SGM has received honoraria, travel support, and research funding from Bayer, Biogen, Sanofi, Merck, Novo Nordisk, Genzyme, MSD, and Teva. PA has received honoraria, travel support, and

research funding from Novartis, Biogen, Merz, Teva, Ipsen, Allergan, Celgene, Janssen Cilag, Roche, Merck, Sanofi, and Sandoz. JIL has received honoraria, travel support, and research funding from Boehringer Ingelheim, Daiichi Sankyo, Allergan, AbbVie, Ipsen, Novartis, Teva, Lilly, and Pfizer, as well as research grants from Merz to the University Hospital Düsseldorf for projects involving JIL.

EPO-243 | Does migraine predict dizziness?

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Background and aims: Headache and dizziness combined account for more than 50% of consultations in Neurology outpatient clinics. Both vestibular migraine and Persistent Postural Perceptual Dizziness (PPPD), are common causes of dizziness. In this study, we aimed to understand the coexistence of these symptoms and whether the dizziness intensity can be predicted by migraine features.
Methods: Consecutive patients attending the General Neurology and Headache Clinic at Queen Elizabeth Hospital (Jan 2024-Dec 2024, n=120) were asked to fill the Dizziness Handicap Inventory (DHI) and the Niigata PPPD Questionnaire (NPQ) if they experienced vestibular symptoms. DHI was developed to assess vestibular disorders and the NPQ for PPPD.
Results: Median age was 50 years (IQR, 72% females). A migraine diagnosis as per the 3-item ID migraine could be applied to 112 patients. Ninety-seven out of 120 (81%) complained of vestibular symptoms and completed the questionnaires. Median DHI was 14 (IQR 2-36.5), median NPQ was 20 (IQR 5 – 43). A Wilcoxon test showed no significant difference between median DHI and NPQ (W=1467; P=0.210). Respective linear regression models with the DHI and NPQ scores as dependent variables, using gender, headache and migraine frequency, nausea, photophobia, osmophobia, movement sensitivity as predictor variables, showed migraine frequency as the only predictor variable for both (B=6.85 95% CI 4.22 – 9.47; P=0.004 for DHI and B=3.872 95% CI 0.181 – 7.562; P=0.04 for NPQ).
Conclusion: Even if the DHI and NPQ may reflect the severity of different aspects of vestibular symptoms, migraine frequency may predict more severe presentations of vestibular disorders and PPPD.
Disclosure: Nothing to disclose.

EPO-244 | Medication overuse headache in cluster headache

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Background and aims: Medication overuse headache (MOH) is a well-described major driver of chronification in migraine. However, it is a topic of debate if MOH exists in cluster headache (CH). Therefore, we aimed to examine this and to describe the clinical characteristics associated with MOH in CH. Additionally, we aimed to explore the impact on CH treatment.
Methods: A large cohort of people diagnosed with CH, mainly deriving from a tertiary headache clinic, participated in a retrospective, semi-structured interview investigating MOH according to existing criteria (ICHD-3).
Results: A total of 433 people with CH were included with a male:female ratio of 2:1. Concurrent MOH could be diagnosed in 16%. Simple analgesics were the most frequently overused drug (52.2%), followed by triptans (37.3%), opioids (29.9%) and combination therapies (20.9%). Chronic phenotype (OR11.4, $p<0.00001$) and comorbid migraine (OR2.35, $p<0.05$) were associated with having concurrent MOH. Clinically, people with MOH had longer attack duration (30.0 vs. 20.0 minutes, $p<0.01$) and less effect of acute and preventive medication than those without MOH (20.0 vs. 55.9%, $p<0.05$ and 13.3 vs. 37.3%, $p<0.01$, respectively).
Conclusion: Our findings indicate that MOH can also occur in other headache disorders than migraine and tension-type headache, including CH. If suspecting concurrent MOH in a patient with CH, we recommend that triptans should be continued due to the severity of CH attacks, but other analgesics could be discontinued, and preventive treatment sought to be optimized. Further prospective studies are warranted to identify better CH treatment and understand the effect of MOH on CH disease burden.
Disclosure: Nunu Lund has received a personal research grant from the Capital Region of Denmark's research foundation.

EPO-245 | A rare case of secondary paroxysmal hemicrania caused by a thoracic schwannoma affecting the sympathetic chain

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Background and aims: Paroxysmal hemicrania (PH) is a rare headache disorder commonly classified as a trigeminal autonomic cephalalgia (TAC). Only few cases were reported, where a PH presentation could be convincingly aligned to a secondary pathology (e.g. a tumor).
Methods: Case description of a patient (male, 64y) with a rare cause of secondary PH.
Results: With an onset in 2011, the patient had frequent attacks of typical PH responsive to indometacin. During the attacks, the patient reported tearing and miosis of the ipsilateral eye, and a drop of heart rate (documented by a health tracker). Initially, MRI (brain and cervical spine) and neurological examination revealed no pathologies. In 2022, an MRI of the thoracic spine was performed due to new-onset shoulder pain and tingling of legs. It depicted an extra-spinal 2x1cm tumor at Th1-level, locally compressing the spinal cord. After surgical removal in 2023 (pathology: schwannoma grade 1), the headache thereafter ceased

completely. A reevaluation of the case led to the diagnosis of a secondary PH provoked by the Th1-nerve root schwannoma.
Conclusion: A presumed sympathetic deficit has long been discussed in the pathophysiology of PH. The reported case highlights, that an affection of the Th1-nerve root, which carries sympathetic fibers to the forehead/periorbital region, can induce PH possibly via the sympathetic-trigeminal complex or an altered meningeal vasoregulation. Considering this, the role of sympathetic dysfunction in PH pathophysiology should be reevaluated.
Disclosure: Nothing to disclose.

EPO-246 | A new rat model of nocebo-related nausea involving observational learning and conditioning mechanisms

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Background and aims: The nocebo effect, such as nausea and vomiting, is one of the major reasons patients discontinue therapy. The underlying mechanisms remain unknown due to a lack of reliable experimental models. The goal of this study was to develop a new animal model of nocebo-related nausea by combining observational learning and Pavlovian conditioning paradigms.
Methods: Male Sprague-Dawley rats with nitroglycerin-induced migraine were given 0.9% saline (a placebo) or LiCl (a nausea inducer) following headache relief, according to different paradigms.
Results: Both strategies provoked nocebo nausea responses, with the conditioning paradigm having a greater induction impact. The superposition of two mechanisms led to a further increase in nausea responses. A preliminary investigation of the underlying mechanism revealed clearly raised peripheral and central cholecystokinin (CCK) levels, as well as specific changes in the 5-hydroxytryptamine and cannabinoid systems. Brain networks related to emotion, cognition, and visceral sense expressed higher c-Fos-positive neurons, including the anterior cingulate cortex (ACC), insula, basolateral amygdala (BLA), thalamic paraventricular nucleus (PVT), hypothalamic paraventricular nucleus (PVN), nucleus tractus solitarius (NTS), periaqueductal gray (PAG), and dorsal raphe nucleus-dorsal part (DRD). We also found that nausea expectances in the model could last for at least 12 days.
Conclusion: The present study provides a useful experimental model of nocebo nausea that might be used to develop potential molecular pathways and therapeutic strategies for nocebo.
Disclosure: Nothing to disclose.

EPO-247 | Aryl hydrocarbon receptors alleviate migraine-like pain in rats by regulating Treg/Th17 cell-related balance

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Background and aims: Migraine is a neurovascular disorder with unclear pathophysiological mechanisms, but recent studies suggest immune dysfunction may play a role. The aryl hydrocarbon receptor (AHR), involved in autoimmune diseases, may be implicated in migraine, though its role remains unclear.
Methods: A chronic migraine rat model was created using repeated nitroglycerin (NTG) injections. Mechanical and thermal pain thresholds were measured. AHR expression in the trigeminal nucleus caudalis (TNC) was assessed, alongside Treg/Th17-related factors. The AHR agonist ITE and antagonist CH-223191 were used to examine their effects on pain behavior, c-Fos, CGRP, AHR, and Treg/Th17 factors.
Results: NTG administration increased nociceptive hypersensitivity and enhanced c-Fos and CGRP expression, while AHR levels in the TNC decreased. Treg/Th17-related transcription factors showed an imbalance, with forkhead box protein P3 and STAT5 decreased, and RORγt and STAT3 increased. AHR agonist ITE alleviated pain behaviors and corrected Treg/Th17 imbalances, while AHR antagonist CH-223191 worsened pain.
Conclusion: The AHR participates in the development of CM by regulating Treg/Th17-related homeostasis. Therefore, treatments targeting the AHR/Treg/Th17 signaling pathway could be new effective interventions for CM treatment.
Disclosure: Nothing to disclose.

Movement Disorders 2

EPO-248 | Fecal microbiota transplantation for Parkinson's disease: A systematic review and meta-analysis

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Background and aims: Dysregulation of the microbiome–gut–brain axis is a key pathophysiological mechanism preceding the onset of motor symptoms in PD. FMT has been evaluated in several randomized controlled trials (RCTs) as a novel intervention for PD. However, it remains inconclusive whether FMT significantly improves PD symptoms.
Methods: MEDLINE, Web of Science, Scopus, and the Cochrane Library databases were systematically searched for RCTs comparing FMT with placebo in PD patients. We assessed efficacy using the Unified Parkinson's Disease Rating Scale

(MDS-UPDRS), the PD Questionnaire (PDQ-39), Irritable Bowel Syndrome Scale (IBSS), and Wexner Constipation score.

Results: 3 RCTs and 145 patients were included, of whom 79 (54,48%) underwent FMT. UPDRS-III showed no difference between groups (Mean Difference [MD] -2.30; 95% CI -4.94 to 0.34; p=0.08; I2=45%) but both MDS-UPDRS-II and MDS-UPDRS-IV subscales favored the FMT group (MD 0.78; 95% CI 0.34 to 1.23; p=0.0005; I2=0%; and MD 0.28; 95% CI 0.05 to 0.51; p=0.01; I2=0%, respectively). There was no difference in PDQ-39, IBSS, and Wexner scale between groups (PDQ-39 MD -1.35; 95% CI -3.55 to -0.86; p=0.23; I2=95%; IBSS MD 9.57; 95% CI -30.50 to 49.64; p=0.63; I2=40%; Wexner score MD -0.85; 95% CI -2.12 to 0.43; p=0.19; I2=87%).

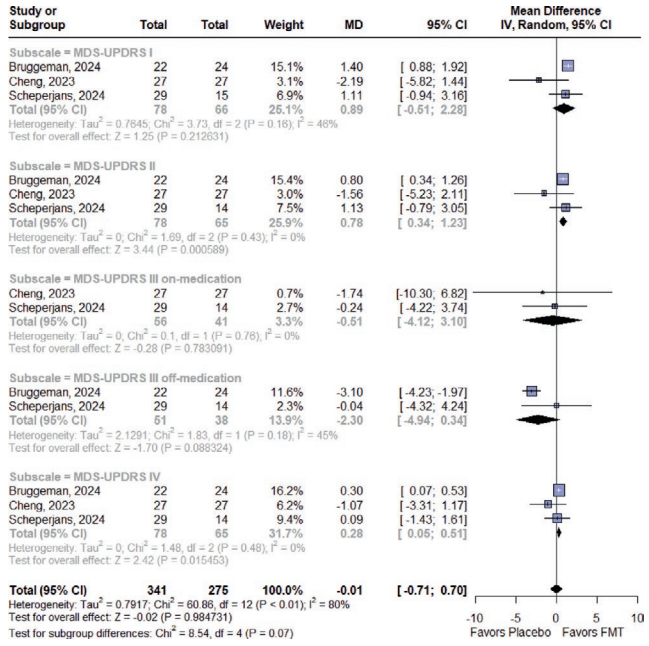

FIGURE 1 Mean Unified Parkinson's Disease Rating Scale (MDS-UPDRS) post treatment.

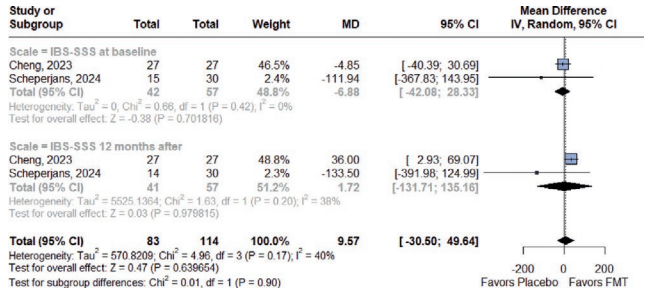

FIGURE 2 Mean Irritable Bowel Syndrome Scale (IBSS) post treatment.

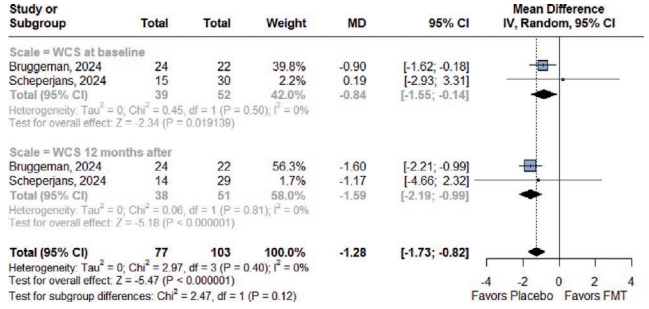

FIGURE 3 Mean Wexner Constipation score post treatment.

Conclusion: Our findings indicate an improvement in Non-Motor Experiences of Daily Activity (MDS-UPDRS-II) and Motor Complications (MDS-UPDRS-IV) in patients receiving FMT. However, we did not observe any impact on motor or constipation scores. Further trials without baseline differences between groups are needed to clarify the effects of FMT on PD.

Disclosure: Nothing to disclose.

EPO-249 | The impact of multimorbidity on symptom severity and quality of life in functional motor disorder

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Background and aims: Functional motor disorder (FMD) is common, often associated with multiple persistent, disabling symptoms and impaired health-related quality of life (HRQoL). The impact of co-occurring physical illness comorbidities is underexplored; however, it may contribute to symptom manifestations and significantly affect HRQoL. Objective: To investigate the cumulative effect of multimorbidity on motor symptom severity, self-reported symptom severity and HRQoL in FMD.

Methods: A total of 357 FMD patients (270 females, mean age=47.6 years, SD=12.8) years underwent detailed clinical evaluation including the Simplified FMD Rating Scale (SFMDRS) assessing motor severity. All patients completed an adapted Physical Health Questionnaire (PHQa) assessing subjective physical and neurological symptom severity, the Beck Depression Inventory (BDI), the Short Form Survey (SF-12) for HRQoL. Based on reliable medical reports, a multimorbidity index (MMi) was calculated as a sum of major physical illness, neurological comorbidities including migraine and any psychiatric comorbidity.

Results: MMi significantly correlated with BDI (r=0.24, p<0.001), SFMDRS (r=0.13, p<0.05), SF-12 (r=-0.28, p<0.001), PHQa (r=0.34, p<0.001) scores. When controlling for age and gender a linear regression revealed the MMi was a significant predictor of PHQa (β=0.22, p<0.001) and SF-12 (β= -0.25, p<0.001), but not motor symptom severity. These associations remained significant after correction for depression.

Conclusion: Our findings suggest that multimorbidity contributes substantially to the clinical complexity of FMD. Higher multimorbidity is associated with increased self-reported somatic symptom severity and poor HRQoL. Further studies should investigate the role of multimorbidity in the pathophysiology of FMD to better understand its impact and inform targeted interventions.

Disclosure: Supported by NW24-04-00456.

EPO-250 | Intrajejunal levodopa infusion therapy – comparison of real-world data from the ELEGANCE, GLORIA and DUOGLOBE registries

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Background and aims: The therapeutic options for patients with advanced Parkinson's disease (PD) who choose intrajejunal levodopa infusion treatment are levodopa–carbidopa intestinal gel (LCIG) or levodopa–entacapone–carbidopa intestinal gel (LECIG). GLORIA and DUOGLOBE are completed observational studies that have captured real-world efficacy, safety and quality of life data (QoL) for LCIG. ELEGANCE is an ongoing international non-interventional study (NCT05043103) collecting similar data on the routine clinical practice use of LECIG.
Methods: We compared published 12-month outcomes data from GLORIA (Global LOng-term Registry: DUODOPA® In patients with Advanced PD, a 2-year international observational study) and DUOGLOBE (DUOdopa in Patients with Advanced Parkinson's Disease – a GLobal Observational Study Evaluating Long-Term Effectiveness, a 3-year international observational study) with those of the ELEGANCE planned interim analysis.
Results: The ELEGANCE analysis includes 167 patients with effectiveness data from at least one visit following their baseline assessment (V1) and who were followed up to V3 (6–12 months of treatment). The baseline demographics and clinical history of patients included in all three registries were similar (Table 1). Results showed significant reductions in daily OFF time following 12 months of LCIG or LECIG treatment with similar improvements across datasets in UPDRS part II, sleep parameters (PDSS-2) and QoL (PDQ-8).

TABLE 1 Comparison of study outcomes from the ELEGANCE interim analysis and the GLORIA and DUOGLOBE studies.

Parameter	ELEGANCE interim data*	GLORIA 12-month data	DUOGLOBE 12-month data
Number of patients included in analysis	167	172	195
Mean (± SD) age (years)	68.2 ± 7.7	66.5 ± 9.3	70.2 ± 8.2
Mean (± SD) duration of PD (years)	13.3 ± 6.3	12.6 ± 6.6	11.2 ± 4.8
Mean (± SD) daily OFF time at baseline	5.2 ± 3.1 (n=167)	7.1 ± 3.5 hours (n=172)	6.0 ± 3.4 (n=164)
Mean (± SD) reduction in daily OFF time from baseline	-3.5 ± 2.9 p<0.0001 (n=57)	-4.7 ± 3.4 hours p<0.0001 (n=46)	-3.9 ± 3.6 hours p<0.001 (n=128)
Mean (± SD) UPDRS II scores (activities of daily living) in ON state at baseline	20.7 ± 8.2 (n=78)	16.5 ± 10.7 (n=172)	14.8 ± 7.8 (n=173)
Mean (± SD) reduction in UPDRS II scores in ON state	-3.4 ± 7.4 p=0.0198 (n=29)	-3.1 ± 8.7 p=0.0107 (n=56)	0.7 ± 7.7 NS (n=137)
Mean (± SD) PDSS-2 total scores at baseline	25.2 ± 10.6 (n=110)	Not assessed	26.6 ± 11.7 (n=171)
Mean (± SD) reduction in PDSS-2 scores	-6.6 ± 9.5 p<0.0001 (n=41)	Not assessed	-6.5 ± 12.2 p<0.001 (n=136)
Mean (± SD) PDQ-8 summary index (quality of life) at baseline	46.3 ± 20.1 (n=135)	48.6 ± 19.0 (n=172)	45.1 ± 18.1 (n=171)
Mean (± SD) PDQ-8 summary index decrease (improvement)	-11.1 ± 16.3 p<0.0001 (n=52)	-8.6 ± 22.6 p=0.0100 (n=50)	-9.0 ± 21.6 p<0.001 (n=135)

NS, not statistically significant; PDQ-8, Parkinson's Disease Questionnaire 8-item; PDSS-2, Parkinson's Disease Sleep Scale 2; UPDRS, Unified Parkinson's Disease Rating Scale.

Conclusion: At an early stage of treatment with LECIG (up to 12 months) patients in ELEGANCE showed significant improvements in PD motor symptoms, sleep and QoL. These findings are directly comparable to observations after 12 months of treatment with LCIG in the GLORIA and DUOGLOBE studies.
Disclosure: Nothing to disclose.

EPO-251 | Limited success of GPi-DBS in DYT-THAP1 dystonia: Report of three cases

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Background and aims: DYT-THAP1 dystonia is a rare genetic movement disorder caused by mutations in the THAP1 gene. While globus pallidus internus deep brain stimulation (GPi-DBS) is an established treatment for dystonia, its efficacy in DYT-THAP1 remains inconsistent. Here, we report the clinical response to GPi-DBS in three patients with DYT-THAP1 dystonia.
Methods: A retrospective review of three DYT-THAP1 patients treated with GPi-DBS at Ankara University included data on age at onset, symptom duration prior to surgery, Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS) motor and disability scores, and speech outcomes.
Results: All patients exhibited spasmodic dysphonia with varying degrees of cervical, axial, and limb dystonia. Disease onset ranged from ages 7 to 25, with surgery performed after 4–27 years of symptoms. Post-surgical motor improvement was limited, with no significant benefit observed in speech. When comparing pre- and post-surgical BFMDRS scores, motor

improvements of 18.8%, 0%, and 4.55% were observed. Also, no change was noted in the BFMDRS disability scores for any of the patients (Table 1). Two patients chose not to replace the battery after it had drained. Predictive factors such as early onset, long disease duration, and laryngeal involvement may have contributed to poor outcomes.

Table 1: The characteristic features of DYT-THAP1 patients

Patient number	Age at symptom onset (years)	Age at GPi-DBS (years)	Disease duration before GPi-DBS (years)	Preoperative BFMDRS-M[a]	Postoperative BFMDRS-M[a]	Benefit	Preoperative BFMDRS-D[b]	Postoperative BFMDRS-D[b])	Speech improvement
1	25	32	7	33	33	0%	8	8	no
2	11	15	4	44	36	18.8%	12	12	no
3	7	34	27	44	42	4.55%	16	16	no

[a] BFMDRS-M: Burke-Fahn-Marsden Dystonia Rating Scale- Motor Score

[b] BFMDRS-D Burke-Fahn-Marsden Dystonia Rating Scale-Disability Score

Conclusion: The variability in response to GPi-DBS among patients with DYT-THAP1 dystonia underscores the need for further studies to identify determinants of surgical efficacy. Our findings emphasize the critical role of patient-specific factors in optimizing individualized treatment strategies and highlight the essential need for comprehensive reporting of both favorable and unfavorable outcomes to enhance evidence-based clinical decision-making.
Disclosure: Nothing to disclose.

EPO-252 | Subthalamic nucleus deep brain stimulation in a patient with digenic Parkinson's disease

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Background and aims: Homozygous deletions in PARK2 and PINK1 are both associated with autosomal recessive forms of Parkinson's disease (PD). We present a patient with a homozygous deletion in the PARK2, combined with a heterozygous deletion in the PINK1, who underwent bilateral subthalamic (STN) deep brain stimulation (DBS).
Methods: We present the clinical and genetic features of an early-onset PD patient with pathogenic structural variants in PARK2 and PINK1. We also assessed local field potential recordings (LFP) using the DBS device. Finally, we provide a brief literature review on STN-DBS in genetic PD.
Results: Favourable motor outcome of STN-DBS is reported in PARK2- and PINK1-associated PD. However, only few patients with limited follow-up duration have been reported. LFP recordings in genetic PD patients undergoing DBS offer novel technology to longitudinally assess phenotypic features.
Conclusion: We report DBS outcome in a PD patient with digenic inheritance, and provide an overview of the reported monogenic PD patients undergoing DBS. Collection of additional data in longitudinal multicenter studies is needed to establish robust data and establish evidence-based guidelines for device-aided therapies in monogenic PD.
Disclosure: Nothing to disclose.

EPO-253 | Sex differences in Spinocerebellar ataxia type 1: clinical presentation and progression

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Background and aims: Both motor and cognitive symptoms characterise spinocerebellar ataxia type 1 (SCA1), but sex-specific differences in disease presentation and progression remain poorly understood. This study investigates the role of sex on motor and cognitive outcomes in SCA1 patients.
Methods: We conducted a monocentric, longitudinal observational cohort study at the University Hospital of Ferrara between 2021-2024. Consecutively genetically confirmed SCA1 patients were evaluated at baseline and after 24±3 months. Assessments included comprehensive neuropsychological testing and auditory event-related potentials (aERPs). Motor function was assessed using the Scale for Assessment and Rating of Ataxia (SARA).
Results: Sixteen SCA1 patients (9 males, seven females) were enrolled at baseline, with 10 patients (5 males, five females) completing follow-up at 24±3 months. At baseline, while most cognitive functions were preserved in both sexes, male patients showed significantly worse performance in emotion attribution tasks than females (42.8±8.5 vs 53.1±5.7, p=0.029). At follow-up, males demonstrated more pronounced deficits in verbal fluency, visual memory recall, and emotion attribution, while females maintained normal ranges across all tests. Although both sexes showed slightly worsening cognitive performance over time, the differences were not statistically significant. Motor impairment was more severe in males at follow-up, though not significantly (SARA: 18.8±6.8 vs 14.0±6.5, p=ns). Analysis of aERPs revealed no differences between sexes at follow-up.
Conclusion: These findings highlight both the importance of considering sex-specific approaches in the clinical management of SCA1 patients and the higher values of neuropsychological assessment compared to neurophysiological approach to reach these slight changes over time.
Disclosure: no

EPO-254 | Impact of deep brain stimulation on impulsive-compulsive behaviors in Parkinson's disease patients

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Background and aims: Parkinson's Disease (PD) is a neurodegenerative disorder with motor and non-motor complications, including impulse-control disorders (ICDs), mainly due to dopaminergic medications used to treat the disease. While medication is the primary treatment, its effectiveness in managing impulsivity may be limited. Deep Brain Stimulation (DBS) alleviates motor symptoms, but its effect on ICDs is unclear. We aim to compare ICD between patients with PD treated with DBS as an adjunct to medication therapy versus medication alone.

Methods: We conducted a systematic review and meta-analysis, searching PubMed, Embase, Cochrane Library, Web of Science, and Scopus. The inclusion criteria were patients with PD treated with DBS as an adjunct to medication therapy or alone. The primary outcomes analyzed were the Barratt Impulsiveness Scale (BIS) and decision-making performance, assessed by the Iowa Gambling Task (IGT). Data on ICD severity, frequency, types, and adverse events were analyzed.

Results: For impulsiveness, measured by BIS, no significant difference was found between groups (MD = 0.47, 95% CI: -7.82 to 8.77; p = 0.91, I^2 = 88%). Decision-making performance, assessed by the Iowa Gambling Task (IGT), was better with DBS OFF than DBS ON (MD = -8.81, 95% CI: -16.45 to -1.18; p = 0.02, I^2 = 23%), indicating potential adverse effects of DBS on impulsivity.

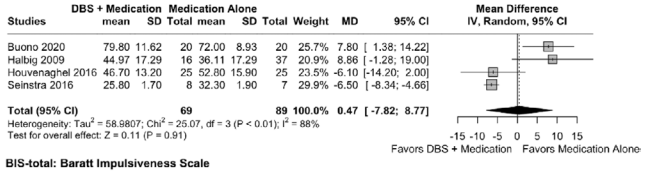

FIGURE 1 Forest plot of Barratt Impulsiveness Scale (BIS)

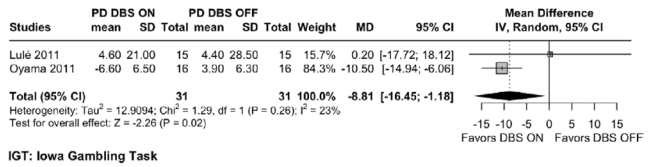

FIGURE 2 Forest plot of Iowa Gambling Task (IGT)

Conclusion: Your findings suggest that managing ICDs with DBS in PD patients is promising. Findings may guide clinical decision-making regarding the use of DBS in this population and inform future research directions.

Disclosure: Nothing to disclose.

EPO-255 | Actigraphic sleep monitoring in patients with Parkinson's disease and Deep Brain Stimulation

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Background and aims: Deep Brain Stimulation (DBS) represents an effective therapeutic strategy to improve both motor and non-motor symptoms of Parkinson's disease (PD), such as sleep-related issues. Actigraphy, based on the detection of triaxial accelerometric impulses, could become a useful innovation to monitor sleep even in these patients, allowing a continuous monitoring of patients' conditions with better compliance and economic advantages.

Methods: We investigated the reliability of Actigraphy in the definition of sleep-wake patterns, through a comparison with the gold-standard Polysomnographic method, both in terms of epoch-by-epoch sleep recording and the definition of sleep-related metrics such as Total Time of Sleep (TST), Wakefulness after Sleep Onset (WASO) and Sleep Efficiency (SE) in PD patients with Subthalamic DBS. Sleep recordings were collected using Axivity AX3 wrist Actigraphy and Polysomnography on 10 patients.

Results: An individually variable predictive capacity of Actigraphy in defining sleep-wake patterns was present in our study, in agreement with literature. We estimated an average sensitivity of 74% in detecting sleep status, with an accuracy of 55%. Actigraphy globally underestimates TST values, but differences with Polysomnography are not statistically significant, given the wide variability detected between different patients' data. Greater agreement was reported between the SE and WASO values.

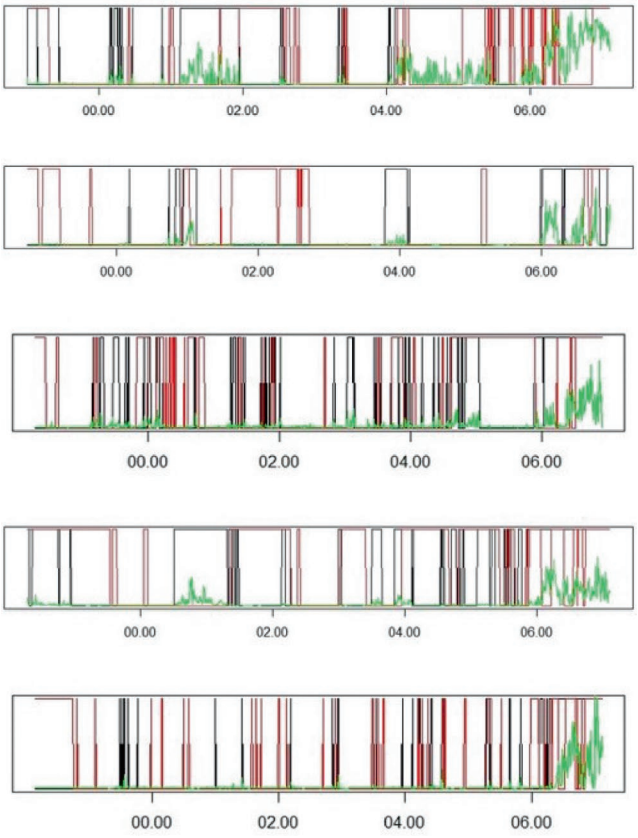

FIGURE 1 Epoch by Epoch graphics of 5 patients, monitored across an entire night. In black, the Actigraphic binarized sleep-wake trace; in red, the Polysomnographic trace; in green the trace of movement intensity detected by the Actigraphic device.

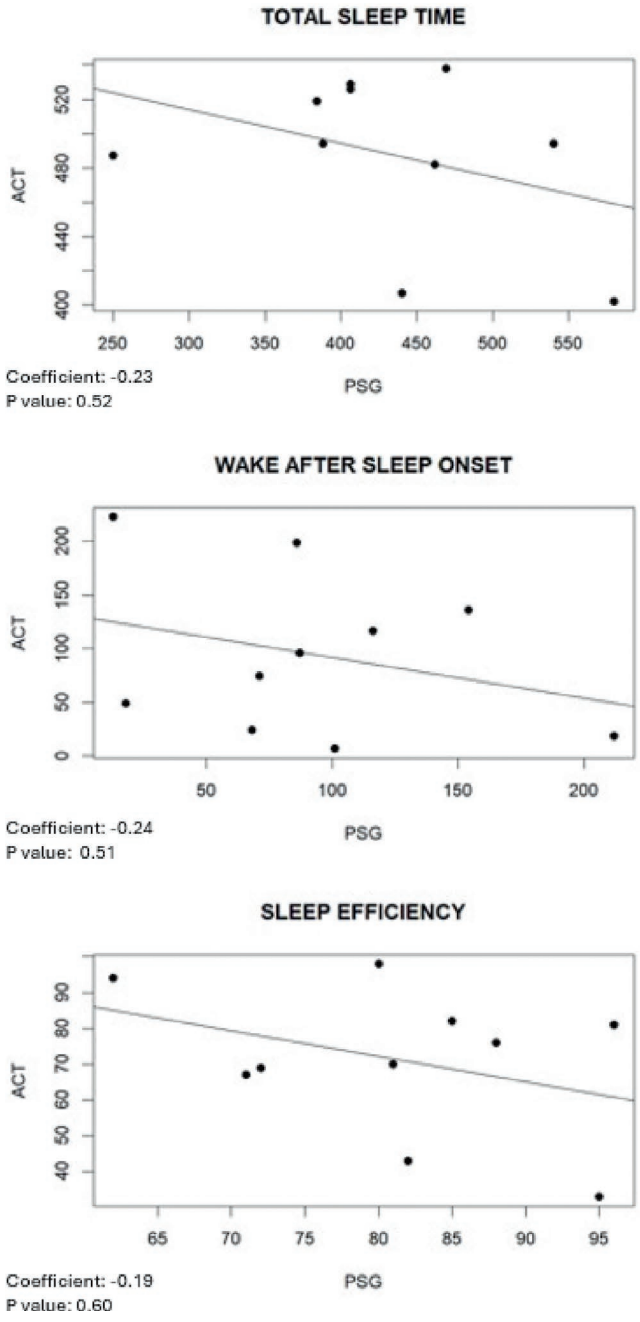

FIGURE 2 Spearman correlations obtained by comparing Polysomnographic (PSG) and Actigraphic (ACT) sleep records. Each point of the graph represents a patient and his relative values: TST (minutes), WASO (minutes), SE (percentage).

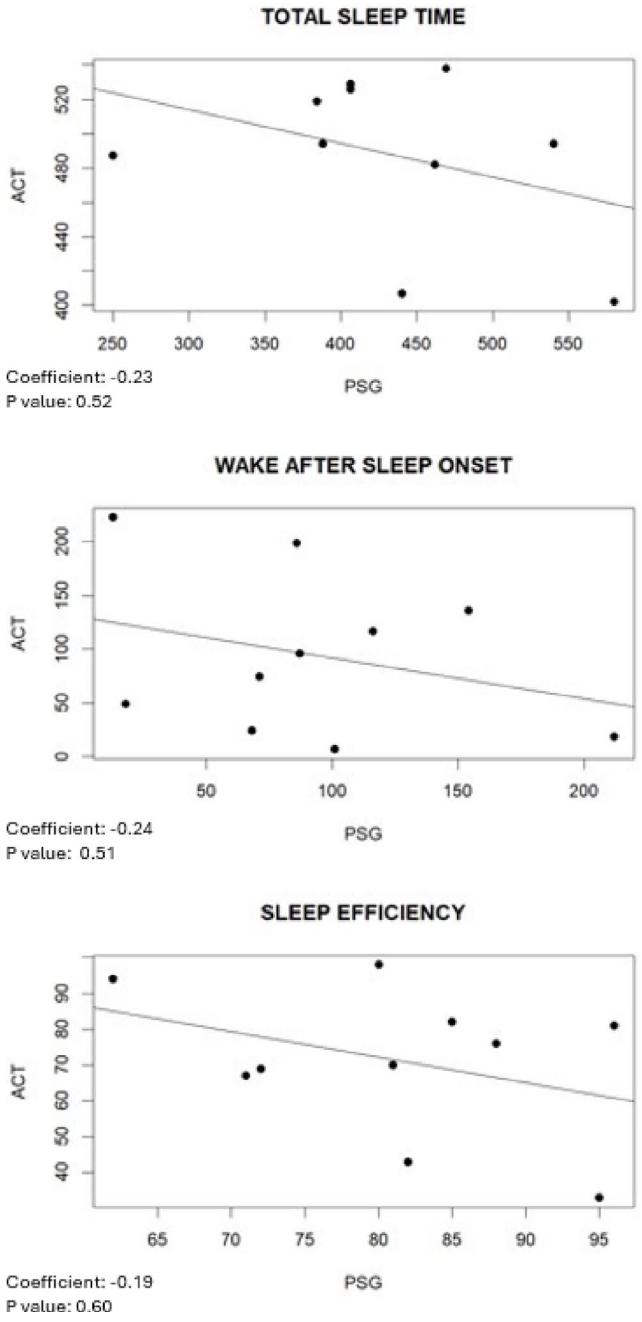

FIGURE 3 Bland-Altman plots comparing sleep measures of patients reveal an unsignificant tendency of Actigraphy to TST underestimation (mean difference = 55.3 minutes), WASO underestimation (1.9 minutes) and SE overestimation (10%) vs Polysomnography.

Conclusion: The study shows the potential applicability of Actigraphy in the assessment of sleep for PD patients undergoing DBS, with several clinical implications. However, we also highlight the inter-patient variability in the reliability of the sleep-related data obtained with this instrument in this population.
Disclosure: Nothing to disclose.

EPO-256 | Gender-differences in efficacy and tolerability of opicapone in add on of levodopa. A real-world observational study

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Background and aims: Opicapone is a peripheral catechol-O-methyltransferase inhibitor, approved in add on to levodopa (LD) in Parkinson's disease (PD) patients with motor fluctuations. Aim of the study is to evaluate gender-differences in efficacy and tolerability of opicapone in add on to LD treatment.
Methods: PD patients with motor fluctuations who started opicapone and who were followed up for at least 6 months were enrolled.
Results: Seventy-seven PD patients (51 men; 66.2%) with a mean age at onset of 57.3±9.4 years and a disease duration of 11.0±4.2 years were enrolled. Baseline characteristics were not significantly different between sexes. At follow-up a significant reduction of the total daily OFF time was observed. Overall 41.6% reported some adverse events (AEs) and incidence of AEs was significantly higher among women (65.4% versus 29.4%; p-value 0.002). At multivariate analysis, adjusting by LEDD, female sex was significantly associated with the presence of AEs (OR 4.42; p-value 0.004); 27.3% patients discontinued opicapone due to AEs and women had significantly higher odds of discontinuation (OR 3.00; p-value 0.04).

TABLE 1 Gender-differences in baseline and follow-up clinical features in our PD sample.

	Men N=51	Women N=26	Total N=77	*p-value*
BASELINE (T0)				
Sex	51 (66.2)	27 (33.8)	51 (100)	/
Age at onset	56.4±9.2	58.8±9.7	57.3 ±9.4	0.3
Disease duration	10.5±3.9	11.8±4.6	11.0±4.2	0.2
LEDD	885.4±338.7	828.2±225.5	866.1±304.9	0.4
OFF time	90.2±51.0	85.6 ±55.8	88.7±52.3	0.7
Dyskinesia	24 (48.0)	13 (50.0)	37 (48.7)	0.9
UPDRS-ME	45.2±15.3	43.6±15.3	44.6±14.6	0.6
FOLLOW-UP (T1)				
LEDD	1100.7± 343.1	1063.8 ± 373.0	1090.7± 350.4	0.7
OFF time	68.6 ± 47.33	113.9 ± 159.4	81.5 ± 94.6	0.03
OFF time No dropped	65.8 ± 48.4	71.9 ±70.5	67.3 ± 54.1	0.7
OFF time dropped	79.5 ± 43.6	205.0± 254.8	126.6± 163.5	0.1
Dyskinesia	30 (60.0)	16 (72.7)	46/72 (63.9)	0.3
UPDRS-ME	41.4 ± 10.7	43.3± 13.0	42.0 ± 11.5	0.6
AEs	15 (29.4)	17 (65.4)	32 (41.6)	**0.002**
Type of AE				**0.01**
Dyskinesia	9 (60.0)	10 (58.8)	19 (59.4)	/
Other	5 (33.3)	6 (35.3)	11 (34.4)	/
Psychosis	1 (6.7)	1 (5.9)	2 (6.2)	/
Drop out	10 (19.6)	11 (42.3)	21 (27.3)	**0.03**

Conclusion: Opicapone is highly effective for the treatment of motor fluctuations. Women experienced significantly higher AEs resulting in a higher frequency of drug discontinuation. The higher frequency of AEs, including dyskinesias, may be explained by higher levodopa bioavailability among women. To avoid an early discontinuation due to the presence of AEs in women with motor fluctuations, LD dosage should be reduced

before the introduction of opicapone. Our study provides novel insights regarding gender-differences in PD treatment, suggesting a personalized management for women with PD.
Disclosure: Nothing to disclose.

EPO-257 | Importance of moderate to vigorous physical activity for bone health in Parkinson's disease

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Background and aims: Parkinson's disease (PD) is associated with significant alterations in bone metabolism, yet the relationship between different intensities of physical activity and bone health in PD remains unexplored. This study aimed to assess bone health and its association with physical activity in PD patients.
Methods: PD patients underwent bone densitometry and physical activity was measured using a waist-worn accelerometer (ActiGraph wGT3X-BT) for seven days. Obtained data included total steps, time spent in light and moderate to vigorous physical activity (MVPA), and sedentary time. Demographic, clinical, and disease-related data were collected.
Results: Among the 40 patients studied (mean age 70.5 ±7.5years; disease duration 6.5 ±5years), seven (17.5%) were osteoporotic. Patients with and without osteoporosis showed no differences in age (74.5 ±8.6 vs. 69.7 ±7.1; p=0.129), sex (males 57.1% vs. 63.6%; p=0.747), disease duration (7.5 ±3.8 vs. 6.3 ±5.2; p=0.194), or disease severity (UPDRS III: 30.5 ±13.4 vs. 28.8 ±14.7; p=0.630). Regression analysis, adjusting for age, sex, and BMI, revealed that total physical activity was positively associated with total hip bone mineral density (BMD) (β=0.310; p=0.026). Only MVPA was significantly related to total hip BMD (β=0.376; p=0.009), whereas light activity was not (β=0.109; p=0.457).
Conclusion: MVPA is associated with higher bone mineral density in PD patients. Encouraging this type of activity is recommended to support better bone health in this population.
Disclosure: Nothing to disclose.

EPO-258 | Subthalamotomy induced dyskinesia in Parkinson's disease: A sign of positive response rather than a problem

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Background and aims: Unilateral magnetic resonance-guided focused ultrasound (MRgFUS) subthalamotomy is a minimally invasive effective treatment for Parkinson's disease (PD) patients with asymmetrical motor signs. Dyskinesias may develop in the treated hemibody. We aimed to assess the effect of MRgFUS subthalamotomy in PD patients with dyskinesias post-procedure in terms of patient-reported changes, motor improvement and quality of life (QoL).
Methods: Thirty-five PD patients underwent MRgFUS subthalamotomy in a randomized controlled trial. Retrospectively, they were grouped into those with (PD-Dysk, n=13) and without dyskinesias (PD-NoDysk, n=22) post-procedure. The primary outcome was the between-group difference in Patient's Global Impression of Change (PGI-C) at four months. Secondary outcomes included long-term PGI-C, MDS-UPDRS III scores, levodopa equivalent daily dose (LEDD) reduction, and QoL (PDQ-39) at 4,12 and 24-36 months. Mann-Whitney U tests with Bonferroni correction were used.
Results: At four months, the PD-dysk group reported greater improvement on PGI-C (median 2.0 vs. 2.5, p=0.019), with a trend persisting at 24-36 months (p=0.061). Motor improvement measured by MDS-UPDRS III was comparable between groups except for greater reduction in treated-side off-medication score in the PD-dysk group at 4 and 12 months (median -14 vs. -9.5; -14 vs. -9). LEDD reduction was greater in the PD-dysk group at four months (-175 vs 0, p=0.015) but not sustained. QoL scores showed no significant differences.

TABLE 1 Analysis of primary and secondary outcomes.

	Group		*p* value
	PD-Dysk	PD-NoDysk	
4-month visit (n=35)	n=13	n=22	
PGI-C	2.00 [1.00, 2.00]	2.50 [2.00, 3.00]	0.027
Total On MDS-UPDRS III change	-10.00 [-14.00, -7.00]	-8.50 [-10.75, -3.25]	0.843
Total Off MDS-UPDRS III change	-17.00 [-24.00, -15.00]	-13.00 [-17.75, -10.25]	0.078
Treated Side On MDS-UPDRS III change	-10.00 [-10.00, -7.00]	-7.00 [-8.00, -5.00]	0.447
Treated Side Off MDS-UPDRS III change	-14.00 [-16.00, -11.00]	-9.50 [-12.75, -7.25]	**0.027**
LEDD change	-175.00 [-300.00, 0.00]	0.00 [-41.25, 73.75]	**0.015**
PDQ-39 score	9.74 [5.00, 14.48]	17.86 [10.62, 23.85]	0.303
12-month visit (n=33)	n=13	n=20	
Total On MDS-UPDRS III change	-8.00 [-13.00, -6.00]	-10.00 [-13.25, -5.75]	1
Total Off MDS-UPDRS III change	-15.00 [-24.00, -14.00]	-11.50 [-15.50, -9.00]	0.111
Treated Side On MDS-UPDRS III change	-10.00 [-13.00, -5.00]	-8.00 [-9.25, -6.00]	0.447
Treated Side Off MDS-UPDRS III change	-14.00 [-16.00, -12.00]	-9.00 [-11.25, -7.00]	0.003
LEDD change	-100.00 [-200.00, 0.00]	6.50 [-20.25, 162.50]	0.054
PDQ-39 score	14.69 [7.97, 24.48]	17.66 [8.46, 23.80]	1
30-month visit (n=23)	n=10	n=13	
PGI-C	2.00 [1.00, 2.00]	3.00 [2.00, 3.00]	0.061
Total On MDS-UPDRS III change	-3.50 [-8.75, 1.75]	-12.00 [-15.00, -9.00]	0.246
Total Off MDS-UPDRS III change	-13.50 [-16.75, -7.50]	-11.00 [-15.00, -9.00]	1
Treated Side On MDS-UPDRS III change	-8.00 [-10.75, -5.50]	-9.00 [-10.00, -6.00]	1
Treated Side Off MDS-UPDRS III change	-13.00 [-14.00, -10.25]	-10.00 [-11.00, -9.00]	0.168
LEDD change	18.50 [-358.00, 253.75]	205.00 [0.00, 350.00]	0.342
PDQ-39 score	12.81 [5.92, 20.07]	14.43 [13.12, 22.97]	1

Data are reported as median [IQR]. IQR, Interquartile range; LEDD, Levodopa equivalent daily dose; MDS-UPDRS III, Movement Disorders Society-Unified Parkinson's Disease Rating Scale part III; PD-Dysk, Parkinson's disease patients with dyskinesia, PD-NoDysk, Parkinson's disease patients without dyskinesia; PDQ-39, 39-Item Parkinson's Disease Questionnaire; PGI-C, Patient's global impression of Change. P value corrected for multiple comparisons.

Conclusion: PD patients with MRgFUS subthalamotomy-related dyskinesias had a more favorable impression of health

improvement than those without dyskinesias. Dyskinesias did not significantly impact QoL in either direction.
Disclosure: Nothing to disclosure.

EPO-259 | Non-motor symptoms in GBA1-Parkinson's disease: Analysis from the Parkinson's progression markers initiative

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Background and aims: Parkinson's Disease (PD) progression varies, particularly with non-motor symptoms (NMS), which significantly affect quality of life. GBA-PD is linked to GBA1-gene mutations, encoding the beta-glucocerebrosidase enzyme. On average, GBA-PD shows earlier onset and a faster progression compared to idiopathic PD (iPD). Using data from the Parkinson's Progression Markers Initiative (PPMI), we compared GBA-PD and iPD progression based on NMS severity.
Methods: PPMI, a multicenter, longitudinal cohort study was used (data-cut: Dec-11th, 2024). Non-motor scales with continuous variables (cognitive, behaviour and sleep-assessments) were included if the sample size at the longest follow-up (6 years) was >=40. Mixed-Effects-Model for Repeated-Measures (MMRM), corrected for baseline value and disease duration, was employed.
Results: In total, 95 GBA-PD and 495 iPD patients were included. At baseline, GBA vs iPD patients were 62.2 ±10.55 (mean ± standard deviation) vs 64.1 ±9.70 years-old and had PD for 3.2 ±1.97 vs 2.2 ±1.18 years, respectively (Table 1). Patients with GBA-PD consistently show worse severity and significantly faster progression in 54.5% of the scales vs iPD. Longitudinally, 6 non-motor scales for GBA-PD and 4 for iPD (out of 11) show Minimal Clinical Important Difference (MCID) from baseline, with GBA-PD reaching MCID 1-2 years earlier than iPD. Among group differences (Figure 1), four scales reached MCID: MDS-UPDRS-Part-1A, Symbol-Digit-Modalities-Score, Hopkins-Verbal-Learning-Test, and State-Trait-Anxiety-Index, with scores worse for GBA-PD vs iPD.

TABLE 1 Baseline Characteristics.

Baseline Variable	statistics	GBA-PD	Idiopatic PD
Number of Patients	n	95	495
Age at Baseline* (years)	mean (sd)	62.2 (10.55)	64.1 (9.70)
Time since PD diagnostics (years)	mean (sd)	3.2 (1.97)	2.2 (1.18)
Sex (%)			
Female	n (%)	42 (44.2)	160 (32.3)
Male	n (%)	53 (55.8)	335 (67.7)
Clinical Questionnaires	mean (sd)		
Benton Judgement of Line Orientation Score		11,9 (2,66)	12,5 (2,42)
Epworth Sleepiness Scale Score		6,6 (4,20)	6,4 (4,14)
Geriatric Depression Scale Score		3,00 (3,12)	2,4 (2,7)
Hopkins Verbal Learning Test: Immediate/Total Recall t-score		45,4 (11,10)	44,6 (11,46)
MDS-UPDRS Part 1A		7,9 (5,00)	7,1 (4,57)
MDS-UPDRS Part 1B		6,2 (3,90)	5,6 (3,55)
Montreal Cognitive Assessment		26,0 (3,13)	26,6 (2,87)
Questionnaire for Impulsive-Compulsive Disorders in Parkinson's Disease		0,54 (0,90)	0,25 (0,63)
REM Sleep Behavior Disorder Screening Questionnaire (RBDSQ) total score		5,2 (3,55)	4,5 (2,97)
State-Trait Anxiety Index (STAI) Total Score		67,8 (18,50)	64,2 (18,41)
Symbol Digit Modalities Score		38,0 (12,72)	40,6 (10,74)

* Baseline was adjusted to the first visit in the study each participant reported taking PD-medication

FIGURE 1 Heatmap of yearly visits with statistically significant differences between GBA-PD and iPD. Darker Red gradients indicate lower p-values <=0.05; Purple asterisks denote Minimal Clinically Important Difference (MCID) between groups.

Conclusion: This analysis suggests that, over 6-years, NMS present with more severity and faster progression in GBA-PD compared to iPD-patients (adjusted for covariates baseline value and disease duration).
Disclosure: Daniel S. Ramos, Miguel M. Fonseca, and Valentina Di Foggia are employees of Bial.

EPO-260 | Mobile health technology postural and turning assessment in progressive supranuclear palsy and Parkinson's disease

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Background and aims: Progressive supranuclear palsy (PSP) is a neurodegenerative disease characterized by earlier postural instability compared to Parkinson's disease (PD). The aim of this study is to evaluate differences in postural and turning performances between patients with PSP and PD using Mobile Health Technology (MHT).
Methods: 250 subjects entered the study: 27 with PSP, 44 with PD who have experienced at least 1 fall in the last year, 63 with PD who have not experienced any fall in the last year and 116 healthy subjects. Static balance was evaluated with instrumented (lower back accelerometer, Rehagait®, Hasomed, Germany) 30-s trials in side by side, semitandem and tandem positions. Turning was evaluated with instrumented Timed Up and Go test. Data were analysed to determine what parameters discriminate PSP from PD and HC and to detect correlations of technological measures with clinical assessment.
Results: Compared to HC and PD, PSP and PD fallers showed similar static parameters. PSP exhibited lower volume of perturbation compared to PD with falls. Turning parameters significantly differed between HC, PD without falls and PD fallers as well as PSP, with no differences between the latest groups.

Conclusion: PSP patients exhibit similar postural pattern compared to PD with falls but lower perturbation volume. Different pathophysiology and compensations mechanism are probably related to postural instability in these patients. Turning parameters instead are more sensitive in the detection of fallers and further studies are needed to determine if they could be used as markers of risk of falls or early markers of disease progression.
Disclosure: Nothing to disclose.

EPO-261 | Machine learning predicts risk of motor dysfunctions in Parkinson's Disease patients in a multicentric study

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Background and aims: Dyskinesia, freezing, and motor fluctuations are conditions occurring during the course of Parkinson's Disease (PD) and significantly impacting the quality of life in patients. This study aims to identify patterns of clinical variables as predictors for each of the three outcomes—dyskinesia, freezing, and motor fluctuations—using a standardized Machine Learning (ML) strategy that ensures results reliability.
Methods: Demographic, motor, clinical, and pharmacological data of 265 PD patients followed at Movement Disorder Clinic in three Italian centers were retrospectively collected at four time points (baseline, after 12, 24, and 36 months) in the context of the project NeuroArtP3[1] (NET-2018-12366666). Four different classifiers were evaluated, namely Random Forest (RF), Extra Trees Classifier (ETC), XGBoost (XGB), and Logistic Regression (LR) on each outcome using a Randomized Nested Grid Search Cross Validation (RNGCV) strategy. Models performance was measured using Area Under the Receiver Operating Characteristic Curve (AUC), Matthews Correlation Coefficient (MCC) and F1-score. To understand how clinical features influence each specific outcome, a SHAP explainability analysis was performed on the best-performing classifiers.
Results: Best models' performances (AUC) for 3 outcomes ranged from 0.81 to 0.86 and are shown in Figure 1. Significant predictors for the three motor dysfunctions are shown in Figure 2.

Motor Dysfunction	Best Model	Performance		
		MCC	F1	AUC
Dyskinesia	ETC	0.48 +- 0.12	0.64 +- 0.09	0.81 +- 0.05
Freezing	XGB	0.55 +- 0.11	0.65 +- 0-09	0.86 +- 0.04
Fluctuations	XGB	0.48 +- 0.09	0.71 +- 0.05	0.82 +- 0.05

FIGURE 1 Classification performances of the best models for each outcome.

Motor Dysfunction	Most Predictive Features
Dyskinesia	motor fluctuations at baseline, dyskinesia at baseline, levodopa administration, levodopa years of treatment, hyposmia
Freezing	motor fluctuations at baseline, levodopa years of treatment, LEDD, depression, MDS-UPDRS3 ON Total, age at baseline
Fluctuations	freezing, Age at baseline, LEDD, years from symptom onset to diagnosis, MDS-UPDRS3 ON Total

FIGURE 2 Most important predictors for the three outcomes.

Conclusion: ML analysis showed a robust performance in predicting the risk of motor dysfunctions in PD patients. Comprehending the aspects that anticipate the risk of these outcomes could provide valuable insights for targeted clinical interventions.
Disclosure: Nothing to disclose.

EPO-262 | Limb-kinetic apraxia of legs in Parkinson's disease: Prospective clinical investigation

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Background and aims: The study of dynamic organization of motor acts is important for investigation of motor impairment, and a possible sign of a disorder of fronto-parietal areas of the brain in Parkinson's disease (PD). We aimed to prospectively investigate whether limb-kinetic apraxia in legs (LKA-L) is a heretofore unrecognized manifestation of PD independent of bradykinesia and rigidity.
Methods: Patients with PD and healthy controls (HC) performed bipedal reciprocal coordination (BRC) and monopedal reciprocal coordination (MRC) tests as a foot modification of the Oseretzky exam (originally alternate antiphase clenching and unclenching of the fists of the right and left hands). While MRC allowed for alternating movements of one leg per unit of time, BRC required synchronous movements of both legs in antiphase. Leg movement rates and their quality were measured by video recording and compared statistically between the groups of PD and HC.
Results: The cohort consisted of 31 PD patients (mean age 69.3±7.1 years, 16 males) and 12 HC (mean age 69±6.2 years, 6

males). No differences between PD and HC groups were identified in MRC rate of performance, which were used as a measure of legs movement speed, although the quality of MRC movements was poorer in PD patients (p=0.022). BRC rate and its performance quality were significantly flawed in PD compared to controls (P = 0.002 and P = 0.003, respectively).

Conclusion: Testing for dynamic organization of LKA-L revealed disorder in individuals with PD. LKA-L analyses should be considered in the diagnosis of leg movements and gait disorders in PD.

Disclosure: Nothing to disclose.

Movement Disorders 3

EPO-263 | Patient based retrospective reporting of motor and nonmotor symptoms in LRRK2-related vs idiopathic Parkinson's disease

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Background and aims: The clinical phenotype of LRRK2-PD overlaps with iPD, making routine clinical identification challenging without family history or in low mutation frequency populations. Our study aims to retrospectively compare motor and nonmotor symptoms in LRRK2- PD vs iPD.

Methods: We conducted a retrospective and cross-sectional study comparing LRRK2-PD with iPD in a single tertiary center. From a cohort of 654 Parkinson's disease patients who underwent genetic screening, 42 heterozygous carriers of LRRK2 mutations were identified. Of these, 24 were included and matched 1:2 with iPD patients (n=48) selected to match age at disease onset, disease duration, and gender. Participants completed structured questionnaires and underwent clinical evaluations using MDS-UPDRS, NMSS, NMSQ, HADS, AES, MoCA, MMSE, and PDSS.

Results: Our retrospective questionnaire showed that LRRK2-PD patients were less likely to report urinary urgency (p=0.014), REM sleep behavior disorder (p=0.004), pain (p=0.031), and falls (p=0.005). No significant differences between groups were identified for age at disease onset, disease duration and gender, in accordance with study design. Cross-sectional evaluation found no significant differences between LRRK2-PD and iPD groups in MDS-UPDRS III, NMSS, NMSQ, HADS, AES, MoCA and MMSE total scores. Acknowledging the limitation of evaluating sub-items in these scales, several showed significant differences between groups: LRRK2-PD patients reported lower frequency/severity of nocturia (p=0.022), sexual dysfunction (p=0.014) and better overall sleep quality (p=0.02).

TABLE 1 Reporting of ever having had motor and nonmotor symptoms.

	LRRK2-PD	iPD	
	n=24*	n=48*	
	% yes	% yes	*P* value
Tremor[a]	100	95.8	0.549
Postural instability[b]	100	87.5	0.169
Falls[c]	75.0	97.9	0.005
Motor fluctuations[d]	91.7	77.1	0.196
Dyskinesia[e]	83.3	68.8	0.259
Dystonia[f]	79.2	70.8	0.575
Freezing[g]	83.3	64.6	0.168
Dysphagia[h]	66.7	85.4	0.121
Dysarthria[i]	83.3	89.6	0.469
Sleep benefit[j] (n=23v.s48)	13.3	4.2	0.320
Depression[k]	87.5	91.7	0.679
Anxiety[l]	83.3	85.4	1.000
Orthostatic hypotension[m]	62.5	75.0	0.286
Psychosis[n]	62.5	77.1	0.265
Memory complaints[o]	50.0	66.7	0.205
Altered sex drive[p]	25.0	31.3	0.784
Restless legs syndrome[q] (n=23.vs47)	87.5	74.5	0.238
RBD[r] (n=19vs.38)	63.2	94.7	0.004
Insomnia[s]	79.2	89.6	0.285
Daytime sleepiness[t]	87.5	89.6	1.000
Sexual impotence[u]	45.8	50	0.806
Taste[v]	12.5	27.1	0.232
Smell[w]	45.8	50	0.806
Constipation[x]	70.8	75	0.779
Urinary urgency[y]	79.2	97.9	0.014
Pain[z]	50.0	77.1	0.031
Apathy[aa]	83.3	85.4	1.000
Vivid dreams[ab]	79.2	89.6	0.285
Punding[ac] (n=22vs.48)	9.1	2.1	0.231

TABLE 2 Demographic and clinical data comparing LRRK2-PD patients vs iPD

	LRRK2-PD n=24* mean (SD)/%	iPD n=48* mean (SD)/%	*P* value
Age at first motor symptoms	53.2 (13.5)	54.0 (10.9)	0.784
Age at examination	68.0 (10.3)	69.3 (9.3)	0.582
Disease duration	16.0 (8.7)	15.3 (8.7)	0.739
Gender (% male)	45.8%	52.1%	0.803
First symptom (% tremor)	70.8%	58.3%	0.439
TD/PIGD/INT	20.0/58.3/20.8%	12.5/64.6/22.9%	0.651
MDS-UPDRS I	13.3 (8.1)	13.6 (7.9)	0.900
MDS-UPDRS II	16.7 (13.3)	18.7 (10.9)	0.511
MDS-UPDRS III	42.3 (21.1)	40.7 (15.6)	0.713
MDS-UPDRS IV	2.1 (2.7)	1.9 (2.8)	0.761
HY	2.6 (1.1)	2.6 (0.9)	0.450
SE	75.0 (27.1)	71.9 (22.8)	0.609
NMSQ			
Nocturia (% yes)	41.7%	70.8%	0.022
NMSS	72.6 (45.1)	66.0 (41.0)	0.534
Mood/cognition	13.7 (12.8)	12.0 (13.4)	0.606
Perceptual problems/Hallucinations	4.4 (6.5)	2.2(4.3)	0.089
Urinary	9.7 (11.0)	13.2(9.5)	0.163
Nocturia	3.2 (4.5)	5.5(4.0)	0.030
Sexual function	3.1 (6.5)	1.0(3.2)	0.147
HADS -Emotional Distress (n=22vs.46)	13.6 (7.3)	13.7(6.5)	0.973
HADS anxiety	6.0 (4.8)	5.9(4.0)	0.889
HADS depression	7.6 (3.8)	7.8(3.9)	0.833
Hamilton DRS (n=21vs.46)	6.0 (4.2)	4.7(4.6)	0.290
Apathy Evaluation Scale (n=22vs.46)			
Patient	33.0 (8.3)	35.2(9.1)	0.342
Clinician (n=24vs.47)	36.9 (8.5)	36.3(8.1)	0.773
MoCA	20.4 (7.1)	20.6(7.0)	0.911
MMSE	25.6 (6.6)	24.6(6.4)	0.452
MDS-PDD level 1 (% yes)	8.3%	22.9%	0.196
SAPS	1.8 (3.5)	1.0 (2.6)	0.283
PPQ (n=23vs.48)	11.3 (4.3)	7.69(7.2)	0.233
QUIP-RS	9.7 (13.4)	9.7 (14.9)	0.991
SCOPA-AUT	12.6 (9.8)	14.5(7.8)	0.395
Sexual dysfunction (n=23vs.48)	0.2 (0.6)	0.9(1.7)	0.014
FSS (n=22vs.46)	5.0 (1.3)	4.5(1.5)	0.287
VAS Fatigue (n=20vs.46)	5.7 (2.7)	5.1(2.5)	0.415
PDSS (n=21vs.45)	100.6 (28.0)	94.6(26.3)	0.397
Overall quality	6.8 (3.0)	5.0(2.7)	0.020
SS-16 (n=23vs.47)	7.43 (2.9)	67(2.9)	0.314
hyposmia	91.3%yes	97.9%yes	0.250
LEDD (mg)	740.3(372.6)	887.7±509.6	0.213
LEDD-DA (mg)	178.3(185.4)	122.1(130.4)	0.005
DBS (% submitted)	45.8%	37.5%	0.396
Time to DBS (years)	14.3(3.8)	15.7(5.9)	0.493

Conclusion: Our retrospective questionnaire investigating if a motor and non-motor symptom was ever present contributed to discriminate between LRRK2-PD and iPD. Structured questionnaires like this one could contribute to inform clinical care and research in PD.

Disclosure: Nothing to disclose.

EPO-264 | 1H-NMR metabolomic analysis identifies disrupted glutamate metabolism as serum signature in Parkinson's disease patients

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Background and aims: Using a High-Performance Liquid Chromatography targeted approach, we recently showed increased CSF and serum serine enantiomers levels as putative biomarker of Parkinson's disease (PD). Recent serum metabolomics evidence showed a dysregulation of multiple amino acids pathways in PD patients compared to healthy controls (HC). Here, we attempted to identify a metabolomic signature distinctive of PD through an untargeted approach.

Methods: We enrolled 69 idiopathic PD patients and 32 age-matched HC. Untargeted metabolomics was carried out using Nuclear Magnetic Resonance (1H-NMR) on serum samples. Partial least-squares discriminant analysis (PLS-DA) and pathway enrichment analysis were used to identify metabolites and biochemical pathways discriminating the two groups.

Results: Serum metabolomics identified two distinct clusters for PD patients and HC (Fig. 1a). Multivariate analyses revealed 11 metabolites independently associated with PD (i.e. with variable importance in projection score>1), including L-glutamate, L-proline, pyruvate and L-serine (Fig. 1b). Univariate analyses showed (i) increased L-glutamate and (ii) reduced L-proline and 2-oxoglutarate levels in PD compared to HC, all showing high predictive power for PD (AUC: 0.99, 0.89 and 0.94, respectively) (Fig. 2a-b). Finally, pathway analysis identified 21 pathways overrepresented in PD at FDR<0.05, almost all involved in amino acids or energy metabolism. Among these, glycine-serine pathway showed the best discriminating value (Fig. 3).

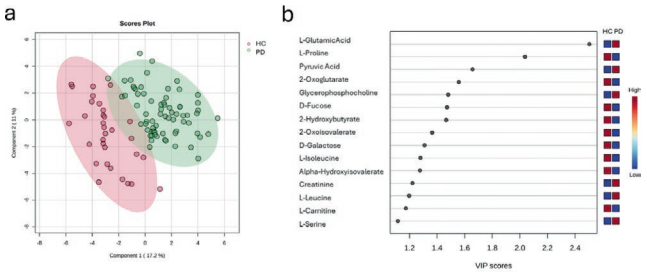

Figure 1. a) PLS-DA score scatter plots related to serum from PD patients (N = 69) and healthy controls (N = 32). The cluster analyses are reported in the Cartesian space described by the main components PC1:17.2% and PC2: 11.0%. PLS-DA was evaluated using cross-validation (CV) analysis. CV tests performed according to the PLS-DA statistical protocol show a significant cluster separation (0.88 and 0.97 accuracy PC1 and PC2, respectively, with positive 0.52 and 0.63 Q2 indices); b) Variable importance in projection (VIP) score graph of metabolites discriminating the two clusters.

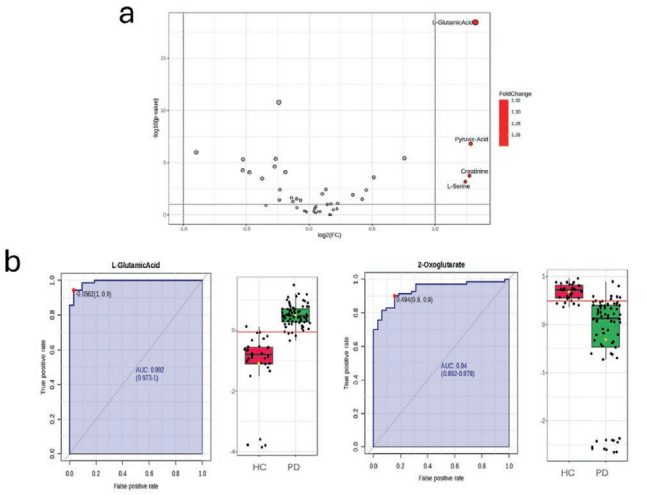

Figure 2. a) Volcano plot analysis of metabolic changes in PD patients and HC sera. Each point on the volcano plot was based on p-value and fold-change (FC) values, set at 0.05 and 2.0, respectively. Red points identify upregulated metabolites. B) Receiver operating characteristic (ROC) curves and box-plots of selected metabolites with significantly different concentrations between PD patients and HC. Red line shows the optimal cutoff value represented in the AUC as cutpoint. Yellow diamond in the bars indicate the average value; black dots represent the individual concentrations of selected metabolites.

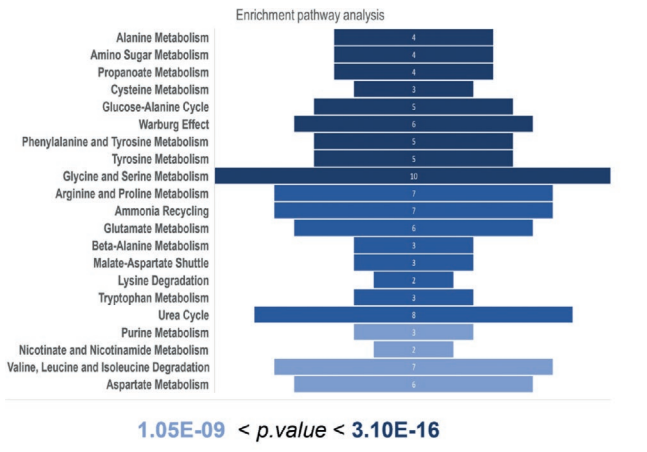

Figure 3. Enrichment pathways analysis. The discriminative pathways are ranked according to p-value and number of hits reported in the bars.

Conclusion: We identified serum glutamate levels and glycine-serine metabolism dysregulation as distinctive signatures of PD. Our results support the hypothesis that dysregulated aminoacids and energy metabolism plays a key role in PD physiopathology and pave the way for future studies evaluating its diagnostic and prognostic value.
Disclosure: Nothing to disclose.

EPO-265 | Low vs. high-frequency STN-DBS in PD patients: results from a two-center, randomized, double-blind, crossover trial

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Background and aims: Subthalamic nucleus deep brain stimulation (STN-DBS) effectively treats Parkinson's disease (PD). Whether low-frequency stimulation (LFS) is more effective than high-frequency stimulation (HFS) on gait and postural disturbances is not entirely elucidated yet.
Methods: We conducted a two-center, randomized, double-blind, crossover trial on sixteen STN-DBS patients (7 females; age 69.7 ± 7.2). Of them, 7 were tremor predominant (TD), and 9 were postural instability/gait disorder (PIGD). Participants randomly received LFS (60 Hz) or HFS (130 Hz) during two separate visits, while in an OFF-medication state. Stimulation amplitude was adjusted to maintain a stable total electrical energy delivered. The MDS-UPDRS part III, the Berg Balance Scale (BBS), and the Time Up-and-Go (TUG) test wearing a wireless inertial sensor were performed both in OFF- and ON-stimulation state.
Results: A significant time, frequency, and motor subtype interaction was found for MDS-UPDRS total ($F_{2,13}=7.19$, $p=0.007$), tremor ($F_{2,13}=10.5$, $p<0.001$), gait score ($F_{2,13}=4.27$, $p=0.03$), and BBS ($F_{2,13}=4.16$, $p=0.04$). Post-hoc tests for the tremor score indicated that in TD patients HFS ON state was significantly different from its OFF state ($p<0.001$) and LFS ON state ($p=0.02$), For the gait score and BBS in PIGD patients both LFS and HFS ON states were significantly different from their OFF states ($p=0.02$ and $p=0.007$, $p=0.006$ and $p<0.001$, respectively), but not from each other ($p=0.77$). A significant effect of time ($F_{1,15}=5.73$, $p<0.03$), but not a significant time, frequency, and motor subtype interaction was found for TUG test duration.
Conclusion: LFS is equally effective as HFS in improving gait and postural stability in PIGD patients.
Disclosure: Nothing to disclose.

EPO-266 | Efficacy and safety of magnetic resonance-guided focused ultrasound pallidothalamic tractotomy for Parkinson's Disease

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Background and aims: Magnetic resonance-guided focused ultrasound (MRgFUS) pallidothalamic tractotomy (PTT) is an incisionless therapy used in Parkinson's Disease (PD). A Phase III trial (NCT04728295) of staged-bilateral PTT-MRgFUS was completed and 12-month follow up data are under FDA review. This systematic literature review (SLR) aims to review

the published evidence to help contextualize those upcoming results.

Methods: An SLR was conducted in Medline and Medline In-Process with no date restrictions (Table 1). Two reviewers independently screened titles and abstracts. Full-text review and data extraction were completed, followed by a narrative synthesis of the findings.

TABLE 1 Inclusion and exclusion criteria.

Criterion	Inclusion criteria	Exclusion criteria
Population	Adult patients with Parkinson Disease.	Studies that include mixed populations and do not provide discrete data for PD and PTT
Intervention	MRI-guided focused ultrasound of the pallidothalamic tract (unilateral or bilateral)	None
Comparator	None	None
Outcomes	Any clinical outcomes but with a focus on cardinal symptoms	None
Study design	Systematic reviews or meta-analyses Primary study designs such as randomized controlled trials, non-randomized controlled studies, before-and-after studies, cohort studies, and case series studies	Case reports, narrative review articles, and editorial letters
Type of publication	Full-text publications and conference abstracts	None
Search period	No restriction on the search period	None
Publication language	English language	Articles published in languages other than English
Geography	No restriction	None

Results: All reports were single-centre studies conducted in Switzerland (5), Taiwan (2), and Japan (1) (Figure 1). Unilateral PTT-MRgFUS (n=102) was an effective treatment reporting statistically significant reductions in tremor (84%), rigidity (70%), bradykinesia (73%), off-medication dystonia (67%) and on-medication dyskinesias (38%). Two staged-bilateral studies (n=25) had a mean interval of 20±10 months between first and second PTT-MRgFUS treatments. Total off-medication UPDRS decreased by 52% ($p<0.007$). Mixed findings were reported for reductions in L-Dopa intake. The most common adverse events included hypoesthesia, speech difficulties, hiccups, and reduced responsiveness to L-Dopa. Recently, a modified approach was introduced by Chen et al, using dual-target VIM-PTT.

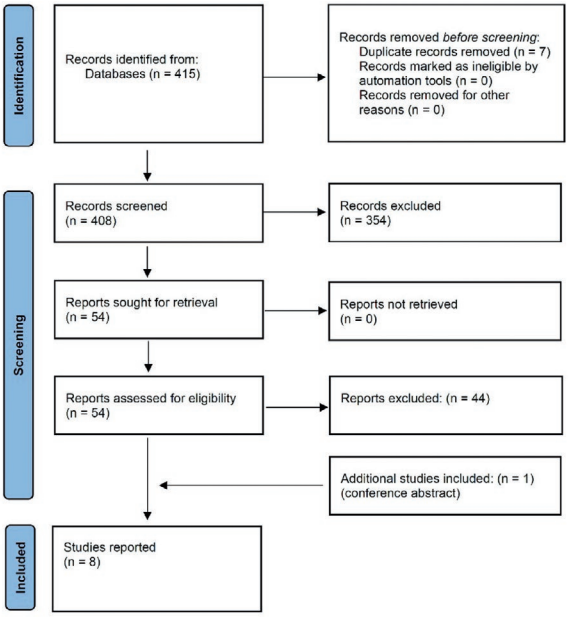

FIGURE 1 PRISMA study selection flowchart.

Conclusion: This SLR provides preliminary evidence that PTT-MRgFUS is effective in reducing motor symptoms and complications, with a generally favorable safety profile. Results from the upcoming Phase III study hold potential to expand bilateral treatment options to patients with idiopathic PD. It will be the first prospective global multicentre study investigating unilateral and staged-bilateral PTT-MRgFUS.

Disclosure: CF, AL, ASF, KG and AG are Insightec employees; SM, AM and OB are MTRC HEOR employees. Writing assistance was provided by Content Ed Net, Madrid, Spain.

EPO-267 | Light chain neurofilaments: A biomarker for differentiating Parkinson's Disease from Atypical Parkinsonism

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Background and aims: Differentiating Parkinson's disease (PD) from atypical parkinsonism (AP) is particularly challenging in the early stages. Emerging evidence suggests that neurofilament light chain (NfL) levels in CSF or serum may facilitate this distinction. This study evaluates the diagnostic utility of NfL in CSF and serum for distinguishing between PD and AP.

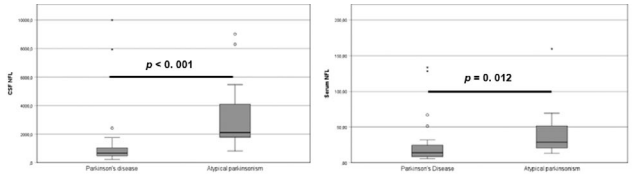
Methods: A retrospective analysis was conducted on clinical records of patients with a probable diagnosis of Parkinson's disease (PD), Multiple System Atrophy (MSA), Progressive Supranuclear Palsy (PSP), and Corticobasal Degeneration (CBD), all of whom underwent NfL testing in CSF and/or serum. NfL levels between

PD and AP were compared using bivariate and multivariate analysis.

Results: We included 49 patients with parkinsonism: 35 PD and 14 AP (5 MSA, 7 PSP, 2 CBD). All had NfL testing in CSF, and 44 also in serum. No significant clinical-demographic differences, except disease duration (PD: 8.0 years [IQR 3.0-12.0]; AP: 2.5 years [IQR 2.0-4.3]; p=0.015) and Hoehn and Yahr stage (PD: 2.0 [IQR 2.0-3.0]; AP: 3.0 [IQR 3.0-4.0]; p=0.002). Bivariate analysis showed higher NfL levels in AP patients compared to PD patients in CSF (p<0.001) and serum (p=0.012). No significant differences in NfL levels were found among AP subtypes. Multivariate analysis, adjusted to disease duration, Hoehn and Yahr score, and CSF/Serum NfL value, found a significant difference in CSF NfL levels (p=0.036), with high diagnostic accuracy (AUC 0.906).

Characteristics (n=49)	Parkinson's Disease (n=35)	Atypical Parkinsonism (n=14)	*p*-value
Females - no. (%)	20 (57.1%)	10 (71.4%)	0.353
Age - years (95%CI)	59.1 (56.0-62.3)	66.9 (61.1-72.8)	0.611
Disease duration - years (IQR)	8.0 (3.0-12.0)	2.5 (2.0-4.3)	**0.015**
MDS-UPDRS part III - score (IQR)	33.0 (24.0-40.0)	32.5 (29.75-46.5)	0.381
Hoehn and Yahr scale - score (IQR)	2.0 (2.0-3.0)	3.0 (3.0-4.0)	**0.002**
Levodopa equivalent daily dose - mg (95%CI)	784.5 (613.8-955.1)	597.5 (352.76-842.2)	0.382

FIGURE 1 Clinicodemographic characteristics and levels of study participants, stratified by final diagnosis



Variable	PD (n=35)	APD (n=14)	*p*-value
CSF NFL - pg/mL (IQR)	672.0 (475.8-1050.9)	2105.3 (1790.9-4442.0)	**<0.001**

Variable	PD (n=35)	APD (n=14)	*p*-value
Serum NFL - pg/mL (IQR) *	14.10 (8.57-24.82)	29.00 (20.46-132.56)	**0.012**

FIGURE 2 Comparison of CSF and serum NfL levels between patients with PD and APD

Parameters	AUC	Cutoff value (pg/mL)	Sensitivity (%)	Specificity (%)
CSF NFL	0.906	1339.5	92.9	82.9
Serum NFL	0.747	26.9	58.3	68.7

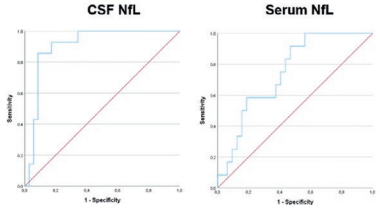


FIGURE 3 Receiver operating characteristic (ROC) analysis of CSF and Serum NFL in the diagnosis of PD and APD

Conclusion: Elevated NfL levels in AP patients compared to PD support NfL as a promising biomarker for differentiation, aiding in therapeutic decisions and prognostic evaluation.

Disclosure: Nothing to disclose.

EPO-268 | Stepwise dual-target MR-guided Focused Ultrasound (dtMRgFUS) for Parkinson's disease: A 2-year follow-up of 3 cases

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Background and aims: Magnetic resonance-guided focused ultrasound (MRgFUS) is a new treatment for medication-refractory Parkinson's disease (PD). Targets like the ventral intermediate nucleus (VIM) and pallidothalamic tract (PTT) have shown varying effectiveness. While single-lesion treatments alleviate specific PD symptoms, our previous research studied the safety and efficacy of a dual-lesion approach targeting both VIM and PTT over one year. This report presents the first three PD patients who underwent dual-target MRgFUS (dtMRgFUS), with outcomes tracked over a two-year follow-up.

Methods: Three tremor-dominant PD patients, previously reported, underwent dual-target MRgFUS treatment, assessed using a comprehensive set of primary and secondary outcome measures. Individual brain MRI scans were used to navigate and precisely target the VIM and PTT. Primary outcomes included the off-medication Clinical Rating Scale for Tremor (CRST) and the Unified Parkinson's Disease Rating Scale Part III (UPDRS-III). Secondary outcomes included UPDRS Parts I, II, and IV, the Hoehn and Yahr scale, the Neuropsychiatric Inventory, the PD Quality of Life Questionnaire (PDQ-39), the Non-Motor Symptoms Scale (NMSS), and the Clinical Global Impression (CGI). Baseline data were compared with results obtained 6 months, 1 year, and 2-year post-treatment.

Results: Tremor severity and motor deficits, as measured by CRST-Part B and UPDRS-III, showed significant improvement following dual-target ablation ($P < 0.05$, nonparametric Mann-Whitney U tests). Non-motor symptoms also demonstrated marked improvement at the 2-year follow-up. No severe adverse effects were reported.

Conclusion: Stepwise dual-lesion targeting of the VIM and PTT using MRgFUS is a safe and effective therapeutic approach for Parkinson's disease patients over a 2-year period.

Disclosure: Nothing to disclose.

EPO-269 | Exploring gender variations in the treatment of motor symptoms in Parkinson's disease

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Background and aims: Existing research highlights the role of gender in Parkinson's disease (PD) with higher prevalence, earlier onset, more severe forms and akinetic-rigid phenotypes seen in males. The study aims to help tailor therapeutic strategies based on the patient's sex by analysing their dopaminergic medication profile.
Methods: This retrospective study involved 1741 PD patients (M-54.9%, n=955; F-45.1%, n=786) of the D. Gherman Institute of Neurology and Neurosurgery stratified based on gender (M-69.01±7.68; F-69.73±7.53 years, p=0.05). PD motor symptoms' phenotype and severity, along to dopaminergic drugs' type and dosages were analysed using IBM-SPSS statistical tools.
Results: The male and female samples showed clinical homogeneity. Akinetic-rigid phenotypes (52.6% vs. 54.1%, df=2, p=0.722) and severe forms were frequent (46.9% vs. 47.7%, df=2, p=0.366), with significantly more fluctuations (33.4% vs. 56.1%, df=1, p<0.01) and dyskinesia (31.1% vs. 50%, df=1, p<0.01) in women. LEDD had minimal variation across genders (1049.15±568.08 vs. 1100.83±584.54, p>0.05). Both had comparable frequencies of levodopa (99.2% vs. 98.7%, df=1, p=0.477) and dopamine agonists (17% vs. 15%, df=1, p=0.294) usage, but amantadine prevailed in women (9.3% vs. 17.7%, df=1, p<0.01). Females employed higher daily dosages (mg) of levodopa (1030.94, ±562.12 vs. 1063.62, ±588.10, p>0.05) and amantadine (225.56, ±89.07 vs. 227.94, ±82.04, p>0.05), whilst males of dopamine agonists (2.02±0.67 vs. 1.73±0.78, p=0.008).
Conclusion: Although samples were generally comparable, female participants had more motor complications and required greater dosages of preventive pharmacological intervention, likely due to metabolic peculiarities that need further research.
Disclosure: Nothing to disclose.

EPO-270 | Tracking the role of the sub-thalamic nucleus in speech: a deep brain stimulation-electroencephalography study

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Background and aims: PD patients often developed hypokinetic dysarthria. Deep brain stimulation of the subthalamic nucleus (STN-DBS) has mixed effects on speech, ranging from improvement to deterioration. An STN–temporal cortex loop oscillating in the alpha frequency band may serve a speech-related function. DBS might therefore impart its negative effects on dysarthria by affecting this network. This study aims to characterize the role of the STN–temporal lobe circuitry in speech production using a speech task performed during STN-DBS, alongside STN local field potentials (LFP) and EEG recordings. The primary objective is to evaluate whether the STN–temporal lobe network is involved in speech production, and if DBS can disrupt this network.
Methods: In this preliminary report, we studied 6 patients with bilateral STN implants, each assessed off-medication (antiparkinsonian drugs were discontinued for 12 hours), in both on- and off-STN-DBS conditions. Patients performed a compensation speech paradigm task involving real-time perturbation of vocal pitch and first formant. High-density EEG and STN LFPs were recorded during these tasks. We evaluated STN–temporal circuit connectivity by computing coherence between STN LFPs and EEG signals across different task phases.
Results: We identified theta–alpha coherence between the left STN and the left frontal and posterior parieto-temporal areas at rest. This coherence showed tendency for modulation during the vocal task. DBS activation tended to reduce this modulation
Conclusion: Our preliminary results suggested the presence of speech modulated coherence in the alpha–theta range between the STN and frontal–parietal areas, possibly originating from a tangential dipole in the temporal regions.
Disclosure: This research was funded by the Brain Entry Clinical Fellowship.

EPO-271 | Predictors of improvement in activities of daily living and QoL in patients treated with foslevodopa/foscarbidopa

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Background and aims: Treatment with foslevodopa/foscarbidopa (LDp/CDp) improved motor experiences of daily living (m-EDL) and quality of life (QoL) for patients with advanced Parkinson's disease (aPD) in a 52-week, multicountry, open-label safety trial (NCT03781167). This post hoc analysis examined baseline characteristics linked to improvements in m-EDL and QoL outcomes.

Methods: A multiple logistic regression model using backward elimination method was used for variable selection and estimating associations between baseline characteristics and efficacy outcomes, namely Movement Disorder Society-Sponsored Unified Parkinson's Disease Rating Scale Part II (MDS-UPDRS-II) and Parkinson's Disease Questionnaire (PDQ-39) Summary Index scores, representing m-EDL and QoL, respectively (Figure 1). The models were adjusted for the respective baseline values of the outcomes. A minimal clinically important difference (MCID) was defined as <=-3.05 for MDS-UPDRS-II and <=-4.72 for PDQ-39 Summary Index scores at the final visit from baseline.

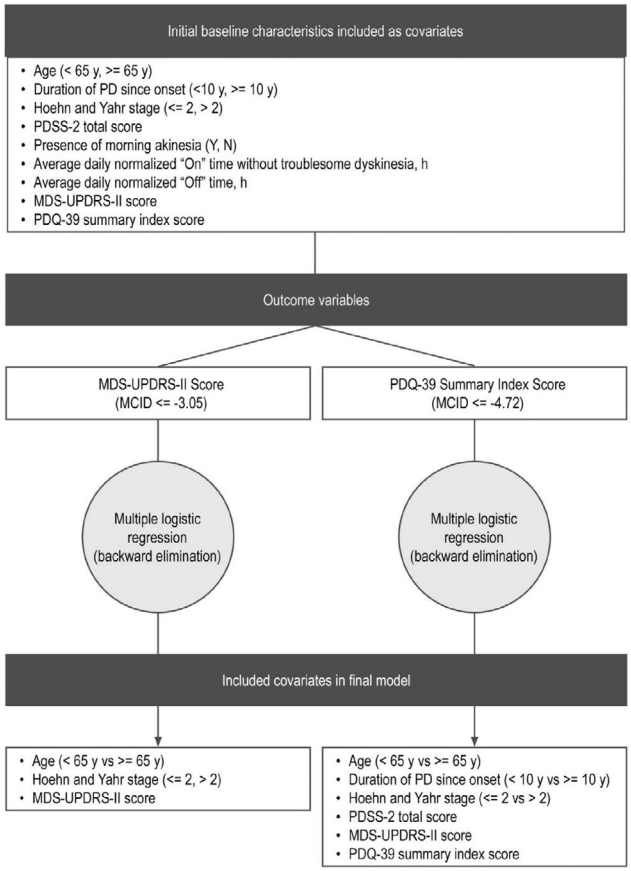

Figure 1. Analytical approach.
Abbreviations: MCID, minimal clinically important difference; MDS-UPDRS-II, Movement Disorder Society-Sponsored Unified Parkinson's Disease Rating Scale Part II; PD, Parkinson's disease; PDQ-39, Parkinson's Disease Questionnaire; PDSS-2, Parkinson's Disease Sleep Scale-2.

FIGURE 1 Analytical Approach with FN

Results: Of the covariates assessed, patients <65 years had a 56% higher likelihood (Odds Ratio [95% CI] = 1.560 [1.06-2.31]) of achieving an MDS-UPDRS-II Score MCID (P=.0258) than patients >=65 years (Table 1). Patients with Hoehn and Yahr (H&Y) stage <=2 had a 77.3% (1.773 [1.07-2.95]) and 80.4% (1.804 [1.06-3.05]) higher likelihood of achieving both an MDS-UPDRS-II Score MCID (P=.0270) and a PDQ-39 Summary Index Score MCID (P=.0282) than patients ≥65 years and with H&Y stage >2 (Table 1).

Table 1. Multiple logistic regression results for the probability of MCID from baseline to final visit (full analysis set).

	MDS-UPDRS-II Score[a]		PDQ-39 Summary Index Score[a]	
Covariate	**OR (95% CI)**	***P* value**	**OR (95% CI)**	***P* value**
Age: < 65 y vs >= 65 y	1.560 (1.06-2.31)	.0258*	1.257 (0.85-1.86)	.2550
Baseline duration of PD since onset: <10 y vs >= 10 y	–	–	1.241 (0.86-1.79)	.2473
Baseline Hoehn and Yahr stage: <= 2 vs > 2	1.773 (1.07-2.95)	.0270*	1.804 (1.06-3.05)	.0282*
Baseline PDSS-2 total score	–	–	0.973 (0.93-1.02)	.2115
Baseline PDQ-39 summary index score	–	–	1.040 (1.00-1.08)	.0330*
Baseline MDS-UPDRS-II score	1.156 (1.09-1.23)	<= .001***	1.042 (0.98-1.11)	.1966

*P <= .05, ***P <= .001.
Abbreviations: MCID, minimal clinically important difference; MDS-UPDRS-II, Movement Disorder Society-Sponsored Unified Parkinson's Disease Rating Scale Part II; PD, Parkinson's disease; PDQ-39, Parkinson's Disease Questionnaire; PDSS-2, Parkinson's Disease Sleep Scale-2.
[a]Baseline values of the respective outcomes were adjusted in the final model.

Conclusion: Although LDp/CDp enhances activities of daily living and QoL for patients with aPD, less advanced disease stage and younger age (<65 years) increase the likelihood of achieving clinically meaningful improvements in these outcomes.

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EPO-272 | Noninvasive deep brain stimulation of subthalamic nucleus in Parkinson's disease: temporal and spatial properties

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Background and aims: Temporal Interference stimulation (TIS) is a novel non-invasive brain electrical stimulation technique that has a potential to modulate deep brain regions. The focal modulation of TIS is possible using two high frequency signals (>1kHz), which interfere to create low frequency envelope

modulating the target area. Recent work presented the capability of TIS to focus the subthalamic nucleus (STN) and to suppress STN beta oscillations in Parkinson's disease. Here, we present temporal and spatial characteristics of this modulation technique.

Methods: Implanted DBS leads were temporally externalized for local field potentials (LFP) recording in 8 patients with Parkinson's disease indicated for STN-DBS. STN-TIS was performed by 2 pairs (f1 = 9.00kHz; f2 = 9.13kHz, 2mA per pair max.) of scalp electrodes placed in frontoparietal regions for 3 minutes. The following 3 minutes of resting-state were then used for LFP evaluation.

Results: Suppressed beta activity in STN re-occurred back in approx. 120 seconds for STN-TIS. In control condition, where conventional DBS was used, the after-effect varied across group and in some patients was more immediate than TIS. No electrical field enhancement around the DBS lead was found in case of transcranial TIS.

Conclusion: TIS is a different type of neuromodulation, applied in a sinusoidal pattern at a sub-threshold intensity; DBS is a pulsed pattern supra-threshold intensity stimulation that generates action potentials. Despite these different mechanisms of action there is growing evidence that TIS has the potential to influence deep brain oscillatory activity and induce clinical effects in a way similar to DBS.

Disclosure: The work was supported by LX22NPO5107 (MEYS), European Union-Next Generation EU.

EPO-273 | Slower turning predicts future Parkinson's disease diagnosis: A longitudinal study

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Background and aims: The use of wearable technology enables precise measurement of turning movements during walking. Cross-sectional studies have shown that a decline in turning can be detected in the early clinical and even preclinical stages of Parkinson's disease (PD). This prospective longitudinal study aims to quantify the change in turning performance among older adults and determine if turning performance predicts future PD diagnosis.

Methods: A total of 933 participants (mean age = 66.1 years) from the TREND study were included for this analysis over five 2-year intervals, with the development of clinically evident PD tracked. Participants walked up and down a 20-meter hallway for one minute at their preferred pace, wearing a digital device on their lower back to capture turning. Longitudinal trajectories of turning performance were modelled using random effects linear mixed models to establish the interval between initial turning changes and PD diagnosis. Cox regression was used to assess whether initial turning measures could predict the time to PD onset, controlling for age and sex.

Results: Of all participants, 23 were diagnosed with idiopathic PD, an average of 5.3 years after baseline assessment. Slower peak angular velocity at baseline was associated with a higher hazard of PD diagnosis, with deviations from controls emerging approximately 8.7 years before diagnosis (Figure 1). Other parameters showed no prediction value of PD diagnosis.

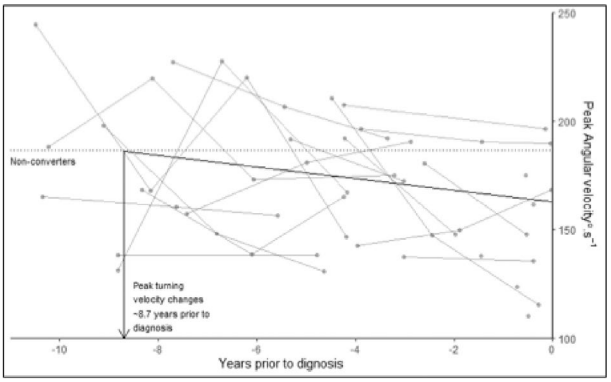

Figure 1: change in peak turning angular velocity in n = 23 older adults prior to a clinical diagnosis of PD (grey points and lines) compared to the mean of n = 910 healthy controls modelled at the average age of PD diagnosis (77.1 y, horizontal dotted line, controls. The sloped black line shows the mean modelled change of peak turning angular velocity (2.71 °.s^{-1}.y^{-1}) in the PD cohort. The solid black vertical line indicates that the mean lines of the PD and controls intersect approximately 8.7 years prior to diagnosis.

Conclusion: Peak angular velocity during turning appears to be a promising marker for identifying and tracking motor progression in the pre-diagnostic phase of PD.

Disclosure: nothing to disclose.

EPO-274 | Unveiling the gut-brain axis in Parkinson's disease: A meta-analysis of randomized-controlled trials

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Background and aims: Gut dysbiosis has been associated with the pathogenesis of Parkinson's disease (PD). Studies show that probiotic supplements may mitigate PD symptoms. However, the effect of broader gut microbiota interventions on PD is not well-defined. Thus, we performed a meta-analysis to explore their role in managing PD symptoms.

Methods: We systematically searched MEDLINE, Scopus, and Cochrane databases from inception until December 05, 2024, for placebo-controlled randomized trials that estimated the effects of probiotics, synbiotics, and fecal microbiota transplantation (FMT) on PD patients. To assess the efficacy of the different interventions, subsequent subanalyses were performed.

Results: A total of 11 RCTs comprising 756 patients were included. Of those, 410 (54%) received gut microbiota interventions. Follow-up ranged from 4 weeks to 6 months. We found that gut microbiota interventions significantly improved motor symptoms (MDS-UPDRS Total: SMD = -0.42; 95% CI -0.67 to

-0.16; p = 0.001) and quality of life (PDQ-39: SMD= -0.43; 95% CI -0.66 to -0.2; p=0.0002) compared to placebo. Depression parameter was also significantly reduced in this group (SMD= -0.41; 95% CI -0.71 to -0.1; p=0.009), with probiotics outweighing FMT. No significant changes in bowel movements and Bristol Stool Form Scale (BSFS) were noted. However, BSFS significantly increased (SMD = 0.55; CI 0.28 to 0.82; p < 0.00001) in patients with low (<= 3) baseline score.

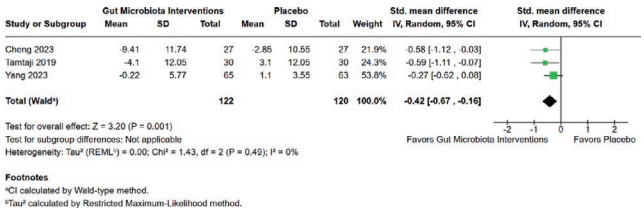

FIGURE 1 MDS-UPDRS total score was significantly reduced in patients receiving gut microbiota interventions compared to placebo.

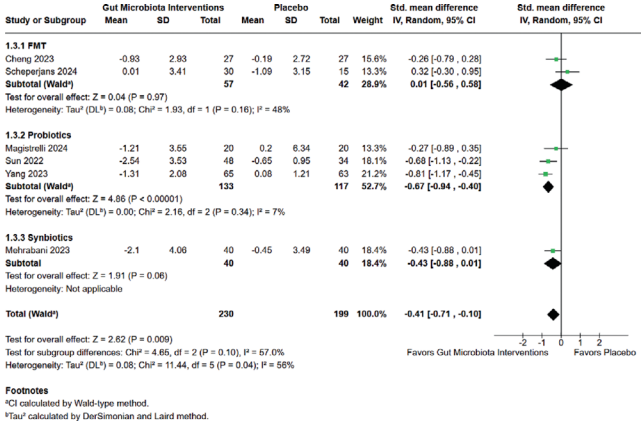

FIGURE 2 Gut microbiota interventions significantly improved depression symptoms in PD patients, with probiotics showing the greatest efficacy.

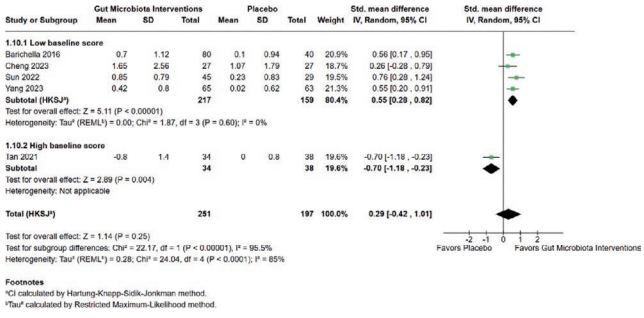

FIGURE 3 Bristol Stool Form Scale (BSFS) was significantly increased in patients with low baseline score treated with gut microbiota interventions.

Conclusion: Gut microbiota interventions seem to alleviate both motor and non-motor symptoms of PD patients. Further research exploring FMT and its impact on the disease's trajectory is needed.

Disclosure: Nothing to disclose.

EPO-275 | Amantadine extended-release tablets for the treatment of parkinson's disease: A phase IV multicenter, single-arm study

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Background and aims: This subset analysis of a phase IV study was performed to assess the safety and efficacy of amantadine extended-release (ER) tablets in Parkinson's Disease (PD) patients.

Methods: A subset of 141 patients from this single-arm, open-label multicenter, phase IV Indian study (CTRI/2023/04/051973), with PD was analyzed for safety and efficacy of amantadine ER tablet. The starting dose was 129 mg orally once; further uptitrated at weekly intervals to a maximum daily dose of 322 mg (administered as a 129 mg and 193 mg tablets) as per patient's response and tolerability. Treatment duration was up to 12 weeks depending on dose uptitration. Primary objective was safety assessment. Efficacy endpoints were change in MDS-UPDRS score (Part I, II, III, IV and total score), OFF hours, ON hours with dyskinesia and PDQ-39-QOL.

Results: Total 29 treatment-emergent adverse events occurred in 16 patients; most common was headache. The mean (±SD) MDS-UPDRS total score decreased significantly (p<0.0001) from 71.24 (±34.17) at baseline across all visits to 47.08 (±29.13) at EOT. Also, the mean (±SD) MDS-UPDRS part I, II, III and IV score significantly decreased from baseline till EOT (p<0.0001). Daily mean (±SD) off hours decreased significantly (p<0.0001) from 1.89 (±2.11) at baseline to 1.04 (±1.43) till EOT. There was significant decrease in mean (±SD) daily ON hours with dyskinesia from baseline till EOT (p<0.0001). The PDQ-39-QOL score decreased from 32.29 (±19.15) at baseline to 19.71 (±14.88) till EOT (p<0.0001).

Conclusion: Amantadine ER tablet was safe and efficacious in Parkinson disease.

Disclosure: The study was funded by Sun Pharma Laboratories Limited (SPLL).

EPO-276 | MR guided focused ultrasound dual lesioning for Parkinson disease

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Background and aims: lesioning procedures have become safe with advent of MRgFUS.
Methods: Dual lesioning of pallido thalamic tract and vim/vo for the past 2 yrs. The pallido thalamic tract was targeted at two sites, one medial and one lateral. The lateral target was located 6.5 to 8.5 mm away from the lateral border of the 3rd ventricle at half the distance from the AC-PC in the same plane. The medial target was located 1.5 mm inferior, 1.5mm posterior and 1.5 mm medial to the lateral target. The subthalamic body, mammillothalamic tract and the internal capsule were marked on the planning MRI and fused later with the live MRI during lesioning. 7 targets were identified for the vim/vo by image based and by standard coordinates. Two are newly described royal care targets. As the vim/vo is a volume multiple lesions were placed monitoring the patient response.

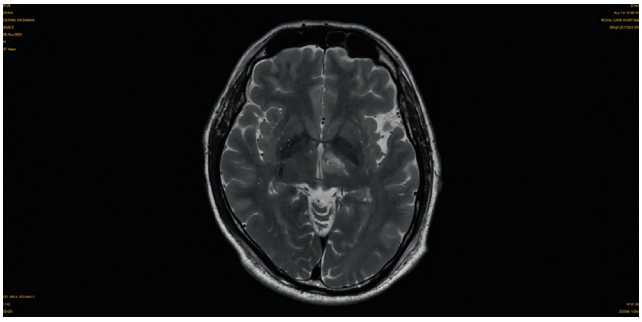

FIGURE 1 MEDIAL PTT TARGET

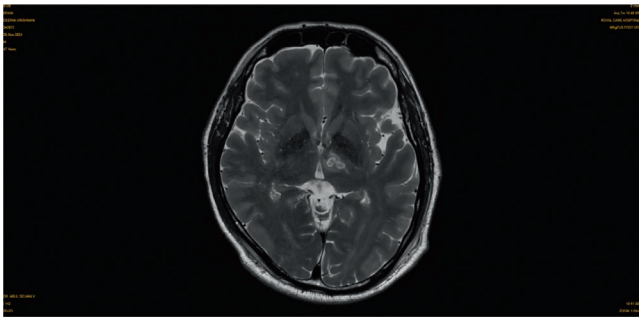

FIGURE 2 LATERAL PTT TARGET

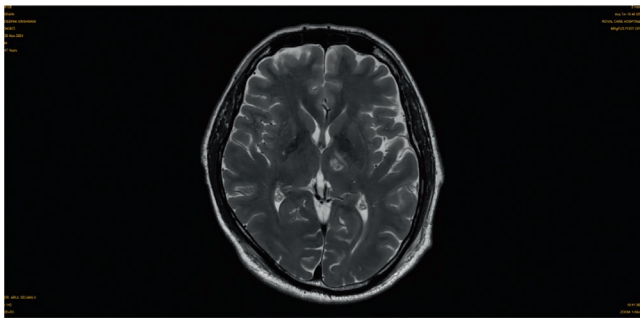

FIGURE 3 VIM-VO TARGET

Results: Total follow up has been for 2yrs. Results of 25 cases of dual lesioning are discussed. There was more than 70% reduction in the UPDRS motor scores. Some improvement in the non-motor symptoms were also noted.
Conclusion: MRgFUS lesioning is safe and effective treatment for PD. Effects are immediate and are also lasting. There is a significant reduction in DOPA dosage. Dyskinesias disappear after PTT lesioning and do not reappear on DOPA challenge. Dual lesioning and sequential bilateral lesioning is also safe and effective. The craving for DOPA is substantially reduced. The quality of life improves over time.
Disclosure: "Nothing to disclose."

EPO-277 | Movement disorders in GLUT1 deficiency syndrome: A systematic review of the literature

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Background and aims: Glut-1 deficiency syndrome (GLUT1-DS) is a rare brain energy failure syndrome caused by impaired glucose transport across brain tissue barriers. Movement disorders (MD) are a prominent feature of the disease. Here we describe in details the clinical presentation of movement disorders in GLUT1-DS by performing a systematic review of the published cases.
Methods: We conducted a comprehensive and systematic review of the literature. The Preferred Reporting Items for

Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed. The search comprised five electronic databases: Medline, Embase, Cinahl, Scopus, Web of Science. Any case reports or case series which report a detailed clinical description of MD in GLUT1-DS patients was included. Data collected from each study included patient demographic characteristics, GLUT1-DS diagnosis, MD and treatments.
Results: The initial search yielded 881 publications. After duplicates' removal, 606 titles were screened, and fifty-nine articles reporting 76 patients (males: 40/76; age at GLUT1-DS diagnosis 14.7 years [±12.70]) met the inclusion criteria. Ataxia was the most frequent MD (43/76) followed by paroxysmal dyskinesia (35/76), dystonia (20/76), tremor (11/76), chorea (7/76) and myoclonus (5/76). Pharmacological treatments determined heterogenous response, whereas ketogenic diet led mostly to complete remission or significant improvement (35/44), and partial or no clinical response in the minority of cases (5/44 and 4/44, respectively).
Conclusion: This review suggests that GLUT1-DS can be associated with a wide range of MD particularly ataxia, paroxysmal dyskinesia and dystonia. The effects of pharmacological treatments were limited while ketonic diet was helpful in the majority of cases.
Disclosure: Nothing to disclose.

MS and Related Disorders 2

EPO-278 | The role of retinal hyper-reflecting foci in axonal damage and retinal vascular density in multiple sclerosis

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Background and aims: Optical Coherence Tomography (OCT) is a key tool in Multiple Sclerosis (MS), detecting neuro-axonal atrophy, which correlates with brain atrophy. OCT Angiography (OCTA) allows assessment of retinal vascular density (VD), reduced in MS patients, especially in the foveal region and optic nerve head (ONH). Hyper-reflecting foci (HRF) are potential markers of activated microglia. This study investigates the relationship between HRF, axonal damage, and VD in relapsing-remitting MS (RRMS) patients.
Methods: We evaluated ganglion cell complex (GCC), retinal nerve fiber layer (RNFL) and VD in superficial and deep capillary plexuses, the ONH and radial peripapillary capillary plexus in RRMS patients. Patients with history of optic neuritis were excluded. HRF were defined as isolated, small-size (<30 mm) elements with moderate reflectivity without any back shadowing. Association between OCT-SD, OCT-A and HRF was assessed through Correlations between SDOCT and OCTA parameters, using linear mixed model using age and sex as covariates and subject as random factor.
Results: We enrolled 19 RRMS patients (mean age 38.9 ± 14.6 years; median disease duration 5 years; median EDSS 2.5). The median number of HRF per subject was 4 (range 1–7). We found a positive inter-eye correlation for HRF (coeff. 0.50, p=0.03). Number of HRF correlated with RNFL (correl. coeff.= -35.3, p=0.03) and with inside disc VD (correl. coeff. = -2.00, p=0.01).
Conclusion: HRF are primarily associated with axonal damage rather than vascular parameters, suggesting they reflect microglial activation driving chronic inflammation and neurodegeneration in MS. These findings position HRF as potential biomarkers for disease monitoring and therapeutic evaluation.
Disclosure: A.E. has received honoraria from Novartis. M.M. has received research grants from ECTRIMS-MAGNIMS, the UK MS Society, and Merck, and honoraria from Biogen, BMS Celgene, Ipsen, Janssen, Merck, Novartis, Roche, and Sanofi-Genzyme. M.P. has received research grants from the Italian MS Foundation and Baroni Foundation, honoraria from Health & Life and Biogen, and sponsorship for travel/meeting expenses from Novartis, Roche, and Merck. R.L. has received honoraria from Biogen, Merck, Novartis, Roche, and Teva. V.B.M. has received research grants from the Italian MS Society and Roche, and honoraria from Bayer, Biogen, Merck, Mylan, Novartis, Roche, Sanofi-Genzyme, and Teva. A.C. has received research grants from Almirall, research grants from ECTRIMS-MAGNIMS, and honoraria from Almirall, Biogen, Roche, Sanofi-Genzyme, Merck, Ipsen, and Novartis. None of the other authors has any conflict of interest to disclose.

EPO-279 | Quantitative clinical observation of neurodegeneration in the case secondary progressive multiple sclerosis (SPMS)

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Background and aims: Neurodegeneration in secondary progressive multiple sclerosis (SPMS) can be manifested by decreased MR density near ventricular horns, old lesions, "black holes" and "dirty" white matter (DWM) on magnetic resonance imaging (MRI). The process of density loss cannot be assessed using a segmentation approach. The evaluation of SPMS neurodegeneration by means of temporal differences of pre-registrated and normalized MR-images was observed.
Methods: MR-data collected for patient with SPMS (2021 – 2024), FSPGR images (256x256x272) at 2021 are recorded to be reference. All others are co-registrated and re-sliced with reference (SPM12) to be located in the similar spatial basis. Then brightness of MR-images is slice-by-slice normalized to the reference one (goal is minimization of brightness differences) to be in the same brightness basis. Consequently, temporal differences (calculated for each pair of years) are in the same spatial and brightness basis. This allows to sum brightness values in specified region of interest (ROI). These sums allow to quantitative compare images over time period. To assess the neurological symptoms, we used EDSS.

Results: This approach allows to analyze ventricle increase, DWM and lesion MR-density reduction (fig. 1). In the case under study, ventricles expand faster, the areas of DWM and especially periventricular lesion density reduces slower (fig. 2,3). The EDSS score increased from 5.5 in 2021-2022 to 6.5 in 2024 (fig. 3)

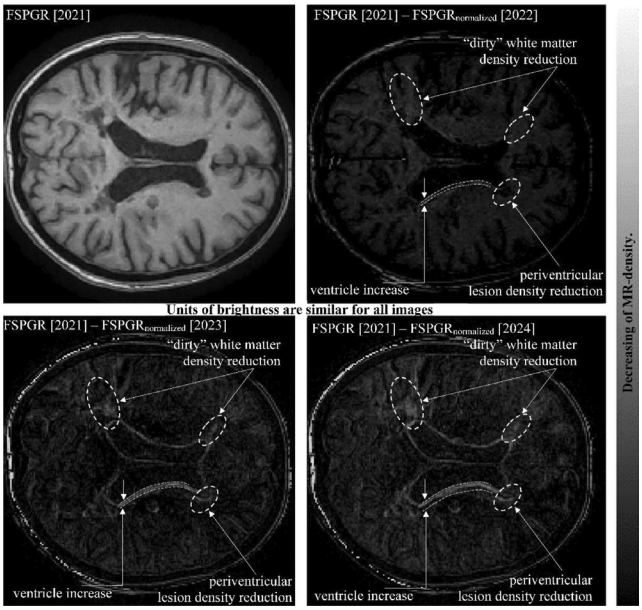

FIGURE 1 Decreasing of MR-density

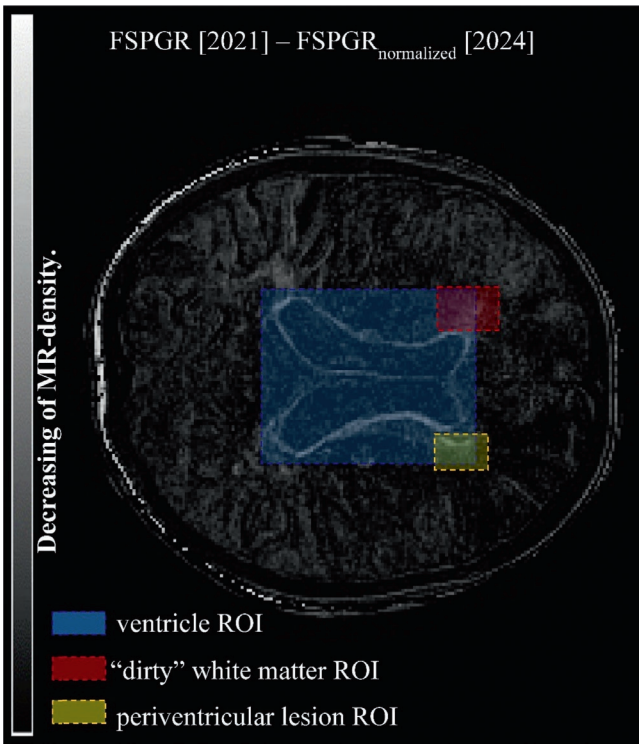

FIGURE 2 ROI with MR-density reduction

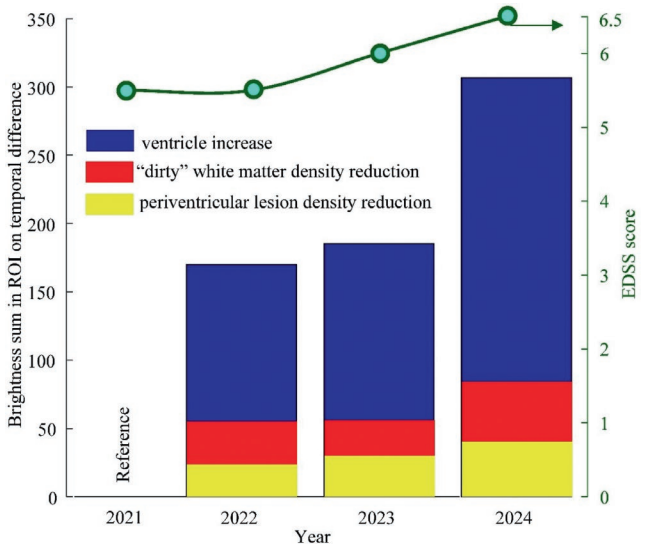

FIGURE 3 Changes in brightness sum in ROI and EDSS score

Conclusion: Calculation of temporal differences of pre-registrated and normalized MR-images allows to visualize and score neurodegeneration quantitatively. Rapid grows of sum brightness values correlates well with EDSS score.
Disclosure: Nothing to disclose.

EPO-280 | The central vein sign: A valuable tool for differential diagnosis of demyelinating diseases

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Background and aims: The central vein sign (CVS), indicative of a vein within a white matter lesion visible (WMLs) on MRI, is considered suggestive of multiple sclerosis and will be incorporated into the new diagnostic criteria.
Methods: To investigate the utility of the central vein sign in clinical practice for patients with WMLs on brain MRI for the differential diagnosis.
Results: The study included 44 patients: 5 with undetermined diagnosis, 4 with confirmed MOGAD, 4 with confirmed NMO and 25 with confirmed RRMS having a disease duration of at least one year. All MS patients showed 70-80% of WML CVS+ on cranial MRI and had at least 6 CVS+ lesions on T2*/FLAIR*. The 4 NMO patients showed no CVS+ lesions, and 3 out of 4 MOGAD patients had fewer than 6 CVS+ lesions on MRI. One MOGAD patient with 20 T2 lesions showed 9 CVS+ lesions but less than 40% of the total. Among the five individuals with unknown diagnoses, two had no CVS lesions: one was later diagnosed with migraine and small vessel disease, while the other tested positive for MOG antibodies. Two others displayed up to 20% CVS-positive lesions: one was recently diagnosed with double-negative NMOSD, and the other with MOGAD. One patient, presenting with headaches, had 45% CVS-positive lesions; however, two lumbar punctures performed were negative for IgG OCBs, and the MRI findings did not meet the MAGNIMS criteria.

Conclusion: The CVS is a useful marker for ruling out MS in patients with WML and uncertain diagnoses in clinical practice
Disclosure: C Oreja-Guevara received honoraria for speaking, consulting and serving on advisory boards from Alexion, Amgen, Biogen Idec, BMS, Horizon, Janssen, Merck, Novartis, Roche, Sanofi-Genzyme, Sandoz, Viatris, Neuraxpharm and Teva. The rest of authors have nothing to disclose.

EPO-281 | Supporting brain-healthy behaviours in MS through lifestyle education and intervention

C. Peel; J. Connor; S. Southward
Overcoming MS, Oxford, England

Background and aims: Evidence shows the importance of lifestyle for brain health, treatment and management, and preventing comorbidities in multiple sclerosis (MS) (Giovannoni 2024) yet awareness and application of lifestyle choices is not widespread (Wills 2024) and supportive education is essential (Bassetti 2022). Charity Overcoming MS developed education to inform and equip people living with MS to make sustainable lifestyle choices to improve their brain health and experience of MS.
Methods: Two education progammes 'Pathways' and 'Retreats' both inform and support an approach to positive living with MS encompassing nutrition, medication, physical activity, stress management and behaviour change. The education includes online group consultation, expert teaching from people with lived experience of MS, group discussion and peer support through online community. (Retreats also include a 3 day residential). Data are gathered pre- and post-course.
Results: From 2022-2024,198 people living with MS attended Retreats (n=78, 2 cohorts) or Pathways (n=120, 4 cohorts). Data across all six cohorts found marked improvements in perceived physical and mental wellbeing; subjective reporting rose by an average of 36% and 37% respectively. Confidence in understanding of, and adherence to the lifestyle medicine Program rose by an average of 44% and confidence in talking to friends and family about lifestyle choices by 31%.
Conclusion: Data from this education suggests people with MS engaging in tailored lifestyle education have improved understanding of, and likelihood of engaging with, healthy behaviours and that this improved self-efficacy has a positive impact on their perceived health quality.
Disclosure: Nothing to disclose.

EPO-282 | Cognitive impairment in multiple sclerosis: An IMSCOGS overview of systematic reviews protocol

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[1]IRCCS, Istituto delle Scienze Neurologiche di Bologna, Epidemiology and Statistics Unit, Cochrane Review Group Multiple Sclerosis and Rare Diseases of the CNS, Bologna, Italy; [2]Azienda USL – IRCCS di Reggio Emilia; [3]Royal Holloway, University of London, Egham, UK; [4]Department of Clinical Neurosciences, Hotchkiss Brain Institute, University of Calgary; Calgary, AB, Canada; [5]Neurological Institute, Cleveland Clinic; Cleveland, Ohio, USA; [6]MS Center Amsterdam, Department of Anatomy and Neurosciences, Vrije Universiteit Amsterdam, Amsterdam Neuroscience, Amsterdam UMC, Amsterdam, The Netherlands; [7]Institute of Systems, Molecular and Integrative Biology, University of Liverpool, Liverpool, UK; Walton Centre NHS Foundation Trust, Liverpool, UK

Background and aims: Cognitive impairment (CI) is a prevalent and disabling symptom in people with multiple sclerosis (PwMS), affecting various cognitive domains and contributing to poorer quality of life. However, the definitions of CI and the screening tools used in research and clinical settings vary widely. This overview of systematic reviews (SRs) aims to provide an outline of the current definitions of CI and the cognitive tests used to screen for CI in studies targeting PwMS. This overview of SRs is part of an International Multiple Sclerosis Cognition Society (IMSCOGS)-European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) collaborative project, aimed at reaching a formal consensus on how to define and assess CI in PwMS.
Methods: Relevant literature will be identified through a comprehensive search of peer-reviewed SRs of diagnosis, intervention or prognosis from the following electronic databases: MEDLINE, Embase, PsychInfo, CINAHL. SRs including PwMS aged >=18, published since January 1, 2001, in English language will be considered. The overview of SRs will be conducted according to the JBI Reviewers' Manual and reported following the PRIOR statement. SRs must provide a clear definition of acquired CI, disorder or dysfunction and may include individual tests or batteries to formally assess CI.
Results: This overview of SRs will summarize the definitions and the screening tools employed to assess CI in PwMS.
Conclusion: These findings may guide future researchers on improving practice.
Disclosure: This project is supported by ECTRIMS. EB, CDS, FN, MS are members of the Cochrane review group MS and rare diseases of the CNS, MMS is president of IMSCOGS, LH is co-chair of steering committee for IMSCOGS, DL has received consultancy, sponsorship, lecture fees or research grants from Bayer, Merck, Novartis and BMS, SAM has served on advisory boards for Amgen, Biogen Idec, BMS/Celgene, EMD Serono, Novartis, Roche, Sanofi Genzyme, and has received research funds or investigator grant from Biogen Idec, MS Canada, National MS Society, and CIHR, CAY has received consultancy, sponsorship, lecture fees or research grants from Biogen, Merck, Roche, Vectura and BMS.

EPO-283 | The blood-brain barrier in MS: correlation between clinical, CSF, MRI signature and albumin quotient in naïve patients

F. De Napoli[1]; V. Mauceri[1]; A. Miscioscia[1]; A. Bertoldo[2]; E. Silvestri[2]; A. Marin[3]; P. Perini[1]; F. Rinaldi[1]; P. Gallo[1]; M. Puthenparampil[1]

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Background and aims: The alteration of the blood-brain barrier (BBBD) plays a key role in the pathogenesis of Multiple Sclerosis (MS) and has been observed even before demyelinating lesions develop. The permeability of the BBB, measured as QAlb (AlbL/AlbS), correlates with central inflammatory load. This study aims to evaluate whether BBBD correlates with clinical, cerebrospinal fluid (CSF) and neuroradiological characteristics in relapsing-remitting MS patients naïve to disease-modifying therapies.

Methods: A retrospective sample of 166 RRMS patients and 30 controls was analyzed. All subjects underwent blood sampling, lumbar puncture, and 3T brain and spinal MRI. Patients were divided into two groups: BBBD– and BBBD+, with BBBD defined by QAlb>QAlbLim. CSF was examined for NfL and YKL-40. The analysis included the EDSS score at baseline and during follow-up (maximum of 8 years), brain volumes, and cerebral lesion volume. Spinal involvement was qualitatively characterized.

Results: Patients had higher QAlb values, and BBBD was detected in 38 patients (22.89%) and none of the controls. The BBBD+ group had a higher proportion of men. The EDSS score was higher in pBBBD+ at baseline and during follow-up. No significant differences in clinical progression or occurrence of PIRA were found. CSF concentrations of NfL and YKL-40 correlated positively with QAlb ($r=0.302$, $r=0.237$, $p<0.005$). pBBBD+ had a higher lesion load and white matter volume, no other significant differences were found in brain volumetrics or contrast enhancement.

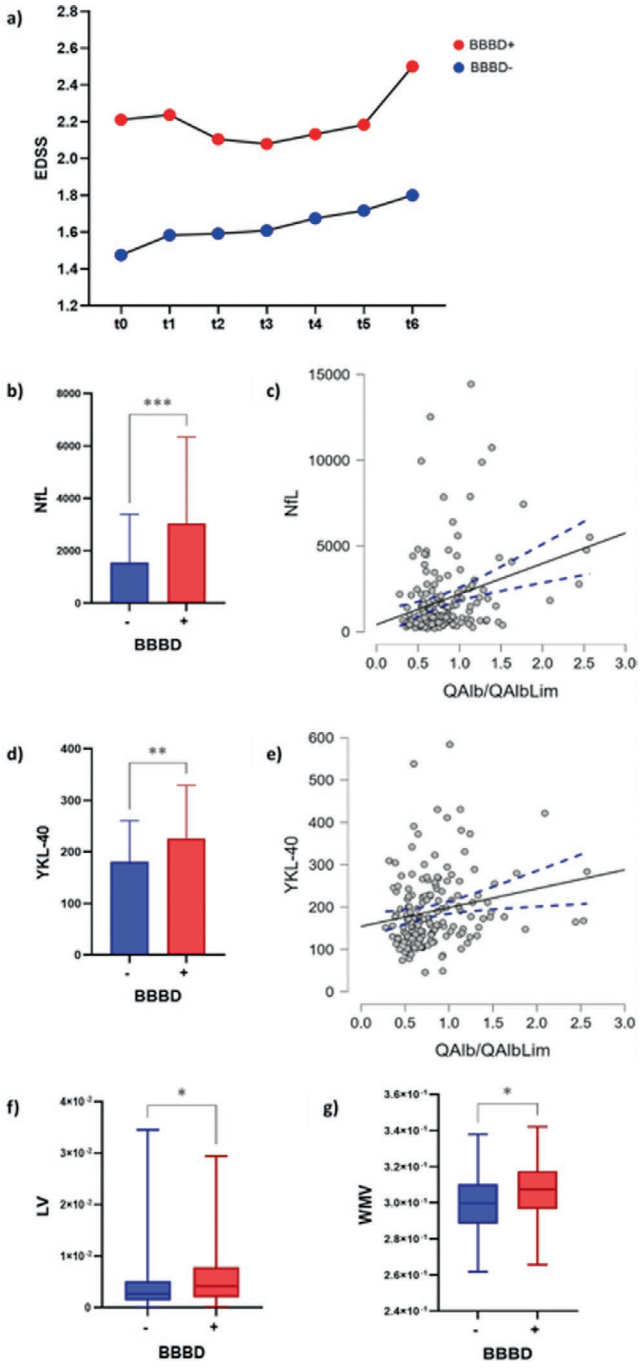

FIGURE 1 EDSS was higher in pBBBD+ (a). CSF concentrations of NfL (b) and YKL-40 (d), brain lesion volume (f), and white matter volume (g) were higher in pBBBD+. QAlb positively correlated with CSF concentrations of NfL (c) and YKL-40 (e).

Conclusion: BBBD correlates with a higher neuroinflammatory burden, defined by brain lesion volume and CSF biomarkers, and is associated with worse clinical impairment.

Disclosure: Nothing to disclose.

EPO-284 | The volume of choroid plexus in MS: correlation with QAlb and clinical, CSF, MRI signature in naïve patients

F. De Napoli[1]; V. Mauceri[1]; A. Miscioscia[1]; E. Barbuti[2]; A. Bertoldo[3]; E. Silvestri[3]; A. Marin[4]; P. Perini[1]; F. Rinaldi[1]; P. Gallo[1]; M. Puthenparampil[1]
[1]Department of Neurosciences, University of Padova, Padua, Italy; [2]Ospedale Sant'Andrea, University La Sapienza, Rome, Italy; [3]Bioingeneer, Department of Information Engineering, University of Padova, Padua, Italy; [4]Department of Biomedical Sciences, University of Padova, Padua, Italy

Background and aims: An emerging factor in MS is the alteration of the blood-cerebrospinal fluid barrier (BCSB), which seems to play a significant role in the early stages of MS. The choroid plexuses (ChP) volume is considered a marker of BCSB activation and correlates with disease severity. This study aims to evaluate whether the volume of the ChP correlates with clinical, cerebrospinal fluid (CSF) and neuroradiological characteristics in relapsing-remitting MS patients naïve to disease-modifying therapies.
Methods: A retrospective sample of 10 controls and 50 MSRR patients was analyzed. All subjects underwent blood sampling, lumbar puncture, and 3T brain MRI. CSF was examined for QAlb (AlbL/AlbS), oligoclonal bands, NfL, and YKL-40. The analysis included the EDSS score at baseline, brain volumes, and cerebral lesion volume. The volume of the ChP was obtained from manual segmentation at the level of the lateral ventricles in 3D-T1 sequences. All brain volumes were normalized for total intracranial volume.

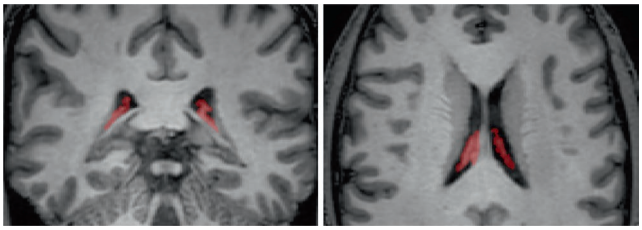

FIGURE 1 Images of the segmentation process of the choroid plexuses in an RRMS patient, coronal (a) and axial (b) sections.

Results: The ChP volume was higher in patients compared to controls (p=0.035) and in MS patients it correlated positively with QAlb (r=0.338, p=0.016) and negatively with total brain volume, grey matter volume, and white matter volume (r=-0.379, r=-0.283, r=-0.353, p<0.05). No correlation was detected with the other variables under analysis.

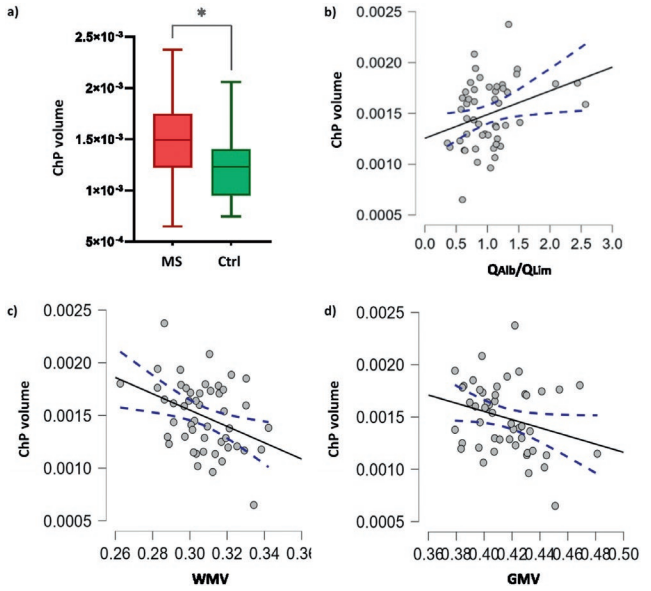

FIGURE 2 The volume of the ChP was higher in MS patients compared to controls (a) and positively correlated with the QAlb (b). The volume of ChP negatively correlated with the white matter volume (WMV, c) and with the gray matter volume (GMV, d).

Conclusion: The volume of the choroid plexuses correlates with disease progression defined by the degree of brain atrophy.
Disclosure: Nothing to disclose.

EPO-285 | EEG microstate dynamics as biomarkers for neural network dysfunction in multiple sclerosis

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Background and aims: Multiple Sclerosis (MS) progression involves brain network dysfunctions, but assessment tools are limited. EEG microstates, representing transient stable brain activity, provide a non-invasive approach to investigate brain network dynamics. This study evaluated microstate metrics to differentiate healthy volunteers (HV) from MS patients and explore their associations with cognitive impairment (CI).
Methods: We compared 45 HVs to 46 MS patients and 57 CI to 31 non-CI MS patients.
Results: TANOVA revealed no significant topographical differences between HV and MS. MS patients had significantly higher Class B explained variance (ExpVar), occurrence, and coverage but shorter durations for Classes C, F, and G. ExpVar of class B and D, Total ExpVar, and class F occurrence were the most relevant features for distinguishing groups, achieving 76.9% classification accuracy (sensitivity 73.9%, specificity 80%). We found significant topographical differences in Classes C, F, and G between CI and non-CI patients. CI patients demonstrated significantly lower Class F ExpVar, duration, occurrence, and coverage. Class F ExpVar emerged as the sole predictor of cognitive impairment, with 64.8% classification accuracy (sensitivity 68.4%, specificity 58.1%). EDSS significantly positively

correlated with Class B ExpVar, Occurrence, and Coverage, controlling for age and education.

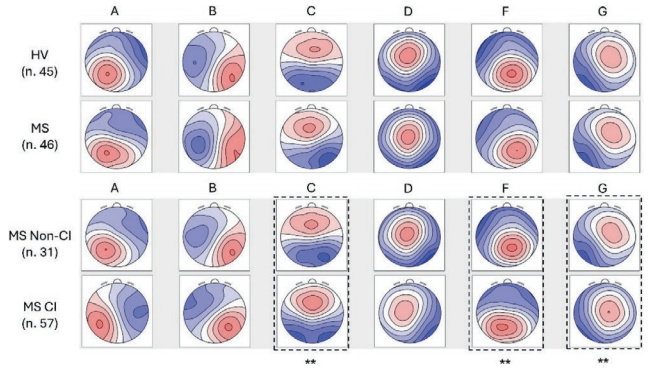

FIGURE 1 Topographical maps of microstate classes (A–G) for healthy volunteers (HV), multiple sclerosis (MS) patients, and MS subgroups with (CI) and without (non-CI) cognitive impairment. **: significant topographical differences, as tested by TANOVA ($p < 0.01$).

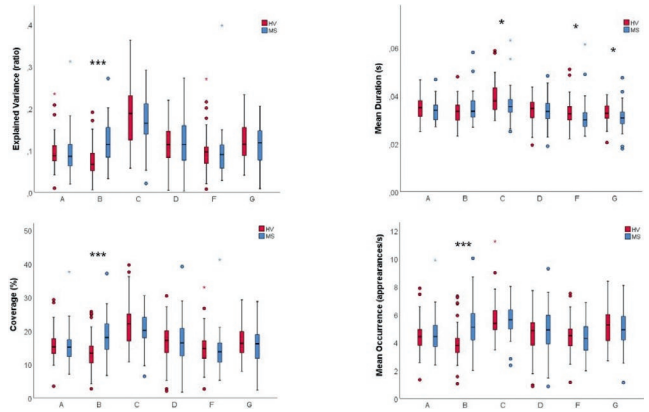

FIGURE 2 Boxplots comparing microstate metrics across classes between HV (red) and MS patients (blu). Significant differences are indicated: ***$p < 0.001$, **$p < 0.01$, *$p < 0.05$.

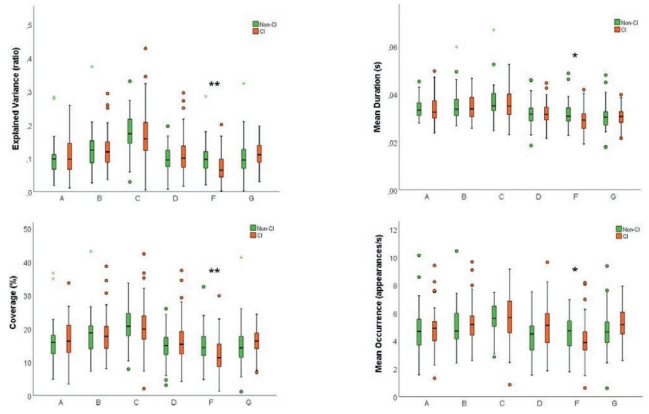

FIGURE 3 Boxplots comparing microstate metrics across classes between Non-CI (green) and CI (orange) MS patients. Significant differences are indicated: **$p < 0.01$, *$p < 0.05$.

Conclusion: Microstates reveal increased visual network (B) activity linked to disability and strong MS-HC discrimination, with reduced stability in salience/DMN (C/F) and sensorimotor (G) networks. Salience network (F) hypo-representation strongly associates with cognitive impairment. Microstates hold promise as biomarkers for MS progression and cognitive dysfunction, warranting longitudinal validation.

Disclosure: None

EPO-286 | First insights on the ocrelizumab route administration switch from IV to SC in MS: data from CONFIDENCE and trotzMS

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[1]Caritas-Krankenhaus, Bad Mergentheim, Germany; [2]Department of Neurology, University Clinic Düsseldorf, Heinrich-Heine-University Düsseldorf, Düsseldorf, Germany; [3]Health Centre, St Johannes Hospital, Bonn, Germany; [4]Institute of Neuropathology, Department of Neurology, University Medicine Göttingen, Göttingen, Germany; Fraunhofer-Institute for Translational Medicine and Pharmacology ITMP, Göttingen, Germany; [5]Roche Pharma AG, Grenzach-Wyhlen, Germany; [6]F. Hoffmann-La Roche AG, Basel, Switzerland; [7]Center of Clinical Neuroscience, Neurological Clinic, Carl Gustav Carus University Clinic, University of Technology, Dresden, Germany

Background and aims: The phase III OCARINA II study demonstrated that subcutaneous (SC) ocrelizumab (OCR) had a non-inferior pharmacokinetic area under the curve (weeks 1–12) compared to intravenous (IV) OCR in people with relapsing (pwRMS) and primary progressive multiple sclerosis (pwPPMS). The SC formulation may offer a more convenient route of administration. We present preliminary real-world experience with this switch.

Methods: We included pwMS from the German non-interventional post-authorization study CONFIDENCE (ML39632, EUPAS22951) who switched from OCR IV to SC. The incidence of adverse events (AEs), serious AEs (SAEs) and reasons for switching were collected. Additionally, we included pwMS from the trotzMS patient-support program who switched from OCR IV to SC or newly started OCR SC and analyzed satisfaction and convenience using the Treatment Administration Satisfaction Questionnaire (TASQ).

Results: In CONFIDENCE, 31 pwMS switched from OCR IV to SC (RMS: n=24; PPMS: n=7) between 22/07 and 11/10/2024. One person experienced an AE (1/31; 3.2%), classified as urinary tract infection, which occurred in the PPMS group and was considered unrelated to OCR. No SAEs were reported. Reasons for switching included patient wish (16/31, 51.6%), physician wish (capacity reasons: 9/31, 29.0%; patient compliance: 1/31, 3.2%) and were missing for 5/31 pwMS (16.1%). Baseline characteristics and TASQ results of pwMS who switched from OCR IV to SC or newly starting OCR SC will be presented.

Conclusion: The preliminary real-world experience of initiating/switching to OCR SC highlights the importance of treatment convenience for pwMS and showed no new safety signals after switching from OCR IV.

Disclosure: MB: Honoraria/travel: Biogen, BMS, Das Fortbildungskolleg, Florian Schmitz Kommunikation, Janssen, Merck, Novartis, RG Ärztefortbildung, Roche, Sandoz, Sanofi, Teva, Viatris SGM: Honoraria/travel: Academy2, Argenx, AstraZeneca, Bayer, BioNtech, Celgene, Datamed, Desitin,

Diaplan, DIU, DPmed, Gen Medicine&Healthcare, IGES, Impulze GmbH, KWMedipoint, MedDay, Medmile, MICE, Mylan, Neuraxpharm, Neuropoint, OxfordPharmaGenesis, QuintilesIMS, Sanofi, Springer, STADA, Chugai, UCB, Viatris, Wings for Life int, Xcenda;research:BMBF, BfR, DFG, EKFS, G-BA, Hertie Fdn, IZKF, DGN, Ministry of Culture&Science NRW, Daimler&Benz Fdn, dmsg, Peek&Cloppenburg Fdn, Hempel Fdn, German Alzheimer Society, Bayer, DGM, FME, GFFU, HERZ Burgdorf; honoraria/travel/research: Alexion, Almirall, Amicus, Argenx, BGP, Biogen, BMS, Demecan, Diamed, Genzyme, Hexal, Janssen, MerckSerono, Novartis, NovoNordisk, ONOPharma, Roche, Teva SS: Advisory Boards/honoraria/travel: F Hoffmann-La Roche, Novartis, MerckSerono, Bayer, Biogen, Genzyme, Teva MSW: Research: DFG (WE3547/5-1, WE3547/7-1, SFBTRR274), Novartis, TEVA, Biogen, Roche, Merck, Uniklinik Göttingen(ProFutura);honoraria/travel:Biogen, MerckSerono, Novartis, Roche, TEVA, Bayer, Genzyme; editor: PLoSOne Employees: SW, CA, JL, SHS, Roche Pharma AG; GF, F Hoffmann-La Roche AG JL: F Hoffmann-La Roche AG shareholder TZ: Personal: Biogen, Roche, Merck, TEVA, NovoNordisk, Neuraxpharm, BMS, Novartis, Sanofi, Sandoz, Viatris; research: Genzyme, Novartis, Roche, Sanofi, Teva, Neuraxpharm.

EPO-287 | Self-report of bladder issues in the UK MS Register

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Background and aims: The United Kingdom Multiple Sclerosis Register (UKMSR) has collected regular Patient Reported Outcomes and Clinical data from people with MS (pwMS) and clinicians since 2011. Following participant co-creation we included more specific instrumentation related to bladder. We deployed a modified version of the PROMIS Bladder Short Form (mPBSF) and carried out linkage with existing demographics, epidemiology and most recent normalised Multiple Sclerosis Impact Scale motor component (MSIS29-motor). Aim Assess the response and impact of bladder issues on the UKMSR population.
Methods: We emailed the active population of the UKMSR about the availability of the mPBSF. Standard 2 question instrument with 7 potential responses, expanded to include data about catheterisation, cystitis/Urinary Tract Infection (UTI), and treatments. Availability was 14/12/2024-14/01/2025. We carried out logistic regression modelling on the cohort.
Results: 3,011 pwMS completed the instrument (52% RMS, 43% PMS, 5% Other MS). 801 had a UTI in the last 12 months (36%) With 57% having had a UTI treated with antibiotics. PMS patients were more likely to have a permanent indwelling catheter (9.3%) and higher disability (MSIS-motor 60(±21)). Controlling for age MS type was significant ($p<0.0001$) in likelihood of having UTI/cystitis. There were significant differences ($p<0.001$) between PMS and RMS populations who had Severe or Moderate need to pass urine, and felt they had not completely emptied their bladders in the last 7 days.
Conclusion: In this community based cohort bladder problems and cystitis/UTI are major issues for MS. Given the impact that UTIs can have on outcome, more proactive management should be considered.
Disclosure: Nothing to disclose.

EPO-288 | Optimizing rapid inflammation control and risk management in highly active multiple sclerosis: The role of natalizumab

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[1]Department of Neuroscience, Rehabilitation, Ophthalmology, Genetics, Maternal and Child Health (DiNOGMI), University of Genoa, Genoa, Italy; [2]IRCCS Ospedale Policlinico San Martino, Genoa, Italy

Background and aims: The rapid initiation of disease-modifying therapies (DMTs) in patients with Highly Active Multiple Sclerosis (HAMS) facilitates prompt suppression of inflammatory activity. However, this approach requires a careful balance between efficacy and safety, particularly when starting continuous high-efficacy DMTs. The objectives of our study were to evaluate whether the early initiation of natalizumab (NTZ) in treatment-naïve HAMS patients allows for a rapid suppression of inflammatory activity while allowing for vaccination for long term risk minimization. We assessed the risks of disease reactivation and the occurrence of progressive multifocal leukoencephalopathy (PML) after transitioning from NTZ to other treatments.
Methods: Baseline clinical, demographic, and MRI data were collected. Disease activity and safety outcomes were monitored throughout the follow-up period.
Results: A total of 102 treatment-naïve HAMS patients were included, 43 of whom were anti-JCV positive at treatment initiation. All patients underwent a tailored immunization program (including live attenuated vaccines) during NTZ therapy without adverse events. During NTZ treatment, only 10 patients (9.8%) experienced subtle disease activity. 48 patients were switched to other therapies during the follow-up with an average wash-out period of 61 days. Of these patients, in only 2 cases was observed MRI activity near the time of the switch. No infection-related adverse events, including PML, were reported.
Conclusion: The rapid initiation of NTZ in treatment-naïve HAMS patients achieves robust and timely suppression of inflammatory activity, while also enabling safe vaccination protocols. This strategy offers a valuable therapeutic window for managing highly active disease, minimizing the risks of delayed treatment and infection-related complications.
Disclosure: GB received personal compensations from Novartis, Sanofi Genzyme, Roche, BMS and Merck, unrelated to the present work. CL received travel grants from Roche, Merck, Sanofi and honoraria for speaking from Novartis, Roche, Merck, Horizon and BMS. MC received personal compensations from Novartis, Sanofi Genzyme, Teva and consulting fees from Zambon. MI received grants NIH, NMSS, FISM; received fees for consultation from BMS; Janssen, Roche, Genzyme, Merck, Biogen and Novartis. None of these personal compensations were related to this work. AL received fees for consultation

from Roche, Genzyme, Merck, Biogen, Novartis, Bristol-Myers Squibb TS, NC, SA, AU, VDB and EC have nothing to disclose.

EPO-289 | Fist-Palm Test (FiPaT): a novel bedside test to screen for cognitive impairment in Multiple Sclerosis

U. De Marca[1]; S. Cuoco[1]; S. Scannapieco[2]; F. Di Filippo[1]; M. Consalvo[1]; C. Giordano[1]; M. Rotolo[1]; A. Rienzo[1]; A. D'Amico[1]; M. Pellecchia[1]; M. Amboni[1]; R. Capuano[2]; M. Di Gregorio[2]; P. Barone[1]

[1]Department of Medicine, Surgery and Dentistry "Scuola Medica Salernitana", University of Salerno; [2]Neurology Clinic, Medical Sciences Department, AOU San Giovanni di Dio e Ruggi d'Aragona, Salerno

Background and aims: Fist-Palm Test(FiPaT) is a novel non-verbalmotor task, able to screen for global cognitive status and to predict cognitive impairment. The aim of our study was to evaluate if FiPat could screen for cognitive status in patients with Multiple Sclerosis(pwMS).

Methods: One-hundred-eleven pwMS with mild disability(EDSS<2) and 28 age, sex and education matched Healthy-Subjects(HS) underwent: Neurological assessment with EDSS and nine-hole-peg test(9HPT), FiPaT (defined altered if final score was>=1); Brief Repeatable Battery of Neuropsychological tests

Results: PwMS were more cognitive impaired than HS (28.8% pwMS vs 0% HS, p=0.001). FiPaT scores were higher in pwMS than HS (mean 0.69 vs 0.21, p=0.03); FiPaT was impaired in 30.6% pwMS and in 14.3% HS (p=0.08). PwMS with altered FiPaT were older (46 vs 39.4 years old, p=0.01) and showed higher times at dominant hand 9HPT(9HPT-DH) (23.2 vs 21.1, p=0.005) than pwMS with normal FiPaT, whereas the two PwMS groups displayed no differences in gender, EDSS, disease duration, treatment type, non-dominant hand 9HPT(9HPT-NDH). Symbol digit modality Test(SDMT) (mean 0.24 vs -0.46, p<0.001); Selective–Reminding-Test(SRT) Consistent Long-Term-Retrieval(SRT-CLTR) (-.51 vs -1.31, p=0.002), SRT-Long-Term-Storage (SRT-LTS)(-.64 vs -1.17, p=0.03), SRT delayed(SRT-D)(-.52 vs -1.11, p=0.02) 10/36 Spatial Recall Test (SPART) (-.25 vs -.88, p=0.002) were significantly lower in pwMS with altered FiPaT. In pwMS, FiPaT was a predictor of SRT-CLTR (FiPaT p=0.008; beta-.27) and SPART (FiPaT p=0.002; beta-.3), whereas FiPaT and 9HPT-DH were predictors of SDMT (FiPaT p=0.002; beta -.3; 9HPT-DH p0.004, beta -.24) independently from age, education, disease duration, EDSS, 9HPT-NDH. ROC analysis, to evaluate the accuracy of FiPaT in identifying cognitive impairment in MS, showed an Area Under the Curve of 0.59 (95% conf. int. 0.49-0.69) whit a sensitivity of 43.7% and specificity of 74.4%.

Conclusion: FiPaT could be a quick tool to screen cognitive status in pwMS.

Disclosure: Nothing to disclose.

EPO-290 | Baseline EDSS and age predict progression risk independently of relapse/MRI activity in natalizumab-treated MS patients

V. Mauceri[1]; M. Puthenparampil[1]; M. Passamonti[1]; M. Rozzi[1]; E. Basii[1]; F. Rinaldi[2]; M. Nosadini[3]; S. Sartori[3]; P. Gallo[1]; P. Perini[2]

[1]Department of Neurosciences, University of Padua, Padua, Italy; [2]Multiple Sclerosis Centre, Azienda Ospedaliera di Padova, Padua, Italy; [3]Paediatric Neurology and Neurophysiology Unit, Department of Women's and Children's Health, University Hospital of Padova, Italy

Background and aims: Together with clinical relapse, Progression independent of relapse and MRI activity (PIRMA) is the main driver of disability accumulation in patients with MS (pwMS) and NTZ pwMS. The effect of Natalizumab (NTZ) on the risk of PIRMA is still unclear.

Methods: In this retrospective, longitudinal observational study, we included 288 NTZ-treated pwMS. During NTZ therapy, all patients performed MRI and clinical evaluation (with EDSS) every 6 months. We defined the Progression independent of relapse and MRI activity (PIRMA) as patients with PIRA conditions and in absence of any evidence of M RI activity. Finally, sustained PIRMA required the persistence of the increased disability for 12 months.

Results: At the end of their follow-up, 79 patients developed PIRA. Cox regression analysis demonstrated that both EDSS and age at baseline strongly predicted PIRMA event (H.R.: 1.770, p<0.001, and H.R.: 1.028, p=0.014 respectively). ROC analysis identified a cut off in the EDSS score of 4.0 (AUC 0.7332, p<0.0001) and survival analysis confirmed an increased risk of PIRMA in patients with high baseline EDSS value than in patients with low (log rank p<0.0001). ROC curve (AUC 0.6609, p<0.0001) identified a cut-off of 42.5 yo to predict PIRMA and survival analysis revealed a higher risk of PIRMA in elder patients compared to younger (H.R. 2.910, 95% IC 1.688 – 5.020, p<0.0001).

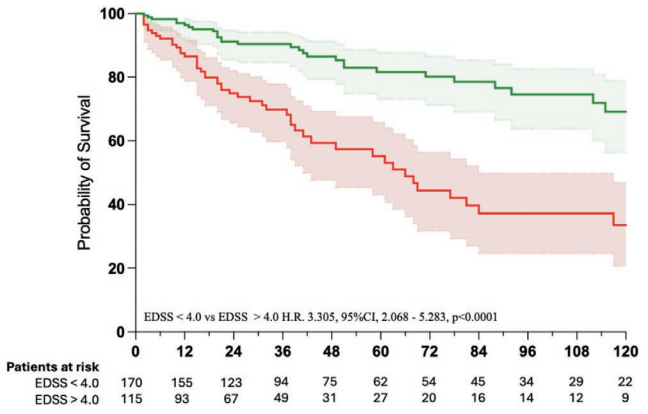

FIGURE 1 The effect of EDSS on the risk of PIRMA

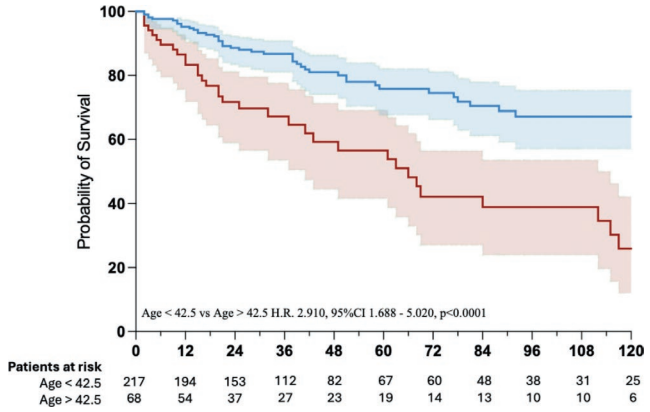

FIGURE 2 The effect of age on the risk of PIRMA

Conclusion: The risk of sustained PIRMA in NTZ-treated pwMS associated with baseline EDSS and age, supporting the early use of NTZ.

Disclosure: M.Pu., report grants from Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis; consultancy for Novartis, Biogen Italy, Sanofi Genzyme; board membership Sanofi Genzyme, Novartis, Biogen Italy. VAM, MP, MR, EB, MN and SS have nothing to disclose. RF report grants from Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis; consultancy for Novartis, Biogen Italy, Sanofi Genzyme. P.G. reports grant from Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis, Roche, Bristol Myers Squibb; consultancy for Novartis, Biogen Italy, Sanofi Genzyme, Roche, Bristol Myers Squibb; board membership Sanofi Genzyme, Novartis, Biogen Italy, Roche, Merck Serono, Bristol Myers Squibb. P.P. reports grants from Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis, Roche; consultancy for Novartis, Biogen Italy, Sanofi Genzyme, Roche.

EPO-291 | The clinical relevance of Hyper-Reflective foci in the inner retina at the time of the diagnosis of Multiple Sclerosis

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Background and aims: HyperReflective foci (HRF) increased in the inner retina (IR) of in patients with Multiple Sclerosis (pwMS). Their clinical prognostic relevance (marker of acute rather than chronic inflammation) is still unclear. The main objective consisted into the evaluation of the risk of disease activity based on HRS count at baseline.

Methods: Fifty-seven pwMS were included in this retrospective, cohort single-centre study. All patients were enrolled at clinical onset and were disease free. No evidence of optic nerve inflammation was acquired by means of clinical, radiological and OCT parameters. Patient were divided at baseline based on the MS treatment indicated by their neurologist as plat-therapy pwMS (PTpwMS) and as High efficacy therapy pwMS (HETpwMS). Then, all patients that started a plat-therapy (PT)were followed up for at least 24 months: the main outcome was the time to switch for lack of efficacy on inflammatory (clinical relapse and MRI new/enlarging/gadolinium-enhancing lesion) outcomes. HRF count was expressed as the sum of both eyes in GCIPL, INL and IR (GCIPL+INL).

Results: At baseline HETPwMS had increased HRS count in all IR layer (HRF-GCIPL: 19.0±5.3 vs 25.8±4.4; HRF-INL 37.1±9.4 vs 50.2±9.9, HRF-IR: 56.1±12.3 vs 76.0±12.2 all p<0.001) compared to PTpwMS. ROC analysis identified a best cut-off in the IR-HRS (75 foci), whose application off on PT pwMS identified an earlier switch (HR 6.5, 95% IC 1.5-28.8, p=0.007).

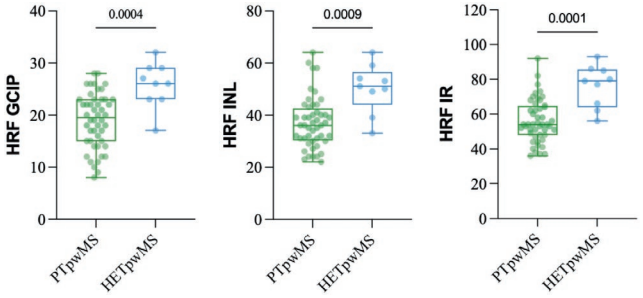

FIGURE 1 HRF count in GCIPL, INL and IR.

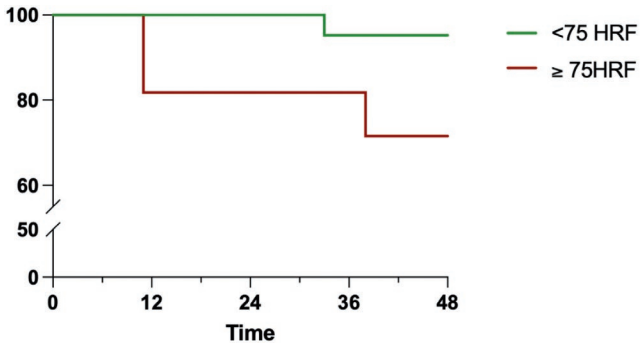

FIGURE 2 Survival analysis on PTpwMS.

Conclusion: HRS might be a useful marker to predict the risk of acute demyelination in MS and might give clues to Neurologist for choosing HET earlier

Disclosure: M.Pu., report travel grants, consultancy, and board membership from Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis, Bristol Myers Squibb, Janssen, and Alexion. M.Pe, E.B., E.P., and E.M. have nothing to disclose. V.A.M reports travel grants from Sanofi Genzyme, Biogen, and Viatris. P.P. reports grants from Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis, Roche, Alexion, Janssen, Brystol Mayer Squibb; consultancy for Novartis, Biogen Italy, Sanofi Genzyme, Roche, Janssen, Brystol Mayer Squibb. RF report grants from Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis, consultancy for Novartis, Biogen Italy, Sanofi Genzyme. P.G. reports grant, consultancy, and board membership for Almirall, Teva, Sanofi Genzyme, Merck Serono, Biogen Italy, Novartis, Roche, Bristol Myers Squibb, Janssen, and Alexion.

EPO-292 | Pain in idiopathic longitudinally extensive transverse myelitis compared to neuromyelitis optica spectrum disorder

Y. Jin[1]; D. Seo[2]; H. Yoon[1]; I. Jang[2]; L. Choi[2]; J. Kim[2]; W. Shin[2]; H. Lee[2]; S. Kim[2]; H. Jung[2]; J. Kim[2]; H. Kim[2]; Y. Lim[2]; E. Lee[2]
[1]University of Ulsan College of Medicine, Seoul, Republic of Korea; [2]Department of Neurology, Asan Medical Center, University of Ulsan, Seoul, Republic of Korea

Background and aims: Chronic pain is a common consequence of longitudinally extensive transverse myelitis (LETM), potentially exacerbated by inflammation. While pain in seropositive neuromyelitis optica spectrum disorder-associated TM (NMOSD-TM) has been frequently studied, less attention has been given to idiopathic LETM (I-LETM), which lacks autoantibodies. We aimed to compare the prevalence and characteristics of chronic pain in I-LETM and NMOSD-TM.
Methods: We prospectively enrolled patients with I-LETM or seropositive NMOSD-TM (anti-aquaporin-4 antibodies) who were in the chronic phase, at least 3 months after their last clinical attack. LETM was defined as transverse myelitis (TM) affecting ≥3 spinal segments, with I-LETM characterized by the absence of aquaporin-4 and myelin oligodendrocyte glycoprotein antibodies. Pain was evaluated using the Pain DETECT Questionnaire (PDQ) and Short Form-Brief Pain Inventory (SF-BPI), while quality of life was assessed using EuroQoL-5D (EQ-5D) at baseline and follow-up (6–12 months).
Results: Among 54 patients (I-LETM: 9, NMOSD-TM: 45; median age: 57 years), I-LETM patients had fewer affected spinal segments (median, 4 vs. 10, p <0.001) and less cervical cord involvement (44% vs. 87%, p=0.012). Chronic pain was reported in all I-LETM patients and 87% of NMOSD-TM patients. Pain severity and neuropathic pain prevalence were comparable, though numbness was more severe in I-LETM (median score: 4 vs. 0, p=0.027). Pain severity negatively correlated with quality of life and remained stable at follow-up.
Conclusion: Chronic pain is highly prevalent and severe in both groups, suggesting that the presence of autoantibodies does not significantly influence LETM pain characteristics. Pain management should be prioritized for all LETM patients.
Disclosure: Nothing to disclose.

Muscle and Neuromuscular Junction Disorder 2

EPO-293 | Understanding muscle biopsy pain: What to expect during and after

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Background and aims: Open muscle biopsy (OBM) is a valuable diagnostic tool, but patients frequently express concerns about the surgical risks and potential discomfort. The aim of this observational study is to describe the characteristics of pain encountered during and after OBM and to assess the prognostic factors that may influence patient's pain perception.
Methods: Patients aged > 18 years who underwent OBM at the Pitie-Salpetriere Hospital in Paris and provided informed consent were enrolled in the study. Clinical data and frailty assessment were collected prior to the intervention. Following OBM, patients completed a detailed questionnaire, including the numerical rating scale (NRS) for pain assessment, and the PHQ-9 questionnaire. Follow-up phone calls were performed at 15 and 30 days.
Results: Forty-seven patients (13 males) were enrolled, with a mean pain score of 2.6 on the NRS. The most painful phase of the OBM was the sampling collection phase (24/47, 51.1%), followed by the local anesthesia phase (10/47, 21.3%). No major complications were observed in the follow-up period, available for 36 patients. Fourteen patients (38.8%) reported mild pain (NRS 1-3), lasting up to 48 hours (11/14), while four patients (11.1%) experienced a moderate pain (NRS 4-6). Overall, only fourteen patients (38.8%) took an antalgic treatment after OBM, with paracetamol being the first line analgesic (12/14, 85.7%), yielding a good therapeutic response. Pre-interventional anxiety wasn't associated with higher pain perception during OBM.
Conclusion: Pain experienced during OBM is usually mild. After OBM, patients generally report little to no discomfort. Therefore, OBM is a safe and well-tolerated procedure.
Disclosure: Nothing to disclose.

EPO-294 | Genome sequencing unveils new insights into LGMD in Tunisia: From misdiagnosis to accurate insights

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Background and aims: Limb-girdle muscular dystrophies (LGMD) are rare hereditary genetic disorders that affect the muscles of the pelvic and shoulder girdles. Due to the rarity of the disease and the phenotypic similarities between its 32 forms, achieving an accurate diagnosis of LGMD is often challenging.
Methods: A total of 48 patients presenting with progressive muscular weakness were included in this study. Targeted gene panel sequencing and whole exome sequencing (WES) were utilized for genetic analysis. Afterwards, Sanger sequencing and multiplex ligation-dependent probe amplification (MLPA) were employed to validate the identified variants.
Results: Genome sequencing confirmed a diagnosis of dysferlinopathy (LGMDR2) for 28 patients, highlighting that this form is the most prevalent form of myopathy in Tunisia, contrary to previous assumptions that sarcoglycanopathy was more relevant. In addition, we confirmed diagnoses of LGMDR1 and LGMDR9 in 12 patients with the identification of new mutations. We also identified unreported rare forms of LGMD in Tunisia, including LGMDR11, LGMDR12, and Bethlem myopathy. Furthermore,

we identified mutations that refined the diagnosis for some patients previously classified as having LGMD. Specifically, these patients carried mutations associated with McArdle disease, mitochondrial myopathy, and AMPD1 myopathy, which mimicked the phenotype of LGMD.
Conclusion: In conclusion, our study marks a turning point in the epidemiology of limb-girdle muscular dystrophies (LGMD) in Tunisia, challenging the previously prevailing data in the region. By incorporating genome sequencing, we identified rare myopathies and corrected misdiagnoses, leading to more precise diagnoses and better treatment adjustments for affected patients
Disclosure: Nothing to disclose.

EPO-295 | Rapid onset of efficacy of Eculizumab in single-center cohort of patients with refractory generalized Myasthenia Gravis

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Background and aims: Eculizumab is a humanized monoclonal antibody that targets complement protein C5 that has been approved in Italy for treatment of patients positive for anti-acetylcholine receptor antibodies (AChR+) refractory generalized myasthenia gravis (gMG). The main objective of our study is to evaluate the time of efficacy onset of Eculizumab in the cohort of patients with refractory acetylcholine receptor antibody-positive (AChR+) gMG.
Methods: All patients with refractory AChR+ gMG treated with eculizumab (900 mg/week for 4 weeks then 1200 mg the fifth week and then every 2 weeks) followed by our Department were included. Outcome measures were MyastheniaGravis-Activities of Daily Living (MG-ADL) scores, Quantitative MyastheniaGravis (QMG) evaluations, number of exacerbations and adverse events. Data were collected before Eculizumab start (BL), 5-weeks after (T1) and then at regular intervals of three months.
Results: Data were available for 6 adult patients (4F; 2M). Two patients had a history of thymoma surgically treated. The mean MG-ADL score reduced from 7.5 at baseline to 2.6 at week 5 ($p=0.02$). The mean QMG score dropped from 17.1 at baseline to 7.6 at week 5 ($p=0.004$). This improvement was stationary at subsequent follow-up. No meningococcal infections neither adverse drug reactions were reported. No patients required additional rescue therapy. One death was reported during FU and was considered unrelated to Eculizumab treatment.
Conclusion: This single-center study confirm a rapid and sustained efficacy of Eculizumab in a real-world setting in patients with refractory gMG and allow to hypothesize future clinical trials designed to evaluate the possible use of eculizumab in gMG exacerbations.
Disclosure: Nothing to disclose.

EPO-296 | Assessing efficacy and safety of gefurulimab in generalised Myasthenia gravis: Baseline characteristics from PREVAIL

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Background and aims: Complement component 5 (C5) inhibitors are effective treatments for anti-acetylcholine receptor antibody-positive (AChR-Ab+) generalised myasthenia gravis (gMG). Gefurulimab (ALXN1720) is a new investigational C5 inhibitor designed for weekly subcutaneous (SC) self-injection. The ongoing phase 3, multicentre, randomised, double-blind, placebo-controlled PREVAIL study is evaluating the efficacy and safety of gefurulimab in adults with AChR-Ab+ gMG (NCT, NCT05556096; EudraCT, 2023-508284-77-00). Here, we describe summary baseline characteristics of participants in the PREVAIL study.
Methods: Adult patients with AChR-Ab+ gMG were randomised 1:1 to weekly SC self-injection of gefurulimab or placebo. The study consists of an initial screening period (up to 4 weeks), a randomised controlled treatment period (26 weeks), and an open-label extension (up to 105 weeks). Patients may continue previously prescribed allowed therapies, including immunoglobulins. The primary endpoint is change from baseline in Myasthenia Gravis Activities of Daily Living (MG-ADL) total score at week 26. Secondary endpoints include change from baseline in Quantitative Myasthenia Gravis (QMG) total score and Myasthenia Gravis Composite (MGC) total score. Safety, pharmacokinetics, pharmacodynamics, immunogenicity, and quality of life are also assessed.
Results: As of 09 Dec 2024, 260 participants have been enrolled. At baseline (n=259), ~60% of participants were female and mean±SD MG-ADL total score was 9.0±2.2. At first dose of study intervention (n=259), mean±SD age was 52.8±15.8yrs, and ~83% of patients were using any immunosuppressive therapy.
Conclusion: This study examines the potential of gefurulimab as an effective treatment for patients with AChR-Ab+ gMG self-administered once-weekly as a SC injection. Additional baseline characteristics will be presented.
Disclosure: FS: speaking honoraria/ad board/consulting fees/ PI-clinical trials: Alexion, Amgen, argenx, AstraZeneca, Alexis, Biogen, Dianthus, Genpharm, Immunovant, JnJ, Leadiant, Lexeo, MedPharm, Medison, Neopharm Israel, Novartis, Prilena, Reata, RemeGen, Roche, Sandoz, Sanofi, Takeda, UCB, Zai Lab. KG: honoraria: AcademicCME, Alexion, AstraZeneca Rare Disease, Amgen, argenx, UCB. MM: honoraria/ad boards: Alexion Pharma GK, AstraZeneca Rare Disease, argenx, Asahi Kasei Medical, Hanall Biopharma, Japan Blood Products Organization, Takeda, UCB. AAH: research support: Alexion, AstraZeneca Rare Disease, argenx, Cabaletta, Genentech/ Roche, Immunovant, Pfizer, Regeneron, UCB, Viela. SP: honoraria/research/travel grants/consulting fees: Adoc, Amgen, argenx, AstraZeneca, Berlin Chemie, Biogen Idec, Dianthus,

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EPO-297 | Eculizumab as a new option for thymoma-associated myasthenia gravis after thymectomy: A prospective case series

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Background and aims: The perioperative efficacy and safety of eculizumab in patients with thymoma-associated myasthenia gravis (TAMG) after thymectomy have not been evaluated. This study aims to report a case series of TAMG who have eculizumab as an add-on therapy for perioperative treatment.
Methods: This is a single-centre observational prospective study. TAMG cases with thymoma burden and initiated eculizumab before thymectomy were enrolled. The MG-activities of daily living (ADL) score, lymphocytic phenotypes, and adverse events were assessed pre-thymectomy and post-thymectomy.
Results: Seven TMG patients were finally recruited with a mean age of 53.0±14.95 years. The duration from MG onset and initiation of eculizumab to thymectomy was 7.17±6.21 months and 2.35±2.19 weeks, respectively. Upon eculizumab initiation, MG-ADL score rapidly reduced from 9.83±6.52 to 5.50±6.38 by 1 week and 2.50±6.17 by 4 weeks. The thymectomy was performed successfully, and the patients were discharged from the hospital after recovery in 13.17±15.01 days. The percentages of CD3+CD4+Th lymphocytes in peripheral blood significantly declined from 45.14%±6.07% to 31.82%±6.77%($p<0.05$), while there were no significant changes in CD3+CD8+Tc lymphocytes and CD19+B lymphocytes.
Conclusion: This small case series highlights the use of eculizumab in TAMG as a rapid symptom-control treatment during the perioperative period. Future prospective cohort studies with a large sample size are expected to validate these findings, particularly for those TAMG with moderate to severe myasthenia before thymectomy.
Disclosure: Nothing to disclose.

EPO-298 | A real-world experience with Efgartigimod for new-onset generalized myasthenia gravis

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Background and aims: The real-world experiences with efgartigimod, as reported in various studies confirmed that efgartigimod is effective across diverse subtypes of patients and can be integrated into personalized treatment strategies for myasthenia gravis (MG). But there remains a paucity of relevant evidence regarding its use in patients with new-onset AChR antibody positive generalized MG.
Methods: We conducted a prospective study to evaluate the real-world safety and efficacy of efgartigimod in 29 new-onset AChR-gMG patients with a three-month follow-up. The MG-ADL, QMG score, dose of prednisone, laboratory data and adverse events were assessed at every follow-up.
Results: At 4, 8, 12 weeks, the change in MG-ADL score was 8.13±3.66, 7.41±4.22, and 6.37±4.67, respectively. 96% (28/29) of patients demonstrated an MG-ADL response (ADL ≥2-point) compared with baseline after one cycle and the time to response was 0.81 ±0.53 weeks (5.67 ±3.71 days). 52% (15/29) patients achieved MSE after one cycle, while 41% maintained MSE by 12 weeks. Moreover, 89% and 72% MG-ADL responder was sustained for 8 and 12 consecutive weeks. Additionally, TMG patients presented worse response to efgartigimod and required to apply two infusion cycles. All patients were able to reduce their daily dose of steroids. The treatment was well tolerated with few adverse events reported.
Conclusion: Our study shows that efgartigimod is clinically beneficial and offers rapid symptom control for new-onset AChR-gMG patients. More aggressive application of efgartigimod in combination with corticosteroids may lead to a smoother therapy transition, which will further maintaining the favorable condition and improve longitudinal prognosis.
Disclosure: Nothing to disclose.

EPO-299 | Long-term safety of rozanolixizumab treatment cycles in patients with generalised myasthenia gravis

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Background and aims: In the MycarinG study (MG0003/NCT03971422), one 6-week cycle of rozanolixizumab was generally well tolerated and significantly improved myasthenia gravis (MG)-specific outcomes versus placebo. After MycarinG, patients could receive additional cycles of rozanolixizumab in the open-label extension study MG0007, which is now complete. We evaluate the long-term safety of repeated rozanolixizumab treatment cycles in patients with generalised MG (gMG).

Methods: Safety data up to Cycle 13 were pooled for patients receiving >=1 rozanolixizumab cycle across MycarinG and MG0007 (NCT04650854).

Results: 188 patients received a total of 1094 cycles of rozanolixizumab 7mg/kg or 10mg/kg, equating to 310.25 years of exposure. Across all cycles, treatment-emergent adverse events (TEAEs; mostly mild/moderate) occurred in 93.1% (n=175/188) of patients. Incidence varied across 13 cycles, from 37.5% (Cycle 12) to 74.5% (Cycle 1) in the 7mg/kg group and 44.4% (Cycle 12) to 88.9% (Cycle 5) in the 10mg/kg group (Table 1). Incidence of any TEAE did not increase with repeated cyclic treatment compared with Cycle 1. Most common TEAEs were headache (50.0%), diarrhoea (33.5%), COVID-19 (21.8%) and pyrexia (20.7%). Overall incidence of infection or infestation (58.0%) and headache did not increase across cycles. Serious TEAEs occurred in 29.3% (n=55/188) of patients; events occurring in >1% of patients across all cycles were MG (9.6%), MG crisis (2.1%), COVID-19 (1.6%), nephrolithiasis (1.1%) and pneumonia (1.1%). Four deaths occurred, all deemed unrelated to rozanolixizumab by investigators.

TABLE 1 Incidence of TEAEs by treatment cycle.

	RLZ 7mg/kg		RLZ 10mg/kg	
Any TEAE	N	n (%)	N	n (%)
Cycle 1	94	70 (74.5)	94	79 (84.0)
Cycle 2	73	47 (64.4)	72	57 (79.2)
Cycle 3	51	30 (58.8)	66	46 (69.7)
Cycle 4	43	24 (55.8)	59	41 (69.5)
Cycle 5	40	22 (55.0)	54	48 (88.9)
Cycle 6	35	23 (65.7)	51	40 (78.4)
Cycle 7	31	17 (54.8)	47	35 (74.5)
Cycle 8	29	14 (48.3)	42	28 (66.7)
Cycle 9	26	13 (50.0)	33	21 (63.6)
Cycle 10	20	14 (70.0)	30	17 (56.7)
Cycle 11	13	8 (61.5)	24	15 (62.5)
Cycle 12	8	3 (37.5)	18	8 (44.4)
Cycle 13	8	5 (62.5)	10	6 (60.0)
All cycles	135	112 (83.0)	133	126 (94.7)

Patients who switched rozanolixizumab dose between cycles are included in both treatment groups. RLZ, rozanolixizumab; TEAE, treatment-emergent adverse event.

Conclusion: Rozanolixizumab was generally well tolerated in patients with gMG with an acceptable and consistent safety profile across repeated treatment cycles.

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EPO-300 | Assessment of patient-reported outcomes from the phase 3 vivacity-MG3 study of nipocalimab in gMG

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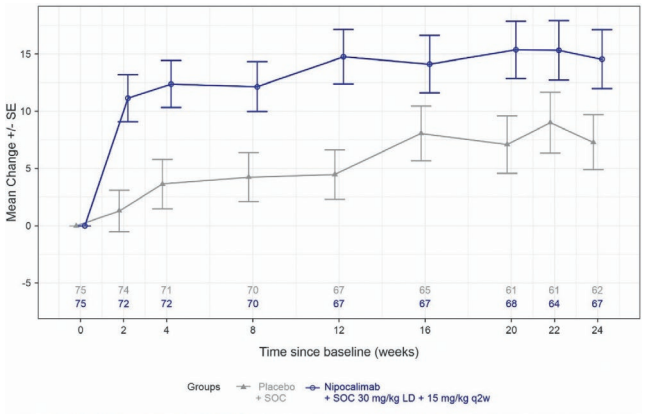
Background and aims: Due to the heterogeneity of generalized myasthenia gravis (gMG), it is crucial to capture health-related quality of life data, including treatment satisfaction

for this rare condition. Examining patient-reported outcomes (PROs) helps to better understand the overall impact of the disease and the effectiveness of treatments from the patients' perspectives. Nipocalimab+SOC demonstrated positive efficacy in Vivacity-MG3 (NCT04951622) vs placebo+SOC in gMG. The analysis of comprehensive PRO measures from the Vivacity-MG3 trial offers valuable insights into treatment satisfaction and overall disease status from the viewpoint of patients treated with nipocalimab+SOC vs placebo+SOC.

Methods: The efficacy analysis population included participants who were antibody-positive for a gMG-related pathogenic antibody (anti-acetylcholine receptor [AChR], anti-muscle-specific tyrosine kinase [MuSK], or anti-low density lipoprotein receptor-related protein 4 [LRP4]). PROs were reported from week-2 (W2) through week-24 (W24) descriptively and included: EuroQol 5-Dimension Visual Analogue Scale (EQ-5D VAS), Patient Global Impression of Severity/Change-Fatigue (PGIS/PGIC), and Treatment Satisfaction Questionnaire for Medication (TSQM-9).

Results: EQ-5D-5L VAS mean (95% confidence interval [CI]) change-from-baseline scores were significantly improved for nipocalimab+SOC (11.1[7.1, 15.2]) vs placebo+SOC (1.3[-2.2, 4.8]) by W2; improvement was sustained up to W24 (Figure). At W24, 56.5% of nipocalimab+SOC-treated patients reported their fatigue as 'much better' or 'moderately better' since the start of study medication, a difference of 15.5% vs placebo (Table). Mean scores (95% CI) in TSQM-9 Global Satisfaction domain at W24 were numerically higher in nipocalimab (65.7[59.4, 72.0]) vs placebo (56.1[50.1, 62.1]).



EQ-5D-VAS score range is 0-100. Positive score changes indicate improvement.
Abbreviations: EQ-5D-VAS=European Quality of Life Group, 5 Dimension, 5 Level version, Visual Analog Scale; LD=Loading dose; SE=Standard error; SOC=Standard of care; q2w=Every 2 weeks

Figure. EQ-5D-5L Visual Analog Scale

Table Outcome scores	Placebo + SOC	Nipocalimab + SOC	Difference in scores between Nipocalimab + SOC arm and Placebo + SOC arm
PGI Measures			
PGIS-Fatigue "None" at W24	n=61 4.9%	n=63 14.3%	9.4%
PGIS-Fatigue "None", "Mild", or "Moderate" at W24	80.3%	93.7%	13.4%
PGIC-Fatigue "Much better" at W24	n=61 14.8%	n=62 33.9%	19.1%
PGIC-Fatigue "Much better" or "Moderately better" at W24	41.0%	56.5%	15.5%
EQ-5D-VAS (0 to 100 scale)			
EQ-5D-VAS mean (SE) change from BL at W22	n=61 9.00 (2.65)	n=64 15.33 (2.61)	6.33
EQ-5D-VAS mean (SE) change from BL at W24	n=62 7.27 (2.39)	n=67 14.55 (2.56)	7.28
TSQM-9 (0 to 100 scale			
TSQM-9 mean (SD) Global satisfaction domain at W24	n=63 56.1 (24.17)	n=67 65.7 (26.91)	9.6
TSQM-9 mean (SD) Effectiveness domain at W24	57.9 (19.75)	63.1 (24.48)	5.2

PGIS response options: "None", "Mild", "Moderate", "Severe", "Very Severe"
PGIC response options: "Much better", "Moderately better", "A little better", "No change", "A little worse", "Moderately worse", "Much worse"
TSQM-9: 'Global satisfaction' and 'Effectiveness' domains each consists of 3 items
Note: There was no formal testing strategy used for the PROs in this table
Abbreviations: BL=Baseline; EQ-5D-VAS=European Quality-of-Life, 5Dimension, 5-level version Visual Analogue Scale; PGI=Patient Global Impression; PGIS=Patient Global Impression of Severity; PGIC=Patient Global Impression of Change; SD=Standard deviation; SE=Standard error; SOC=Standard-of-care; TSQM-9=Treatment Satisfaction Questionnaire for Medication; W=Week.

Conclusion: Nipocalimab-treated patients reported numerically greater improvements on patient-reported health status and treatment satisfaction compared with placebo-treated patients.

Disclosure: This study was sponsored by Johnson & Johnson. Elena Cortés Vicente: Received consulting/advisory from Argenx BV, Alexion Pharmaceuticals Inc., Janssen Pharmaceuticals Inc., UCB Pharma SA. Sheryl Pease, Nida Imran, Kavita Gandhi, Maria Ait-Tihyaty, Ibrahim Turkoz, Charlotte Gary, Zia Choudhry, and Sindhu Ramchandren: Employees of Johnson & Johnson, may hold stocks/stock options in Johnson & Johnson. Geoffroy Coteur: Owner of IPATH Solutions and received consultant fees from Johnson & Johnson. John Vissing: Participated in paid advisory boards for Alexion Pharmaceuticals Inc., Argenx BV, Dianthus Therapeutics, Horizon Therapeutics (now Amgen Inc.), Janssen, Regeneron, Roche, and UCB Pharma SA.

EPO-301 | Rehabilitation (R) and function of external respiration in outpatient myasthenia gravis (MG) patients

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Background and aims: It is important to diagnose respiratory disorders (RD) in MG that often stay unrecognized. The R-possibilities in MG are limited and require special attitude.

Methods: The study was carried out in 36 outpatient MG patients (13(36%) men and 23(64%) women), 62.0[46.0;68.0] years, BMI 27.0[24.0;30.0]. All patients with generalized MG, 13(36%) with bulbar disorders and 23(64%) without, 35(97%) with the second and 1(3%) with the third MGFA class. The control group 14 patients (4(29%) men and 10(71%) women) without

signs of neuromuscular pathology, 57.5[51.0;61.0] years, BMI 26.5[26.0;31.0]. Groups comparable in age (U, p=0.18), BMI (U, p=0.93), gender (χ2, p=0.61). The R-complex included diaphragmatic breathing, exercises involving arms.

Results: When comparing spirometry in outpatient MG with control group significant decrease in Vital Capacity (VC) was found in MG: sitting 78,0[71,5;96,5]%/99,0[91,0;108,0]%, U, p=0.005 and lying 80,0[67,5;94,5]%/94,5[83,0;101,0]%, U, p=0.01. MG patients with low VC in the sitting position (n=21) underwent R. Significant increase was achieved in VC (72, 0[69,0;78,0]%/82,0[77,0;89,0]%, W, p=0.01) and Inspiratory Reserve Volume (IRV) (1.14[1.02;1.56]l/1.65[0.96;1.93]l, W, p=0.03). Spirometry in MG patients before and after R were compared with spirometry in MG patients without R (n=35). VC and IRV before R comparable in both groups: 72,0[69,0;78,0]% /75,0[70,0;83,0]%, U, p=0.57 and 1.14[1.02;1.56]l/1.04[0.71;1.56] l, U, p=0.28. After R significant improvement was found: 82, 0[77,0;89,0]%/75,0[70,0;83,0]%, U, p=0.04 and 1.65[0.96;1.93] l/1.04[0.71;1.56]l, U, p=0.02.

Conclusion: Preventive spirometry in outpatient MG patients is necessary for early diagnosis and active correction of latent RD.

Disclosure: Nothing to disclose.

EPO-302 | Respiratory studies in dystrophic myotonia patients

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Background and aims: Breathing disorders during the day and at night are common non-specific clinical manifestations in patients with dystrophic myotonia (DM) but often missed.

Methods: The study included 21 DM patients with identified mutation (2(10%) men, 19(90%) women): 17-DM1, 4-DM2, 44,0[36,0;50,0] years, BMI 24,0[21,0;29,0]. The control group 24 patients (3(13%) men, 21(87%) women), 40,0[33,0;55,0] years, BMI 26,5[23,0;31,0]. There was no statistical difference in age, gender and BMI. The external respiratory function (ERF) was performed using the MAC-2 BM spirometer Belarus), and night respiratory monitoring was performed using the Pulsar portable pulseoximeter (Belarus).

Results: The results of spirometry and nocturnal pulseoximetry are presented in Tables 1 and 2. The following parameters were significantly reduced in 47,6% DM patients (47%): VC, l/min (U, p=0.001), VC, l % (U, p=0.003), FVC, l/min (U, p=0.04), FVC, l % (U, p=0.001), FEV1, l/min (U, p=0.003), FEV1, l % (U, p=0.004). A decrease in the main respiratory parameters of the pulseoximetry was observed in 42,8% DM patients: average total SpO2, % (U, p=0.001), minimum total SpO2, % (U, p=0.002) and average SpO2 during the sleep period, % (U, p=0.001), AHI, epis/hour (U, p=0.004), DI, epis./hour (U, p=0.02).

TABLE 1 Spirometry parameters of patients with DM and the control group, Me[LQ;UQ].

Parameters	DM, n=21	Control, n=24	U, p
Vital capacity (VC), l best	2,5 [2,3;3,1]*	3,7 [3,0;4,0]*	**0,001**
VC, l %	71,0 [57,0;92,0]*	94,0 [81,0;100,0] *	**0,003**
Forced vital capacity (FVC), l best	3,0 [2,2;4,0]*	3,8 [3,3;4,1] *	**0,04**
FVC, l %	85,5 [63,0;103,0]*	100,0 [93,0;113,0] *	**0,001**
Forced expiratory volume in 1 minute (FEV1), l best	2,6 [1,9;3,4] *	3,1 [2,7;3,6] *	**0,003**
FEV1, l %	88,0 [64,0;106,0]*	105,0 [95,0;112,0] *	**0,004**
FEV1/ FVC, % best	85,0 [83,5;88,0]	83,0 [76,0;86,5]	0,06
FEV1/VC, % best	92,5 [78,0;116,0]	87,0 [81,0;93,0]	0,6

TABLE 2 Parameters of overnight pulseoximetry in patients with DM and the control group, Me[LQ;UQ].

Parameters	DM, n=21	Control, n=24	U, p
Average total SpO2, %	93,1 [91,6;95,5] *	96,1 [95,9;96,3]	**0,001**
Minimum total SpO2, %	65,0 [52,0;71,0] *	79,0 [70,0;89,0] *	**0,002**
Average total heart rate, %	67,5 [59,0;74,3]	70,2 [66,9;71,7]	0,2
Average SpO2 during the sleep period, %	94,2 [93,0;95,5] *	96,1 [95,3;96,2] *	**0,001**
Minimum SpO2 during the sleep period, %	80,0 [70,0;84,0]	80,0 [70,0;90,0]	0,8
Average heart rate, during the sleep period, %	66,4 [56,4;67,5]	63,9 [63,7;66,2]	0,7
Apnea/hypopnea index (AHI), epis./hour	3,9 [2,3;9,5] *	1,4 [0,2;5,6] *	**0,004**
Desaturation index (DI), epis./hour	5,5 [1,1;10,6] *	1,7 [1,1;5,0] *	**0,02**

* - significant differences at p< 0.05 (according to the Mann-Whitney criterion)

Conclusion: Respiratory disorders have been identified in DM patients: ERF, nocturnal hypoxemia and increased AHI. Persistent nocturnal hypoxemia, a result of sleep-disordered breathing, leads to cardiovascular and pulmonary failure.

Disclosure: Nothing to disclose.

EPO-303 | Establishing the REaDY LGMD registry: A czech national database for limb girdle muscular dystrophies

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Background and aims: Limb Girdle Muscular Dystrophies (LGMD) are rare, genetically diverse neuromuscular disorders with prevalence estimates ranging from 1:14,500 to 1:123,000. Understanding their natural history and genetic background is crucial for patient monitoring and biomarker identification in clinical trials. To address these gaps, we established the REaDY

LGMD National Registry in Czechia to: Collect epidemiological and genetic data, Gather longitudinal disease progression data, Set diagnostic and care standards, Support clinical trial feasibility studies.
Methods: Launched in June 2020, the registry collects clinical, genetic, and diagnostic data from seven neuromuscular centres. Patients can access their records and complete a Quality-of-Life survey (SF-36). Operating under ethical approval and Czech Neurological Society oversight, it adheres to the TREAT-NMD dataset and is a TGDOC member, enabling international data sharing.
Results: The registry includes 136 patients (58% men, 42% women), primarily aged 11 to 50. The most common LGMD subtypes are: LGMD R1 (calpain-3 related) in 38 patients (28%), LGMD D4 (calpain-3 related) in 27 patients (20%), FKRP-related LGMD in 16 patients (12%). Detailed analysis of allele frequencies, age of onset, age at diagnosis, and clinical features will be presented in a subsequent poster.

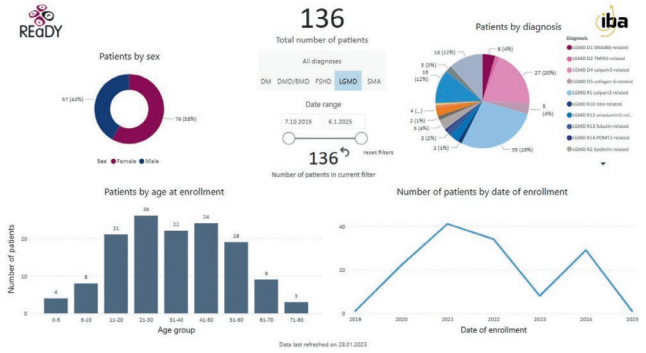

FIGURE 1 REaDY LGMD basic statistics.

Conclusion: The registry continues collaborating with seven neuromuscular centres, with subtype distribution consistent with previous studies. Future plans include expanding enrolment, securing funding, and integrating data within the European TREAT-NMD network.
Disclosure: Nothing to disclose.

EPO-304 | Bioequivalence, injection speed, and usability of subcutaneous efgartigimod PH20 administered with a prefilled syringe

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Background and aims: Efgartigimod is a human immunoglobulin G1 (IgG1) antibody Fc fragment that reduces IgG levels through neonatal Fc receptor blockade. Efgartigimod administered subcutaneously (SC, coformulated with recombinant human hyaluronidase PH20) is approved for adult patients with generalized myasthenia gravis (gMG; US, EU) and chronic inflammatory demyelinating polyneuropathy (CIDP; US). The 1000-mg fixed dose of efgartigimod SC is administered via separate vial and syringe (V+S). These studies evaluated the bioequivalence, safety, and usability of efgartigimod SC administered via prefilled syringe (PFS) vs V+S.
Methods: Bioequivalence of efgartigimod SC 1000 mg administered via PFS vs V+S was assessed in a phase 1, open-label, randomized, 2-period, crossover study. Seventy-two healthy participants were randomized to receive 1 injection of efgartigimod SC via PFS or V+S in a crossover design. Separate studies tested injection speed and usability of efgartigimod SC administered via PFS.
Results: Bioequivalence between efgartigimod SC administered via PFS and V+S was established according to predefined criteria. Efgartigimod serum concentration vs time profiles were similar following a single injection with PFS or V+S. Most adverse events were mild to moderate, and no difference in the incidence of injection-site reactions was observed. Rapid (20-second) administration was feasible, and human factor validation studies determined that the PFS could be successfully administered by caregivers and participants with gMG or CIDP.
Conclusion: Efgartigimod SC was bioequivalent and demonstrated similar safety and usability profiles when administered via PFS or V+S. A PFS may offer a convenient treatment option for patients with gMG or CIDP.
Disclosure: This study was sponsored by argenx; MR, FB, KA, and CDM are employees of argenx; and JN is a consultant for argenx.

EPO-305 | Autoantibodies in myasthenia gravis: Cluster analysis, and clinical correlations

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Background and aims: This study aims to explore autoantibody clusters and their correlations with clinical features in 644 myasthenia gravis (MG) patients.
Methods: Medical records of 664 MG patients were reviewed. Five autoantibodies (AChR, MuSK, titin, RyR and LRP4) were selected for cluster analysis. The various clinical manifestations were compared between clusters. Separate association analyses between individual autoantibodies and clinical manifestations as well as among different MGFA subtypes were also performed without prior clustering.
Results: Two separate autoantibody clusters were identified, with significantly in review different clinical manifestations. Cluster 1 (485 patients) was characterized by higher proportions of RyR-, titin-, and AChR-, while cluster 2 (179 patients) had higher proportions of RyR+, titin+, and AChR+. Cluster 2 patients were older and had elevated QMG scores and odds of complications, particularly hypertension, diabetes, cardiovascular and cerebrovascular diseases, and eye conditions. Individual antibody analysis revealed male cases were more likely to be AChR+ and titin+, and older age was associated with AChR+, RyR+ and titin+. Among MGFA subtypes, significant differences were detected in AChR, MuSk, titin, complications, thymoma, and hypertension. As MG severity increased from type I to type V, AChR+, RyR+, and titin+ proportions peaked at stage IIa. MuSK+ patients were relatively rare and mostly present in the subtype b group. Type b patients had higher MuSk+ prevalence and increased cardiovascular and cerebrovascular disease incidence rates compared with type a cases.

Conclusion: Overall, cluster 2 features were less favorable to patients. This study provides valuable insights into the clinical and autoantibody profiles of Chinese MG patients.
Disclosure: Nothing to disclose.

EPO-306 | Empasiprubart vs immunoglobulin in chronic inflammatory demyelinating polyneuropathy: EMVIGORATE phase 3 study design

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Background and aims: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) is a rare, immune-mediated neuropathy characterised by progressive muscle weakness and sensory dysfunction. The complement system plays a key role in promoting macrophage-mediated demyelination. Empasiprubart binds C2, blocking activation of classical and lectin complement pathways. EMVIGORATE will compare intravenous (IV) empasiprubart and IV immunoglobulin (IVIg) in CIDP.
Methods: This Phase 3, randomised, double-blinded, double-dummy study will randomise ~218 adults on stable maintenance IVIg to receive either empasiprubart IV or continue the stable IVIg dose in a 24-week double-blind treatment period (Part A), followed by a 24-month open-label period (Part B) and a 15-month safety follow-up (Figure). In Part A, participants will receive either empasiprubart IV plus IVIg placebo or empasiprubart IV placebo plus IVIg. In Part B, all participants will receive empasiprubart IV, while IVIg treatment will not be permitted. No study treatment will be administered during the safety follow-up period.

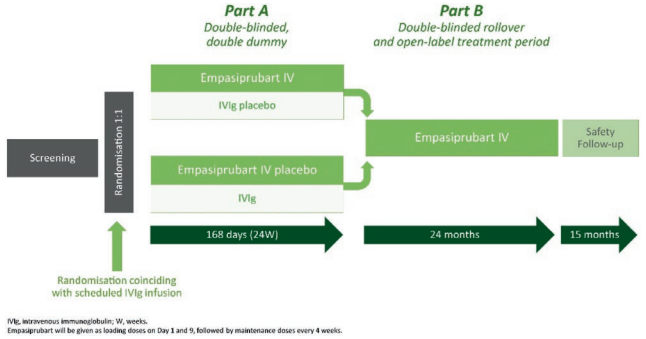

FIGURE. EMVIGORATE study design.

Results: The primary endpoint is the percentage of participants achieving ≥1-point improvement versus baseline in adjusted Inflammatory Neuropathy Cause and Treatment (aINCAT) score at Week 24. Secondary endpoints (Week 24) include changes from baseline in Inflammatory Rasch-Built Overall Disability Scale score, Medical Research Council sum score, dominant hand grip strength and Timed Up and Go, time to decrease of ≥1 point in aINCAT score, and Patient Global Impression of Change actual values.
Conclusion: This Phase 3 study will compare the efficacy and safety of empasiprubart IV and IVIg in CIDP, focusing on functional ability, muscle strength/function, gait performance, and patient-reported outcomes.
Disclosure: TB: argenx, Janssen, Immunovant, Sanofi PED: argenx, CSL Behring, Kedrion KLG: Annexon Biosciences, argenx, CSL Behring, Grifols, Immunovant, Sanofi KG: Annexon Biosciences, argenx, Genentech, Momenta, Pfizer, UCB SR: Annexon Biosciences, argenx, the Beijing Association of Holistic and Integrated Medicine, British Medical Association, CSL Behring, Dianthus, Excemed, Fresenius, GBS/CIDP Foundation International, Guillain-Barré syndrome and Related Inflammatory Neuropathies (GAIN) charity, Hansa Biopharma, the Irish Institute of Clinical Neuroscience, Medical Research Council (UK), National Institute of Health Research (NIHR), the Pathological Society of Great Britain Ireland, Peripheral Nerve Society, Takeda, UCB, the University of Oxford's John Fell Fund, Wellcome Trust MS: argenx, Bayer, Biogen Idec, Biotest, CSL Behring, Genzyme, Grifols, Immunovant, Kedrion, Merck, Novartis, Octapharma, PPTA, Roche, Sanofi-Aventis, Teva, UCB JAA: Akcea Therapeutics, Alexion, Alnylam Pharmaceuticals, Annexon Biosciences, argenx, CSL Behring, Grifols, Immunovant, Immupharma, Johnson & Johnson, Pfizer, and Takeda OVdS, KBudding, IVdW, SE, and MM are employees of argenx.

EPO-307 | Quality of life in patients with generalised myasthenia gravis receiving rozanolixizumab: Post hoc analysis of MycarinG

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Background and aims: Generalised myasthenia gravis (gMG) is a chronic autoimmune disease that can significantly impact many aspects of patients' quality of life (QoL). In the MycarinG

study (NCT03971422), rozanolixizumab significantly improved myasthenia gravis (MG)-specific outcomes versus placebo in patients with gMG. In this post hoc analysis, we identified three themes of the MG-QoL 15-items revised (MG-QoL 15r) tool to evaluate the impact of rozanolixizumab on QoL.

Methods: Patients received six weekly infusions of rozanolixizumab 7mg/kg, 10mg/kg or placebo to Day 43. We grouped the 15 items of MG-QoL 15r (total score 0–30; higher scores reflect worse QoL) into three themes: physical (e.g., eating, walking; 0–14), social (e.g., hobbies, family; 0–8) and emotional (e.g., frustration, depression; 0–8). Descriptive analyses of the change from baseline (CFB) in scores at Day 43 for each theme were conducted.

Results: Overall, 200 patients received rozanolixizumab 7mg/kg (n=66), 10mg/kg (n=67) or placebo (n=67). Least squares mean (standard error) CFB in MG-QoL 15r total score at Day 43 was greater for both rozanolixizumab groups than placebo – 7mg/kg: −4.35 (0.93), p=0.018; 10mg/kg: −5.81 (0.97), p<0.001; placebo: −2.11 (0.95). Mean scores CFB were greater for rozanolixizumab than placebo patients for all three themes – physical: −1.6, −2.4 and −0.6; social: −1.3, −1.5 and −0.3; emotional: −1.0, −1.4 and −0.4 for 7mg/kg, 10mg/kg and placebo, respectively.

Conclusion: Rozanolixizumab led to greater improvements in scores for the physical, social and emotional themes of the MG-QoL 15r versus placebo, demonstrating the benefit of treatment across the spectrum of MG symptoms that affect patients' QoL.

Disclosure: This study was funded by UCB. Jos Bloemers, Fiona Grimson, and Thais Tarancón are employees and shareholders of UCB. Full disclosure of all industry relationships will be made during congress presentation if accepted.

Neuroimmunology 1

EPO-308 | Neurology crossroads: Unravelling the Enigma of NMDA encephalitis in patients with multiple sclerosis

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Background and aims: The co-occurrence of multiple sclerosis and anti-NMDAR encephalitis is rarely documented, with only a handful of case reports available. Our understanding of the shared pathogenic processes between these two conditions remains significantly limited.

Methods: We describe a trio series of NMDAR Encephalitis/MS overlap.

Results: Case 1: A 31-year-old female presented with NMDA encephalitis in 2019, experiencing anxiety, hallucinations, and paranoia. A relapse occurred two years later. Both episodes were treated with steroids, plasma exchange, and rituximab. Her 2021 relapse included neurological symptoms, revealing spinal and brain demyelinating lesions. Positive NMDAR antibodies and oligoclonal bands confirmed overlapping NMDA encephalitis and relapsing-remitting MS. Treatment with Ocrevus stabilized both conditions, preventing further NMDA encephalitis relapses. Case 2: A 27-year-old female presented with gait ataxia and ophthalmoplegia. MRI showed cervical demyelination. CSF revealed unmatched oligoclonal bands. She later developed psychiatric symptoms. NMDAR antibodies were positive in serum and CSF. A left ovarian teratoma was discovered and removed, leading to NMDAR antibody disappearance. High-dose steroids were administered. The patient experienced no further NMDAR encephalitis or MS relapses. Case 3: A 30-year-old woman diagnosed with relapsing-remitting MS in 2019 developed NMDA receptor antibody encephalitis in 2020, with a relapse in 2021. After breakthrough relapses of her MS on Cladribine and natalizumab, she responded well to Ocrelizumab, started in November 2022. By June 2023, CSF NMDA antibodies disappeared, with no further disease activity.

Conclusion: These cases highlight the rarity and complexity of cases involving both MS and anti-NMDAR encephalitis, emphasizing the need for thorough clinical vigilance and tailored treatment approaches.

Disclosure: Nothing to disclose.

EPO-309 | Evaluating cognitive outcomes in multiple sclerosis: Real-world impact of ozanimod on processing speed using BICAMS

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Background and aims: Cognitive dysfunction represents a major burden in Multiple Sclerosis (MS). The impact on cognitive outcomes of ozanimod in real-world settings remains to be fully elucidated.

Methods: In this single-center observational study, we evaluated cognitive performance in 67 MS patients (74.6% female) receiving ozanimod (mean treatment duration 17.7 ± 3.0 months). Cognitive assessment was performed using the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) battery, comprising Symbol Digit Modalities Test (SDMT), California Verbal Learning Test-II (CVLT-II), and Brief Visuospatial Memory Test-Revised (BVMT-R) collected at different time points.

Results: Analysis suggested significant improvement in SDMT Z-scores (mean improvement 0.337, SD 0.638; Cohen's d = 0.42, p = 0.0111). Baseline SDMT z-score emerged as the sole significant predictor of cognitive change (coefficient -0.345, p < 0.001), accounting for 32.4% of variance. CVLT-II and BVMT-R scores remained stable across time points.

Conclusion: This real-world study suggests that ozanimod treatment is associated with significant improvement in information processing speed, independent of traditional prognostic factors. These findings complement existing clinical trial data and warrant further investigation through larger, multicenter studies with extended follow-up periods to validate these cognitive benefits.

Disclosure: Nothing to disclose.

EPO-310 | Blood metabolites: Predictors of axonal damage and recovery biomarkers in multiple sclerosis

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Background and aims: Multiple sclerosis (MS) is a disorder with an unpredictable outcome at the time of diagnosis. Measurement of serum neurofilament light chain (sNfL) and glial fibrillary acidic protein (sGFAP) opened the field to new biomarkers for MS disease activity and progression. However, additional diagnostic and prognostic tools are needed. The aim of this study was to evaluate the predictive capacity of plasma metabolites, gut microbiota, and clinical/lifestyle factors on MS outcome measures including MS-related fatigue, MS disability, and sNfL and sGFAP concentrations.
Methods: We conducted a prospective cohort study of 54 people with MS and collected anthropometric, biological, and lifestyle parameters. Untargeted metabolomics of plasma samples was performed. Fecal microbiota composition was assessed by 16S rRNA metagenomics sequencing. Nutritional, lifestyle parameters, including sleep and physical activity were obtained. We utilized the least absolute shrinkage and selection operator (LASSO) algorithm with ten-fold cross-validation to identify MS disease outcome parameters predictors based on plasma metabolomics, microbiota sequencing, and clinical and lifestyle measurements derived from questionnaires and anthropometric measurements.
Results: Circulating metabolites emerged as superior predictors for sNfL and sGFAP concentrations, while clinical and lifestyle data were associated with EDSS scores. Both plasma metabolites and clinical data significantly predicted MS-related fatigue. Combining multiple multi-omics data did not consistently improve predictive performance.
Conclusion: This study demonstrates that plasma metabolites are valuable predictors of sNfL and sGFAP, and fatigue in MS. Our findings suggest prioritizing metabolomics over other methods for more accurate prediction of MS disease.
Disclosure: This project was supported by grants from the Swiss MS Society (grant no. 2021-13) and the Panacée Foundation. J.R., N.E.P., G.T., T.H.C. have nothing to disclose. J.K. received speaker fees, research support, travel support, and/or served on advisory boards by the Progressive MS Alliance, Swiss MS Society, Swiss National Research Foundation (320030-189140), University of Basel, Biogen, Celgene, Merck, Novartis, Octave Bioscience, Roche, Sanofi. M.T. received travel grants, advisory board/lecture and consultancy fees from Biogen, Sanofi, Novartis, Merck and Roche. R.D.P. reports that the Lausanne University Hospital received speaker honoraria and travel grants for his activities with Biogen, Genzyme, Merck, Novartis, Roche, and Sanofi. None of them were related to this work. C.P. reports that the Lausanne University Hospital received speaker honoraria, travel grants and consulting services for her activities with Novartis, Roche, Biogen, Merck, Sanofi-Aventis none related to this work.

EPO-311 | The unexpected guest: GABA A autoimmune encephalitis with GAD67 positivity

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Background and aims: The diagnosis of autoimmune encephalitis (AE) is challenging because of overlapping phenotypes and variable testing availability: comprehensive antibody testing may detect rare reactivities such as GABA A and GAD67, but multiple positivity can occur. We present the case of a myeloma patient with ictal aphasia, cacosmia, cognitive impairment, multifocal brain lesions, oligoclonal bands, CSF monoclonal CD5- lymphocytes, but no corresponding antibodies on AE panels: brain biopsy was needed to confirm AE and CSF retesting revealed GABA A and GAD67 (but not GAD65) positivity.
Methods: This case was compared with literature reports: concurrent GABA A/GAD65 positivity may be common, while CSF antibodies exclusively against GAD67 are less studied and associated with heterogeneous, GAD65-like, phenotypes (epilepsy, cerebellar ataxia, AE, stiff person syndrome).
Results: The significance of anti-GAD67 antibodies remains elusive, due to limited diagnostic use and sparse literature. GAD67 autoimmunity may represent an epiphenomenon in syndromes like GABA A- AE, but a diagnostic and/or pathogenic role for GAD67 antibodies cannot be excluded, as they may potentially worsen the GABAergic dysregulation and perpetuate the inflammation and consequent neuronal damage.
Conclusion: Further research is needed to understand the nuances of multiple antibody positivity in AE, particularly when rare and less characterised antibodies such as GAD67 are involved. Brain biopsy and expert pathology review are essential not only for identifying rare antibody patterns, but also for speculating on the dominant drivers of the disease.
Disclosure: Nothing to disclose.

EPO-312 | Commercial tissue-based assays are suboptimal to detect intracellular antibodies in autoimmune neurological syndromes

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Background and aims: Current techniques to identify autoantibodies against intracellular neural antigens (IC-abs) include tissue-based assays (TBAs) alongside line-blot or cell-based assays (CBAs). Most clinical laboratories rely on commercially available TBAs, whose diagnostic accuracy has not been assessed. Here, we evaluated the performance of two commercial TBAs.
Methods: We tested samples from 100 patients with autoimmune neurological syndromes harbouring IC-abs (determined by in-house TBAs and line-blot or CBAs) and from 50 negative controls. IC-abs samples included sera (10 of each: Hu, Yo, Ri, SOX1, CV2, Ma2, Tr, amphiphysin, GAD65) or CSF (10 GFAP). Two commercial indirect immune-fluorescent TBAs (INOVA and EUROIMMUN) were blindly evaluated by two experienced and three less-experienced investigators; discordant results were re-evaluated in an interrater discussion.
Results: The two experienced raters showed substantial agreement (>95% after interrater agreement) on negative or positive results. They correctly identified 118/150 (79%) and misclassified 28/150 (19%) samples with INOVA, whereas they correctly identified 106/150 (71%) and misclassified 39/150 (26%) samples with EUROIMMUN. Sensitivity was 73% for INOVA and 66% for EUROIMMUN. Specificity was 96% for INOVA and 88% for EUROIMMUN. Among the positive samples, antibody-specific immunostaining patterns were correctly identified in 62/100 samples with INOVA and 55/100 with EUROIMMUN (p=0.39). Both TBAs failed to identify CV2 antibodies. INOVA better identified Ma2 antibodies (9/10 vs. 1/10, p=0.001), while EUROIMMUN better identified Hu/Ri antibodies (19/20 vs. 12/20, p=0.02). Less-experienced raters showed higher rate of false positive results.
Conclusion: The performance of commercial TBAs for IC-abs is suboptimal, particularly for CV2 (both kits), Ma2 (EUROIMMUN) and Hu/Ri (INOVA) antibodies.
Disclosure: M. Spatola receives research support from La Caixa Foundation (Junior Leader) and Spanish National Health Institute Carlos III (ISCIII) and co-funded by the European Union (FIS grant PI23/01366). J. Dalmau receives research support from CaixaResearch Health 2022 (HR22-00221), Spanish National Health Institute Carlos III (ISCIII) and co-funded by the European Union (FIS grant PI23/00858), Cellex Foundation, Fundació Clínic per a la Recerca Biomèdica (FCRB) Programa Multidisciplinar de Recerca, Generalitat de Catalunya Department of Health (SLT028/23/000071), Edmond J Safra Foundation. He receives royalties from Euroimmun for the use of NMDA as an antibody test. He received a licensing fee from Euroimmun for the use of GABAB receptor, GABAA receptor, DPPX and IgLON5 as autoantibody tests; he has received a research grant from Sage Therapeutics. All the other authors report no disclosures.

EPO-313 | Risk assessment for progressive multifocal leukoencephalopathy using the two available tests

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Background and aims: Patients treated with natalizumab are at an increased risk of PML caused by the reactivation of JC virus (JCV). The main risk factors include treatment duration, prior immunosuppression, and the presence of anti-JCV antibodies in the blood. StratifyJCV™ is a Biogen risk stratification algorithm that combines anti-JCV antibody status using an ELISA test, prior immunosuppression, and natalizumab treatment duration (by treatment year). Recently, Sandoz developed the ImmunoWELL™ JCV IgG test, which also uses a two-step ELISA technique validated by the European Medicines Agency, demonstrating non-inferiority compared to the StratifyJCV test with a sensitivity of 95%.
Methods: Eighty patients (72% women) with a diagnosis of relapsing-remitting MS (RRMS) under natalizumab treatment and follow-up at our center were recruited. Both risk stratification tests, StratifyJCV and ImmunoWELL, were performed simultaneously using the same sample.
Results: 34% of StratifyJCV tests were positive, whereas 60% of ImmunoWELL tests were positive. When comparing the results, 29% of them did not match, with StratifyJCV yielding negative results while ImmunoWELL was positive. Additionally, two patients showed differences greater than one point in the test results.
Conclusion: More than 25% of the results showed discrepancies between the two JCV antibody tests. The percentage of positive results was higher with ImmunoWELL. These discrepancias create difficulties for risk management strategies in conditions like PML.
Disclosure: Nothing to disclose.

EPO-314 | Immune checkpoint inhibitors trigger and exacerbate anti-CV2/CRMP5 paraneoplastic neurological syndromes

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Background and aims: Immune-checkpoint inhibitors (ICI) may trigger or worsen paraneoplastic neurological syndromes (PNS). We described CV2/CRMP5-PNS patients treated by ICI, compared post-ICI cases with ICI-naïve, and estimated the overall survival of ICI-treated patients with CV2/CRMP5-PNS, Hu-, and Ma2-PNS.
Methods: All patients positive for anti-CV2/CRMP5 antibodies and treated with ICI in a French referral center (2016-2024) were included.
Results: Fourteen ICI-treated CV2/CRMP5-PNS patients were included. Eight [median age, 73 years; 87.5% men] developed post-ICI PNS after a median of 3.5 ICI cycles. Frequency and distribution of clinical phenotypes [isolated neuropathy (n=3), or multifocal involvement (encephalopathy, limbic, brainstem, cerebellar, ocular, neuropathy, and/or dysautonomia; n=5)] was similar to ICI-naïve CV2/CRMP5-PNS (n=48). Frequency of severe presentations [modified Rankin Scale (mRS) >3] at diagnosis was similar between post-ICI and ICI-naïve CV2/CRMP5-PNS (63% vs 48%, p=0.7), but non-significantly higher at last visit in post-ICI patients (88% vs 54%, p=0.12). Anti-CV2/CRMP5 antibodies were undetectable in one patient with a pre-ICI serum sample. Among 6 patients with pre-existing CV2/CRMP5-PNS [median age, 66 years; 50% men], PNS worsened in 5 (83%) (median mRS increase of 1.5 points) after ICI. Median overall survival (22 months) was significantly longer in ICI-treated CV2/CRMP5-PNS compared to Hu- and Ma2-PNS (4 months and 8 months, respectively, p=0.0069).
Conclusion: ICI may trigger the onset and exacerbate the progression of CV2/CRMP5-PNS. Post-ICI forms are clinically undistinguishable than ICI-naïve. Pre-ICI antibody negativity in one case challenges the role of baseline onconeural antibody testing as predictive biomarker for the development of PNS. Post-ICI PNS have variable prognosis according to associated onconeural autoantibodies.
Disclosure: This work is supported by a public grant overseen by the Agence Nationale de la Recherche (ANR; French research agency) as part of the Investissements d'Avenir program (ANR-18-RHUS-0012), also performed within the framework of the LABEX CORTEX of the Université Claude Bernard Lyon 1 (program Investissements d'Avenir, ANR-11-LABX-0042, operated by the ANR) and supported by the European Reference Network RITA. G.S.C and A.F were awarded a research fellowship by the European Academy of Neurology. M.V-G. is funded by a research grant from Fundación Alfonso Martín Escudero (Spain).

EPO-315 | Preoperative efgartigimod benefits myasthenia gravis patients undergoing thymectomy

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Background and aims: Thymectomy is an effective way to alleviate muscle weakness for Myasthenia Gravis (MG) patients with and without thymoma. However, thymectomy may exacerbate MG. Efgartigimod as a neonatal Fc receptor blocker has been found to be effective in generalized MG, and this study aims to explore whether application of efgartigimod before surgery can also benefit MG patients who undergo thymectomy.
Methods: We retrospectively included 44 patients from Shijiazhuang People's Hospital via propensity score matching analysis (nearest neighbor 1:3 matching). Clinical features, quantitative antibody test results, Myasthenia Gravis Foundation of America (MGFA) type at different periods, thymic pathology, operation information, and muscle functional change as evaluated by both MG-ADL and QMG scores were collected. Patients were divided into two groups: the efgartigimod group and the non-efgartigimod group.
Results: Patients in the Efgartigimod group had a shorter time to reach surgical criteria (efgartigimod vs. non-efgartigimod, 4 days vs. 55 days, $p < 0.001$) (Figure 1) and a shorter time to postoperative treatment in the ICU (36 h vs. 44 h, $p = 0.007$) compared with patients in the non-efgartigimod group (Figure 2d). In addition, MG-ADL (9 vs. 1, $p = 0.002$) and QMG scores (7 vs. 2, $p < 0.001$) showed greater functional improvement and greater decline in antibody titers (3.73 vs. 0.39, $p < 0.001$) (Figure 2a-c). The efgartigimod group had a higher incidence of better postoperative MGFA type (Figure 3).

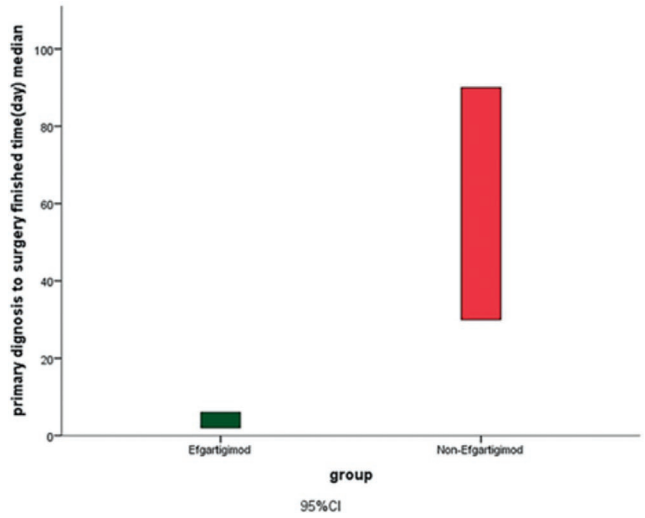

FIGURE 1 Lower primary-diagnosis-to-finished-surgery time was observed in the efgartigimod group.

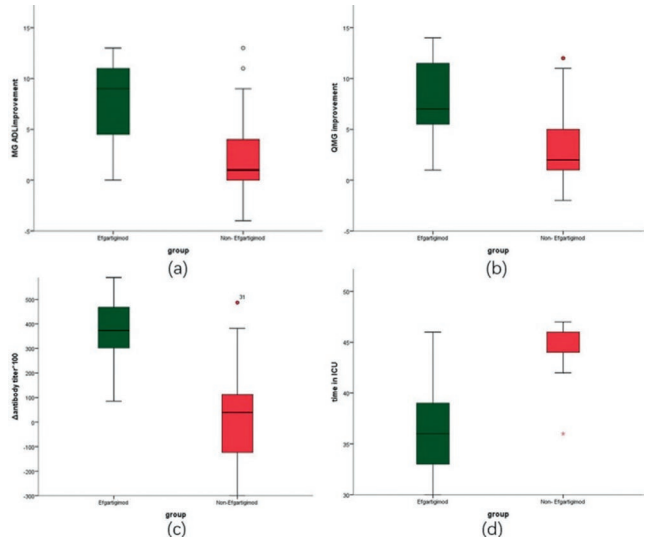

FIGURE 2 (a-c) Changes of MG ADL, QMG score and antibody titer after operation compared with those before operation. (d) Patients with preoperative efgartigimod spent less time in the ICU post-surgery.

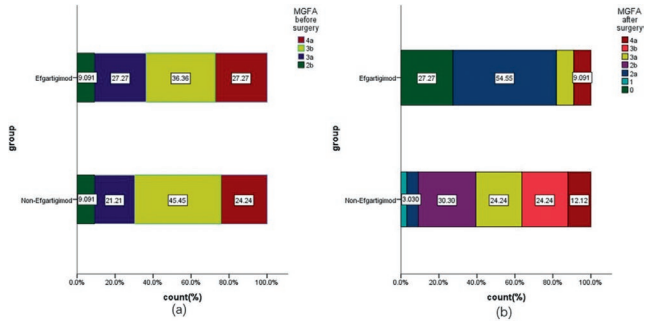

FIGURE 3 (a) There were similar MGFA types before surgery in both groups; (b) Patients in the efgartigimod group obtained better MGFA types post-surgery compared to the non-efgartigimod group.

Conclusion: Using Efgartigimod is a good way for unstable MG patients to become more stable prior to surgery.

Disclosure: This work was supported by the National Natural Science Foundation of China (No.: 82274582), Central Guidance for Local Scientific and Technological Development Funding Projects (No.: 246Z7706G) and the Hebei Province Innovation Capability Enhancement Plan Project (No.: 20577715D).

EPO-316 | Tracking eye movements to detect motor and cognitive decline in Multiple Sclerosis: A novel approach

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Background and aims: Multiple sclerosis (MS) is a neurological disorder characterized by physical and cognitive impairments. Abnormal eye movements, commonly observed in MS, may reflect underlying cognitive dysfunction. However, their relationship with disease severity remains unclear. This study investigates the association between motor and cognitive functions and eye movement parameters during the n-back and Go/No-Go tasks in individuals with MS.

Methods: A cross-sectional study was conducted with 71 participants with MS (pwMS). Eye movements were tracked during the n-back and Go/No-Go tasks using a head-mounted display with eye-tracking technology. Parameters analyzed included saccade amplitude, gaze duration, task duration, number of fixations, single fixations, and refixations. Motor and cognitive functions were assessed with the Expanded Disability Status Scale (EDSS), Nine Hole Peg Test (NHPT), Timed 25-Foot Walk (T25FW), Symbol Digit Modalities Test (SDMT), Paced Auditory Serial Addition Test (PASAT), California Verbal Learning Test (CVLT), and Brief Visuospatial Memory Test-revised (BVMT-R). Statistical analyses were performed, with significance set at $p<0.05$.

Results: Participants (mean age 40.2±12.03 years, disease duration 9.7±6.8 years) showed significant associations between eye movement patterns and disability. In the n-back task, longer fixation duration correlated with higher disability and lower SDMT scores, while saccade amplitude was shorter with higher disability ($p<0.05$). In the Go/No-Go task, increased refixations and reduced single fixations were linked to greater disability and poorer cognitive scores ($p<0.05$).

Conclusion: Eye movement parameters significantly correlate with motor and cognitive impairments in pwMS, highlighting their potential as biomarkers for monitoring MS progression.

Disclosure: María Barbara Eizaguirre, Natalia Ciufia, Aldana Marinangeli, Lucia Bacigalupe, Lucia Ibarra, Lucas Nicolas Lapalma, Magdalena Casas, Ricardo Alonso: nothing to disclose. Gerardo Fernandez, Danilo Verge, and Matías Shulz are employees of ViewMind.

EPO-317 | Microglial NFAT5 aggravates neuroinflammation via mediating NLRP6 inflammasome in experimental Ischemic stroke

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Background and aims: Microglial activation triggers the inflammatory cascade and exacerbates brain injury following ischemic stroke. Middle cerebral artery occlusion (MCAO) model increased the expression of Nuclear factor of activated T cells 5 (NFAT5) in microglia. However, the role of microglial NFAT5 in ischemic stroke remains unclear.
Methods: The MCAO and Oxygen-Glucose Deprivation/Reoxygenation (OGD/R) were utilized to emulate ischemia-reperfusion injury. In addition, recombinant Adeno-Associated Virus (rAAV) was employed for the specific silencing of microglial NFAT5 in vivo. In vitro, short hairpin RNA (shRNA) was utilized to knock down NFAT5.
Results: Here, our findings indicated that microglial NFAT5 knockdown reduced the expression of pro-inflammatory factors, microglial activation, and neutrophil infiltration, ultimately ameliorating cerebral infarction and neurological deficits in mice following MCAO. Additionally, we treated hippocampal neuronal cells (HT22) with conditioned culture medium from a microglia cell line (BV2) to simulate microglia-induced neuronal injury in vitro. We observed that NFAT5 knockdown attenuated the expression of pro-inflammatory factors in BV2 cells and reduced apoptosis in HT22 cells. Previously, our published work reported that the NOD-like receptor pyrin domain-containing 6 (NLRP6) inflammasome contributes to inflammatory injury after MCAO. In this study, we discovered that NFAT5 promotes the transcriptional activity of the Nlrp6 promoter through its -1527bp to -1518bp element. Notably, our results also demonstrate that NFAT5 regulates the stability of NLRP6 mRNA via the 5'UTR of Nlrp6.
Conclusion: Our research indicates that the transcription factor NFAT5 may potentially exacerbates neuroinflammation and cerebral ischemia-reperfusion injury by modulating the mRNA level of NLRP6 at both the transcriptional and post-transcriptional stages.
Disclosure: Nothing to disclose.

EPO-318 | Treatment utilization and clinical outcomes by serostatus in a real-world US generalized myasthenia gravis population

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Background and aims: Generalized myasthenia gravis (gMG) is characterized by impaired transmission at the neuromuscular junction that is mostly driven by autoantibodies, including those directed against the acetylcholine receptor (AChR-Ab+) and other targets (non-AChR-Ab+), though some patients are seronegative. This study describes treatment utilization and clinical outcomes in patients with gMG based on serostatus.
Methods: Data were from the Adelphi gMG II Disease Specific Programme™, conducted in the US from February–August 2024. Neurologists provided cross-sectional and chart-pulled patient data (demographics, Myasthenia Gravis-Activities of Daily Living [MG-ADL] score, clinical events, treatment utilization) in patients with varying serostatus.
Results: Fifty-two neurologists provided data on 336 patients with gMG (mean [SD] time since diagnosis, 3.8 [5.6] years, 53.9% male, mean [SD] age, 54.9 [13.3] years). Most patients were AChR-Ab+ (73.5%), 10.1% were non-AChR-Ab+, 11.3% were seronegative and 5.1% had unknown serostatus. Maintenance treatment was prescribed in 95.5% of AChR-Ab+ patients (mean [SD] number of regimens used since diagnosis, 1.8 [1.0]), 94.1% of non-AChR-Ab+ patients (1.4 [1.0]), 89.5% of seronegative patients (1.4 [1.0]) and 52.9% of patients with unknown serostatus (0.6 [0.6]). Mean (SD) MG-ADL scores in AChR-Ab+, non-AChR-Ab+, seronegative, and unknown serostatus patients were 4.3 (3.3), 4.9 (4.0), 3.2 (3.1), and 3.8 (3.3), respectively. Since diagnosis, myasthenic crises or symptom exacerbations were reported in 45.8%, 39.4%, 27%, and 7.1% of patients, respectively.
Conclusion: Patients with gMG experience clinical events and activity impairment despite treatment and regardless of serostatus. Additional treatment options are needed for all patients to optimize clinical outcomes.
Disclosure: LAMW, LL and YE are employees of Immunovant, Inc., JC, SLB, HC and GG are employees of Adelphi Real World

EPO-319 | Kappa index in multiple sclerosis: A pivotal study to determine any correlation to recent disease activity

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Background and aims: kappa index (K-index) is a marker of intrathecal synthesis widely studied for its diagnostic role in multiple sclerosis (MS). Increasing evidence suggests its prognostic value, yet the factors influencing K-index levels require further exploration 2.3. This study aimed to investigate clinical and biological correlates of the K-index, particularly its relationship with inflammatory activity and disease course.
Methods: This cross-sectional study included 100 patients diagnosed with MS from two Italian centers. Data collection included cerebrospinal fluid (CSF) analyses, clinical parameters, and disease course characteristics. Linear regression models were used to evaluate associations between K-index and variables such as recent clinical or radiological activity, time from disease onset, Link index, lambda index, and CSF cellularity.
Results: No significant correlation was observed between K-index and recent disease reactivation (N=100; p=0.865), recent brain or spinal MRI with contrast-enhancing lesions (N=32; p=0.394), time from disease onset (N=76; p=0.166), or lambda index (N=55; p=0.393). K-index significantly correlated with Link index (N=87; p<0.001, estimate=95.219, 95% CI=57.67–132.77) and CSF cellularity (N=77; p<0.001, estimate=3.603, 95% CI=1.93–5.28).
Conclusion: Our findings suggest that the K-index is not influenced by recent clinical relapse or the presence of

contrast-enhancing lesions, indicating that its value is more reflective of ongoing and temporally disseminated inflammation rather than acute disease reactivation. The significant correlation with the Link index and CSF cellularity supports its role as a marker of chronic intrathecal inflammation. Further studies are needed to confirm its prognostic utility and potential implications for therapeutic decision-making in MS.
Disclosure: Nothing to disclose.

EPO-320 | Clinical features of patients with myasthenia gravis with initial worsening after high-dose methylprednisolone pulse

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Background and aims: Myasthenia gravis (MG) is treated with high-dose methylprednisolone pulse (HMP) as a rescue treatment for acute exacerbations. However, initial worsening may occur after treatment (often 2–5 days after administration). There are few reports on the characteristics and treatment strategies of MG patients with initial worsening after HMP. We investigated the clinical characteristics of MG patients with initial worsening following HMP.
Methods: We reviewed the electronic records of 123 MG patients admitted between April 2019 and June 2024, who underwent initial HMP. The patients were divided into two groups: 31 patients who developed an initial worsening (IW group) and 92 patients who did not (Non-IW group). Clinical characteristics, such as gender, age, presence of thymoma, MG-Activities of Daily Living scale, current and maximum prednisolone (PSL) doses, use of intravenous immunoglobulin/plasmapheresis (IVIg/PP) at HMP, and incidence of bulbar symptoms, were compared between the two groups.
Results: The IW group showed a higher frequency of bulbar symptoms [IW, n (%) vs. Non-IW, n (%); 19 (61.3%) vs. 27 (29.7%); $p < .0025$] and the use of IVIg/PP [IW, n (%) vs. Non-IW, n (%); 28 (90.3%) vs. 50 (54.4%); $p < .0002$]. The Non-IW group had a higher frequency of ocular MG [IW, n (%) vs. Non-IW, n (%); 3 (9.7%) vs. 38 (41.3%); $p < .0009$].
Conclusion: Initial worsening should be anticipated in generalized MG treated with HMP, even when IVIg/PP is combined. The dosage regimen of HMP should be determined considering clinical features of individual MG patients such as ocular or bulbar symptoms.
Disclosure: Dr. Genya Watanabe has received honoraria for lectures from Argenx Japan, UCB Japan, and Alexion Pharmaceuticals.

EPO-321 | Targeting ROS-dependent NET formation with natural molecules: A potential approach for managing multiple sclerosis

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Background and aims: Neutrophil extracellular traps (NETs) are released by neutrophils as a defense mechanism, but in autoimmune diseases like multiple sclerosis (MS), excessive NET formation contributes to neuroinflammation and tissue damage.
Methods: Four natural molecules (oleuropein, phenylethanol, tyrosol, and tyrosol3) were tested for their capacity to inhibit NET formation in primary human neutrophils in vitro. To evaluate the potential cytotoxic effects of these molecules, we used the Trypan blue exclusion test. Since NET formation is primarily ROS-dependent, the luminol-amplified chemiluminescence assay was employed to assess intra- and extracellular ROS levels. Fluorescence microscopy, with Hoechst as a DNA intercalating dye, was used to visualize NET production.
Results: Our results showed that our four molecules do not have an acute cytotoxic effect on neutrophils maintained in culture for 48 hours. A high anti-radical effect of these four molecules was translated by a strong inhibition of the production of superoxide anion by neutrophils. Fluorescence microscopy showed that the treatment of neutrophils with the four molecules has significantly reduced the production of NETs.
Conclusion: Our results revealed for the first time an inhibitory effect of four natural molecules on ROS-dependent NET release. These four molecules could be considered in the future as a palliative treatment for patients with autoimmune diseases.
Disclosure: Nothing to disclose.

Neuroimaging and Neurosonology

EPO-322 | Visual inspection of dorsolateral nigral hyperintensity in idiopathic REM sleep behaviour disorder

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Background and aims: Early detection of idiopathic REM sleep behaviour disorder (iRBD) through neuroimaging can enhance prognostication and support the identification of phenoconversion to Parkinson's disease (PD). This study explores the clinical utility of dorsolateral nigral hyperintensity (DNH) loss on iron-sensitive MRI in iRBD.
Methods: We searched MEDLINE, Scopus, Web of Science, ProQuest and Google Scholar for observational studies, assessed eligible studies with QUADAS-2 and performed proportional and diagnostic test accuracy meta-analysis. Heterogeneity was quantified with I2 statistics and investigated with meta-regression.

Results: Among 349 search results, 5 studies of satisfying quality were eligible (420 patients, iRBD, n = 117, PD, n = 175, healthy controls, HCs, n = 128). Pooled difference in prevalence of STS loss between PD and iRBD was 0.37 [0.12; 0.72], with high heterogeneity (I2 = 94.6%). Pooled sensitivity and specificity for iRBD vs HCs differentiation were 0.49 [0.34; 0.64], I2 = 62.4%, and 0.91 [0.82; 0.95], I2 = 0.0%, respectively. Summary Area Under the Curve (SAUC) was 0.64. Meta-regression eliminated heterogeneity, showing longer disease duration linked to increased sensitivity. Three studies investigated the capacity of DNH loss in detecting iRBD patients with abnormal nuclear scans, with sensitivity and specificity of 0.79 [0.65; 0.88], I2 = 0.0%, and 0.77 [0.54; 0.91], I2 = 57.2%, respectively. SAUC was 0.80.

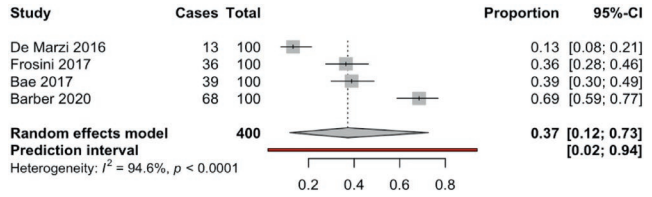

FIGURE 1 Forest plot of meta-analysis regarding the difference in prevalence of STS loss between PD and iRBD subjects (PD-iRBD).

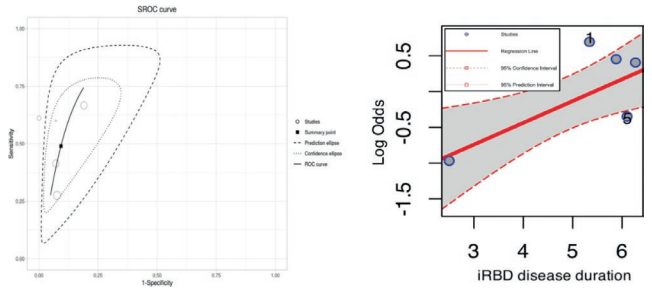

FIGURE 2 Diagnostic accuracy meta-analysis: Summary receiver-operating characteristic curve (left) and meta-regression analysis (right), with a significant positive association between sensitivity in differentiating iRBD from HCs and disease duration.

TABLE 1 Pooled diagnostic accuracy measures. STS: swallow tail sign; iRBD: idiopathic REM sleep behavior disorder; HCs: healthy controls; SAUC: Summary Area Under the Curve; PLR: positive likelihood ratio; NLR: negative likelihood ratio; NA: not applicable.

	No of Studies	SAUC	DOR	Sens.	Spec.	PLR	NLR	Area 95% Prediction Ellipse
Differentiation of iRBD subjects from HCs	5	0.64	9.38 [4.31; 20.42]	0.49 [0.34; 0.64]	0.91 [0.82; 0.95]	5.27 [2.79; 9.95]	0.56 [0.43; 0.74]	0.243
Detection of iRBD patients with abnormal nuclear scans	3	0.80	13.48 [3.70; 49.10]	0.79 [0.65; 0.88]	0.77 [0.54; 0.91]	3.47 [1.52; 7.93]	0.28 [0.15; 0.50]	NA

Conclusion: Prevalence of DNH loss differs between iRBD and PD. Iron-sensitive MRI may aid identification of iRBD among other sleep disorders, especially in association with disease duration, and may comprise a stratification tool for the conduction of nuclear scans.

Disclosure: Nothing to disclose.

EPO-323 | The tsiogkaspaeth grid for detection of neurological visual field defects: A validation study

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Background and aims: The TsiogkaSpaeth (TS) grid is a new, low cost and easy to access portable test for visual field (VF) screening which could be used by clinicians in everyday clinical practice. Our study aimed to determine the validity of an innovative screening grid test for identifying neurological disease associated VF defects.

Methods: We enrolled two groups of participants: We assessed the one eye of 10 consecutive adult patients with different types of neurological disease associated VF defects and 10 eyes of controls in each group. The TS grid test was performed in each group. Sensitivity, specificity, and positive and negative predictive values of the TS grid scotoma area were assessed using the 24–2 VF Humphrey Field Analyser (HFA) as the reference standard.

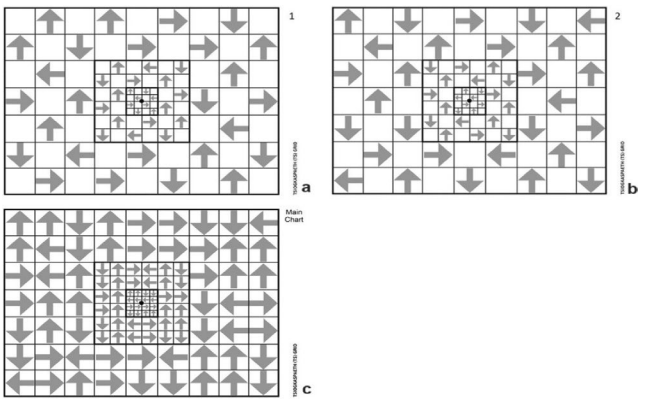

FIGURE 1 TS grid 1 (a), TS grid 2 (b) and TS grid Main Reference Chart (c) for the clinical examination

Results: Sensitivity and specificity of the TS grid test were 100% and 90.91% respectively. The Area Under Curve was 0.9545 with 95% CI 0.87-1.00. There was a significant correlation between the number of missed locations on the TS grid test and the Visual Field Index of the HFA 24-2 (r = 0.9436, P < .0001).

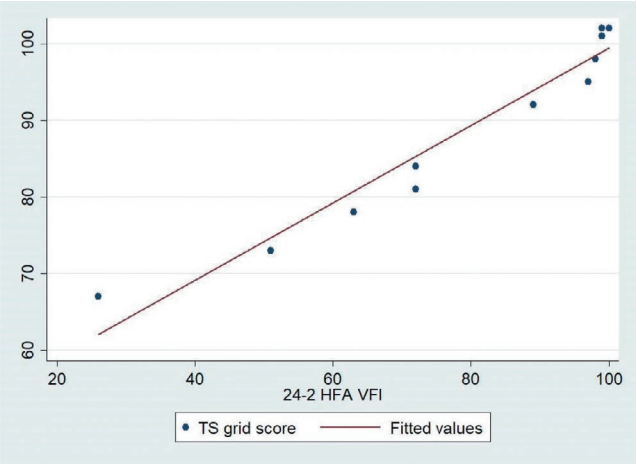

FIGURE 2 Scatter plots of The TS grid score and HFA 24-2 visual field parameters

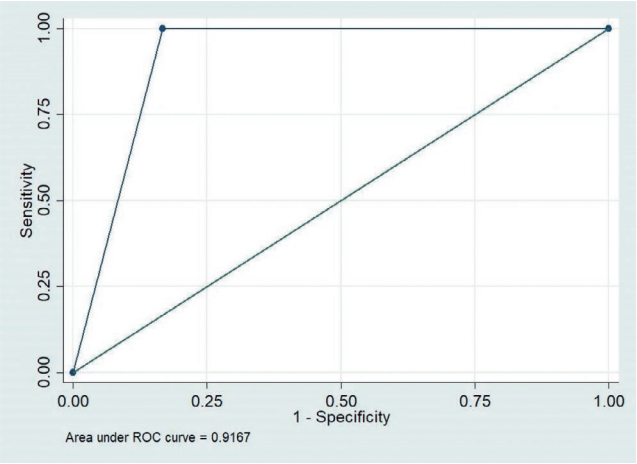

FIGURE 3 TS grid ROC curve (blue line) and HVA 24-2 ROC curve (green line) for detection of neurological disease associated VF defects

Conclusion: The sensitivity and specificity of the TS grid test were high in detecting VF defects in neurological disease. The TS grid test appears to be a reliable, low cost and easily accessed alternative to traditional VF tests in diagnosing typical neurological patterns of visual field defects. It would be useful in screening subjects for neurologically derived ocular morbidity in everyday clinical practice and in remote areas deprived of specialized health care services.
Disclosure: Nothing to disclose.

EPO-324 | Correlation between cerebral vasoreactivity and retinal vessel density in patients with internal carotid artery stenosis

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Background and Aims: The retinal and cerebral circulation are developmentally, anatomically, and physiologically similar. We aimed to investigate the relationship between cerebral and retinal circulation in patients with atherosclerotic Internal Carotid Artery (ICA) stenosis.
Methods: 24 patients with significant ICA stenosis were consecutively enrolled. Cerebrovascular reactivity was estimated from the change in ipsilateral MCA blood flow velocity (measured by TCD) and resistance to the common carotid artery compression (CCC) test. Cerebral Arterial Resistance Transient Hyperemic Response Ratio - CAR-THRR (the change of flowresistance after CCC relative to the baseline value) and CARAUC (area under curve of CAR response to CCC) were calculated. Optical Coherence Tomography Angiography (OCTA) was performed to determine the vessel density (VD) on the papilla (P) whole image (WI) and in the peripapillary (PP) region for all vessel types (VDP-WIall) and selectively for small vessels (VDP-WIsmall) only.
Results: A significant, negative correlation was found between CAR-THRR, CARAUC and VDPPsmall vessel type ($p=0.003$; Spearman's $r=-0.57$), ($p=0.002$; Spearman's $r=-0.56$), as well as between VDPPall vessel types ($p=0.01$; Spearman's $r=-0.48$), ($p=0.03$; Spearman's $r=-0.46$). There was also a significant, negative correlation between CAR-THRR, CARAUC and VDP-WIsmall ($p=0.01$; Spearman's $r=-0.52$), ($p=0.01$; Spearman's $r=-0.54$) and between VDP-WIall ($p=0.02$; Spearman's $r=-0.45$), ($p=0.006$; Spearman's $r=-0.47$) too.
Conclusion: The study showed a significant correlation between decreased cerebrovascular reactivity and retinal functional vessel density in patients with ICA stenosis suggesting common mechanisms of action. The combined use of OCTA and TCD was found to be suitable for assessing the condition of cerebral vasculature in significant ICA stenosis.
Disclosure: Nothing to disclose.

EPO-325 | Association between stroke pattern and prior anticoagulant/antiplatelet use: A retrospective study

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Background and Aims: The association between the structure of thrombus or thrombus source and infarct lesion patterns on diffusion-weighted imaging (DWI) is a subject of interest. However, it is even more interesting whether the use of antiaggregants or anticoagulants affects the infarct pattern by changing thrombus formation. Our aim was to investigate the relation between prior antiplatelet or anticoagulant use and infarct patterns.
Methods: We retrospectively examined 938 stroke patients with etiologies including cardioembolic, small vessel disease (SVD), large-artery atherosclerosis (LAA) using DWI. Infarct patterns were categorized as single cortical, medium/large corticosubcortical, subcortical less/more than 15 milimeters, borderzone, confluent and additional, small-scattered lesions. Prior

medication use were categorized as anticoagulant, antiplatelet, both, none. The association between infarct pattern and prior anticoagulant/antiplatelet use was investigated (Table 1).

Table 1: Prior Anticoagulant/Antiplatelet Use Rates in Infarct Patterns

		PATTERN							
Prior Anticoagulant or Antiplatelet Use		**Single Cortical**	**Large Cortico subcortical**	**Medium Cortico subcortical**	**Subcortical < 15 mm**	**Subcortical > 15 mm**	**Confluent and additional**	**Small-Scattered**	**Borderzone**
None	n	33	20	61	249	67	27	44	66
N=567 (60,4%)	%	5,8%	3,5%	10,8%	43,9%	11,8%	4,8%	7,8%	11,6%
Antiplatelet	n	25	14	33	137	27	13	18	34
N=301 (32,1%)	%	8,3%	4,7%	11,0%	45,5%	9,0%	4,3%	6,0%	11,3%
Anticoagulant	n	2	1	4	29	7	4	8	10
N=65 (6,9%)	%	3,1%	1,5%	6,2%	44,6%	10,8%	6,2%	12,3%	15,4%
Both	n	0	1	0	2	1	0	0	1
N=5 (0,5%)	%	0,0%	20,0%	0,0%	40,0%	20,0%	0,0%	,0%	20,0%
Total N=938		60 (6,4%)	36 (3,8%)	98 (10,4%)	417 (44,5%)	102 (10,9%)	44 (4,7%)	70 (7,5%)	111 (11,8%)

P=0,666

Results: Cardioembolic infarctions are known to cause small-scattered, confluent and additional lesions as well as large single infarctions. Although anticoagulant/antiplatelet use was considered to affect thrombus structure, it was not found to be associated with a specific infarction pattern in our study. Small-scattered and confluent were higher, large corticosubcortical lesions were lower in the anticoagulant group. It may be due to the fact that the patients with cardioembolic etiology were chosen from the ESUS/PAF+ subgroup.
Conclusion: Contrasting the literature, prior anticoagulant/antiplatelet use was not found to be associated with a specific infarction pattern, and may be explained by their etiology. To better understand the effects of anticoagulant/antiplatelet on the clotting mechanism and its association with infarct patterns, it may be useful to include patients not only ESUS/PAF also with known AF.
Disclosure: Nothing to disclose.

EPO-326 | Synthetic data integration in neurological research: Enhancing analysis accuracy and data privacy with EPICOSAI

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Background and Aims: Neurological research faces challenges such as data privacy concerns, small sample sizes, and complex datasets. Synthetic data offers a scalable solution, preserving confidentiality while replicating real-world data. The EPICOSAI platform integrates Monte Carlo simulations with statistical distributions—normal, binomial, Bernoulli, and exponential—to generate synthetic datasets. This study explores EPICOSAI's potential to address data limitations and improve neurological research outcomes.
Methods: Key statistical properties demographic data and clinical variables were extracted from real datasets to guide synthetic data generation. Monte Carlo simulations modeled continuous variables (e.g., age, mean = 65 years, SD = 7 years) using the normal distribution, binary outcomes biomarker presence, 60%) using the binomial distribution, and time-to-event data (e.g., relapse time, mean = 2.5 years) using an exponential distribution. Validation confirmed fidelity, with less than 5% deviation in key metrics such as mean and variance.
Results: Synthetic datasets expanded sample sizes from 100 to 10,000 patients, enabling robust modeling of rare neurological conditions. Machine learning models trained on synthetic data achieved 90–95% accuracy, comparable to real data models. These datasets facilitated simulations of clinical scenarios, such as treatment efficacy in Alzheimer's disease, overcoming real-world data limitations.
Conclusion: EPICOSAI provides scalable, privacy-preserving synthetic data solutions that address critical challenges in neurological research. By ensuring data reliability and enabling advanced analyses, EPICOSAI supports impactful and ethical studies, establishing itself as a transformative tool in neurology.
Disclosure: The authors acknowledge EPICOSAI for providing the tools and resources necessary for generating synthetic data and conducting the analyses presented in this study.

EPO-327 | Diagnostic value of the 'insular knife-cut' Sign in patients with suspected herpes simplex virus encephalitis

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Background and Aims: The "insular knife-cut" sign, a sharp demarcation between insular FLAIR abnormalities and basal ganglia on axial images, is associated with herpes simplex virus encephalitis (HSVE). We assessed its prevalence and diagnostic accuracy in a cohort of patients with suspected HSVE.
Methods: A multi-center, retrospective cohort of patients with suspected HSVE was carried out. Inclusion criteria were: (1) CSF sample tested with polymerase chain reaction for HSV-1/2; and (2) acute brain MRI. We evaluated the relationship between insular knife-cut sign and other clinical and radiological variables.
Results: A total of 188 patients were selected: 44 with HSVE, and 144 with alternative diagnoses (51 with autoimmune encephalitis; 22 with infectious encephalitis; 71 with other acute encephalopathies). The insular knife-cut sign was found in 53% cases of HSVE and in 1% with alternative diagnoses ($p < 0.001$) at baseline. Specificity and sensitivity of the sign were 99.3% (95% CI, 96–100) and 52% (95% CI, 38–66), respectively. In eight HSVE patients the insular knife-cut sign appeared on the subsequent MRI obtained acutely, increasing sensitivity to 70.5% (95% CI, 56–82). On multivariate regression, the insular knife-cut sign was the strongest independent predictor (odds ratio [95% CI]) of HSVE (42.4 [7.3–486.4]), followed by temporal pole involvement (12.9 [3.7–54.6]), abnormal brain MRI (7.4 [1.6–34.3]), and CSF pleocytosis (4.9 [1.4–19.4]).
Conclusion: Detection of the insular knife-cut sign on MRI strongly predicts HSVE diagnosis in patients with suspected acute encephalitis. This marker could help early diagnosis and

treatment of HSVE, especially when other diagnostic tests are equivocal/unavailable.
Disclosure: Nothing to disclose.

EPO-328 | Detection of microembolic signals in patients with carotid web

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Background and Aims: The mechanism by which the carotid web (CW) produces ischemic strokes is still not well understood. We describe the clinical characteristics and results of microembolic signal (MES) recording in a series of patients with CW and ischemic stroke or transient ischemic attack (TIA).
Methods: Patients admitted in our hospital between 2020 and 2024 with ischemic stroke or TIA and CW were identified. 60 minutes MES monitoring with transcranial Doppler (TCDX, Atys medical) was performed in MCA ipsilateral to CW.
Results: We included 9 patients, 5 women, 4 men. Median age 62 years (IQR 53 - 74). Six patients suffered an ischemic stroke and three a TIA. CW was bilateral in 3 patients, ipsilateral to the vascular event in 3 and contralateral (asymptomatic) in 3 (table 1). MES monitoring was positive in three patients, all women. In two of the three MES+ cases, the CW was ipsilateral to the event and contralateral in the remaining case (patient with atrial fibrillation). The etiologic diagnosis at discharge was undetermined in 5 cases, cardioembolic in two, and small vessel in two (table 2). Carotid revascularization was not performed in any patient. With a median follow-up of 8 months, no recurrences were recorded.

	Pt1	Pt2	Pt3	Pt4	Pt5	Pt6	Pt7	Pt8	Pt9
Age	57	53	58	81	62	90	62	45	74
Sex	Female	Female	Female	Male	Female	Female	Male	Male	Male
Hypertension	No	No	No	Yes	No	Yes	Yes	No	Yes
Diabetes	No	No	No	No	No	No	No	No	No
Hypercholesterolemia	Yes	No	No	No	No	Yes	No	No	Yes
Smoker	Former	Yes	Yes	No	No	No	Former	No	No
Ischemic heart disease	No	No	No	No	No	No	No	No	No
Atrial fibrillation	No	No	No	No	No	Yes	No	No	No
Clinical presentation	A. Fugax	Ischemic stroke	Ischemic stroke	Ischemic stroke	TIA	Ischemic Stroke	Ischemic stroke	TIA	Ischemic stroke
Carotid web location	Bilateral	Ipsilateral to the event	Ipsilateral to the event	Bilateral	Ipsilateral to the event	Contralateral to the event	Contralateral to the event	Bilateral	Contralateral to the event
Microembolic signals (number)	No	No	Yes (7)	No	Yes (12)	Yes (1)	No	No	No
Etiology	Undetermined	Undetermined	Undetermined	Cardioembolic	Undetermined	Cardioembolic	Small vessel	Undetermined	Small vessel
Treatment after the event	Single-antiplatelet	Single-antiplatelet	Single-antiplatelet	OAC	Single-antiplatelet	OAC	Dual-antiplatelet	Single-antiplatelet	Single-antiplatelet
Recurrence in follow-up	No	No	No	No	No	No	No	No	No

FIGURE 1 Characteristics of included patients

	MES + (n=3)	MES – (n=6)
Age, mean (SD)	70 (17,4)	62 (13,4)
M/F ratio	0/3	4/2
Hypertension	1	3
Diabetes	0	0
Hypercholesterolemia	1	2
Smoker	1	1 (2 formers)
Atrial fibrillation	1	0
Clinical presentation		
Ischemic stroke	2	4
TIA/ A. fugax	1	2
Etiology		
Undetermined	2	3
Small vessel	0	2
Cardioembolic	1	1
Carotid web location		
Bilateral	0	2
Ipsilateral to the event	2	1
Contralateral to the event	1	2
Treatment after the event		
Single-antiplatelet	2	4
Dual-antiplatelet	0	1
OAC	1	1

FIGURE 2 Characteristics according to the presence or absence of MES

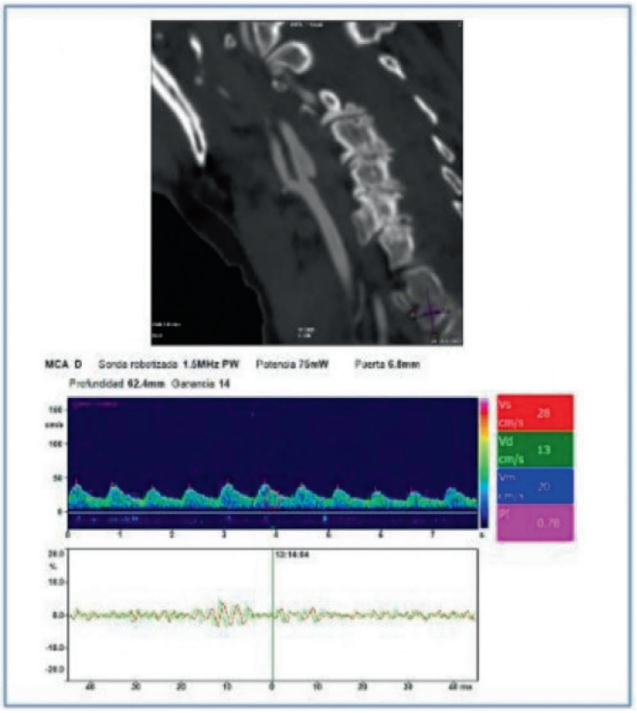

FIGURE 3 CTA showing a CW in right ICA. MES (9 dB, 17 ms) detected during right MCA monitoring

Conclusion: Previous studies have described a high recurrence risk in patients with CW, which contrasts with what was observed in this series. It is difficult to establish a causal relationship between CW and ischemic stroke. MES monitoring with TCD could help to better understand the mechanism of cerebral ischemia in patients with CW.
Disclosure: Nothing to disclose.

EPO-329 | MRI features of central nervous system involvement in 104 Moroccan patients with Neuro-Behcet's syndrome

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Background and Aims: Behçet's disease (BD) is a recognized as a chronic relapsing heterogeneous multisystem inflammatory disorder and a vasculitis of unknown origin which has a peculiar epidemiology. Neurologic involvement has been reported to be less common than other systemic manifestations, but can cause substantial disability.
Methods: This is a retrospective study of 104 patients presenting with BD and neurological involvement, collected over a period of 23 years. The MR images of patients with BD, associated with neural parenchymal involvement in 86 cases (82.7%) and CVT in 18 cases (17.3%) were reviewed.
Results: Concerning parenchymal CNS pattern, brain MR imaging (MRI) showed hypointense lesions on T1-weighted and hyperintense lesions on T2 and FLAIR-weighted images, involving mostly the brainstem (84.8%), basal ganglia (68.6%), cerebral white matter (53.4%), internal capsule (47.6%) and thalamus (46.5%). For the extraparenchymal pattern, the brain MRI results of our series showed that the venous involvement was isolated superior sagittal sinus (SSS) thrombosis in 8 patients (44.4%), isolated lateral sinus (LS) thrombosis in 4 patients (22.2%), and concomitant SSS and right lateral sinus thrombosis in 3 patients (16.6%).
Conclusion: Brain MRI study including contrast and MR angiography (MRA) especially MR venography (MRV), are mandatory in categorizing the neurological involvement and both should be used routinely in cases of suspected NBD.
Disclosure: Nothing to disclose.

EPO-330 | Altered hippocampal volume in patients with cognitive impairment associated with post-COVID-19 condition

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Background and Aims: The post-acute sequelae of the SARS-CoV-2 infection are known as Long COVID or Post-COVID-19 Condition (PCC) and often manifests neurocognitive symptoms. Understanding the mechanisms driving this cognitive impairment is crucial for accurately characterizing the disease and developing effective therapeutic interventions. This study aims to investigate volumetric changes with subfield hippocampal analysis in PCC patients, building on prior evidence of structural brain alterations to better understand the neuroanatomical basis of cognitive impairment.
Methods: A dataset of 60 age- and sex-matched PCC patients and 60 healthy controls (HC) was analyzed, with all PCC patients reporting cognitive deficits and reduced memory satisfaction based on MMQ scores. MRI scans were performed on all participants using a standardized protocol, and the data were processed with Freesurfer for hippocampal and amygdala subfield segmentation. Statistical analysis of hippocampal ROIs was conducted using ANCOVA, controlling for age, sex, and total intracranial volume, with false discovery rate (FDR) adjustments applied to *p*-values. Multiple regression was employed to explore the relationships between volumetric brain measurements, neurocognitive performance, and the presence of autoantibodies in the cerebrospinal fluid of PCC patients.
Results: Significant volume reductions were observed in the hippocampal body, particularly in the CA4, subiculum, and molecular layer bilaterally, with FDR-adjusted significance retained for the left CA3, dentate gyrus, and hippocampal fissure. No alterations were detected in the hippocampal head. Further modeling of imaging and clinical data is currently being conducted.
Conclusion: Reduced volume in several hippocampal body ROIs was found in PCC patients, suggesting susceptibility of the hippocampus to neuroinflammation following SARS-CoV-2 infection.
Disclosure: Nothing to disclose.

EPO-331 | Decision-making made easy: Algorithmic approach to fetal and neonatal ventriculomegaly

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Background and Aims: Ventriculomegaly (VM) is a common neurodevelopmental anomaly characterized by cerebral ventricular enlargement. As a non-specific sonographic finding, VM may be associated with a range of pathological and genetic conditions, making accurate diagnosis essential for appropriate prognosis and management. We aim to improve the differential diagnosis of VM by utilizing a structured, algorithmic approach which involves a step-by-step algorithmic framework that categorized etiology of VM based on imaging characteristics.
Methods: The diagnostic algorithm was developed through a systematic review of literature, analysis of clinical cases, and expert consultations. Imaging data from ultrasonography and magnetic resonance imaging (MRI) formed the basis for the algorithm's structured diagnostic flow. Key diagnostic steps included classifying the severity of VM, assessing associated anomalies, and categorizing potential etiologies. Validation was performed retrospectively on ten clinical cases, comparing algorithmic diagnoses with established clinical and imaging findings.

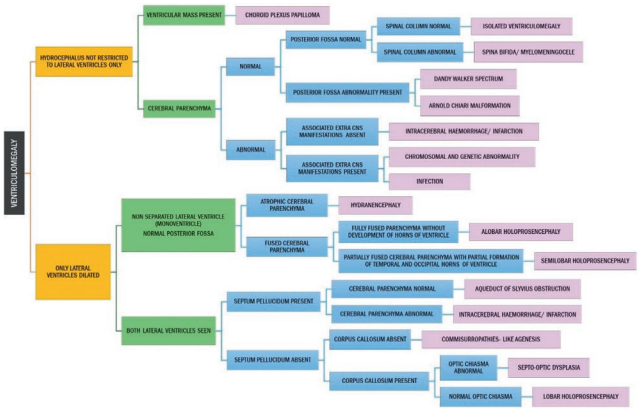

FIGURE 1 Designed Algorithm for Fetal and Neonatal Ventriculomegaly

Results: The algorithm facilitated precise identification of various etiologies of VM, including semilobar holoprosencephaly, Dandy-Walker malformation, intracerebral infarction, choroid plexus papilloma, corpus callosal agenesis, congenital infections (e.g., toxoplasmosis, cytomegalovirus), and congenital muscular dystrophy. Each diagnosis aligned with clinical and imaging findings, underscoring the algorithm's reliability.

Conclusion: This algorithmic approach offers a structured, evidence-based tool for the differential diagnosis of VM, enabling clinicians to navigate its complex etiological spectrum. By integrating detailed imaging analysis with clinical findings, the algorithm supports early and accurate diagnosis, improves prognostication, and facilitates timely interventions, ultimately optimizing outcomes for affected neonates, fetuses, and their families.

Disclosure: Nothing to disclose.

EPO-332 | Is the T1-w/T2-w marker affected by iron deposition in patients with secondary progressive multiple sclerosis?

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Background and Aims: MRI and histological studies have shown altered brain iron levels in the brains of patients with multiple sclerosis (MS). Quantitative Susceptibility Mapping (QSM) provides quantitative distribution of susceptibility sources in tissue, especially iron in ferritin or deoxygenated hem. The ratio of T1-w/T2-w images is a marker of microstructural damage in MS that might be affected by paramagnetic ions in the tissue.

Methods: 22 patients with a diagnosis of secondary progressive MS (EDSS: 6.1 ±1.1, 53.3 ±8.1 years, 9M, duration of disease 18.3 ±7.5 years) with various load of hypointense lesions on T1 and without enhancing lesions on MRI were included. High resolution T1-w and T2-w images were obtained at 3T. For QSM, a 3D multi-echo gradient-echo sequence (SWAN) was obtained (1 ×1 ×2 mm 39 TE values ranging from 4.5 to 48 ms). Susceptibility maps were calculated with MEDI. Regions of Interest (ROI) were outlined using SAMSEG.

Results: 12 patients had regions of increased susceptibility (Figure), among others 3 had rims (Figure 1), suggesting the presence of smoldering lesions. The corresponding mean values of T1-w/T2-w and susceptibility did not correlate in any ROI (e.g., Figure 2 and Figure 3).

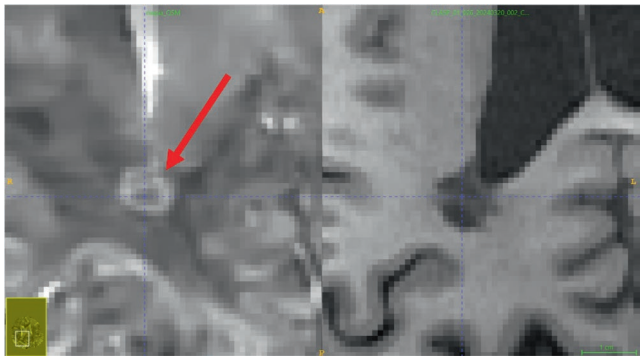

FIGURE 1 Exemplary rim on QSM suggesting presence of a smoldering lesion and corresponding anatomy on T1-w image.

Conclusion: The T1-w/T2-w ratio does not appear to be affected by tissue paramagnetic biometals, such as iron, associated with inflammatory states.

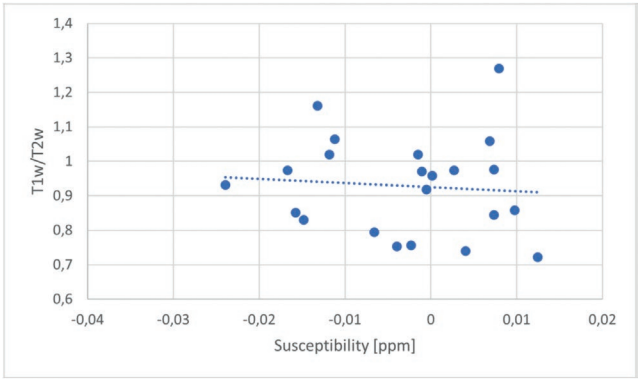

FIGURE 2 No correlation in White Matter Signal Hyperintensities.

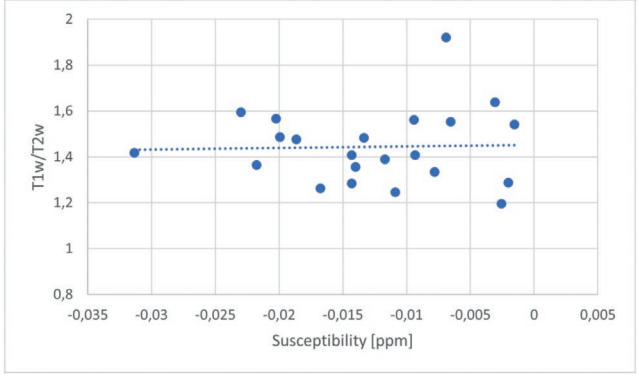

FIGURE 3 No correlation in Normal Appearing White Matter.

Disclosure: Nothing to disclose. This study was supported by Medical Research Agency of Poland, grant 2021/ABM/02/00002-00.

EPO-333 | Clinical and radiological correlations in patients with generalised epilepsy: A single center f-MRI study

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Background and Aims: In patients with generalized epilepsy (PwGE) there is a bidirectional correlation between seizure outcome and comorbidities .The aims of the study are: a) to analyze the clinical features of a sample of PwGE b) to investigate the functional connectivity by using resting state (rs-f-MRI) c) to highlighted clinical and (functional) radiological correlations.
Methods: we enrolled 31 PwGE, 16 SFp and 15 DREp (3), and 15 age-gender-matched healthy controls (HCs). We used an ANOVA to compare the groups of PwGE and HCs on demographic, clinical, cognitive, and behavioural features. Moreover, we compared by one-way ANOVA SFp and DREp subgroups with each other and the HCs. MRI at 3 Tesla was collected in all PwGE and HCs.
Results: DREp compared with SFp showed executive disfunction and behavioural abnormalities scoring worse to TMT and semantic fluency test, epitrack and apathy evaluation scale (AES). Moreover in DREp a reduction of functional connectivity of the limbic network (LN) and an increased functional connectivity of the salience network (SN) was detected. Correlation analyses showed a negative correlation between the scores to TMT test and LN functional connectivity; thus functional connectivity changes could represents a compensatory event to executive deficits in PwGE. Conversely a positive correlation between AES and SN connectivity was observed; this could represents an ineffective attempt to apathy.

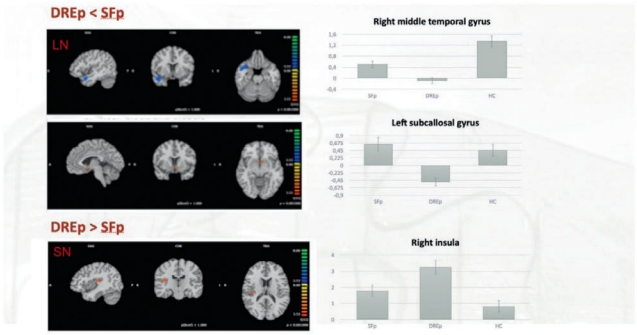

FIGURE 1 MRI functional connectivity abnormalities in patients with treatment-resistant generalized epilepsy (DREp) compared with seizure-free patients (SFp)

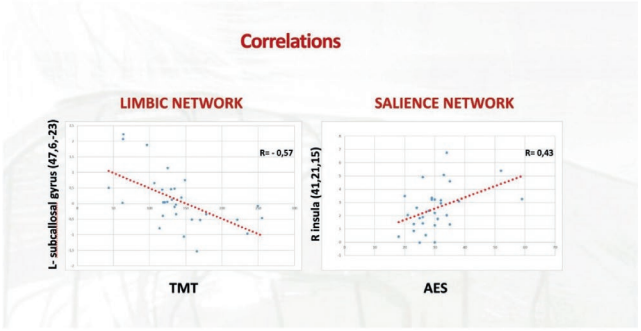

FIGURE 2 Clinical and radiological correlations

Conclusion: In our single center rs-fMRI study we confirmed both a bidirectional correlation between seizures outcome and cognitive/behavioural comorbidities and functional connectivity abnormalities between DREp and SFp. Moreover interesting clinical and radiological correlation were observed.
Disclosure: Nothing to disclose.

EPO-334 | AI-detected brain atrophy pattern associated with progression independent of relapse activity in multiple sclerosis

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Background and Aims: Progression independent of relapse activity (PIRA) represents the main driver of clinical disability accrual in multiple sclerosis (MS). Brain atrophy is the MRI outcome that better correlates with disease progression, however it is difficult to detect at a subject-level in the clinical practice. Also, its functional correlate still remains uncertain. The primary goal of this study was to identify the brain atrophy pattern (BAP) associated with PIRA using Artificial Intelligence (AI); secondarily, we aimed to assess the resting state functional connectivity (RS-FC) correlated to this pattern and its implications on clinical performance.
Methods: We included MS-patients treated with Natalizumab with PIRA ($n=14$) and clinically stable (CS) ($n=10$) disease. Patients underwent a motor/cognitive evaluation (EDSS/SDMT) and a brain MRI (MPRAGE,3D-FLAIR,RS-fMRI). Brain volumetrics was analyzed through an AI software (Pixyl) detecting global/regional atrophy. Comparisons of clinical/MRI volumetric measures between PIRA and CS groups were performed. We then assessed the RS-FC of PIRA-associated BAP through a seed-based analysis using CONN-toolbox.
Results: PIRA group showed a higher patients proportion with global/total WM atrophy than CS. No differences were found for total GM, however when analyzing the single GM regions, PIRA group showed a greater patients percentage with atrophy (88% vs. 40%; p-value = 0.03241) of the left thalamus compared to CS. Patients with left thalamus atrophy (leftTA) showed a RS-FC

alteration of the Default Mode Network(DMN) and a lower SDMT-score than those without leftTA.
Conclusion: AI enables to identify BAP associated to clinical phenotypes. PIRA is associated with leftTA, which correlates to a RS-FC alteration of the DMN, possibly linked to decreased cognitive performance.
Disclosure: Rinaldi V. has nothing to disclose Moltoni G. has nothing to disclose Le Mura L. has nothing to disclose Romano A. has nothing to disclose Buscarinu C. has nothing to disclose Salvetti M. has nothing to disclose Bozzao A. has nothing to disclose.

Neuro-oncology

EPO-335 | A rare neurological immune-related adverse event in a melanoma patient

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Background and Aims: Immune checkpoint inhibitors (ICI) are used as immunotherapy in different neoplasms. Neurological immune-related adverse events (nirAE) are rare. Of these, headache/hypophysitis (2–9%), neuromuscular disorders (0.5–2.5%), encephalitis (0.5–1%), meningitis (<0.5%) and demyelinating disease (<0.5%) are usually considered. Symptoms typically present 6-13 weeks after treatment initiation.
Methods: Case report.
Results: A 63-year-old woman with metastatic melanoma to the lymph nodes and lung (BRAF+) started nivolumab and ipilimumab. After 2 sessions, a rash, thyroiditis and grade 3 autoimmune hepatitis were identified. ICI were suspended and oral corticosteroids were administered for 8 weeks. Fourteen weeks after ICI start (11 weeks after stopping), the patient reported unsteadiness, and isolated gait ataxia was observed. Brain MRI showed multiple punctiform hyperintensities (1–5 mm size) in dark-blood and T2/FLAIR with gadolinium enhancement. Lumbar puncture revealed 13 lymphocytes/mm^3, without neoplastic cells, oligoclonal bands or antineuronal antibodies. Infectious serologies, MOG and AQP4 antibodies were negative. Clinical improvement was observed after another 6 weeks of corticosteroids. Melanoma treatment was switched to BRAF/MEK inhibitors. Brain MRIs showed a rapid regression of contrast enhancement and of most previous lesions (last MRI 12 months after symptom onset).
Conclusion: In this case, we hypothesize a nir-AE with multifocal and monophasic inflammatory/demyelinating lesions. Although brain metastases were the main differential diagnosis, concomitant lymphocytic meningitis and systemic immune-related adverse events strongly support that diagnosis. Neurological complaints may have initially been masked by steroids for the first ir-AEs.
Disclosure: Nothing to disclose.

EPO-336 | Bridging neurology and oncology: Unraveling the complexities of primary central nervous system lymphoma

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Background and Aims: Primary central nervous system lymphomas are rare and, usually, with very poor prognosis. In these cases, the most described subtype is diffuse large B cell lymphoma. We intend to explore the clinical presentations of such cases.
Methods: Description of cases diagnosed with this pathology observed in neurology hospitalization regimen.
Results: We obtained nine cases. Five were confirmed as primary central nervous system lymphomas. No biopsy was performed in the others. Considering the confirmed ones, the clinical presentation was variable: motor deficits or gait impairment if brain located ones; headaches and peripheral face palsy in brainstem located one and, finally, a cauda equina lymphoma presented with progressive paraparesis. The lymphoma subtype confirmed in all was diffuse large B cell lymphoma. Two of them were treated with high dose methotrexate, meanwhile the two most recent ones were treated with MATRIX regimen. As for the non-confirmed cases, they presented with state of consciousness alterations, motor deficits or gait impairment. Three of them didn't perform biopsy considering their poor neurological status; one due to its difficult location. The only treatment performed was corticosteroids. The first group had a mean lifetime between diagnosis and obit of 1.75 months, while the other had a mean of 4.75 months. The patient diagnosed with cauda equina lymphoma is still alive and regained autonomous walk.
Conclusion: Despite the small sample, these cases show the challenges regarding this diagnosis considering its phenotypic variability. The poor prognosis associated highlights the extreme importance of an early diagnosis, allowing timely beginning of the treatment.
Disclosure: Nothing to disclose.

EPO-337 | Acute neurological sequelae in leptomeningeal carcinomatosis cases

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Background and Aims: Leptomeningeal carcinomatosis (LMC) is a neurological complication of various systemic cancers.
Methods: The data were retrospectively collected from the hospital database with patient consent.
Results: A 60-year-old female patient with a diagnosis of breast cancer who was receiving pembrolizumab presented with speech impairment. On examination, her speech was dysarthric, and her gait was ataxic. Cranial MRI findings were normal

except for cerebral atrophy. She was admitted with a preliminary diagnosis of autoimmune cerebellitis and leptomeningeal disease. Lumbar puncture (LP) was performed. CSF glucose was low, and microprotein and microalbumin levels were elevated. CSF cytology showed suspicious results. The patient received radiotherapy with a preliminary diagnosis of leptomeningeal involvement and immune-related encephalitis. A 51-year-old female with a diagnosis of metastatic breast cancer presented with complaints of dizziness. Diffusion MRI revealed diffusion restriction, and she was subsequently admitted to the hospital. During follow-up, her consciousness deteriorated. A lumbar puncture (LP) was performed. CSF glucose levels were low, and malignant cells were observed in the CSF cytology. Control MRI showed contrast uptake in the cerebellum. The diagnosis of leptomeningeal carcinomatosis was confirmed.

Conclusion: Headache is the most common symptom of leptomeningeal carcinomatosis, with various neurological signs present. CSF cytology and imaging techniques are crucial for early diagnosis.In patients with a history of breast cancer presenting with stroke-like neurological symptoms, leptomeningeal carcinomatosis should be considered in the differential diagnosis.In patients with a history of breast cancer presenting with stroke-like neurological symptoms, leptomeningeal carcinomatosis should be considered in the differential diagnosis.

Disclosure: Nothing to disclose.

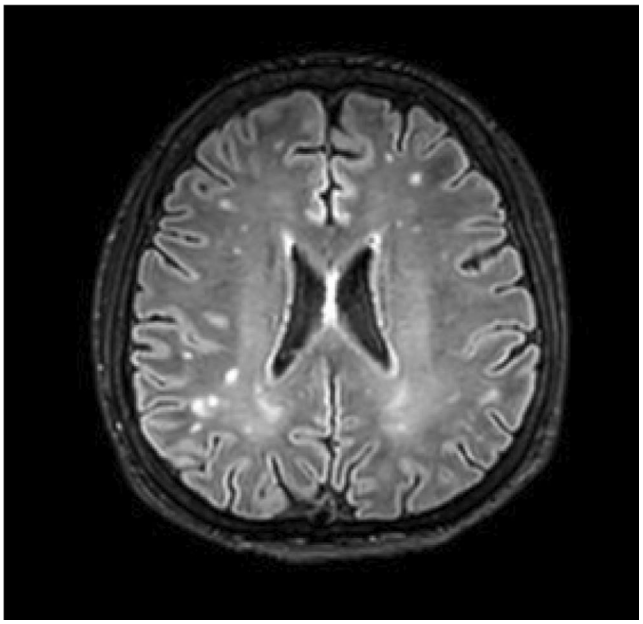

FIGURE 1 Patient 1. Parenchymal lesions in both cerebral hemispheres, asymmetric, FLAIR hyperintense with an inflammatory appearance.

EPO-338 | Description of 2 cases of intravascular large B-cell lymphoma (IVLBCL) with CNS involvement: A diagnostic challenge

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Background and Aims: IVLBCL is a rare form of lymphoma, characterized by intravascular proliferation of lymphomatous cells, obstructing small and medium-sized vessels. Neurological signs are diverse but present in up to 2/3 of patients and generally accompanied by constitutional symptoms. There are no specific laboratory or radiological findings, and histopathological diagnosis is required, unfortunately with autopsy in many cases.

Methods: We retrospectively analysed data from 2 patients diagnosed with IVLBCL in Hospital General Universitario Doctor Balmis in 2024. 1. A 66-year-old woman, history of pulmonary tuberculosis 20 years ago. Constitutional symptoms and post-infectious paraparesis. MRI showed inflammatory ADEM like lesions in the brain and conus medullaris. 2. A 68-year-old woman, anticoagulated atrial fibrillation. Recurrent hospital admissions with encephalopathy and focal signs. MRI showed multiterritorial diffusion-restricted lesions.

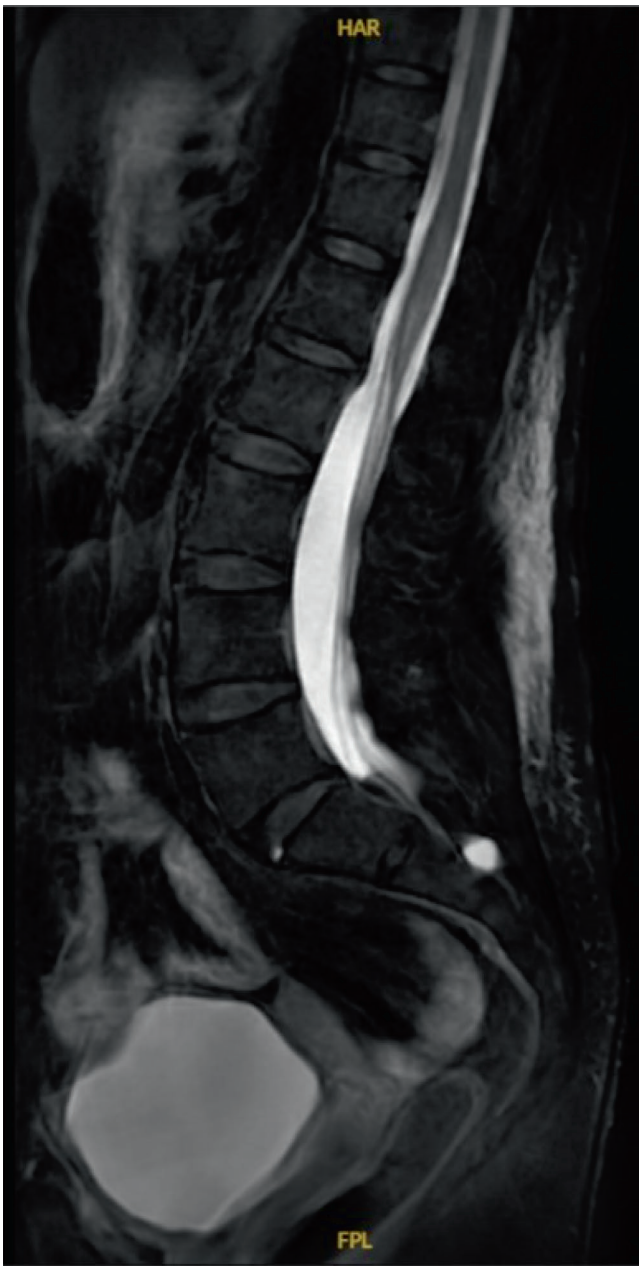

FIGURE 2 Patient 1. Signal alteration of the conus medullaris, hyperintense on T2, involving the territory from T12 to L1, with central localization.

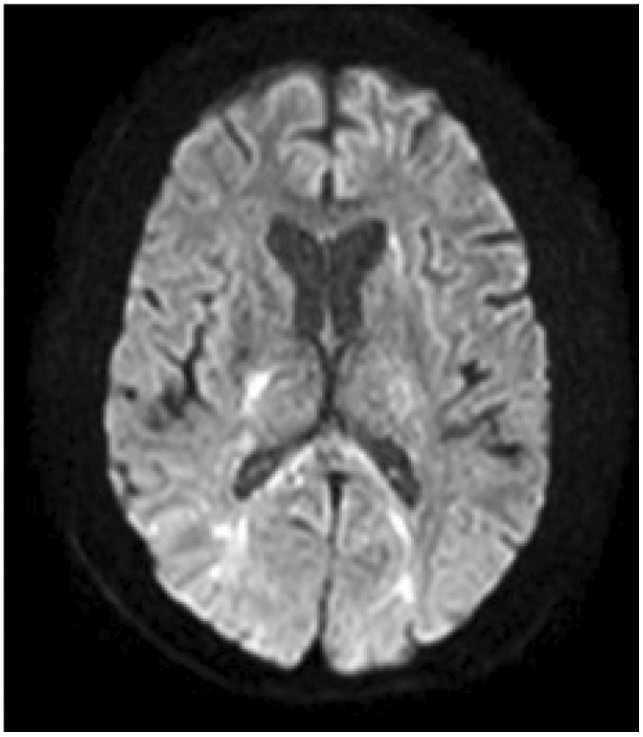

FIGURE 3 Patient 2. Multiple areas of bilateral diffusion restriction, temporo-occipital, in the corpus callosum and right basal ganglia, suggestive of ischemic foci of cardioembolic etiology.

Results: An extensive blood and CSF analitical study was negative (immunological, infectious, tumor markers, flow citometry...) in both. 1. CSF: mild hyperproteinorrachia. Body PET-CT: chronic inflammatory lung changes. Clinico-radiological improvement after high dose corticosteroids but worsening after tapering. New pulmonary infiltrates and mediastinal lymphadenopathy observed on PET-CT. Lung biopsy confirmed the histopathological diagnosis of IVLBCL. 2. CSF: lymphocytic pleocytosis and mild hyperproteinorrachia. Body PET-CT and vessel-wall MRI showed no evidence of vasculitis. Brain biopsy of the right parietal lession confirmed the histopathological diagnosis of IVLBCL.
Conclusion: Neurologists must be aware of IVLBCL in patients with recurrent inflammatory or ischemic multifocal lesions with inadequate response to treatment. Early histopathological diagnosis and treatment are crucial in this fatal condition.
Disclosure: Nothing to disclose.

EPO-339 | Diagnosis and treatment of gestational hemangioblastoma: A systematic review of case reports and case series

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Background and Aims: Tumor occurrence during pregnancy is rare, with breast cancer being the most common type. Hemangioblastomas in pregnancy, though less studied than meningiomas and gliomas, pose significant diagnostic and management challenges due to overlapping symptoms and the complexity of timing tumor resection. This study systematically reviews the clinical features, diagnostic implications, and maternal and fetal outcomes of hemangioblastoma in pregnant females, drawing on case reports and series.
Methods: A comprehensive search was conducted in PubMed, Scopus, WOS, and Cochrane databases from inception to November 2024. Screening identified 81 case reports and series papers, encompassing 116 pregnant females.
Results: The mean maternal age was 31.72 ±6.27 years, and the mean gestational age at diagnosis was 20.18 ±8.63 weeks. Among 116 cases, 42 patients were multigravida, and 58 had von Hippel-Lindau syndrome. Hemangioblastomas were predominantly infratentorial (74 cases), with 62 central lesions, including 37 in the brain and 20 in the spine, primarily in the cerebellum (30 cases). Headache was the most common symptom (33 cases), followed by weakness (15 cases) and vomiting (14 cases). MRI was the primary diagnostic tool (83 cases). Obstetric complications were underreported, with a low mortality rate of one miscarriage and three preterm deliveries. Neurological outcomes improved in 50 patients, with only three deaths recorded.
Conclusion: Management strategies should be individualized, considering the patient's neurological status and gestational age. Symptomatic management is common, especially for spinal hemangioblastomas, while urgent tumor resection can be performed safely with thorough maternal and fetal monitoring.
Disclosure: Nothing to disclose.

EPO-340 | Emerging therapeutic strategies for leptomeningeal metastases: Targeting the tumor microenvironment and immune evasion

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Background and Aims: Leptomeningeal metastases (LM) are a severe complication of advanced malignancies, characterized by the dissemination of cancer cells to the leptomeninges and cerebrospinal fluid (CSF). Prognosis remains dismal, with median survival ranging from 2 to 6 months. Traditional treatments like radiotherapy and systemic chemotherapy have shown limited success. Recent advances in understanding the tumor microenvironment and immune evasion mechanisms have led to the development of novel therapeutic strategies.
Methods: A review of studies published between 2015 and 2024 was conducted, including clinical trials, observational studies, and preclinical research. Data sources included PubMed, ClinicalTrials.gov, and oncology conference proceedings. Outcomes assessed were overall survival (OS), progression-free survival (PFS), response rates, and adverse events.
Results: Intrathecal immune checkpoint inhibitors, such as nivolumab, improved median OS to 7.5 months compared to 4.2 months with standard care (HR: 0.65; $p=0.002$). Nanoparticle-based drug delivery systems increased CSF drug concentrations by 30%, extending PFS by 2.8 months ($p=0.01$). CSF microenvironment modulation through CXCL12/CXCR4 axis targeting reduced CSF tumor cell count by 25% ($p=0.005$). Adverse events were mostly mild (grade 1–2), with no significant increase in severe events ($p=0.45$).
Conclusion: Therapies targeting the tumor microenvironment and immune evasion offer promising strategies for LM. Intrathecal immunotherapies and advanced drug delivery systems show potential to improve survival outcomes. Large-scale trials are essential to confirm these findings and inform clinical practice.
Disclosure: No disclosure is to be made

EPO-341 | Isolated cranial hypertrophic pachymeningitis as the sole manifestation of mantle cell lymphoma

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Background and Aims: Mantle cell lymphoma (MCL) constitutes approximately 5% of non-Hodgkin lymphomas, typically presenting with generalized lymphadenopathy and extranodal involvement. CNS involvement in MCL is rare and associated with poor prognosis.
Methods: We report a 62-year-old immunocompetent female presenting with a two-week history of headaches, dizziness, vertigo, slurred speech, and blurry vision.
Results: Imaging revealed diffuse dural thickening. Histopathological examination confirmed MCL infiltrating the dura mater, presenting as hypertrophic pachymeningitis.
Conclusion: This case represents the first documented instance of hypertrophic pachymeningitis as the sole manifestation of MCL. This case underscores the importance of considering MCL in differential diagnoses of hypertrophic pachymeningitis and highlights the diagnostic value of dural biopsy in such atypical presentations.
Disclosure: Nothing to disclose.

EPO-342 | Microsurgery vs. radiotherapy for vestibular schwannoma: A systematic review and meta-analysis

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Background and Aims: Vestibular schwannomas are benign tumors arising from Schwann cells of the vestibulocochlear nerve. Treatment options include microsurgical resection (MS), which offers immediate tumor removal but carries risks such as cranial nerve deficits and prolonged recovery, and stereotactic radiosurgery (SRS), a minimally invasive approach like Gamma Knife or CyberKnife, designed to control tumor growth with reduced morbidity. While SRS is associated with improved

auditory preservation and fewer complications, comparative data on short-term outcomes, particularly within a one-year follow-up, remain limited.

Methods: A systematic search of the Cochrane Library, Embase, and MEDLINE was conducted through December 2024. Data extraction included study design, population characteristics, interventions, and outcomes. Risk of bias was assessed using the Cochrane Risk of Bias 2.0 tool. A random-effects meta-analysis was performed using R software (v4.3.1), with heterogeneity quantified by the I^2 statistic and publication bias assessed via funnel plots.

Results: From 1,319 records, 4 studies met inclusion criteria, analyzing 199 MS-treated and 239 SRS-treated patients. MS was associated with better hearing preservation rates (OR 0.55, 95% CI 0.36–0.84, I^2 =92%) and lower incidences of tinnitus (OR 0.84) and deafness (OR 0.72). SRS reduced vertigo (OR 0.69) and headaches (OR 1.37). Heterogeneity across outcomes was noted.

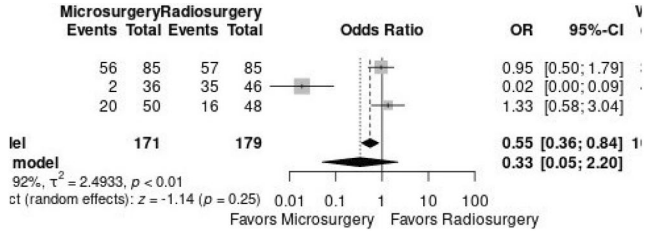

FIGURE 1 Forest plots of the meta-analysis on the proportion of patients with hearing serviceable after radiosurgery and microsurgery treatment.

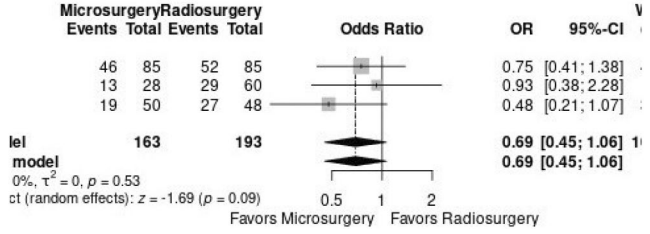

FIGURE 2 Forest plots of the meta-analysis on the proportion of patients with vertigo after radiosurgery and microsurgery treatment.

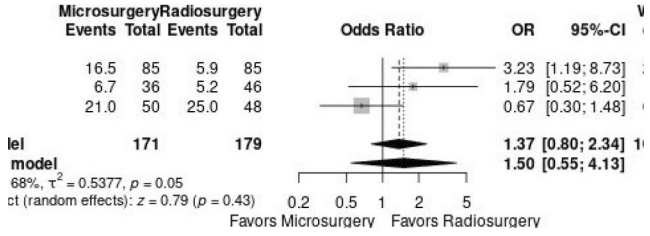

FIGURE 3 Forest plots of the meta-analysis on the proportion of patients with headache after radiosurgery and microsurgery treatment.

Conclusion: Both treatments offer specific benefits, highlighting the importance of individualized strategies for acoustic neuromas. Further high-quality studies are needed to confirm these findings and guide clinical decision-making.

Disclosure: Nothing to disclose.

EPO-343 | When the storm recedes and returns: Reactivation of ICANS in CAR-T therapy and the critical role of timely intervention

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Background and Aims: Immune effector cell-associated neurotoxicity syndrome (ICANS) is a recognized complication of CAR-T therapy, primarily presenting with neurological symptoms. Although most cases occur early, delayed onset or reactivation of ICANS can pose significant challenges to recovery. This report describes a case of ICANS reactivation in a patient treated with CAR-T therapy, with emphasis on its clinical progression, diagnostic findings, and management strategies.

Methods: A 39-year-old woman with grade IV follicular lymphoma underwent CAR-T therapy on September 17 without immediate complications. Five days later, she developed aphasia and altered consciousness, necessitating ICU admission. Corticosteroid therapy resulted in significant improvement, and she was discharged. On December 22, she was readmitted with fever, renal failure, and hypoxia. Respiratory and renal function deteriorated but improved with methylprednisolone. Two days later, she experienced three tonic-clonic seizures.

Results: CT imaging was unremarkable. Lumbar puncture revealed an opening pressure of 27 mmHg, no evidence of infection, and elevated IL-6 at 6.7 pg/mL. MRI demonstrated asymmetric vasogenic cerebral edema involving supratentorial and infratentorial regions. Corticosteroid therapy escalation led to marked neurological improvement.

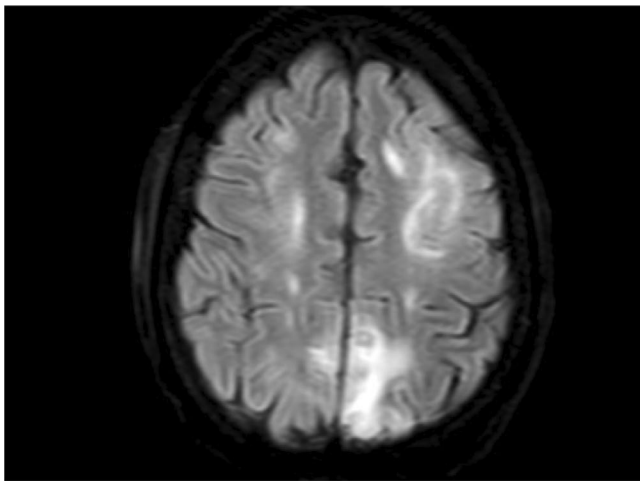

FIGURE 1 Bilateral parasagital hypersignal noted, FLAIR.

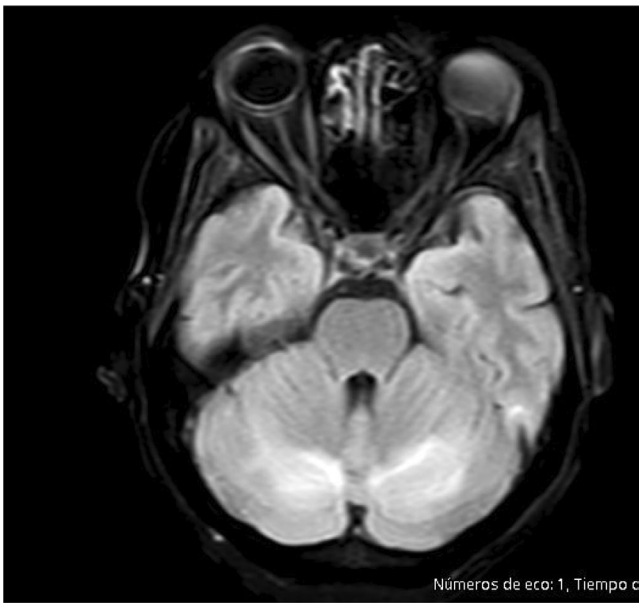

FIGURE 2 Hypersignal in both cerebellar hemispheres, FLAIR.

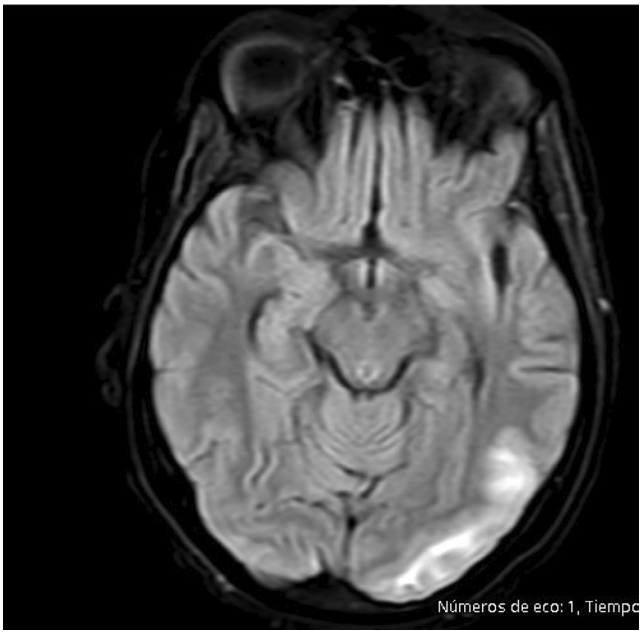

FIGURE 3 Left temporoocipital hypersignal, FLAIR.

Conclusion: This case highlights the reactivation of ICANS following CAR-T therapy. While ICANS and posterior reversible encephalopathy syndrome (PRES) share overlapping features, key differentiators include the patient's CAR-T history, elevated inflammatory mediators (e.g., IL-6), and multisystem involvement (respiratory, renal, cardiovascular). Prompt corticosteroid escalation is crucial for ICANS management. Antiepileptics may be used prophylactically or therapeutically, while tocilizumab is indicated only for severe cytokine release syndrome (CRS).
Disclosure: Nothing to disclose.

EPO-344 | The immune landscape of brain tumors: Implications for neuroimmunology and neuro-oncology therapies

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Background and Aims: The intersection of neuroimmunology and neuro-oncology is an emerging field that investigates how the immune system influences brain tumor progression and how tumors evade immune detection. Brain tumors, including gliomas, glioblastomas (GBMs), and metastatic cancers, create an immunosuppressive environment that aids tumor growth and resistance to therapies. This review explores the complex relationship between the immune system and brain tumors, focusing on immune cells like microglia, macrophages, T cells, and dendritic cells, and their roles in either supporting or inhibiting tumor progression. We also discuss promising immunotherapies that target the tumor microenvironment, including immune checkpoint inhibitors, adoptive T-cell therapy, and oncolytic viruses.
Methods: We conducted a systematic review of recent studies from 2015 to 2023, sourced from PubMed and Scopus. The review includes clinical trials, preclinical studies, and key articles on immune-tumor interactions, immune evasion, and immunotherapy for brain tumors.
Results: Our findings show that brain tumors manipulate their microenvironment to suppress immune responses, using mechanisms like immune checkpoint activation and recruitment of immunosuppressive cells. Although immune checkpoint inhibitors and adoptive T-cell therapies show potential, their clinical efficacy remains limited. Emerging combination therapies that integrate immune modulation with traditional treatments like chemotherapy and radiation offer new possibilities for improved outcomes.
Conclusion: A deeper understanding of immune-tumor interactions is crucial for developing effective treatments. Combining immunotherapy with conventional therapies could lead to better outcomes for patients with aggressive brain cancers like GBM.
Disclosure: Nothing to disclose.

EPO-345 | Spinal metastasis in pleomorphic liposarcoma: A rare location for a rare malignancy

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[1]Institute of Medical Scineces, Banaras Hindu University, Varanasi, India; [2]Mahamana Pandit Madan Mohan Malaviya Cancer Centre & Homi Bhabha Cancer Hospital, Varanasi, India

Background and Aims: Soft tissue sarcoma (STS) are rare mesenchymal tumors, originating from the non-epithelial connective tissue. The most common subtype of liposarcoma is well differentiated and dedifferentiate liposarcoma. Abdominal wall is a rare site of origin of liposarcoma.
Methods: NA.
Results: We present a rare case of 58-year-old male presented with painless lump in left side lower abdomen for five months. Histopathological examination and immunohistochemistry of biopsy from the lump confirmed the diagnosis of

dedifferentiated liposarcoma (vimentin and MDM2 strongly positive). 18FDGPET CT findings confirmed it to it to be a localized disease, FDG avid heterogeneously enhancing soft tissue mass with central necrosis noted at subcutaneous plane of left iliac fossa at anterior abdominal wall abutting anterior abdominal wall muscle with peripheral fat stranding measuring 6.5(AP) × 5.3(T) × 6.0(CC) cm (SUV max-13.41). Patient underwent wide excision of mass and followed by adjuvant radiotherapy. Within a week of completion of radiotherapy patient developed acute backache and pain was radiating to lower back. Patient soon within a week developed acute paraparesis. MRI dorso-lumbar spine revealed altered marrow signals with soft tissue component of D10 vertebra level, reaching into spinal canal and causing cord compression likely metastatic lesion.

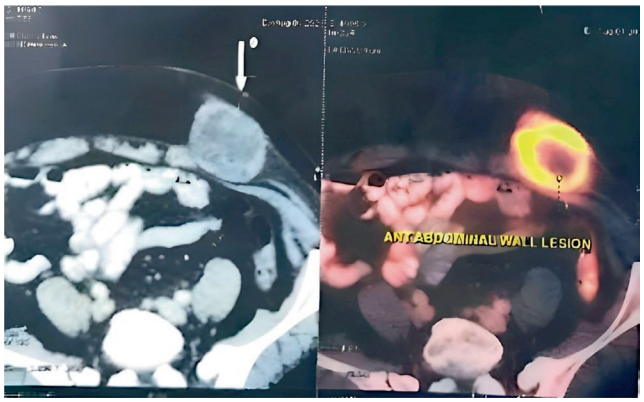

FIGURE 1 CECT abdomen showing well-defined oval hypodense lesion of size 5.3 × 5.2 × 4.2 cm seen in deep subcutaneous plane of anterior abdominal wall with maintained fat plane. (b) FDG avid heterogeneously enhancing soft tissue mass with central necrosis.

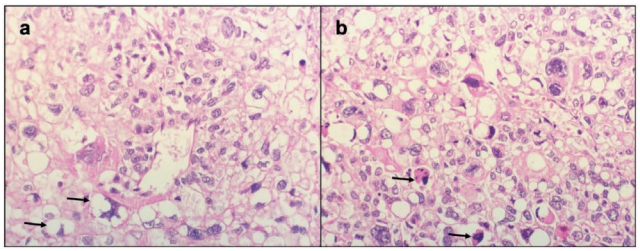

FIGURE 2 shows sheets of tumor cells having marked nuclear pleomorphism. Cells have an abundant amount of clear cytoplasm. Scattered lipoblasts are noted (arrow), [H&E, 40×] (b) Numerous bizarre tumor cell nuclei are noted along with frequent multinucleated tumor

Conclusion: This unique case of localized abdominal wall dedifferentiated liposarcoma showed early dissemination to D10 vertebra and patient landed with acute paraparesis. Meticulous clinical examination and aid of MRI helped in earliest possible diagnosis. Patient received palliative radiotherapy to involved site of vertebra.

Disclosure: Nothing to disclose.

EPO-346 | Cognitive outcomes of sterotactic radiosurgery vs. stereotactic radiotherapy in skull base meningioma patients

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Background and Aims: Meningiomas are the most common primary intracranial tumors, with their localization at the skull base posing a significant clinical challenge. While surgery is considered the gold standard treatment for meningiomas, alternatives such as stereotactic radiosurgery (SRS) and stereotactic radiotherapy (SRT) have emerged as less invasive and effective options. However, their long-term cognitive impacts remain incompletely understood.

Methods: This study aimed to compare the effects of SRS and SRT on cognition in patients with skull base meningiomas, providing evidence to guide more informed therapeutic decisions that balance oncological efficacy with the preservation of quality of life. A quantitative, comparative, and prospective analysis was conducted at two tertiary care hospitals in São Paulo, Brazil. Cognitive evaluation included the Trail Making Test B (TMT-B), administered pre-treatment and repeated at 1 and 2 years post-treatment, and the Brief Visuospatial Memory Test – Revised (BVMTR-R), conducted at 6 and 18 months post-treatment.

Results: The study sample consisted of 57 patients with skull base meningiomas, with 54.4% treated with SRT and 45.6% with radiosurgery RS. No statistically significant changes were observed in the cognitive test results or quality-of-life scores over time or between the two groups.

Conclusion: The results indicate that both SRS and SRT are equally effective and safe for preserving cognition in patients with skull base meningiomas, particularly in the domains of focused and alternating attention as well as visuospatial memory.

Disclosure: Nothing to disclose.

EPO-347 | Innovations in biomarker discovery for DMD: A systematic review of current research trends

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Background and Aims: Duchenne muscular dystrophy (DMD) is a debilitating genetic disorder characterized by progressive muscle degeneration. Biomarkers play a critical role in advancing DMD management by facilitating early diagnosis, monitoring disease progression, and evaluating treatment responses. Recent advancements in biomarker discovery offer

potential for improving patient care and accelerating therapeutic development.

Methods: A systematic search of PubMed, Embase, and Cochrane Library identified studies published up to 2024 that investigated biomarkers for DMD. Eligible studies included preclinical and clinical research evaluating biomarker utility in diagnosis, prognosis, and therapeutic monitoring. Data were synthesized to highlight current trends and key findings.

Results: Analysis of 30 studies identified promising biomarkers, including serum creatine kinase as a traditional diagnostic marker and microRNAs (e.g., miR-206 and miR-1) for monitoring muscle damage. Imaging biomarkers such as MRI-based fat fraction quantification provided insights into disease progression. Novel biomarkers, including dystrophin quantification and inflammatory cytokines, demonstrated potential for evaluating treatment responses in clinical trials. Limitations included variability in biomarker standardization and validation.

Conclusion: Innovations in DMD biomarker discovery are transforming disease management by enabling precise monitoring and personalized therapeutic strategies. Continued research is essential to validate novel biomarkers and integrate them into clinical practice, advancing outcomes for patients with DMD.

Disclosure: Nothing to disclose.

EPO-348 | Primary CNS lymphoma with simultaneous brain and spinal cord involvement: A challenging rarity

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Background and Aims: Primary central nervous system (CNS) lymphoma is a rare and aggressive neoplasm. Known risk factors include advanced age, immunosuppression, and Epstein-Barr virus (EBV) infection. They are mostly diffuse large B-cell lymphomas with predominant brain involvement.

Methods: Case report.

Results: A 50-year-old female patient, with known hypothyroidism and atrophic gastritis treated accordingly, developed a two-month history of constitutional symptoms followed by psychomotor slowing, dysphagia, constipation, limb paresthesia, muscle weakness, and loss of walking ability. Brain MRI showed bilateral T2 and T2/FLAIR hyperintense thalamic lesions without diffusion restriction or gadolinium enhancement, and spinal cord lesions from C5 to D11. Laboratory results revealed positive EBV IgG serology and cerebrospinal fluid (CSF) pleocytosis. The remaining infectious study was unremarkable, and neuronal surface, anti-AQP4, and anti-MOG antibodies were negative. No CSF oligoclonal bands were detected. CSF cytology and immunophenotyping were normal. PET imaging showed diffuse brain hypometabolism and mild hypermetabolism in the cervical spinal cord. The patient underwent treatment with methylprednisolone, human immunoglobulin, plasmapheresis and rituximab. Despite imaging improvement of the spinal lesions, the brain lesions further expanded and there was clinical deterioration to coma. Brain biopsy confirmed a diffuse large B-cell primary CNS lymphoma. Palliative care was prioritized, and the patient passed away five months after symptom onset.

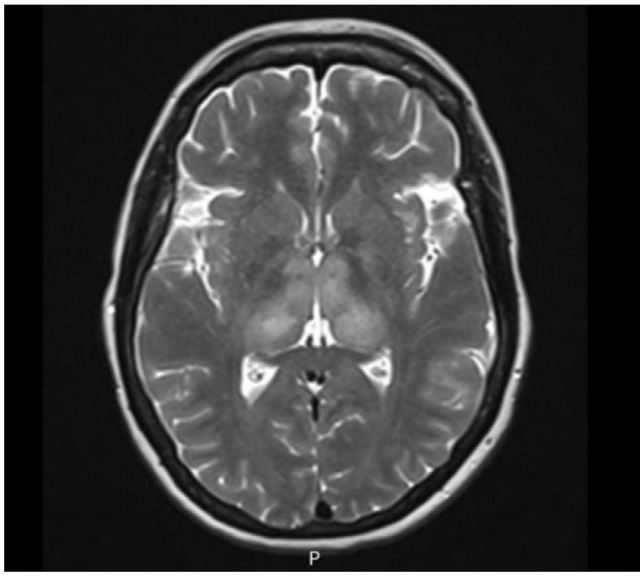

FIGURE 1 Brain lesions in MRI T2 sequence

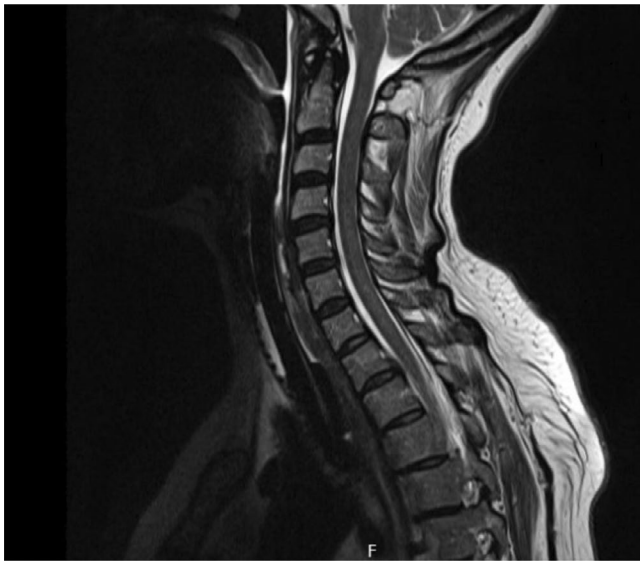

FIGURE 2 Spinal cord lesions in MRI T2 sequence

Conclusion: This case highlights the diagnostic challenges posed by a rare presentation of primary CNS lymphoma. It also notes the importance of multidisciplinary collaboration to ensure a timely diagnosis and improved survival for these patients.

Disclosure: Nothing to disclose.

EPO-349 | Management of adult-onset paraneoplastic opsoclonus-myoclonus ataxia syndrome: Results from a "meta-cohort"

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Background and Aims: Treatment guidelines of adult-onset paraneoplastic opsoclonus-myoclonus-ataxia syndrome (pOMAS) are limited compared to paediatric cases, owing to its rarity and heterogeneous pathogenesis. We aim to systematically review individual cases of adult-onset pOMAS to evaluate treatment efficacy.

Methods: We searched MEDLINE, SCOPUS and Web of Sciences through October 2024 with synonyms for "opsoclonus-myoclonus-ataxia syndrome". Individual patient data were extracted from eligible pOMAS case reports/series. For analysis we grouped treatment into tumour-directed (TD) and immunotherapy (IT). We dichotomised outcomes as clinical improvement or no benefit (relapse/non-response) and used univariable and multivariable logistic regression models, adjusting for age and sex.

Results: We included 101 articles, pertaining to 141 patients. Lung cancer was the most common malignancy (52/141, 36.9%). Outcome was reported in 134 patients. Clinical improvement after any treatment was demonstrated in 91/134 patients (67.9%). TD and IT combination demonstrated significantly greater efficacy than IT alone (OR = 3 [1.09–8.38], $p = 0.034$). However, this finding was not sustained in multivariable analysis, with age being the sole significant predictor of clinical improvement (OR = 0.95 [0.92–0.99], $p = 0.007$). Gynecological- and breast-cancer-associated pOMAS was more likely to present clinical improvement (OR = 3.1 [1.11–9.66], $p = 0.03$ and OR = 4.44 [1.43–16.99], $p = 0.01$, respectively).

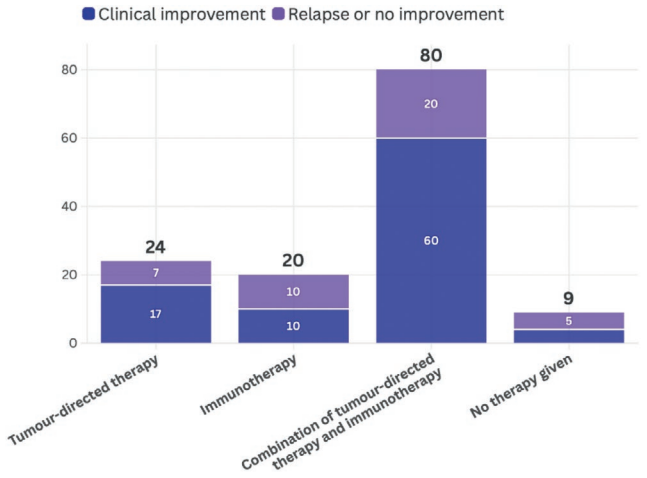

FIGURE 1 Tumour-directed treatment and immunotherapy combination demonstrated significantly greater efficacy than IT alone (OR = 3 [1.09–8.38], $p = 0.034$) in univariable analysis.

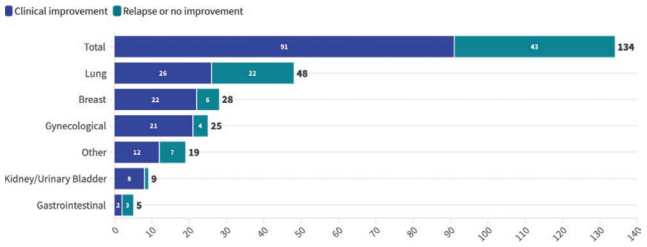

FIGURE 2 Patients with gynaecological or breast cancer were more likely to present clinical improvement of OMAS symptomatology compared to patients with lung cancer (OR = 3.1 [1.11–9.66], $p = 0.03$ and OR = 4.44 [1.43–16.99], $p = 0.01$, respectively).

	Univariable Analysis			Multivariable Analysis		
Variables	OR	95% CI	*p* value	OR	95% CI	*p* value
Sex (Male/Female)	0.49	0.23, 1.03	0.06	0.71	0.31, 1.66	0.49
Age	0.94	0.91, 0.98	**.001**	0.95	0.91, 0.98	**.007**
Treatment						
None / IT	0.8	0.16, 3.91	0.78	0.60	0.60, 1.10	.55
TD / IT	2.42	0.71, 8.74	0.16	1.97	0.54, 7.41	.30
TD and IT / IT	3.00	1.08, 8.38	**0.03**	1.91	0.65, 5.64	.23

Table 1: Logistic regression models for clinical symptomatology improvement in patients with paraneoplastic opsoclonus-myoclonus-ataxia syndrome

OR: Odds Ratio, CI: Confidence Intervals, TD: tumour-directed therapy, IT: immunotherapy

Conclusion: We present the largest "meta-cohort" of adult-onset pOMAS. Despite indications for the superiority of TD and IT combination over IT alone, prognosis is mostly influenced by age and cancer type. Limitations related to study design and missing data, highlight the need for future registry-based studies.

Disclosure: Nothing to disclose.

EPO-350 | Abstract withdrawn

EPO-351 | 2years of experience from the administration of adecanumab in a 33-year-old patient with genetic AD

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Background and Aims: Aducanumab was the first etiological treatment for Alzheimer's disease (AD). It is a recombinant monoclonal antibody that targets beta-amyloid plaques, though its results so far have been controversial. We present our two-year experience with the infusions of this new treatment in a 35-year-old patient.
Methods: Case presentation.
Results: We present a 33-year-old patient with no family history of AD, who was examined in the Emergency Department in January 2021 after an episode of generalized seizures. The neurological examination revealed significant impairment of higher cognitive functions, with ideomotor apraxia being the most prominent feature. Her relatives reported behavioral disturbances and difficulty with work demands for approximately three years. Neuropsychological testing showed moderate cognitive decline, while Brain MRI revealed generalized cortical atrophy. The biological markers in the CSF indicated Alzheimer's disease, and genetic testing revealed a pathogenic mutation in PSEN1. After approval from the Geek National Organization for Medicines, treatment with Aducanumab (Aduhelm) was initiated, with one infusion per month and gradual titration, starting with the first dose in August 2021. She has received a total of 24 doses. She has tolerated the treatment without any adverse effects, and follow-up MRI scans have shown no imaging findings related to β-amyloid destruction (Amyloid-Related Imaging Abnormalities), either in the form of hemorrhages (ARIA-H) or brain edema (ARIA-E).
Conclusion: We present a rare case of a genetic form of Alzheimer's disease with an exceptionally early onset, in which the first targeted treatment for the disease was administered for the first time in a European country.
Disclosure: Nothing to disclose.

EPO-352 | Genetic evidence for a link between frontotemporal dementia and Parkinson's disease: The case of RAB32 Ser71Arg

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[1]Scuola Universitaria Superiore IUSS di Pavia, Italy; [2]Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy; [3]Centogene GmbH, Rostock, Germany

Background and Aims: Frontotemporal dementia (FTD) is a heterogeneous group of neurodegenerative disorders primarily affecting behavior and cognition, often overlapping with parkinsonism. A recently discovered gene associated with familiar Parkinson's disease (PD), i.e. RAB32, has been suggested as susceptibility gene in other neurodegenerative syndromes. Hereby, we report a case study on the first RAB32 Ser71Arg mutated patient with a FTD phenotype.
Methods: A case study on a 76-year-old female proband including family history, neurological examination, neuropsychological and instrumental evaluations, was conducted.
Results: Family history revealed five affected relatives with cognitive and/or motor phenotypes. The proband showed predominant executive and social cognition deficits and no motor impairments, fulfilling criteria for the behavioral variant of FTD (bvFTD). Genetic testing confirmed the RAB32 Ser71Arg mutation in a heterozygous state, with no variants in the main autosomic dominant FTD-associated genes.
Conclusion: The RAB32 Ser71Arg mutation is implicated in a rare bvFTD phenotype, broadening the mutation's known clinical spectrum beyond PD. The high phenotypic variability within the proband's family supports incomplete penetrance mechanism and potential additional modifiers influencing disease expression. Strong collaboration between FTD and PD experts should be promoted to better capture the complexity of RAB32 Ser71Arg mutated cases.
Disclosure: MR, SL, JJP, FCu, PB and CB are employees of CENTOGENE GmbH. The other authors have nothing to disclose.

EPO-353 | Implementation of cerebrospinal fluid biomarkers for the diagnosis of Alzheimer's disease: A single-center study

E. Conesa-García[1]; M. Martínez-Zarco[1]; M. Tomás Orgaz[2]; E. Martínez-Alonso[3]; J. Bermejillo-Barrera[1]; B. Gómez-Gozálvez[1]; M. Ruiz-Perello[1]; F. Salazar-Hernández[1]; J. Sánchez-Villalobos[1]; A. Savolainen[1]; D. López-Segura[1]
[1]Neurology, Hospital Santa Lucía, Cartagena, España; [2]Clinical Analysis, Hospital Santa Lucía, Cartagena, Spain; [3]Cell Biology and Histology Department, Universidad de Murcia, Murcia, España

Background and Aims: Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive cognitive decline, with cerebrospinal fluid (CSF) biomarkers serving as essential tools for early and accurate diagnosis. This study aims to retrospectively evaluate the application of CSF biomarkers in the diagnosis of AD within our hospital.
Methods: We conducted a retrospective observational study involving 116 patients evaluated for cognitive impairment. CSF samples were obtained via lumbar puncture and analyzed for amyloid-beta 1-42 (Aβ1-42), the Aβ1-42/Aβ1-40 ratio, total tau (t-tau), and phosphorylated tau 181 (p-tau181), using CLEIA on the Lumipulse G600II Platform. Diagnostic categorization was based on established cut-off values for these biomarkers. Statistical analysis was performed to calculate the predictive values of disease as well as the intrinsic efficacy parameters of the technique.

Results: Preliminary results show that 65% of patients had abnormal Aβ1-42 levels, 46% exhibited reduced Aβ1-42/Aβ1-40 ratios, and elevated t-tau and p-tau181 levels were found in 31% and 27%, respectively. The biomarker demonstrating the highest positive predictive value (PPV) was p-tau181 (92%), whereas Aβ1-42 exhibited the lowest PPV (36%). Incorporating the Aβ1-42/Aβ1-40 ratio enhanced the PPV of Aβ1-42 by 17%, corresponding to an approximate 30% reduction in the false-positive rate. The prevalence of biomarker-defined AD in this cohort was 25%.
Conclusion: Our findings support the implementation of CSF biomarkers as a reliable diagnostic tool for Alzheimer's disease, emphasizing the utility of Aβ1-42/Aβ1-40 ratio in routine clinical practice. This study highlights the importance of integrating biomarker analysis in diagnostic workflows for early and accurate identification of AD.
Disclosure: Nothing to disclose.

EPO-354 | Bernese brain health consultations: First experience

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Background and Aims: The Swiss Brain Health Plan (Bassetti et al., 2023) emphasizes raising awareness and fostering interdisciplinary approaches to brain health. The Bernese Brain Health Consultations aimed to provide comprehensive care for patients, while promoting public awareness of brain health (BH). This analysis summarizes our first experience to guide future brain health initiatives.
Methods: We conducted 74 ambulatory BH consultations involving 69 patients at Inselspital Bern in 10/2023–07/2024. Of these, 56 patients provided general consent and were included in the current analysis of 61 consultations. Each one-hour consultation provided individualized recommendations addressing key aspects of BH.

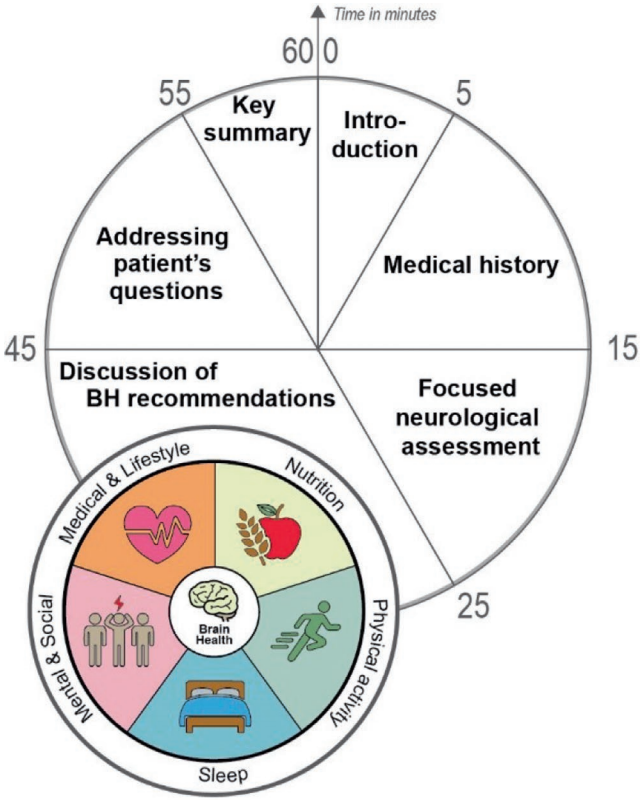

FIGURE 1 BH consultation: suggested plan for one hour.

Results: The consultations included men and women equally (age: 55.1 ± 16.0 years; Figures 2 and 3). Patients had various diagnoses, including psychiatric, neurological, and cardiovascular disorders. Initial referrals originated from general practitioners, neurologists and other sources, including self-referral, in nearly equal proportions. The recommendations of consultations were diverse, with a high prevalence of further referrals to other specialists (i.e., notably somnologists and specialists in cognitive neurology), additional diagnostics, or lifestyle interventions. Most patients did not require follow-up BH consultations.

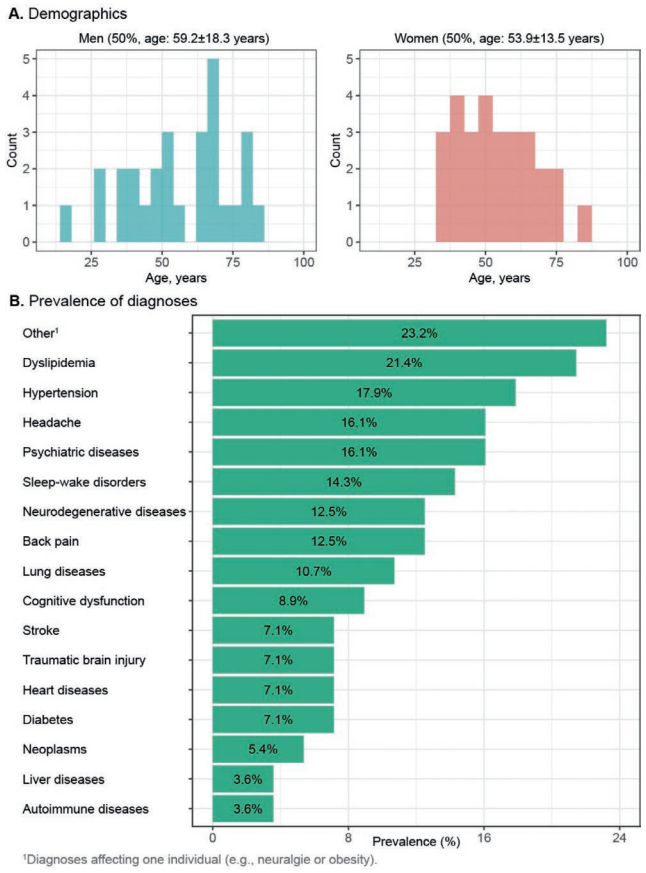

FIGURE 2 Patient population ($n = 56$).

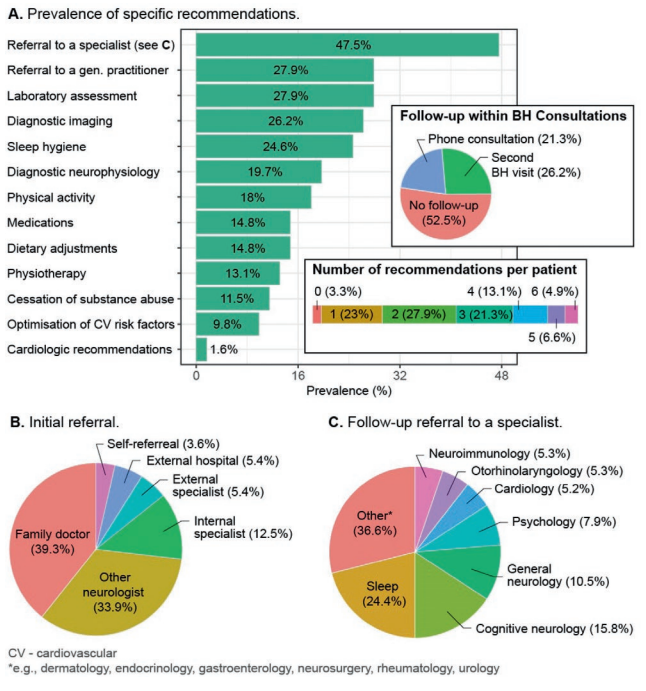

FIGURE 3 BH recommendations (61 consultations in 56 patients).

Conclusion: This is the first description of the BH consultations. BH received high demand from general practitioners and non-neurologic specialists. The complexity of BH recommendations highlights the importance of an interdisciplinary approach for BH. The experience with BH consultation lays foundation for the development of the Swiss Brain Health Questionnaire. Future efforts should focus on integrating BH into routine care and promoting strategies for BH in the general population, including healthy individuals.
Disclosure: Nothing to disclose.

EPO-355 | Yes, I'm forgetful – So what? Public perceptions of cognitive decline in Eastern Serbia: A survey study

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Background and Aims: Rural areas, with predominantly older populations, have a higher prevalence of dementia. A common clinical issue is that individuals with cognitive disturbances often seek care only after significant functional decline. We explored general awareness of cognitive decline and forgetfulness among residents of Knjaževac, Eastern Serbia.
Methods: The questionnaire designed by the authors for this study was given to the patients and caregivers in Health Center Knjaževac in Serbia. Exclusion criteria were previously diagnosed dementia or mild cognitive impairment.
Results: The sample included 745 participants (4.55% of Knjaževac's population), mean age 57.10 ± 14.12, of whom 68.7% lived in municipal areas, 26.7% in rural areas, and 4.56% received geriatric home care. Overall, 62.9% reported disturbances in one or more cognitive domains, and 47.6% of these considered the problem normal for their age. Only 30.7% of those who reported cognitive issues opted for a neurology examination. Among participants who declared memory problems, 58.1% believed frequent forgetfulness is due to lifestyle, 16.6% believed it is not, and 25.2% were unsure ($p < 0.01$). Furthermore, 15.0% were worried and 34.2% were sometimes worried, compared to only 4.9% and 11.3% of those without such problems ($p < 0.001$).
Conclusion: According to our findings, many people minimize or normalize cognitive issues. Improving knowledge about dementia is vital. This is crucial to increase knowledge about normal forgetfulness and dementia. Educational materials, information campaigns, and broader public awareness could support earlier dementia diagnosis.
Disclosure: Nothing to disclose.

EPO-356 | Astrocyte reactivity in Alzheimer's disease: Implications for blood-brain barrier permeability

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Background and Aims: Astrocytes undergo structural and metabolic changes in Alzheimer's disease (AD) progression. These changes impact functions such as blood-brain-barrier

(BBB) support (1), can be traced using biomarkers like CSF Glial Fibrillary Acidic Protein (GFAP) and lactate, and may vary by APOE genotype (2). This study examines the relationship between these astrocytic biomarkers and BBB permeability in AD, considering the effects of APOE genotype.

Methods: We enrolled 98 patients with biomarker-confirmed AD and 17 age-matched healthy controls (HC). CSF GFAP and Lactates, albumin quotient (Qalb) and APOE genotyping were measured. AD patients were subclassified as APOE-ε4 when carrying at least one ε4 allele ($n=49$), as APOE-ε3 otherwise ($n=49$). We performed Kruskal-Wallis tests and multivariate regressions to verify the associations of CSF GFAP and Lactates with Qalb, adjusting for age, sex and p-tau.

Results: There were no significant differences in terms of Qalb nor CSF astrocytic biomarkers across subgroups, with intact BBB throughout. CSF GFAP was negatively associated with Qalb in both APOE-ε3 ($\beta = -0.495$, $p=0.016$) and APOE-ε4 ($\beta = -0.482$, $p=0.022$), but not in HC. Conversely, CSF Lactates showed a moderate positive association with Qalb in APOE-ε4 ($\beta=0.420$, $p=0.002$), but not in APOE-ε3 ($\beta=0.219$, $p=0.128$) nor HC.

Conclusion: Our results underscore the multifaceted nature of astrocyte reactivity in AD, with structural and metabolic markers exhibiting distinct relationships with BBB permeability. Indeed, GFAP appears to be associated with a protective/compensatory mechanism aimed at maintaining BBB integrity (3), while the increase of CSF Lactates alongside BBB disruption in APOE-ε4 patients might represent a genotype-specific response to neuronal bioenergetic dysfunction.

Disclosure: Nothing to disclose.

EPO-357 | DCE-MRI reveals impaired blood brain barrier in basal forebrain region in patients with Alzheimers disease

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Background and Aims: Blood brain barrier (BBB) dysfunctions is one of is one of the possible mechanisms contributing to onset of Alzheimer's disease (AD). Dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) is an imaging technique allowing regional assessment of BBB breakdown by estimating local metrics of capillary permeability such as K-trans. We used DCE-MRI to examine BBB dysfunction in regions affected early in the course of AD - hippocampus, entorhinal cortex (EC) and basal forebrain (BF) nuclei.

Methods: A group of 43 participants – 22 biomarker negative cognitively unimpaired (CU) individuals and 21 biomarker positive patients with mild AD from Czech Brain Aging Study underwent DCE-MRI. K-trans maps were estimated using Patlak algorithm implemented within ROCKETSHIP software toolbox. Segmentations of hippocampal head, body and tail, anterolateral and posteromedial EC and BF nuclei were obtained using in house developed pipeline. Average K-trans values were extracted for each region. Regional differences in BBB permeability between groups were assessed using ANCOVA adjusted for age, sex and ApoE4 positivity.

Results: Participants in the AD group had lower mean K-trans in total BF (K-transCU$=0.573\times10^{-3}$ min^{-1}; K-transAD$=0.270\times10^{-3}$ min^{-1}, $p=0.002$), anterior-intermediate (K-transCU$=0.833\times10^{-3}$ min^{-1}; K-transAD$=0.291\times10^{-3}$ min^{-1}, $p=0.002$) and posterior (K-transCU$=0.536\times10^{-3}$ min^{-1}; K-transAD$=0.237\times10^{-3}$ min^{-1}, $p=0.004$) part of nucleus basalis Meynerti. There were no other significant differences between regional BBB permeability in measured structures ($p>0.05$).

Conclusion: Our data show regional reduction in BBB permeability in BF region in patients with mild AD. Regional BBB dysfunction may be one of the factors contributing to early AD related pathological changes in the BF area.

Disclosure: Nothing to disclose.

EPO-359 | Exploring trends in Alzheimer's disease mortality among aging diabetes patients in the United States over two decades

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Background and Aims: Alzheimer's disease poses a growing public health challenge, particularly among individuals with diabetes. This study investigates two-decade trends in AD mortality rates among aging U.S. adults with diabetes, providing insights into the evolving burden.

Methods: Data from 1999 to 2022 were extracted from the CDC WONDER database. Age-adjusted mortality rates (AAMR), annual percentage changes (APC), and average annual percentage changes (AAPC) were analyzed using Joinpoint regression for adults aged 65 and above.

Results: AD among diabetic patients resulted in 202,802 deaths, with AAMRs rising from 138.48 in 1999 to a peak of 264.35 in 2020 before declining to 223.47 in 2022, reflecting an AAPC of 2.06. The period from 2017 to 2020 saw significant increase in AAMR, with an APC of 9.74, followed by notable decline from 2020 to 2022 (−4.84). Alarmingly, females experienced higher AAMRs than males (198.53 vs. 191.07). AAMRs were highest among Non-Hispanic (NH) Blacks (272.93), followed by Hispanics or Latinos (249.42), while the most pronounced increases were observed in NH Asians (AAPC: 4.28). The West region exhibited the highest AAMR (229.54), followed by the Midwest, South, and Northeast. Additionally, rural areas consistently reported higher AAMRs than urban areas (241.34 vs. 181.72). Among age groups, individuals aged 65–69 showed the highest increase (AAPC: 1.78). Mississippi reported highest AAMR (488) while Nevada reported the lowest (133.5).

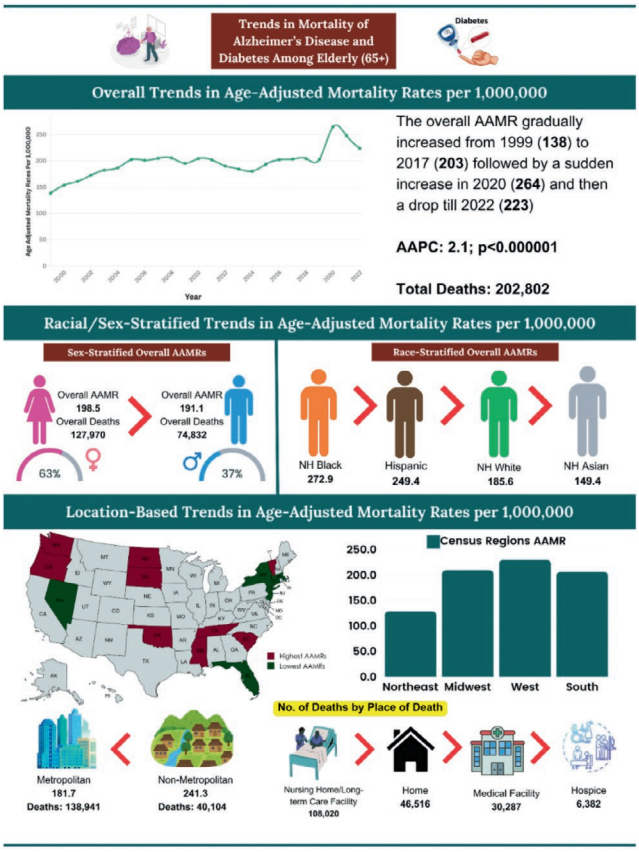

FIGURE 1 Trends in Mortality of Alzheimer's Disease and Diabetes Among Elderly

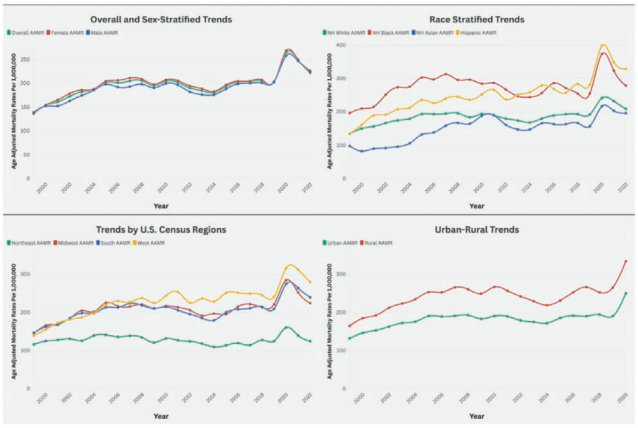

FIGURE 2 Graphical Representation of Trends

Conclusion: AD and diabetes-related mortality increased gradually since 1999, peaking in 2020, with higher rates observed in females, NH Blacks, the West region, and rural areas. The disparities warrant targeted intervention especially for vulnerable groups.
Disclosure: Nothing to disclose.

EPO-360 | Long-term residential exposure to greenspace, bluespace, traffic, and air pollutants and Dementia risk: A cohort study

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Background and Aims: Residential air pollution-related exposures have been implicated in dementia risk, but the underlying pathways remain unclear.
Methods: We analyzed 317,498 UK Biobank participants free of dementia at baseline. Residential exposures to pollutants, traffic, greenspace, and bluespace were assessed. Dementia outcomes included all-cause dementia (ACD), Alzheimer's disease (AD), vascular dementia (VaD), and other dementias (O). Cox proportional hazards models evaluated exposure-dementia associations, with mediation analysis on plasma metabolites and telomere length.

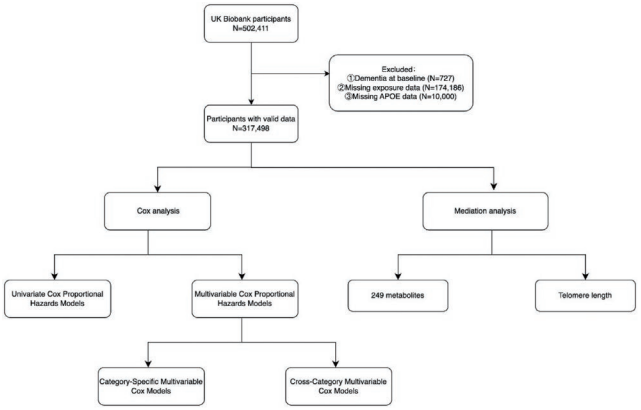

FIGURE 1 Flowchart of the included participants.

Results: Pollutant exposures, especially NO_2 and PM10, were consistently associated with increased dementia risk, with age-specific effects. Greenspace demonstrated protective effects, particularly for ACD and VaD, while traffic proximity significantly elevated VaD risk. Mediation analysis identified 49 metabolites linking PM2.5-10 to ACD in younger participants, with Omega-3% (33.3%) and S-VLDL-TG% (32.99%) as key mediators.

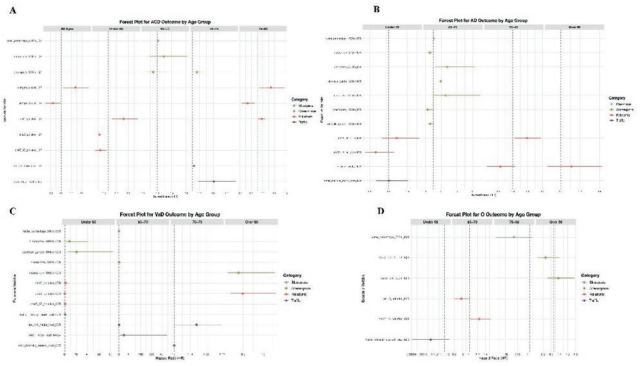

FIGURE 2 Forest plots for cross-category multivariate models.

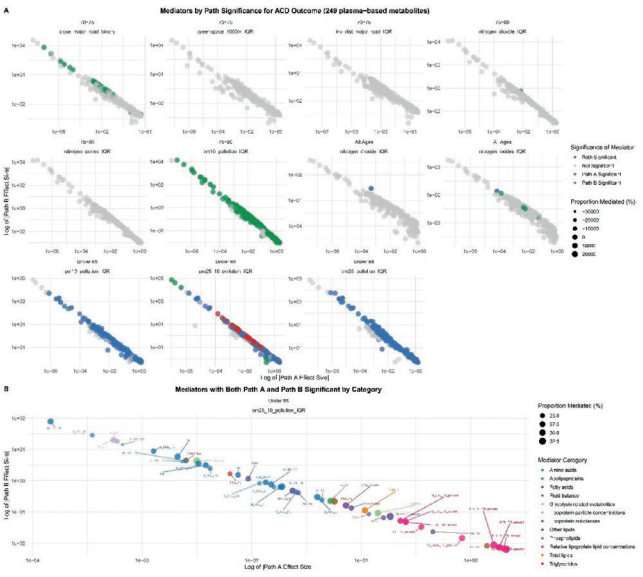

FIGURE 3 Mediators by path significance for ACD outcome (249 plasma-based metabolites).

Conclusion: Air pollution, especially particulate matter, is significantly associated with dementia risk, partially mediated by metabolic pathways, highlighting the need for environmental interventions.
Disclosure: Nothing to disclose.

EPO-361 | Carbon dots conjugated with procyanidin B2 function as diamagnetic CEST MRI theranostic agents for Alzheimer's disease

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Background and Aims: Oxidative stress and neuroinflammation are consistently cited as primary pathological manifestations of Alzheimer's disease (AD). Natural procyanidins can mitigate AD pathological features, by reducing the accumulation of reactive oxygen species (ROS) and neuroinflammation. Implementing in vivo monitoring to assess the impact of antioxidant treatment can contribute to advancing our understanding of this pathophysiological process. Recently, carbon dots (C-dots), which are discrete quasi-spherical carbogenic nanoparticles measuring several nm in size, have emerged as a more biocompatible alternative to heavy metal-based quantum dots. In this study, we developed a C-dots integrated with procyanidin B2 (C-dots@procyanidin B2) MRI theranostic agent for eliminating ROS in the brains of AD mice while simultaneously monitoring drug distribution.
Methods: We synthesized a new class MRI contrast agent C-dots@ procyanidin B2. The C-dots@ procyanidin B2 has chemical exchange saturation transfer (CEST), which enabled the use of CEST imaging for monitoring c-dots distribution and provided the information for ROS and neuroinflammation accumulation.

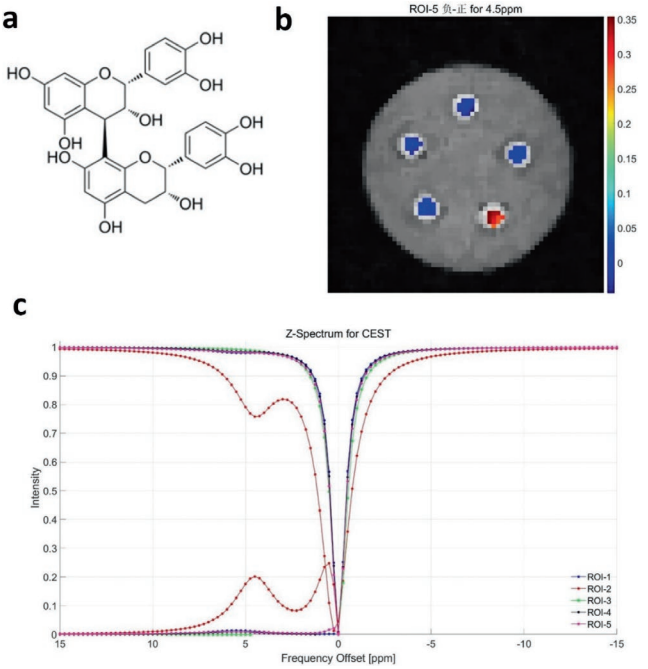

FIGURE 1 We found procyanidin B2, which has a CEST effect near 4.5 ppm in aqueous solution, crucial for MRI contrast enhancement.

Results: Based on in vitro and in vivo studies, we demonstrate that C-dots@procyanidin B2 exhibits CEST effects. Moreover, C-dots@procyanidin B2 efficiently mitigates ROS levels. Furthermore, these C-dots rapidly accumulate in the brains of AD mice and alleviate pathological features such as Aβ plaque deposition, neuronal loss, and neuroinflammation. Additionally, they significantly enhance learning ability and memory function in AD mice.

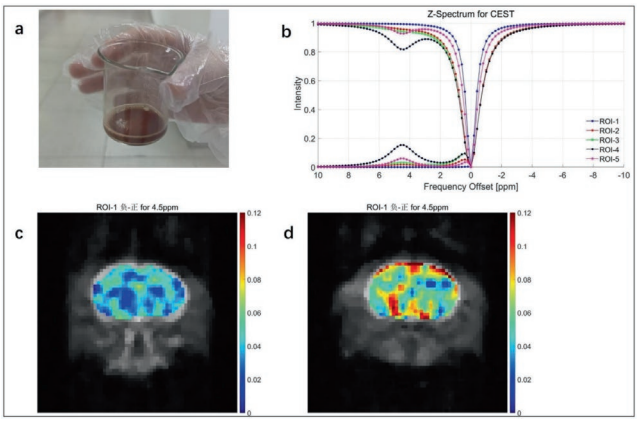

FIGURE 2 The synthesis of AC-dots@procyanidin B2 Agent and CEST MRI.

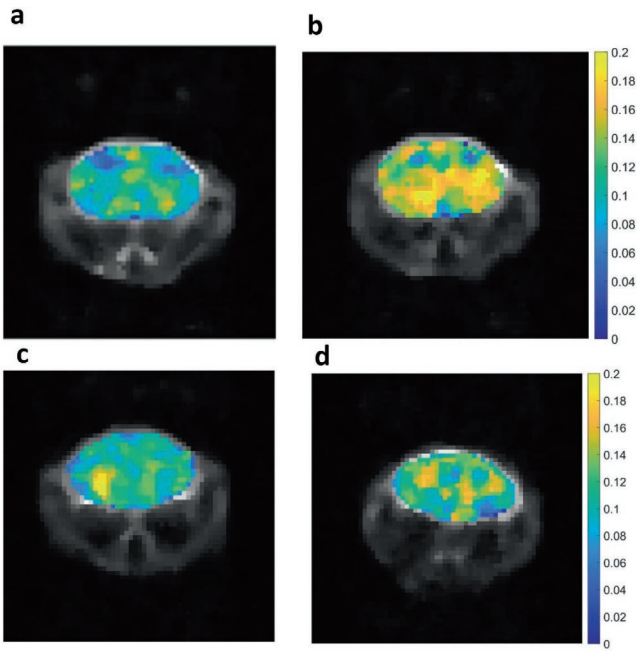

FIGURE 3 Our in vivo studies using 6-month-old APP/PS1 mice demonstrated the efficacy of our nanoparticles. Thirty minutes post-drug administration, CEST imaging revealed a significant increase in signal intensity in the therapy group (a,b) compared to the saline.

Conclusion: This study demonstrates that C-dots@procyanidin B2 can attenuate the progression of AD by reducing levels of reactive oxygen species (ROS) and neuroinflammation accumulation. Additionally, its CEST effects offer a novel approach for developing theranostic agents targeting AD.
Disclosure: Nothing to disclose.

Epilepsy 2

EPO-362 | Imaging of epilepsy in children in Abidjan, Cote D'Ivoire

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Background and Aims: Epilepsy is a neurological chronic condition affecting 0.5 to 1% of children. Investigations carried often involve brain imaging. The overall aim of our study was to have a better understanding of the role of brain imaging in the management of child epilepsy, and to contribute to its accessibility in our country.
Methods: This was a retrospective, descriptive study of the records of children followed over a period of three (03) years, from January 2020 to January 2023. It included 129 children who had undergone brain imaging, representing 59.4% of children with epilepsy during this period.
Results: The average age was 5.3 years, and the most represented gender was male. The mean age of onset of seizures was 3 years and 2 months. Motor delay was noted in almost 30% of cases, and language delay in over 45%. Brain imaging performed in all our patients was pathological in 52.7% of cases: brain atrophy was the most frequent abnormality (48%), followed by anoxic-ischemic lesions (29.7%). Predictive factors for pathological imaging were early age of onset, neonatal distress, delayed psychomotor development, focal seizures, and presence of a neurological deficit
Conclusion: Brain imaging remains essential in the search for the cause of epilepsy.
Disclosure: Nothing to disclose.

EPO-363 | Does age matter: Risk of an epilepsy diagnosis in an adult cohort referred to a first-seizure clinic

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Background and Aims: At the Epilepsy Clinic, Aalborg University Hospital, Denmark our clinical observations indicate a rising trend in the referral of older individuals for epilepsy evaluation. We aim to compare the likelihood of receiving an epilepsy diagnosis and the diagnostic yield of brain imaging and EEGs between different age groups.
Methods: This single-center retrospective study include patients referred for epilepsy evaluation April 1, 2022–January 8, 2024, with a one-year follow-up available. Demographics, resulting diagnostic work-up including CT/MRI brain imaging and electroencephalogram (EEG) and final diagnosis were

registered. Descriptive data were calculated as proportions and the relative risk of epilepsy was modeled using Poisson regression with age as the primary predictor and presented using a cubic spline. OSL regression was used to compare the sensitivity and specificity of EEG between age groups.
Results: A total of 530 patients aged 18–95 years were included (mean age: 55, 56.7% male). Of patients referred to the clinic 158 (29.8%) of patients received an epilepsy diagnosis. Poisson regression curve indicated a rising trend in the risk of receiving an epilepsy diagnosis with advancing age. The risk of receiving an epilepsy diagnosis was significantly higher in patients aged >65 years compared to those aged 18-64: RR = 1.36, 95% CI (1.04–1.76 *p*-value: 0.02). MRI, CT-scans of the brain and EEG were key diagnostic tools, with varying diagnostic yield across age groups.
Conclusion: Our study highlights the need for continuous attention to precise patient selection and specialized diagnostic work-up of patients referred to First Seizure Clinics.
Disclosure: Nothing to disclose.

EPO-364 | Detection of clinical, molecular and radiological biomarkers in patients with progressive myoclonic epilepsy

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Background and Aims: Progressive myoclonic epilepsies (PME) are often diagnosed late due to the disease's insidious onset and lack of biomarkers, which accelerates progression. This study aimed to evaluate the clinical, molecular, and radiological findings of PME patients and identify potential biomarkers.
Methods: Seventeen patients aged over 18 with PME, obtained informed consent were included. Clinical findings, cerebrospinal fluid (CSF) neurofilament light chain (nFL) levels, and retrospective cranial MRI findings were analyzed. Expression levels of miRNAs linked to NHLRC1 and EPM2A genes (miR-326 for NHLRC1 and miR-383-5p for EPM2A), key to Lafora Disease (LD) pathogenesis, were evaluated. Statistical analyses were conducted on the collected data.
Results: Nine patients (52.9%) were female, with a mean age of 34.8 ± 15.2 years. The most common genetic variant was LD-NHLRC1. Disease duration averaged 22.2 ± 13.0 years, with other neurological symptoms appearing 5.7 ± 3.8 years post-onset. Twelve patients (70.5%) were independent in walking. Frontal dysfunction (82.3%) dominated the neuropsychological profile. CSF nFL levels did not differ from reference values according to patients and age. However, miR-326 and miR-383-5p expression levels were significantly reduced in patients compared to controls.
Conclusion: The p.Asp146Asn mutation in the NHLRC1 variant of LD is associated with a favorable course. Restrictive symptoms manifesting 5.7 years post-disease onset highlight the importance of early diagnosis with suitable biomarkers. Normal CSF nFL levels suggest a slow neurodegenerative process via different mechanisms. The pronounced reduction in miR-326 and miR-383-5p expression among non-Lafora patients indicates shared pathophysiological processes in PMEs.
Disclosure: This study was supported by Istanbul University Scientific Research Projects Coordination Unit. Project ID: 40136.

EPO-365 | Comparison of subtotal hemispherectomy and other disconnective surgical techniques in epilepsy surgery

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Background and Aims: Disconnective surgery may be an option for refractory epilepsy when the seizure onset zone is too large or resection is not feasible due to the risk of functional loss. Commonly used disconnective techniques today include Functional Hemispherotomy (FH), Posterior Quadrantectomy (PQ), and Subtotal Hemispherectomy (SH). The aim of this study is to retrospectively evaluate the outcomes of SH and other disconnective surgical techniques.

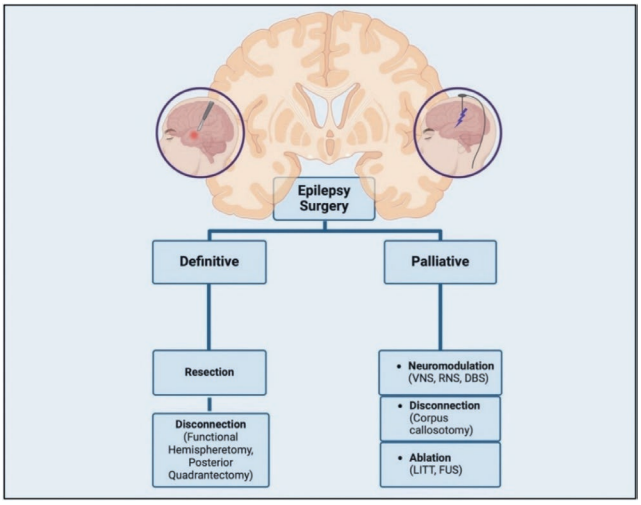

FIGURE 1 Types of Epilepsy Surgery

Methods: Patient records from our center, from 2000 to 2022, were reviewed retrospectively. A total of 48 patients who underwent disconnective surgery and had at least 1 year of postoperative follow-up were included in the study. Gender, age, age at seizure onset, disease duration, postoperative neurological complications, and postoperative seizure frequency were evaluated.
Results: The mean age of the 48 patients (20F, 28M) was 21.29 ± 12.67 years. 23 patients underwent FH, 17 patients underwent PQ, and 8 patients underwent SH. 31 patients were classified as Engel Class 1, 7 as Engel Class 2, 5 as Engel Class 3, and 5 as Engel Class 4. Of the patients who underwent SH, 7

achieved Engel Class 1, while 1 patient remained as Engel Class 4. Postoperative complications were observed in 11 patients. No significant differences were found between the groups regarding Engel classification and complication rates.

TABLE 1 The Demographical Features of The Patients.

		n	%
Gender	*Female*	20	41,7
	Male	28	58,3
Type of the Resection	*FH*	23	47,9
	PQ	17	35,4
	SH	8	16,7
Age at Operation	*≤18 years*	35	72,9
	>18 years	13	27,1
Post-operative Complication	*Present*	12	25,0
	Absent	36	75,0
		Mean±Sd	**Min-Max (Median)**
Age of the patient		21,29±12,67	5-64 (20)
Age at seizure onset		3,56±3,95	1-18 (1)
Age at the operation		13,81±12,88	1-58 (10,5)
Operation Gap (years)		10,25±11,26	0-55 (6,5)
Post-operative ENGEL Score		1,58±1,01	0-4 (1)

Abbreviations: FH: Functional Hemispheretomy, PQ: Posterior Quadrantectomy, SH: Subtotal Hemispherectomy, Sd: Standard deviation, Min: Minimum, Max: Maximum

TABLE 2 Analysis of Age at Seizure Onset, Postoperative Complications and Engel Scores According to the Types of Disconnection Surgery

		Type of the Disconnection			p Value
		FH	PQ	SH	
Postop Engel score; Mean±Sd (Median)		1,48±0,93 (1)	1,82±1,07 (1)	1,38±1,06 (1)	[c]*0,300*
Age at Seizure Onset; Mean±Sd (Median)		1,35±0,93 (1)	5,94±5,04 (5)	4,88±3,44 (4,5)	[c]*0,001***
Postop Complications	*Present; n (%)*	7 (30,4)	3 (17,6)	2 (25,0)	[b]*0,653*
	Absent; n (%)	16 (69,4)	14 (82,4)	6 (75,0)	

[c]*Kruskall Wallis Test* [b]*Pearson Chi-Square* ***p<0,01*

Abbreviations: FH: Functional Hemispheretomy, PQ: Posterior Quadrantectomy, SH: Subtotal Hemispherectomy, Sd: Standard deviation, Postop: Post-operative

Conclusion: The appropriate surgical disconnective procedure should be selected based on the seizure onset zone and individual patient characteristics. Patients with hemispheric structural anomalies but no paresis may be suitable candidates for SH.
Disclosure: Nothing to disclose.

EPO-366 | Effect of cenobamate on sudden unexpected death in epilepsy risk in a Spanish cohort of a phase 3 clinical trial

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[1]Hospital Universitari i Politècnic La Fe, Valencia, Spain; [2]Angelini Pharma S.p.A., Rome, Italy; [3]MeDaStats LLC, Tampa, USA; [4]Angelini Pharma S.p.A., Barcelona, Spain; [5]Angelini Pharma S.p.A., Madrid, Spain

Background and Aims: Effect of cenobamate on sudden unexpected death in epilepsy (SUDEP) accounts for 2-17% of deaths in patients with epilepsy (Ficker 2000, Epilepsia 41 Suppl 2: S7–S12). SUDEP-3 (score 0–4) and SUDEP-7 (score 0–10) scales assess the potential risk of SUDEP. For each point reduction in SUDEP-3, SUDEP odds decrease by 64%; for SUDEP-7, per-point odds decrease is 29% (Rasekhi 2021, Epilepsia 62(7):1536–1545).
Methods: NCT02535091 (C021, $N=1340$) was a global, multicenter, phase 3, open-label safety study of cenobamate as adjunctive treatment in adults with uncontrolled focal-onset seizures (FOS). Efficacy data pre- and post-cenobamate treatment were collected in in a multicenter retrospective observational study of the C021 Spanish cohort ($n=127$). SUDEP-3 and SUDEP-7 risk scores (RS) were calculated for patients in that cohort before and after cenobamate treatment.
Results: At baseline, 76% and 24% patients had SUDEP-3 RS of 2 and 3. After 2 years of cenobamate treatment, 6% had a RS point reduction of 3, 11% of 2, and 14% of 1 point; 69% remained stable (Figure 1). Using the SUDEP-7 inventory, at baseline, 51% of patients had a RS of 1–3 and 49% had a RS of 4–8. After 2 years of cenobamate treatment, 1% had a RS point reduction of 4, 9% of 3, 9% of 2, and 30% of 1 point. 44% remained stable, and 7.5% increased SUDEP risk (Figure 2).

FIGURE 1 Study subjects stratified by SUDEP 3 risk score.

Conclusion: Cenobamate treatment significantly reduced SUDEP risk in some Spanish cohort patients as measured by two SUDEP risk scales. The potential for reducing SUDEP risk should be considered when initiating/changing treatment in patients with uncontrolled FOS.
Disclosure: The original study C021 (NCT02535091) was supported by SK Life Science, Inc. (Paramus, NJ, USA), the Spanish cohort study was supported by Angelini Pharma Spain, and these analyses were supported by Angelini Pharma S.p.A. (Rome,

Italy). VV: Consultant/advisor: Angelini Pharma, BIAL, Eisai, Esteve, GlaxoSmithKline, Jazz, Novartis, Sandoz, Takeda, UCB Pharma, Xenon; Speaker: Angelini Pharma, BIAL, Cevomed, Eisai, Esteve, Jazz, Newbridge, Paladin, UCB Pharma; Research support: Angelini Pharma, BIAL, Eisai, Jazz, UCB Pharma. JPL, PPD, EAB: Employees, Angelini Pharma. KT: Consultant: Angelini Pharma.

EPO-368 | Cortical myoclonus as an manifestation of familial myoclonic epilepsy of adults (FAME)

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Background and Aims: A 51-year-old man reports acute onset 15 years ago of sudden, rapid, asymmetrical, appendicular and axial, asynchronous muscle contractions associated with subsequent generalized hyposthenia. Both father and brother presented the same symptomatology and episodic generalized tonic-clonic seizures.
Methods: The patient underwent routine blood tests, brain MRI, electroencephalography, electroneuromyography, jerck-locked back averaging analysis and genetic panel analysis for genetically determined epilepsies.
Results: Electroencephalography showed (a) isolated, brief clusters of punctate elements and subsequent slow wave clinically followed by upper limb muscle contraction (cortical myoclonus), (b) a photoparoxysmal response to ntermittent photic stimulation. Surface electromyography (long flexor and extensor carpal muscle) confirmed the presence of myoclonus. Genetic analysis showed a pathological pentameric expansion in heterozygosity (ATTTC)n in the STARD7 gene.
Conclusion: The abovementioned findings supported the diagnosis of Familial myoclonic epilepsy of the adult (FAME2). FAME is a genetically determined disorder with autosomal dominant and vertical transmission, with probable involvement of cerebellar structures, characterized by a heterogeneous syndromic cortex of cortical tremor, myoclonic jerks, occasional generalized tonic-clonic and/or myoclonic seizures, and additional symptoms based on the disease phenotype (migraine, night blindness, cognitive impairement, psychiatric deseases). The clinical features of this disorder pose different differential diagnoses (essential tremor, juvenile myoclonic epilepsy, Progressive myoclonic epilepsy) because of the wide etiologic possibility of the myoclonic phenomenon; therefore, it is necessary to identify precise disease phenotypes, including in correlation with the mutated gene, and clinical, radiologic, and electrophysiologic dinstiguous elements to avoid misdiagnosis, inadequate therapeutic treatment, and worsening prognosis.
Disclosure: Nothing to disclose.

EPO-369 | Neurophysiological and clinical correlates of low-dose perampanel in familial adult myoclonus epilepsy type 2

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Background and Aims: Familial adult myoclonus epilepsy (FAME) management relies on antiseizure medications (ASMs), which inadequately address myoclonus and cortical tremor. This study evaluates Perampanel (PER), an AMPA-receptor antagonist, for treating FAME symptoms.
Methods: Fifteen FAME2 patients participated in an observational prospective study. They received up to 6 mg daily of PER and underwent Unified-Myoclonus-Rating-Scale (UMRS) before and after treatment. Neurophysiological evaluations, including somatosensory evoked potentials (SEPs) and transcranial magnetic stimulation (TMS), assessed PER's impact on cortical glutamatergic excitatory and GABAergic inhibitory circuits.
Results: PER treatment significantly reduced UMRS total scores ($p=0.001$) and action-myoclonus subscores ($p=0.002$), irrespective of disease duration, age at onset, or testing time ($p>0.05$). Patients with more severe baseline myoclonus demonstrated significant improvements. Neurophysiological assessments revealed a PER-induced decrease in sensorimotor hyperexcitability, characterized by diminished N33 amplitudes, attenuated glutamatergic facilitation, and enhanced GABAergic inhibition in the motor cortex. In conclusion, low-dose PER is well tolerated and effective in alleviating myoclonus in FAME2 patients, supported by its modulatory effects on glutamatergic and GABAergic neuronal circuits. Plain Language Summary:

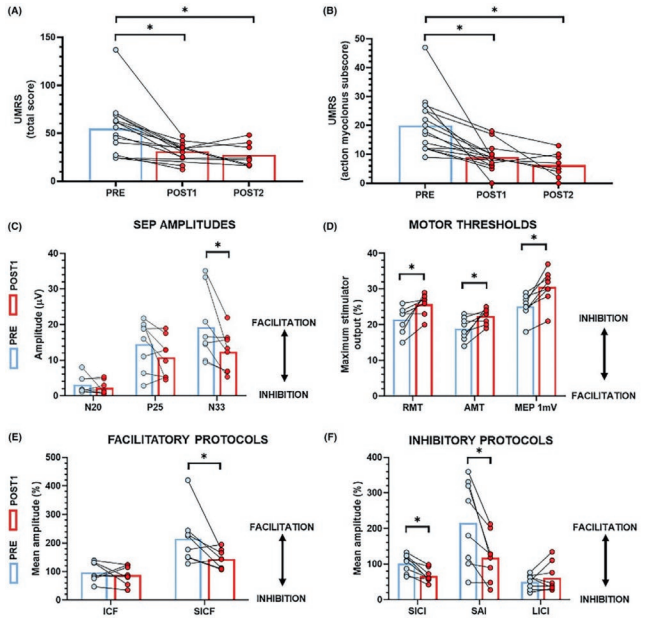

FIGURE 1 The UMRS total score (A) and the action myoclonus subscore (B) were significantly reduced following PER (PER) treatment at both follow-up assessments: POST1 (total score: $p = 0.008$; subscore: $p = 0.031$) and POST2 (total score: $p = 0.006$; subscore: $p = 0.0$)

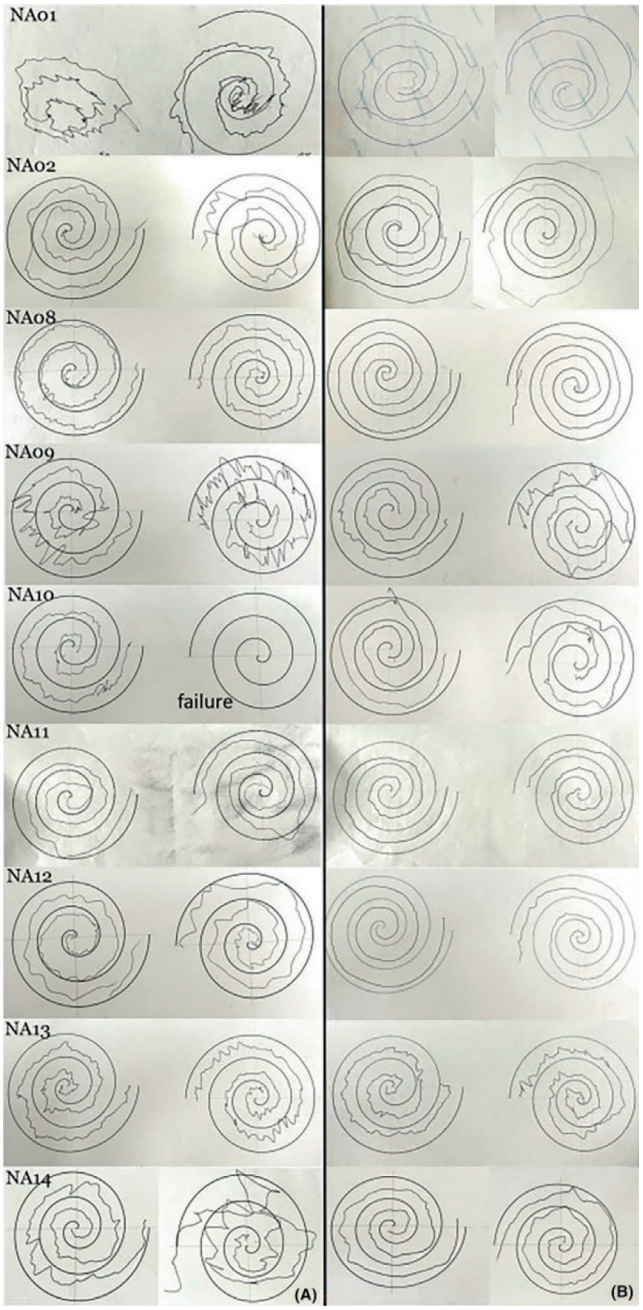

FIGURE 2 (A) Spiral Archimedes drawing executed at baseline and (B) at POST-1. Right-hand drawing is on the right and left-hand drawing is on the left. Note that subject NA10 could not initiate the task for the right hand at baseline.

Conclusion: This study investigated the effects of low-dose perampanel in individuals with Familial Adult Myoclonus Epilepsy2 (FAME2), a hereditary condition characterized by epilepsy and tremors. Perampanel, an antiepileptic drug, blocks AMPA receptors in the brain, reducing excessive neural activity that causes seizures and abnormal movements. The results showed significant symptom improvement, which correlated with changes in brain activity as measured by neurophysiological tests. This study suggests that perampanel helps regulate abnormal brain signals and may help managing FAME2 symptoms.

Disclosure: Nothing to disclose.

EPO-370 | Real-world experience with cannabidiol as add-on treatment in patients with Lennox-Gastaut syndrome

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Background and Aims: The efficacy of Cannabidiol (CBD) has been established in several clinical trials and long-term open-label extension studies on Lennox-Gastaut syndrome (LGS)1,2. This study evaluates the sustained effectiveness and safety of CBD in an adult cohort of LGS patients.
Methods: We retrospectively included all LGS patients referred to the adult Epilepsy Center of our Institute treated with CBD. Follow-ups occurred at 3, 6, and 12 months. The primary endpoint was sustained effectiveness. Secondary endpoints included retention rate, improvement of behavioral/psychiatric disorders, and incidence of adverse effects (AEs).
Results: A total of 37 adult patients (M/F: 22/15, mean age: 36.5 ± 12 years) were included. All had refractory epilepsy previously treated with a mean of 11 anti-seizure medications and had intellectual disability (ID); 21 (56.8%) had concomitant behavioral or psychiatric disorders. Eighteen patients (48.6%) showed a reduction in seizure frequency, and 10 patients (27%) reported improved quality of life. AEs were noted in 23 patients (60%), with drowsiness (29.7%) and elevated transaminases (10.8%) being the most common. At the last follow-up, 16 patients (43.2%) continued CBD therapy at an average dose of 9.7 mg/kg/day: 12 (32.4%) with a sustained reduction in seizure frequency, and 4 (10.8%) with a transient or inadequate response. Conversely, 21 patients (56.8%) discontinued CBD due to long-term inefficacy (29.7%) or AEs (27%) after 7.8 ± 6.7 months.
Conclusion: CBD appears to be a viable alternative in drug-resistant adult patients. Among the responding patients, a significant percentage has shown an improvement of seizures frequency. Moreover, CBD is relatively well tolerated in our cohort.
Disclosure: Nothing to disclose.

EPO-371 | The prediction of seizure freedom in non-lesional temporal lobe epilepsy based on a machine learning approach

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Background and Aims: Introduction: Resective brain surgery represents the only therapeutic option that can lead to long-term seizure cessation in patients with drug-refractory epilepsy. In this study, we focused on predicting surgical seizure-free outcomes in a group of patients with non-lesional temporal lobe epilepsy (TLE).
Methods: Methods: We retrospectively identified a cohort of 19 drug-resistant non-lesional TLE patients who underwent surgical treatment and an extended pre-surgical MRI protocol that included 25 imaging methods (IMs). Each IM was evaluated by three different metrics which were derived based on the known extent of resection, resulting in a total of 75 features for each patient. We then selected the 10 most discriminative features to construct three machine learning (ML) models: Multi-Line Perceptron (MLP), Gaussian Naive Bayes (GNB), and Support Vector Machine (SVM). The performance of each model was assessed by its accuracy.
Results: Results: For 19 non-lesional TLE patients, 10 IMs were selected as the most discriminative. The majority of the most discriminative features were based on a metric that compared tissue features within the resection to the immediate vicinity of the resection. The highest average accuracy of 80 % was obtained in the MLP and GNB model. The average accuracy of the SVM model was 70%. The highest accuracy of 89 % was present in the MLP model that included the nine most discriminative features.
Conclusion: Conclusion: Our study demonstrates that ML models can effectively predict surgical outcomes in patients with non-lesional temporal lobe epilepsy, achieving an accuracy of up to 89% with the MLP model.
Disclosure: Nothing to disclose.

EPO-372 | Ictal and postictal central apnea in focal epilepsy due to NPLR3 pathogenic variants

M. Burani[1]; G. Giovannini[2]; N. Orlandi[1]; M. Pugnaghi[2]; A. Vaudano[1]; A. Ballerini[1]; N. Biagioli[1]; L. Taruffi[1]; S. Scolastico[1]; L. Madrassi[1]; E. Micalizzi[3]; I. Florindo[4]; S. Meletti[1]
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Background and Aims: Recently, the association between mTOR pathway gene mutations and focal epilepsy with ictal and postictal central apnea and the increased risk of SUDEP has been provided in animal models. NPLR3, together with NPLR2 and DEPDC5, make the GATOR1 complex, which regulates mTOR signalling. Our group previously described a cohort of patients with DEPDC5 mutations who exhibited ictal and postictal central apnea (PICA). Here, we describe three new patients with pathogenic sequence variants in NPLR3 with MRI-negative focal epilepsy who presented with PICA.

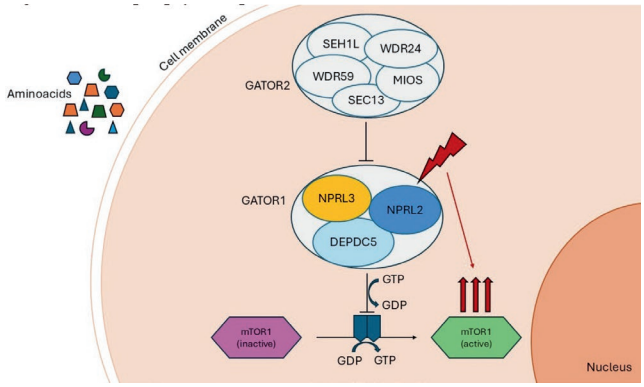

FIGURE 1 A schematic overview of the GATOR1/2-mTOR pathway. Mutations in GATOR genes lead to mTORC1 upregulation, resulting in hyperactivation of this pathway.

Methods: Three patients (two females; mean age 29.7 years), affected by focal epilepsy, were admitted to our Epilepsy Monitoring Unit in 2024 and underwent long-term video-EEG monitoring (LTVM) with cardiorespiratory polygraphy, neuropsychological tests, and 3T brain MRI with HARNESS protocol.
Results: During LTVM, a total of six seizures were recorded (50% during sleep), and in 83.3% of these, we observed ictal and postictal apnea with oxygen desaturation up to 79%. None of the patients were aware of respiratory distress and reported shortness of breath or poor sleep quality. None of them had known structural aetiology. Genetic testing (NGS panel) revealed a pathogenic mutation in NPLR3.

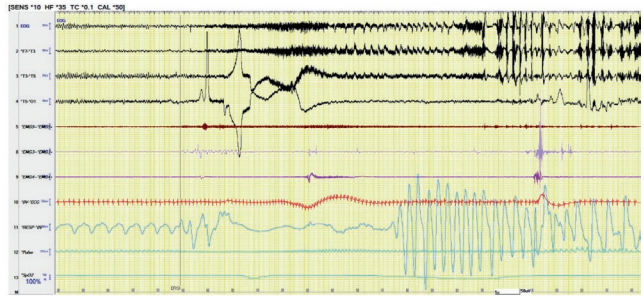

FIGURE 2 2 minutes of long-term EEG monitoring of a temporal lobe seizures with a prolonged apnea (>30 seconds) right after the EEG seizure onset, shown in the RTA channel. The apnea is followed by marked tachypnea and oxygen desaturation.

Conclusion: These three new cases of peri-ictal respiratory alteration associated with NPLR3 mutation confirm the association between mTOR pathway and central apnea, a recognized SUDEP risk factor. Furthermore, our findings highlight: 1) the need of respiratory polygraphy during LTVM in order to detect peri-ictal breathing alterations; 2) the importance of offering genetic testing to patients with focal epilepsy without structural aetiology and peri-ictal breathing disorders.
Disclosure: Nothing to disclose.

EPO-373 | Effectiveness, adherence and safety of cenobamate in patients with focal refractory epilepsy: Results of CiFES study

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Background and Aims: Objectives: We aimed to assess the effectiveness, adherence and safety of cenobamate (CEN) in a cohort of patients diagnosed with refractory focal epilepsy in clinical practice
Methods: Materials and methods: The CiFES (Cenobamate in Focal Epilepsy Study) study is an observational, retrospective study comparing the following variables up to 6 months after initiating CEN: number of monthly epileptic seizures, concomitant antiepileptic drugs (AEDs) compared as the number and as the corresponding Defined Daily Dose (DDD), the retention rate at 6 months and the side effects related with CEN withdrawal or dose adjustment
Results: Results: 41 patients were included. 27 (65.8%) were male, 71% between 30-50 years of age, 57% diagnosed 10-20 years ago, 48% with focal motor seizures and 4.13 ±0.52 seizures per month. Treatment with CEN significantly reduced the number of epileptic seizures from baseline (13.12 ±0.75) at 1 month (9.74 ±0.42, t 1.40 = 4.863; p = 0.001), 3 months (1.96 ±0.57, t 1.40 = 6.810; p = 0.001) and at 6 months (1.69 ±0.48, t 1.40 = 6.938; p = 0.001). 5 (12%) patients were seizure-free at 6 months. Furthermore, the number of concomitant AEDs was significantly lower after 6 months with CEN (2.57 ±0.20 vs. 2.91 ±0.23, t 1.40 = 2.676; p = 0.041) and the DDD significantly (p = 0.007) decreased from 5.87 ±0.31 to 4.34 ±0.29 after 6 months. 5 patients suffered side effects being dizziness the most reported (n = 2, 4.8%). Only 1 patient discontinued CEN after 6 months being the retention rate of 97% in the study period.
Conclusion: Conclusions: CEN is an effective and well tolerated antiepileptic treatment for patients with drug-resistant focal epilepsy.
Disclosure: Nothing to disclose.

EPO-374 | Seizure outcomes and risk of post-stroke epilepsy in patients with acute symptomatic post-stroke seizures

N. Orlandi[1]; G. Giovannini[2]; G. Bigliardi[2]; S. Maffei[2]; M. Pugnaghi[2]; A. Vaudano[2]; N. Biagioli[1]; S. Scolastico[1]; L. Madrassi[1]; M. Burani[1]; L. Taruffi[1]; S. Meletti[2]
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Background and Aims: Acute symptomatic seizures (AS) are considered among the most relevant factors for the development of post-stroke epilepsy (PSE). Herein, we explored seizures' outcome in a cohort of adult patients with AS after a first-ever ischemic stroke.

Methods: Observational, single-center, retrospective study of patients admitted to the Stroke Unit of Modena Academic Hospital (Italy) from January 1st 2004 to December 31st 2022. Acute (AS) and remote (RS) symptomatic seizures were defined according to ILAE definitions. Patients with AS were divided among those who experienced single seizures (SS), seizure cluster (SC) and status epilepticus (SE). Kaplan–Meier survival analyses and Cox proportional hazard regression models were used to estimate seizure freedom as longterm outcome.
Results: 49 patients (mean age: 69.2 y/o; 51% female) were included: 25 (51%) experienced SS, 9 (18%) SC and 15 (31%) SE. Overall, 8 patients (16%) developed RS (mean follow-up: 55.8 months). Cumulative probability of seizure freedom at 5 years after stroke was 96% in SS, 69% in SC and 61% in SE sub-groups, respectively. The risk of RS development was higher in case of SC (HR 7.8 95% CI 0.81–76.5; $p = 0.08$) and SE (HR 16.1 95% CI 1.7–153.2; $p = 0.02$) compared to SS. In 20 out of 49 patients, antiseizures medications were withdrew without further seizures (17 SS, 1 SC and 2 SE; $p < 0.001$).
Conclusion: In our cohort, the risk of PSE appeared to be influenced by the severity of seizures' phenomena in the acute phase after stroke.
Disclosure: Nothing to disclose.

EPO-375 | Risk of seizure recurrence after antiseizure medications withdrawn in patients with acute post-stroke seizures

N. Orlandi[1]; G. Giovannini[2]; G. Bigliardi[2]; S. Maffei[2]; M. Pugnaghi[2]; A. Vaudano[2]; N. Biagioli[1]; S. Scolastico[1]; L. Madrassi[1]; M. Burani[1]; L. Taruffi[1]; S. Meletti[1]
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Background and Aims: The question of whether discontinue antiseizure medications (ASMs) in patients with acute symptomatic post-stroke seizures (AS) represents an important issue. Herein, we explored seizures' outcome in a cohort of adult patients with AS after a first-ever ischemic stroke.
Methods: Observational, single-center, retrospective study of patients admitted to the Stroke Unit of Modena Academic Hospital (Italy) from January 1st 2004 to December 31st 2022. Acute (AS; <1-week from stroke) and remote (RS) seizures were defined according to ILAE classification. Patients with AS were further divided in single seizures (SS) and seizure cluster/status epilepticus (SC/SE). Kaplan–Meier survival analyses was used to estimate seizure freedom as longterm outcome.
Results: 49 patients (mean age: 69.2 y/o; 51% female) were included: 25 (51%) experienced SS and 24 (49%) SC/SE. Overall, 8 patients (16%) developed RS (55.8 months). In 23 patients, ASMs were withdrawn after a mean of 8 months since stroke: 68% of patients with SS (17/25) and 25% of patients with SC/SE (6/24) ($p = 0.003$). After ASMs withdrawn 3 out of 23 patients experienced RS, all in the SC/SE subgroup (follow-up 55.5 months). Cumulative probability of seizure freedom at 1-year after ASMs withdrawn resulted to be significantly lower in case of SC/SE compared to SS (44% vs 100%; $p < 0.001$).
Conclusion: The risk of post-stroke epilepsy after ASMs withdrawn was higher in patients with acute symptomatic status epilepticus or seizure cluster, underlying the role of acute repetitive seizures in the development of the epileptogenic network.
Disclosure: Nothing to disclose.

EPO-376 | Predictors of good VNS response in 129 patients with generalized drug-resistant epilepsy (DRE)

S. Aubert-Conil[1]; R. Carron[1]; D. Scavarda[2]; A. Paz Paredes[2]; N. Villeneuve[3]; A. Lepine[3]; F. Pizzo[1]; F. Bonini[1]; G. Daquin[1]; L. Vaugier[1]; J. Makhalova-Scholly[1]; S. Lagarde[1]; A. Trebuchon[1]; F. Bartolomei[1]
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Background and Aims: Identifying best candidates for VNS among all DRE patients remains challenging, as favorable prognostic factors are not clearly defined and only few large VNS cohorts are reported in the literature. The aim of this research is 1/ to analyze the VNS responder rate in our patients' population and in its subgroups and 2/ to try to delineate favorable prognostic factors for VNS therapy in this population.
Methods: This single-center (Marseille, France) retrospective study collected data from July 2000 to June 2024 from patients with generalized DRE who had VNS implantation with a follow up of at least one year. Univariate, multivariate, univariate logistic regression, stepwise and penalized logistic regression (LASSO) analyses were conducted.
Results: Among all DRE patients with VNS implantation ($n = 401$) and sufficient follow-up, 129 patients had generalized DRE, most of them Lennox-Gastaut Syndrome (LGS, $n = 82$) or Idiopathic Generalized Epilepsy (IGE, $n = 27$). Mean post-implantation follow-up was 8 years and 9 months (1–21 years). In the whole cohort (LGS + IGE patients), regardless of age, 43% were VNS responders (≥50% seizure reduction); 14% had 75–100 % seizure reduction. The variables better associated with a favorable VNS outcome were male gender ($p = 0.00145$) and older age at end of study and at implantation ($p = 0.00585$), regardless of epilepsy subtype.
Conclusion: VNS is a very good treatment option for generalized DRE. Older age and male gender are favorable prognostic factors in this study, but more extensive data analysis are required to confirm these findings.
Disclosure: Nothing to disclose.

EPO-378 | Continuous blood pressure monitoring after thrombectomy for ischemic stroke – Experience of a stroke unit

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Background and Aims: Blood pressure (BP) control after endovascular treatment (EVT) for acute ischemic stroke (AIS) is essential. Elevated BP is linked to an increased risk of hemorrhagic transformation, yet the optimal BP target remains unclear. Most trials have relied on non-invasive, intermittent BP monitoring (<100 measurements/24 h) and reported challenges in controlling BP.
Methods: We included AIS patients undergoing thrombectomy at our center. Continuous BP monitoring with an arterial catheter was performed, and individualized BP targets were defined. We conducted a descriptive analysis of BP control in the first 24 h post-EVT and compared our findings with the literature.
Results: Among 58 patients, 36.2% received intravenous thrombolysis, and 79.3% achieved mTICI2c/3 recanalization. Each patient had a median of 1346 (IQR 178) BP measurements in the first 24 h. Overall, 6.6% of measurements exceeded targets, with 17.4% and 1.3% exceeding targets in strict (SBP <140 mmHg) and permissive (SBP 140–220 mmHg) groups, respectively. The standard deviation of SBP was 16 mmHg (IQR 6). Antihypertensive treatment was used in 37.9% of patients, and 19% required infusions. Symptomatic hemorrhagic transformation occurred in 1 patient (1.7%). At 3 months, 53.4% had mRS 0–2 or their previous mRS, with 10.3% mortality.
Conclusion: The lack of evidence of a clear BP target may result from trial methodologies. In the BP-TARGET and PRAISE trials (<50–100 measurements/24 h), 35–50% and 15–30% of SBP measurements exceeded targets, respectively. In our sample, Continuous monitoring kept patients >90% of the time within BP targets, demonstrating its feasibility for effective BP control.

Clinical trial Year of publication	Intervention	Outcomes	Monitoring	% of SBP measurements above target	Conclusion
ENCHANTED2/MT 2022	SBP <120 vs. <180 mmHg	mRS and hemorrhagic transformation post-EVT	Intermittent (each 15-30 min then each hour)	-	Worsened functional outcome
BP-TARGET 2022	SBP <140 vs. <180 mmHg	mRS and hemorrhagic transformation post-EVT	Intermittent (each 15 min then each hour) or continuous	<140 mmHg: 40-50%; SD SBP 11 mmHg <180 mmHg: 20-30%; SD SBP 17 mmHg	Increased risk of neurological deterioration without decreased risk of hemorrhagic transformation nor functional benefit
BEST 2021	SBP 110–130 mmHg vs. 130–150 mmHg	mRS post-TEV	Intermittent (each 15-30 min then each hour then each 4 hours)	110-130 mmHg: 30-40% 130-150 mmHg: 15-25%	No significant differences in functional outcome (no benefit)
PRAISE 2019	SBP <140 vs. <180 mmHg	Hematoma expansion (conducted in hemorrhagic stroke)	Intermittent (each 15 then each hour) and continuous	<140 mmHg: 35-40% <180 mmHg: 15-20%	Benefit in decreasing hematoma expansion, but without long term benefits
Our study	Individualized targets	Hemorrhagic transformation, mRS, mortality	continuous (1346 measurements/24h)	Any target: 6,6% ≤140 mmHg: 17,4% permissive: 1,3%	...

FIGURE 1 Comparison between the results of our study and the results of clinical trials that have tested different blood pressure targets after endovascular therapy for acute ischemic stroke (and targets after hemorrhagic stroke in the case of the PRAISE trial).

Disclosure: Nothing to disclose.

EPO-379 | Red cell distribution width as inflammatory marker in correlation with intracranial artery calcification

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Background and Aims: Evidence suggests that intracranial artery calcification and red cell distribution width (RDW) are independent risk factors for stroke. This study aims to explore the correlation between these risk factors and their ability to predict the severity of ischemic stroke.
Methods: We included 117 patients in this observational cohort study with a mean age of 67.3 ±11.76 years (50.86% females), who had experienced an ischemic stroke or transient ischemic attack. RDW was recorded from blood samples, and types of intracranial artery calcification were evaluated using non-contrast Computed Tomography (CT) of the head with a standardized method in the anterior and posterior brain arterial circulation systems.
Results: The total anterior intracranial artery calcification score was correlated with RDW. We found a significant correlation between RDW and total anterior intracranial artery calcification Persons correlation coefficient was 0.359 ($p = 0.001$).

TABLE 1 Table presentation of correlation between RDW and subtypes of calcification.

Correlations

		AnteriorTOTAL	RDW
AnteriorTOTAL	Pearson Correlation	1	.359**
	Sig. (2-tailed)		.001
	N	104	89
RDW	Pearson Correlation	.359**	1
	Sig. (2-tailed)	.001	
	N	89	98

**. Correlation is significant at the 0.01 level (2-tailed).

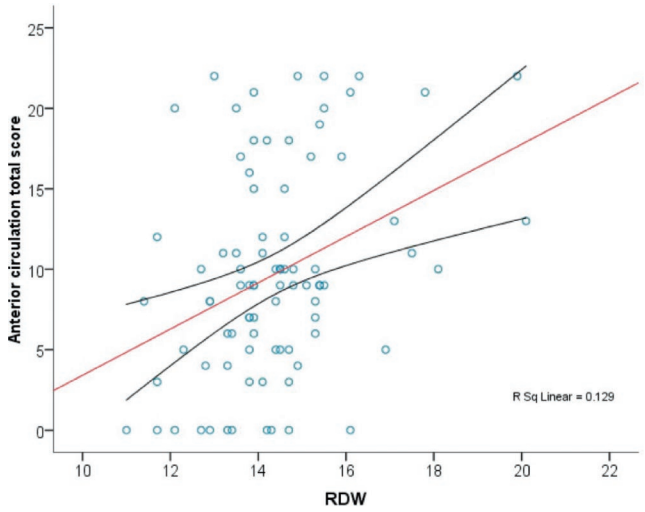

FIGURE 1 Correlation between subtypes of artery calcification in anterior territory with RDW%

Conclusion: The correlation observed between RDW and cerebral artery circulation in the anterior system may be an important marker for the effects of systemic inflammation on intracranial artery calcification, which is an independent risk factor for ischemic stroke.
Disclosure: No.

EPO-380 | The role of post stroke inflammation in acute EEG alterations

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Background and Aims: Post stroke inflammation is a well-known complication which plays a significant role in outcome prediction. Previous studies found a strong association of both slow wave activity (SA) and epileptiform discharges (ED) with stroke outcome. However, there are few data about the relationship between inflammation and on acute phase EEG alteration.
Methods: we retrospectively analysed data of patients with an EEG recording after admission to the SU of Trieste. We excluded haemorrhagic strokes, stroke mimics, infratentorial ischemic strokes, factors which can alter the inflammatory biomarkers (infections, immunosuppressant drugs) and factors which can modify the EEG (previous strokes, antiseizure medication, cognitive impairment). The blood tests were collected after 24h the admission (e.g., C-reactive-protein (CRP), erythrocyte sedimentation rate (ESR), white blood count, neutrophil and lymphocyte count and their ratio (NLR)). We compared the stroke characteristics and risk factors between SA vs no-SA and ED vs no-ED.Then we performed a multivariate analysis (logistic regression).
Results: 316 patients were analysed 0.140 have SA and 67 ED. After multiple adjustment, NLR was not associated with SA (OR 0.98, CI 95% 0.89–1.08, $p = 0.709$), however NLR (OR 1.01, CI 95% 1.03–1.16, $p = 0.002$) remains significantly associated with ED. SA remains associated with some stroke characteristics as admission NIHSS (OR 1.15, CI 95% 1.07–1.24, $p < 0.001$) and haemorrhagic transformation (OR 4.23, CI 95% 1.26–14.21, $p = 0.020$).

TABLE 1 Univariate and multivariate regression for SA.

	UNIVARIATE		MULTIVARIATE	
	OR (95% CI)	**p**	**OR (95% CI)**	**p**
Treatment	2.302 (1.380-3.841)	**0.001**	1.229 (0.667-2.264)	0.509
AF	1.935 (1.077-3.476)	**0.027**	1.140 (0.415-3.131)	0.800
OCSP		**<0.001**		0.144
TACI	8.750 (2.007-38.144)	**0.004**	4.483 (0.823-24.413)	0.083
PACI	1.259 (0.418-3.792)	0.683	1.412 (0.397-5.016)	0.594
LACI	0.625 (0.196-1.995)	0.427	0.981 (0.889-1.083)	0.709
POCI	Ref		Ref	
TOAST		**0.008**		0.275
CE	1.226 (0.599-2.509)	0.576	0.930 (0.299-2.889)	0.900
LAA	0.566 (0.243-1.317)	0.186	0.290 (0.097-0.865)	**0.026**
Lacunar	0.354 (0.181-0.692)	**0.002**	0.761 (0.197-2.936)	0.691
Other	0.755 (0.239-2.382)	0.631	0.780 (0.208-2.933)	0.713
Cryptogenic/indeterminate	Ref			
HT	5.987 (2.022-17.727)	**0.001**	4.233 (1.261-14.207)	**0.020**
NIHSS on admission	1.184 (1.112-1.261)	**<0.001**	1.152 (1.068-1.242)	**<0.001**
NLR	1.143 (1.042-1.254)	**0.005**	0.981 (0.889-1.083)	0.709
Admission to EEG time	1.010 (0.952-1.072)	0.741		

TABLE 2 Univariate and multivariate regression for ED

	UNIVARIATE		MULTIVARIATE	
	OR (95% CI)	p	OR (95% CI)	p
Age	1.016 (0.995-1.037)	0.131		
Sex	2.624 (1.493-4.609)	**0.001**	2.197 (1.166-4.140)	**0.008**
Treatment	1.820 (1.026-3.229)	**0.041**	1.157 (0.605-2.217)	0.661
AF	2.031 (1.163-3.549)	**0.013**	1.011 (0.520-1.966)	0.975
OCSP		**<0.001**		0.136
TACI	2.692(0.804-9.018)	0.108	1.144 (0.287-4.543)	0.849
PACI	0.615 (0.186-2.033)	0.425	0.463 (0.132-1.621)	0.229
LACI	0.538 (0.147-1.967)	0.349	0.560 (0.145-2.157)	0.399
POCI	Ref		Ref	
NIHSS on admission	1.088 (1.046-1.131)	**<0.001**	1.000 (0.946-1.057)	0.902
NLR	1.130 (1.070-1.194)	**<0.001**	1.092 (1.028-1.160)	**0.004**
Admission to EEG time	0.942 (0.824-1.076)	0.378		
CRP	1.020 (0.999-1.041)	0.051		
Slow Activity	4.438 (2.166-9.091)	**<0.001**	2.835 (1.309-6.228)	**0.008**

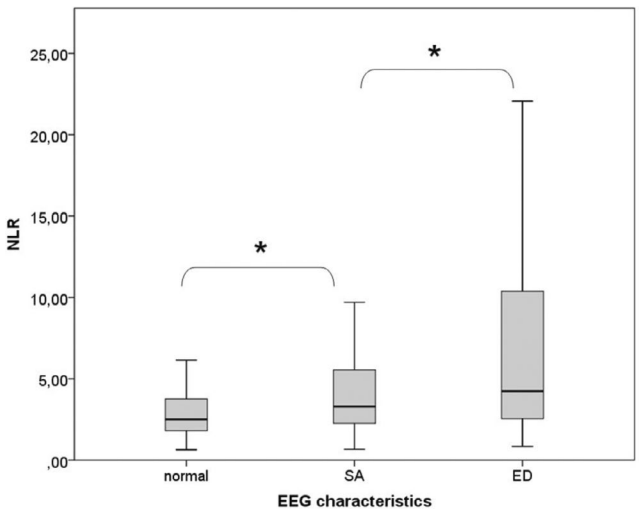

FIGURE 1 NLR levels in the 3 groups. (*) if $p < 0.01$

Conclusion: post stroke inflammation may play different roles in acute EEG. NLR may be more related to the development of ED than SA. SA on EEG is more related to stroke severity and haemorrhagic transformation.
Disclosure: Nothing to disclose.

EPO-381 | Complex functional TCD examinations in patients with significant internal carotid artery stenosis

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Background and Aims: In cases of 48 patients with significant Internal Carotid Artery (ICA) stenosis (ICAS-70%<) a multimodal Transcranial Doppler US examination was performed before undergoing vascular surgery.
Methods: 48 patients were recruited. The applied four vasoactive stimuli were the Valsalva Maneuver (VM), Common Carotid artery Compression test (CCC), Hyperventilation (HV) and Breath Holding (BH) tests. The blood flow velocity changes of both MCA were registered by TCD. The patients' systemic hemodynamic parameters were also simultaneously recorded: ECG, continuous non invasive arterial blood pressure measurement and capnography. A number of time and amplitude variables were defined that took into account arterial blood pressure changes in addition to BFV changes. The Wilcoxon Matched Pair Test was used for the statistical analysis of the variables of the stenotic and contralateral side.
Results: Due to technical reasons VM of 34, HV-BH test of 31 and CCC test of 26 patients were eveluated. In the case of HV-BH tests the BHI did not show a significant difference regarding the stenotic and contralateral side (BHIICAop (mean (SD)): 2.36 ±2.38, BHIICAnonop (mean (SD)): 2.33 ±1.77 Wilcoxon Matched Pair Test $p = 0.89$), while in the dynamic tests (CCC and VM) both time and amplitude variables proved to be sensitive for detecting hemodynamic disturbances.
Conclusion: In cases of carotid stenosis requiring surgical treatment, we recommend the use of stimuli that induce pressure-flow changes for preoperative ischemic risk assessment.
Disclosure: Nothing to disclose.

EPO-382 | AI-based software to support mechanical thrombectomy transfer decision in low-volume primary stroke centers

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Background and Aims: Incorporating artificial intelligence (AI)-based tools into stroke workflows has been shown to significantly reduce the time to endovascular thrombectomy (EVT) in the drip-and-ship model. This study assesses their potential impact on low-volume primary stroke centers.

Methods: We analyzed 95 consecutive anterior circulation stroke patients referred for EVT from 5 low-volume primary stroke centers (≤12 referred patients/year) between January 2019 and April 2023. Remote transmission of radiological images was unavailable. Non-contrast CT and CT angiography studies were retrospectively analyzed using Brainomix 360 software. Clinical data were extracted from our prospective database. EVT-treatment decisions were simulated by two vascular neurologists blinded to outcomes.
Results: LVO was automatically detected in 77 (81.1%) patients. Median door-in-door-out (DIDO) time was 104 minutes (interquartile range [IQR], 87–223), with time from CT angiography to EVT decision accounting for nearly half of it (median 50 minutes; IQR, 30–143). Seventy-three patients (76.8%) could be readily qualified for EVT transfer based on AI-generated imaging data. Transfer would be denied in 4 cases (4.2%) due to both extensive ischemic changes and poor collateral flow; all had unfavorable 3-month outcome (modified Rankin scale of 5–6).
Conclusion: In approximately three-quarters of anterior circulation EVT patients within a drip-and-ship model, referral decisions could be made based on AI-generated neuroimaging data. This is particularly relevant in the workflow of low-volume primary stroke centers, given the relatively long DIDO times. Additionally, AI-based tools may help to prevent the transfer of a small percentage of patients at high risk of futile treatment.
Disclosure: Nothing to disclose.

EPO-383 | Comparative characteristics of stroke morbidity in Russia for 2015–2022 taking into account the impact of COVID-19

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Background and Aims: All types of stroke have high levels of morbidity and disability, up to half of the patients become permanently disabled. The investigation of regional characteristics of incidence of stroke is a fundamental direction for evaluation and regulation of morbidity and mortality, especially in the context of influence on incidence of COVID-19. Objective - to study the dynamics of primary and general incidence of stroke in different regions of Russia and to compare morbidity levels in different periods from 2015 to 2022, taking into account the COVID-19 pandemic.
Methods: By means of continuous statistical observation, official statistics of the primary and general morbidity of adult stroke in Russia in different regions were investigated. Cerebrovascular diseases, transient cerebral ischemic attacks, intracerebral and other intracerebral hemorrhages, brain infarctions and strokes not specified as hemorrhage or stroke were included. Calculated mean primary and general morbidity levels, variation range, standard deviation, coefficient of variation.
Results: In the period 2015-2022, primary and general morbidity levels of individual subtypes of stroke had a different dynamics compared to the average long-term indicators and during the pandemic of coronavirus infection.

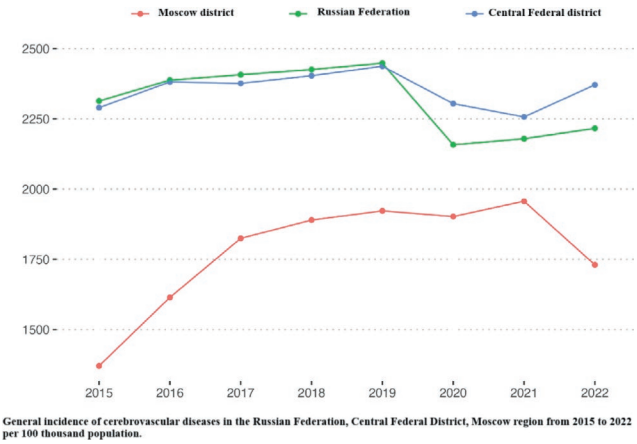

FIGURE 1 Overall incidence of cerebrovascular diseases for 2015–2022

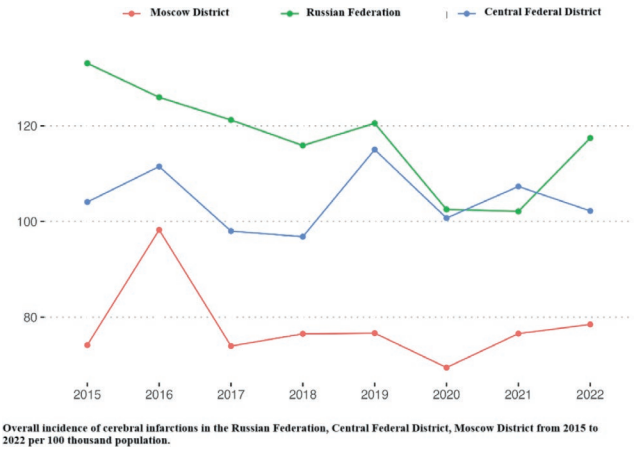

FIGURE 2 Overall incidence of cerebral infarctions for 2015–2022

Conclusion: It is determined that for 2015–2022 the incidence rates are within a limited range of values, which shows the impact of various measures to reduce stroke morbidity in all studied areas. Fluctuations in stroke morbidity rates in the Russian Federation are treated as inaccurate morbidity estimates, incorrect diagnosis coding according to ICD-10, especially in the conditional pandemic COVID-19.
Disclosure: Nothing to disclose.

EPO-384 | One year real-life cohort experience in bempedoic acid in secondary prevention of ischemic stroke

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Background and Aims: Bempedoic acid (BA) antagonizes ATP citrate-lyase, reducing cholesterol synthesis. Recently, it has been approved for the treatment of dyslipidemia, in addition

to statin and ezetimibe. There is still not enough experience regarding its use in patients with ischemic stroke (IS). We aim to describe our experience in secondary prevention of stroke.

Methods: Prospective observational study of patients who started BA therapy as a secondary prevention of IS, treated in a single comprehensive Stroke Centre from September 2023 to December 2024.

Results: Fifty patients (42% female) were included, with a median of 70 years. All patients had multiple vascular risk factors (Table 1). Sixty-five percent were atherothrombotic. We added BA to maximum tolerated statins +/- ezetimibe to achieve two LDL-cholesterol (c-LDL) targets (c-LDL <55 mg/dL in atherothrombotic strokes, or c-LDL <70 mg/dL in the other subtypes). The basal median c-LDL was 79 mg/dL [IQ 37 (69.2–106.2)]. In most of them (78%), BA was combined with statins and ezetimibe, 16% received only ezetimibe, and 6% were on monotherapy. Table 2 shows the determination of c-LDL levels at 3, 6 and 12 months. At 3 months, we observed a reduction of 17.4% in c-LDL. These results were similar during the follow-up with minimum decrease in efficacy. No treatment-related adverse effects were reported. Furthermore, none of the patients suffered new vascular events.

	Frequency (n)	Percentage (%)
Male	29	58
Arterial hypertension	34	68
Diabetes mellitus	18	36
Active/ex-smokers	26	58
Dyslipidemia	45	90
Ischemic stroke	50	100
Atherothrombotic	31	65
Cardioembolic	8	17
Lacunar	4	8
Undetermined	5	10

Table 1. Baseline characteristics

	Median LDL-cholesterol (mg/dL)	Interquartile range
Basal	79	37 (69.2-106.2)
3 month control	66	17,7 (59.2-77)
6 month control	74	35 (59-94)
12 month control	74	17 (70-87)

Table 2. LDL-cholesterol monitoring

Conclusion: In our cohort, Bempedoic acid proved to be safe and effective in lowering LDL-cholesterol in clinical practice. The efficacy of reduction in c-LDL was similar to clinical trial.

Disclosure: Nothing to disclose.

EPO-385 | Good-to-excellent functional outcomes 90 days after large ischemic stroke stratified by ASPECTS in EVT: Meta-analysis

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Background and Aims: Previous randomized controlled trials (RCTs) demonstrated the benefit of endovascular therapy (EVT) in achieving good outcomes for acute ischemic stroke with Alberta Stroke Program Early CT Scores (ASPECTS) ≤5, despite increased intracranial bleeding risk. However, data on 90-day good-to-excellent outcomes for EVT in ASPECTS <3 versus 3–5 remain limited. This meta-analysis compares 90-day functional outcomes stratified into ASPECTS groups: 3–5, ≤3, and ≤5 (combined).

Methods: PubMed and Cochrane databases were searched for RCTs and observational studies comparing EVT versus medical management (MM) in acute ischemic stroke (ASPECTS ≤5), reporting modified Rankin Scale (mRS) 0–2 (good outcomes) and mRS 0–1 (excellent outcomes). Heterogeneity was assessed using I^2, and random-effects models were used where appropriate.

Results: Four studies (three RCTs, one cohort) with 1,225 patients (52.48% EVT) were included. At 90 days, EVT was superior to MM in achieving good outcomes in ASPECTS ≤5 (OR 3.10; 95% CI 1.63–5.88; $p < 0.01$) and ASPECTS 3–5 (OR 3.35; 95% CI 2.08–5.39; $p < 0.01$). Excellent outcomes were four times more likely with EVT in ASPECTS 3–5 (OR 4.01; 95% CI 2.02–7.94; $p < 0.01$) and three times more likely in ASPECTS ≤5 (OR 3.41; 95% CI 1.84–6.31; $p < 0.01$). However, ASPECTS ≤3 showed no significant differences in good ($p = 0.33$) or excellent ($p = 0.60$) outcomes between EVT and MM.

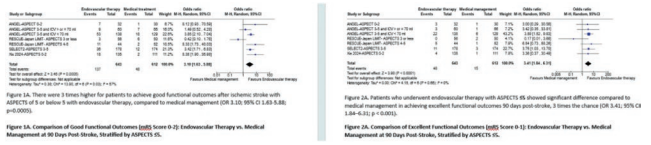

FIGURE 1 Comparison of Functional Outcomes (mRS Score 0–2; versus 0–1): Endovascular Therapy vs. Medical Management at 90 Days Post-Stroke, Stratified by ASPECTS ≤5.

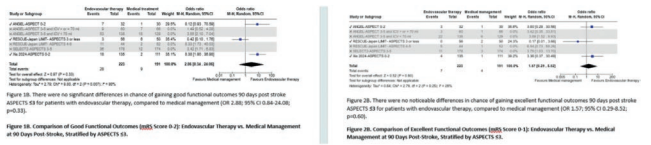

FIGURE 2 Comparison of Functional Outcomes (mRS Score 0–2; versus 0–1): Endovascular Therapy vs. Medical Management at 90 Days Post-Stroke, Stratified by ASPECTS ≤3.

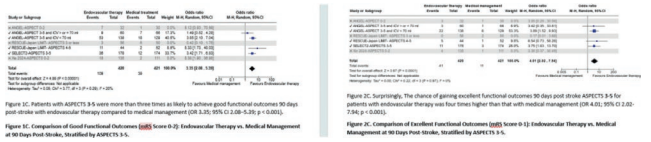

FIGURE 3 Comparison of Functional Outcomes (mRS Score 0–2; versus 0–1): Endovascular Therapy vs. Medical Management at 90 Days Post-Stroke, Stratified by ASPECTS 3–5.

Conclusion: EVT significantly improves good-to-excellent outcomes in ASPECTS 3–5 but shows no benefit over MM in ASPECTS <3. Further RCTs are warranted to explore EVT in ASPECTS ≤3.

Disclosure: Nothing to disclose.

EPO-386 | Herb formula Bao Yuan capsule promotes neurogenesis and neurological functional recovery in ischemic stroke mice model

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School of Chinese Medicine, The University of Hong Kong, Pokfulam, Hong Kong

Background and Aims: Bao Yuan Capsule (BYC) is a patented Chinese medicine formula for health promotion and immunomodulation, but its neuroprotective effects remain unknown. In the present study, we tested the hypothesis that BYC could promote neurogenesis and neurological functional recovery in the mice model of ischemic stroke.
Methods: We firstly performed chemical identification studies by using QIT-TOF-MS technology. Then, we investigated the effects of BYC on improving the recovery of the neurological functions in transient middle cerebral artery occlusion (MCAO) ischemic mice.
Results: We tentatively characterized 36 compounds from the BYC extractions. BYC effectively improved locomotor ability, attenuated anxiety-like behaviors, and enhanced the exploring behaviors, learning and memory capability in the transient MCAO mice. BYC treatment promoted the neural stem cell differentiations in the subventricular zone (SVZ) and subgranular zone (SGZ) of the MCAO mice. BYC also up-regulated the expression of enzymes in oxidative phosphorylation of mitochondria, and its downstream Akt-beta-catenin signaling pathway in the hippocampus of the stroke mice. BYC significantly improved the mitochondrial functions in cultured mouse multipotent neural stem like C17.2 cells. BYC treatment promoted the neuronal differentiations in the C17.2 cells after exposed to oxygen-glucose deprivation (OGD), whose effects were abolished by co-treatments of ATP synthesis inhibitor oligomycin and PI3K/Akt inhibitor wortmannin. Moreover, Akt phosphorylation were dramatically reduced in oligomycin treated C17.2 in differentiation revealing that Akt might be the downstream mechanism of BYC induced neurogenesis.
Conclusion: BYC could promote neurogenesis and neurological functional recovery in post ischemic stroke treatment by regulating the mitochondrial functions.
Disclosure: Nothing to disclose.

EPO-387 | LA strain: A key to uncovering cardioembolic causes of transient ischemic attacks

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Background and Aims: Patients with transient ischemic attacks (TIA) often have undiagnosed paroxysmal atrial fibrillation (AF), a common cause of cardioembolic events. Since AF originates in the atria, this study investigated whether abnormalities in left atrial (LA) structure and function could help identify cardioembolic causes of TIA in patients with sinus rhythm but documented episodes of paroxysmal AF.
Methods: This study included 190 TIA patients, divided into two groups: those with confirmed paroxysmal AF (Group I) and those without (Group II), based on medical record assessments. Cardiac ultrasonography was performed during sinus rhythm, at least 14 days post-TIA onset, to avoid the confounding effects of atrial stunning.
Results: Group I patients were older, more frequently female, had a history of stroke or TIA, and higher CHA2DS2-VASc scores. They also exhibited increased LA volumes, reduced LA emptying fractions, and significantly altered LA deformation patterns. Multivariate logistic regression identified three independent predictors of paroxysmal AF: age >55 years, LA reservoir strain <–17%, and LA emptying fraction <51% ($p < 0.0001$).

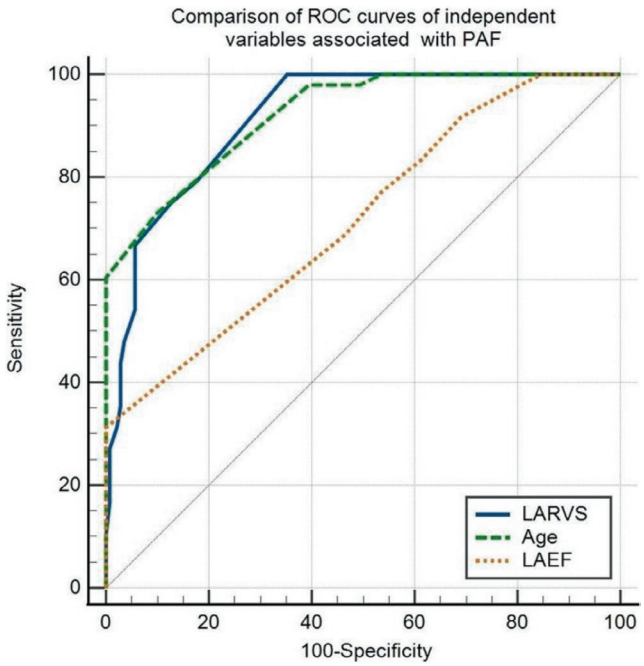

FIGURE 1 ROC curves comparison

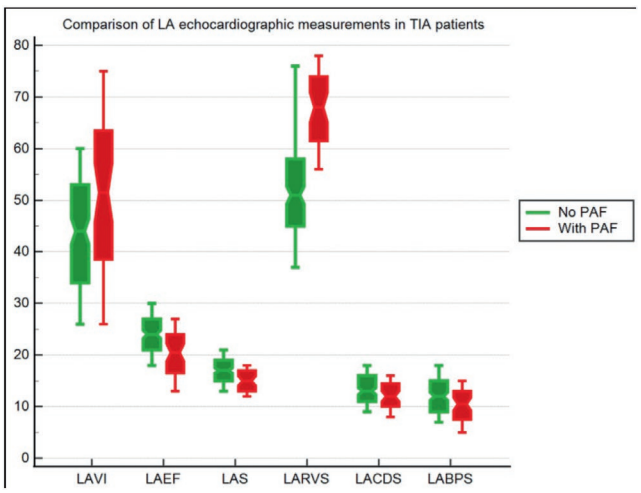

FIGURE 2 Comparison of left atrial echocardiographic measurements in transient ischemic attack patients.

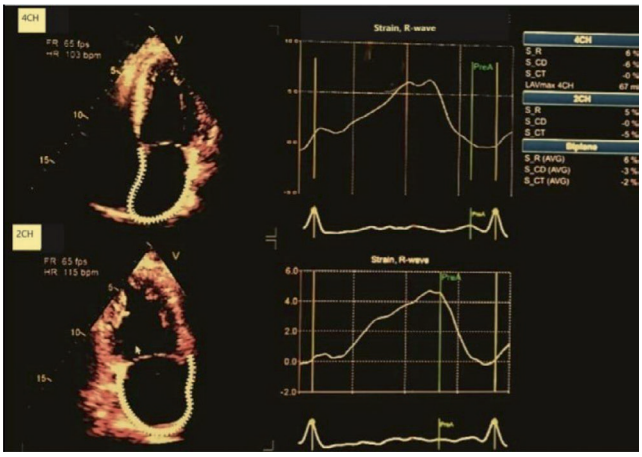

FIGURE 3 Strain curves from left atrial speckle-tracking, in apical four-chamber and two-chamber.

Conclusion: This research demonstrates that LA strains are independently associated with paroxysmal AF in TIA patients and may help identify cardioembolic origins of TIA. These findings have significant clinical implications, as LA 2D speckle-tracking echocardiography (2D-STE), not currently part of routine TIA evaluation, could provide a valuable tool for detecting atrial dysfunction and guiding targeted therapies.
Disclosure: Nothing to disclose.

EPO-388 | Effects of non-invasive brain stimulation on cerebral blood flow in chronic ischemic stroke: A randomised control study

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Background and Aims: Upper extremity impairments are common among stroke survivors. We studied the effect of repetitive transcranial magnetic stimulation (rTMS) and transcranial direct current stimulation (HD-tDCS) on regional cerebral blood flow (CBF) in chronic ischemic stroke using single-photon emission computed tomography (SPECT) imaging.
Methods: In a double-blind, randomized controlled trial, 12 patients with chronic middle cerebral artery ischemic stroke with residual upper limb weakness were assigned to four groups of: combined real HD-tDCS and rTMS (Group A), sham HD-tDCS and real rTMS (Group B), real HD-tDCS and sham rTMS (Group C), and sham HD-tDCS and rTMS (Group D) administered for 10 consecutive days. Pre- and post-treatment SPECT imaging was done using 99mTc-ECD and acquired in Siemens Symbia T6 LEHR Collimator.
Results: No statistically significant changes in regional CBF were observed between the groups ($F=1.76$, $p=0.23$). Group A showed a maximum improved CBF ($+1.67 \pm 2.52$) compared to Group B (-1.67 ± 1.15), Group C ($+0.33 \pm 2.31$) and Group D ($+1.33 \pm 1.53$). Compared to sham NIBS, the NIBS protocols showed no significant differences for the mean change in blood flow.

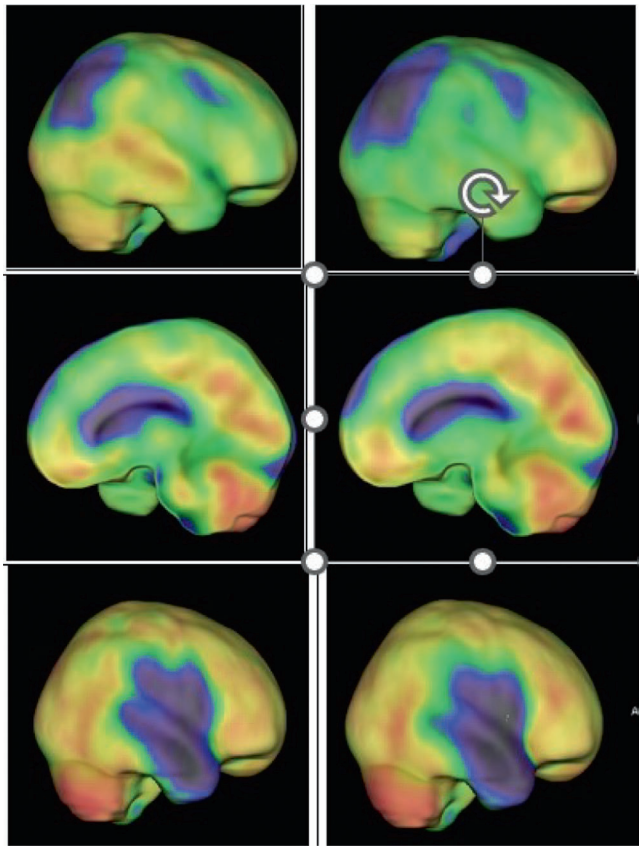

FIGURE 1 GROUP B (Sham tDCS and Real rTMS)

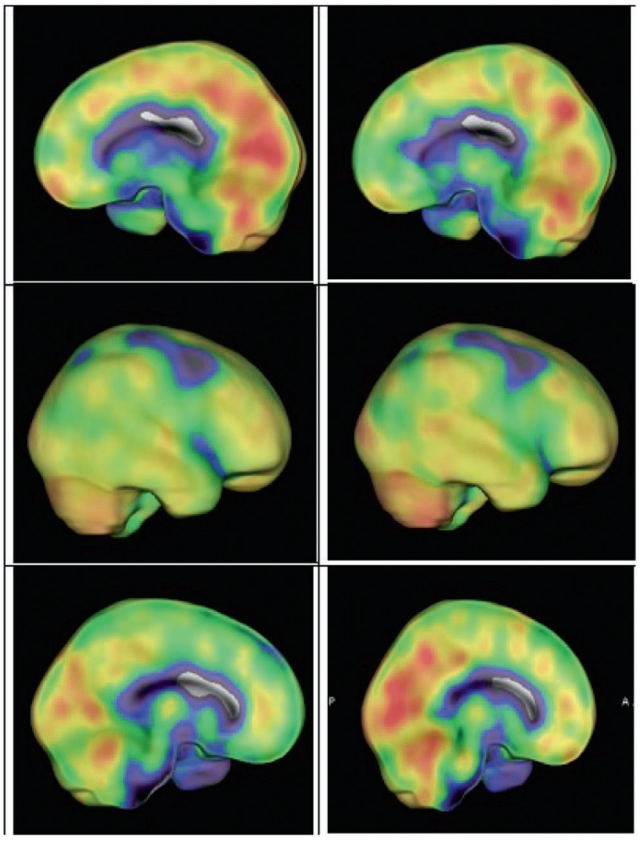

FIGURE 2 GROUP C (Real tDCS and Sham rTMS)

Conclusion: This pilot study demonstrated the feasibility and safety, and potential of NIBS protocols for modifying the regional blood flow on the infarcted hemisphere and the potential for SPECT as a surrogate marker for NIBS induced modification of regional brain flow. Larger-scale studies are warranted to validate these findings, which may give better insights into the physiological mechanisms underlying the effects of NIBS.
Disclosure: Nothing to disclose.

EPO-389 | Prognostic nutritional index as an indicator for in-hospital mortality in patients with cerebral venous thrombosis

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Background and Aims: Prognostic nutritional index (PNI) combines albumin concentration and the lymphocyte count reflecting the nutrition, immunity status and inflammation. Several studies have reported that lower PNI is related to increased mortality in patients with various malignancies, cardiovascular diseases and ischemic stroke. However, little is known about PNI and its relationship with the mortality in cerebral venous thrombosis (CVT). Therefore, we evaluated the prognostic significance of the admission PNI for predicting in-hospital mortality in patients with CVT.
Methods: This retrospective study included 50 consecutive patients admitted within 48 h of CVT onset to our clinic between January 2013 and February 2024. Patients were categorized as survivors discharged from the hospital and those who died during hospitalization. The groups were compared for demographics, risk factors, clinical symptoms, imaging characteristics, admission laboratorial parameters, and PNI. Multivariate logistic regression analysis was performed to confirm if lower PNI was associated with a hospital mortality.
Results: Patients who died in the hospital ($n=14$) were significantly older compared to survivors. These patients were characterized by higher NIHSS scores, a higher prevalence of parenchymal lesion, and higher lymphocyte count. In addition, they exhibited significantly lower PNI value ($p<0.05$). ROC curve analysis also showed that the PNI had a good predictive value for in-hospital mortality with a cut-off value of 41.45.
Conclusion: We suggested that lower PNI may serve as a valuable prognostic indicator for predicting in-hospital mortality in patients with CVT.
Disclosure: Nothing to disclose.

EPO-390 | Impact of recanalisation level and the first pass effect on outcome in patients after M2 MCA occlusion thrombectomy

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Background and Aims: Mechanical thrombectomy (MT) is modality of choice in treatment of acute ischemic stroke (AIS) and large vessel occlusion (LVO). Endovascular treatment of medium and distal vessel occlusions (DMVO) is currently under intensive scientific investigation. Aim of our study was to prove feasibility, effectivity and safety of MT in patients with a primary, isolated M2 MCA occlusion with focus on recanalisation level and first pass effect (FPE) as predictors.
Methods: We prospectively assessed 137 patients during the three years period, since July 2021 to July 2024 (Tab. 1). Primary outcome was defined by modified Rankin Scale (mRS) score 0 - 2, secondary outcome included excellent functional independence (mRS 0–1) and successful recanalisation (mTICI 2c or 3). Safety outcomes included symptomatic intracerebral hemorrhage (sICH), any intracerebral (IC) hemorrhage and 90 days mortality.

Parameter	First pass mTICI 2c/3	Non First pass mTICI 2c/3	p value
n (%)	63 (46)	74 (54)	
Males (%)	29 (46)	30 (40.5)	*0.764*
Age (mean±SD)	70.6±12.5	72.6±11.1	*0.467*
Admission NIHSS (median)	11,5	10,0	
Arterial hypertension (%)	51 (81)	65 (87.8)	*0.269*
Atrial fibrilation (%) - including primomanfestation	32 (50.8)	38 (51.4)	*0.567*
Diabetes mellitus (%)	13 (20.6)	18 (24.3)	*0.772*
Wake-up stroke (%)	8 (12.7)	13 (17.6)	*0.430*
i.v. Thrombolysis (%)	28 (44.4)	24 (32.4)	*0.149*
ASPECTS score (mean±SD/median)	9.4±1.0/10	9.4±1.0/10	
Collateral score (mean±SD/median)	2.2±0.5/2	2.2±0.6/2	
M2 dominant branch (%)	26 (41.3)	37 (50)	*0.307*

NIHSS - National Institutes of Health Stroke Scale, i.v. - intravenous, ASPECTS - Alberta Stroke Program Early CT Score

FIGURE 1 Basic epidemiological parameters and clinical characteristics.

Results: We found that level of reperfusion is linked with better functional outcome, the correlation between good clinical outcome and good reperfusion level (TICI 2c or 3) reached statistical significance ($p=0.024$) (Tab. 2). We failed to prove the importance of first pass effect (FPE) during MT of the M2 segment (Tab. 3). We also noticed a significant 31.3% mortality increase in the group of patients, where recanalisation of the occluded branch was insufficient.

Parameter	mTICI 2b/less (n = 19)	mTICI 2c/3 (n = 118)	p value
mRS 0 - 2 (%)	8 (42.1)	81 (68.6)	*0.024*
mRS 0 - 1 (%)	1 (5.3)	57 (48.3)	*< 0.001*
Mortality = mRS 6 (%)	9 (47.4)	19 (16.1)	*0.002*
Any ICH (%)	6 (31.6)	36 (30.5)	*0.925*
Symptomatic ICH (%)	1 (5.3)	4 (3.4)	*0.686*

mTICI - modified thrombolysis in cerebral infarction, mRS - modified Rankin scale, ICH - intracerebral hemorrhage

FIGURE 2 General characteristics of outcomes divided by mTICI grade

Parameter	First pass mTICI 2c/3 (n = 63)	Non First pass mTICI 2c/3 (n = 74)	p value
mRS 0 - 2 (%)	39 (61.9)	50 (67.6)	*0.489*
mRS 0 - 1 (%)	31 (49.2)	27 (36.5)	*0.133*
Mortality = mRS 6 (%)	12 (19.1)	16 (21.6)	*0.710*
Any ICH (%)	17 (27)	25 (33.8)	*0.390*
Symptomatic ICH (%)	3 (4.8)	2 (2.7)	*0.522*

mTICI - modified thrombolysis in cerebral infarction, mRS - modified Rankin scale, ICH - intracerebral hemorrhage

FIGURE 3 General characteristics of outcomes divided according to presence of FPE.

Conclusion: We conclude, that MT is a powerful and effective treatment method for AIS caused by an occlusion of M2 segment in real life conditions. Patients have higher probability of long term good functional outcome in case that complete or near complete reperfusion is achieved.
Disclosure: Nothing to disclose.

Education in Neurology

EPO-391 | Teaching neurological emergencies through ward-based simulation

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Background and Aims: High-fidelity simulation replicates medical scenarios for students to apply their skills safely. Many medical students experience 'neurophobia' when learning about neurological conditions. This ward-based simulation programme aimed to evaluate confidence in managing neurological emergencies before and after working through a novel simulation programme.
Methods: Scenarios on epilepsy, spinal cord compression and meningitis were designed to run parallel on a simulated ward. Third-year medical students were recruited to act as the patient. The scenarios were completed by final-year medical students working at foundation year 1 doctor level. We collected a pre-simulation data with students rating their confidence in neurological assessment and management on a Likert scale (1–5) and repeated this post-simulation before analysis.
Results: In the first round of simulation, 16 students took part. There was a significant difference in reported confidence in recognising acute neurological deterioration and deficit prior to the simulation ($M = 2.625$, $SD = 0.93$) after the simulation ($M = 3.875$, $SD = 0.70$); $t(15) = -5.84$, $p = 0.00003$. All students agreed or strongly agreed that simulation is a good way to learn. There was a significant improvement in confidence when managing neurological emergencies before the simulation ($M = 2.375$, $SD = 0.72$) and after the simulation ($M = 3.8125$, $SD = 0.66$); $t(15) = -6.45$, $p = 0.00001$.
Conclusion: We found improved self-rated confidence in neurological assessment and management. This exercise encourages students to apply clinical judgement. Our results are limited by the small sample size therefore, this simulation programme is ongoing, and further data is being collected. Multi-centre data is also required to assess the wider impact of ward-based simulation.
Disclosure: Nothing to disclose.

EPO-392 | Neurophobia and the perception of neurology among neurologists in Spain

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Background and Aims: Neurophobia has been well documented in medical students, residents and other specialties, but it has not been explored among neurologists. We aimed to study the awareness neurologists have of neurophobia, as well as our knowledge, fears and insecurities towards our specialty.
Methods: An online questionnaire was distributed through scientific regional societies of neurology. Respondents were questioned about neurophobia and its causes. They were also interrogated about the training received during residency and their perceived current knowledge and insecurities regarding the different subspecialties.
Results: 284 neurologists answered the survey. 60% were familiar with neurophobia. 249 (90%) thought neurophobia was prevalent among other specialties, 244 (88%) in residents, while only 151 (55%) identified neurophobia in medical students. Main reasons for neurophobia were the intrinsic difficulty of neurosciences (211, 74%) and the neurological examination (168%, 59%). Neurogenetics, palliative and sleep-wake neurology were the weakest areas of training during the residency (85%, 84% and 77% respectively). However, neurologists felt the most insecure (Figure 1) in neurogenetics (142, 56%), ataxias (118, 47%), neuro-oncology and neuromuscular diseases and (112, 44%). Reasons adduced were lack of exposure (177, 62%), training gaps during residency (137, 48%) or exclusive dedication to other pathologies (131, 46%).

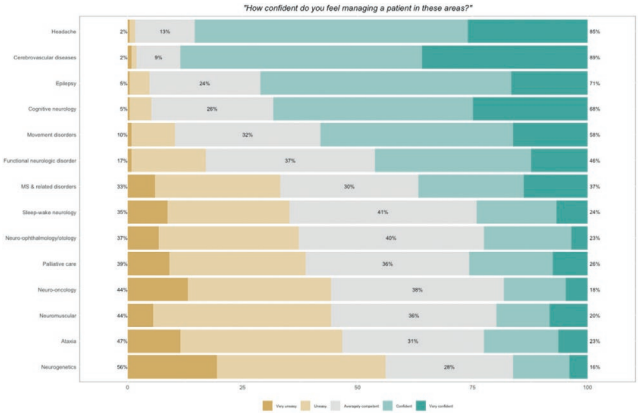

FIGURE 1 Neurologists' confidence levels across different areas.

Conclusion: Neurophobia is not unknown to Spanish neurologists. We also identified a gap in residency training for palliative care, sleep-wake neurology and genetics. However, it was neuromuscular diseases and ataxias where they felt the most insecure. One could argue "partial neurophobia" may exist among neurologists, caused by the lack of exposition more than training or theoretical knowledge.
Disclosure: Nothing to disclose.

EPO-393 | Exploring gender disparities in neurology education: Insights from Spanish medical schools

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Background and Aims: Gender disparities in university faculty roles is a concern across European higher education, with women often underrepresented in senior positions. Women comprise 54% of the Spanish Society of Neurology (SEN) membership, yet their representation within university medical programs remains underexplored. This study aims to analyze neurologists lecturing Neurology in Spanish medical schools, focusing on gender distribution, academic rank, and career progression.
Methods: From July to October 2024, a self-administered survey was distributed to SEN members and medical schools. Data collected included demographics, teaching experience and academic roles. Bivariable and inferential analyses were conducted to assess relationships and statistical significance.
Results: Responses were received from 39 of 43 eligible medical schools. Among 217 respondents, 135 were actively lecturing Neurology, including 49 women (36%). The mean age was 53 ±10 years, with women being younger than men (51 ±8 vs. 55 ±11, $p=0.047$). Women had fewer years of teaching experience than men (10 ±7 vs. 15 ±11, $p=0.004$). Gender distribution across academic ranks varied but did not reach statistical significance ($p=0.112$): women held 25% of Professorships (1/4), 22% of Senior Lecturer roles (4/18), 43% of Lecturer roles (3/7), and 41% of Associate Lecturer or collaborator positions (41/101). None of the three Emeritus Professors were women.
Conclusion: Gender disparities are present in academic Neurology in Spain, with women underrepresented despite their substantial presence in the SEN. Although women hold fewer senior academic roles, these disparities did not reach statistical significance compared to their colleagues. Insight from other European countries would be of interest.
Disclosure: The authors are members of the SEN Council on "Neurology and University".

EPO-394 | Immersive virtual reality education for electroencephalography interpretation

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Background and Aims: Electroencephalography (EEG) is an essential tool in neurology and neuroscience. Its interpretation is time-consuming and requires specialised healthcare professionals for a medical diagnosis. This study introduces a novel Virtual Reality (VR)-based EEG analysis platform that integrates visual and auditory modalities, and artificial intelligence (AI) to detect neonatal seizures.
Methods: An openly available neonatal EEG dataset from the University of Helsinki was used. An EEG analysis application on a VR headset was developed and evaluated. The developed VR environment integrates data and information streams to represent and analyse EEG data, comprised of 8-channels, Fourier transforms, AI-assisted sonification, and an AI-informed 3D visualisation of the brain's seizure activity to detect seizures.
Results: A series of user studies were conducted, evaluating the system's usability, functionality, and overall user experience. User evaluations (20 participants) indicate high satisfaction and reduced cognitive load. Participants performed best when using both sound and visualisation (Combined mean = 7.60), followed by the visualisation alone (Visualisation mean = 6.10) and sound alone (Sound mean = 5.50). The comparative analysis between the two groups (with prior knowledge and no prior knowledge of EEG) shows a slight variation in performance across the three modalities.
Conclusion: This work introduces a VR-based platform to facilitate EEG analysis for seizure detection using a multisensory representation, including 2D and AI-assisted 3D visualisation and AI-assisted sonification and analysis of EEG data. The initial results recommend the tool for applications in educational and clinical settings that require EEG analysis.
Disclosure: Qualcomm sponsored this work through a philanthropic gift UNI-479522. All the authors don't have any conflict of interest to report.

EPO-395 | Focal epilepsy: Virtual patient simulation improves performance in diagnosis and management but uncovers inertia

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Background and Aims: Diagnosing focal epilepsy is challenging due to heterogeneous presentation, limited patient awareness and restricted access to diagnostic tools. Further, management is complicated by diverse aetiologies and numerous potential therapies. Using a patient simulation of a young

female with focal seizures and co-morbid anxiety and depression with partial control on 2 prior monotherapies, we assessed neurologists' performance in diagnosing drug-resistant focal epilepsy and managing nocturnal breakthrough seizures with appropriate combination therapy.
Methods: This CPD-certified virtual simulation allowed European neurologists to select diagnostic and treatment options from a comprehensive database (available at: https://www.medscape.org/viewarticle/998607). After each decision, learners received clinical guidance (CG) based on evidence and faculty recommendations. Pre- and post-CG decisions were analyzed using McNemar's test ($p < 0.05$ is significant). Data were gathered from March to December 2024.
Results: Ninety neurologists participated in the case simulation. Significant improvements were seen post-guidance (CG) for identifying drug-resistant epilepsy (21% to 65%, $p < 0.001$), managing epilepsy (36% to 69%, $p < 0.001$), and evaluating co-morbid anxiety/depression (67% to 75%, $p < 0.01$). Analysing decision flows with a less-stringent diagnostic definition, correct diagnosis and treatment rose from 24% to 29%, while incorrect decisions dropped from 46% to 36%. Among those choosing incorrect treatments, 87% showed inertia pre-CG (no treatment change), decreasing to 74% post-CG.
Conclusion: This study demonstrates the positive effect of online medical education through a virtual simulation on European neurologists' performance in diagnosing and managing drug-resistant focal epilepsy, but in-depth analyses uncovered high levels of inertia in managing drug-resistant epilepsy.
Disclosure: Developed through independent educational funding from Angelini Pharma.

EPO-396 | Virtual patient simulation improves diagnosis and management but uncovers low drug-resistant epilepsy diagnosis rates

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Background and Aims: Diagnosing focal epilepsy is challenging due to heterogeneous presentation, limited patient awareness and restricted access to diagnostic tools. Further, management is complicated by diverse aetiologies and numerous potential therapies. Using a patient simulation of a 62-year old male with post-encephalitic focal seizures with poor control despite 3 different therapies, we assessed neurologists' performance in diagnosing drug-resistant focal epilepsy and managing frequent seizures with appropriate combination therapy.
Methods: This CPD-certified virtual simulation allowed European neurologists to select diagnostic and treatment options from a comprehensive database (available at: https://www.medscape.org/viewarticle/998607). After each decision, learners received clinical guidance (CG) based on evidence and faculty recommendations. Pre- and post-CG decisions were analyzed using McNemar's test ($p < 0.05$ is significant). Data were gathered from March to December 2024.
Results: 106 neurologists participated in the case simulation. Significant improvements were seen post-guidance (CG) for identifying drug-resistant epilepsy (16% to 56%, $p < 0.001$) and managing epilepsy (14% to 29%, $p < 0.001$). Analysing decision flows with a less-stringent diagnostic definition, correct diagnosis and treatment rose from 0.9% to 13%, while incorrect decisions dropped from 93% to 60%. Among those with incorrect treatment, 61% showed inertia pre-CG (no treatment change), decreasing to 46% post-CG.
Conclusion: This study demonstrates the positive effect of online medical education through a virtual simulation on European neurologists' performance in diagnosing and managing drug-resistant focal epilepsy, but more in-depth analyses uncover low levels of diagnosis and management of drug-resistant epilepsy.
Disclosure: Developed through independent educational funding from Angelini Pharma.

EPO-397 | How does the publication of recommendations affect clinical practice? A comparative analysis of patient journeys

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Background and Aims: Quantitative evaluation of the impact of recommendations publication on clinical practice has been poorly investigated in research. This study analysed the systematic changes in the clinical diagnostic process attributable to the publication of the Italian Intersocietal recommendations for biomarker-based diagnosis of neurocognitive disorders (Boccardi, 2000).
Methods: Medical charts of new patients from three Italian memory clinics were reviewed for 2019 (pre-recommendations, P1) and 2023 (post-recommendations, P2). Sociodemographic and clinical data were extracted, and adherence to the recommendations was assessed using a modified Adherence Index (AI). The AI score, ranging from 0 to 5, evaluates diagnostic work-up completeness, with higher scores indicating better adherence. Statistical analyses (Mann-Whitney U and chi-square tests) compared AI scores across periods.
Results: A total of 601 diagnostic work-ups from P1 and 434 from P2 were reviewed. Adherence was computed only in

diagnostic work-up including biomarkers, i.e., 139 cases (23%) in P1 and 178 cases (41%) in P2. Over time, the IA score increased from 2.09 ±1.04 to 2.28 ±1.04 ($U=81$; $p=0.047$). P2 work-ups featured a more thorough neuropsychological assessment (AI: 0.40 ±0.36 in P1 vs. 0.48 ±0.43 in P2, $U=9492$; $p<0.001$) and more adherent use of biomarkers prescription ($X2(3)=39.66$; $p<0.001$).

Conclusion: Adherence analysis highlighted significant changes in clinical diagnostic work-ups following the recommendations release. AI is a straightforward-to-implement measure that provides quantitative indications of the impact of recommendations in actual settings. Process mining will allow for a more in-depth analysis.

Disclosure: We acknowledge unrestricted grants from GE HealthCare LTD and Roche Diagnostics S.p.A. The funders had no role in the conception, design, and implementation of the project nor in data collection, data analysis, interpretation, or discussion of the results. Funders had no privileged access to the project's outputs at any stage.

EPO-398 | Inventory of the knowledge and training needs of professionals in EHPAD for Parkinson's disease

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Background and Aims: Parkinson's disease is a major public health issue, due to its rapidly increasing incidence, which is associated with high levels of dependency and institutionalization. It requires personalized care. The aim of this study is to assess the initial knowledge of professionals working in residential care facilities for the elderly, in order to provide teams with knowledge to adapt to the profiles of their Parkinsonian patients.

Methods: A quantitative study was carried out using a nationally distributed questionnaire. 430 questionnaires were completed by paramedical staff, 92% of them by state-qualified nurses and care assistants. 5 qualitative interviews were conducted with professionals to gain a deeper understanding of their perception of working and training conditions in residential care facilities.

Results: 71% of caregivers felt they knew the pathology. However, trembling (42%) is considered a diagnostic criterion. On the other hand, pain (12%), anxiety (10%) and depression (10%) are little recognized. The role of symptomatic treatments is accepted by 96% of caregivers. Little is known about their non-oral administration. A desire for training (92%) is expressed on pathology (23%) and support (25%). Qualitative interviews underline the central role played by orderlies in dispensing medication, as well as the importance of their knowledge.

Conclusion: EHPAD professionals have an incomplete perception of the pathology. They express a need for training in how to support these patients. In the light of these results, it is essential to develop targeted actions to encourage appropriate care for Parkinson's patients.

Disclosure: The authors would like to thank Tilio Cognard, head of training at France Parkinson, for distributing and passing on the questionnaire feedback.

EPO-399 | The role of knowledge and information sources in empowering patients with multiple sclerosis

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Background and Aims: Empowering patients with multiple sclerosis (MS) is crucial for enhancing their management and quality of life. This study investigates how patient empowerment is reflected in a balance between different types of knowledge (emotional, rational, and spiritual). Additionally, it assesses the impact of verified and unverified information sources on this empowerment.

Methods: A sample of 75 MS patients was consecutively selected, and questionnaires designed to evaluate emotional, rational, and spiritual knowledge were administered. The influence of verified and unverified information sources on patients' decisions was also examined. Data were analysed using the SPSS 4.1 programme through multivariate regression and correlation analysis.

Results: Emotional knowledge demonstrated the greatest effect on patient empowerment ($\beta=0.86$, $p<0.000$), followed by rational ($\beta=0.77$, $p<0.000$) and spiritual ($\beta=0.73$, $p<0.000$). However, the balance between the three types was essential for achieving optimal levels of empowerment. Regarding information sources, verified ones had a greater impact ($\beta=0.31$, $p<0.002$) compared to unverified ones ($\beta=0.21$, $p<0.023$), although both were significant.

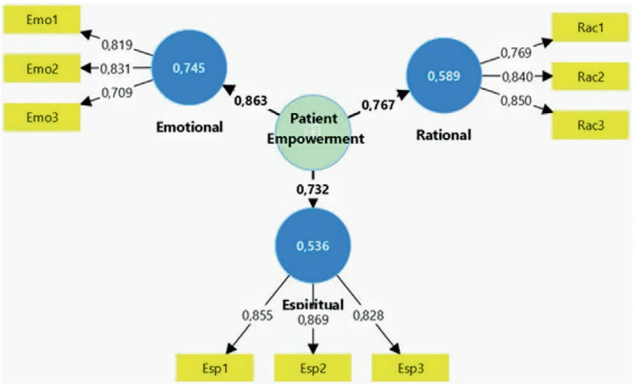

FIGURE 1 Patient empowerment and kinds of knowledge

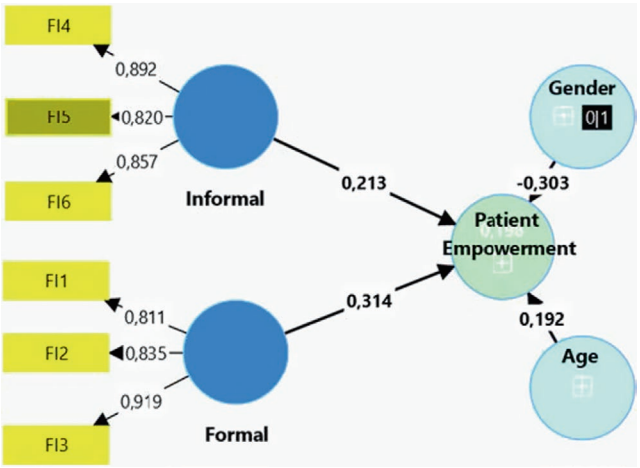

FIGURE 2 Patient empowerment and sources of information (1)

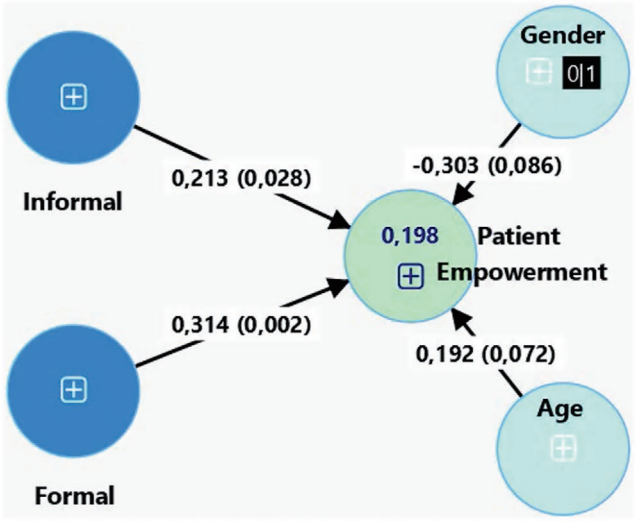

FIGURE 3 Patient empowerment and sources of information (2)

Conclusion: Empowering MS patients requires a balance between emotional, rational, and spiritual knowledge, with emotional knowledge being the most influential, regardless of sex or age. We propose the development of an empowerment measurement scale and a filtering system to improve the quality of unverified information sources.
Disclosure: Nothing to disclose.

EPO-400 | Evaluation of Chat GPT's performance on the pediatric neurology specialty certificate examinations

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Background and Aims: Artificial Intelligence (AI) is being utilized in many aspects of human life, including medicine. Our work focuses on analyzing the effectiveness of AI-based language models in the context of solving the polish State Specialization Examination (SSE) in pediatric neurology.

Methods: The study evaluated the effectiveness of 2 language models: Chat GPT 3.5 and 4.0 in solving two past papers of SSE in pediatric neurology. For the study, questions were divided into 6 thematic groups. The point scores of both models were compared with the results of physicians taking the SSE in the given sessions and the difficulty index of each question.
Results: Chat GPT 4.0 achieved a passing score (60%) in both examination sessions. Considering the total points obtained in both examination sessions, Chat GPT 4.0 achieved similar scores (72%) to physicians (74%). The newer versions of Chat GPT outperformed (72%) its predecessor (48%). Chat GPT 4.0 performed best in the questions connected with metabolic disorders, headaches, CNS tumors, while doctors achieved the highest scores in all other categories.

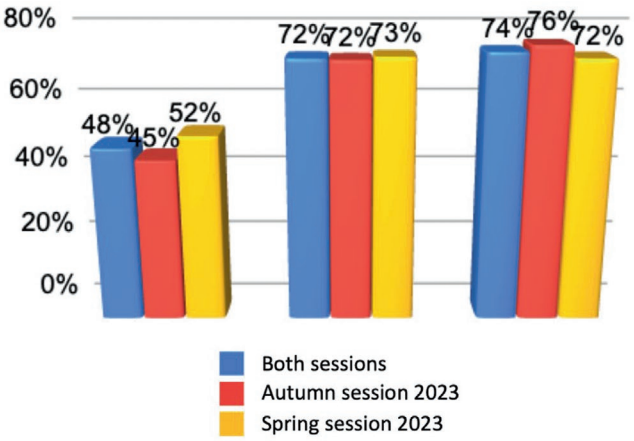

FIGURE 1 Results of the SSE examinations in developmental neurology in the spring 2023 and fall 2023 sessions.

Conclusion: Chat GPT 4.0 outperformed its predecessor, probably due to significant enhancements, such as more advanced contextual understanding, greater language fluency, and a much larger base of learned information. Variations in the Chat GPT's performance in different categories may be a result of inadequate modeling by the engineers and the differences in availability of specialty-specific materials in the training database. Nevertheless, the results presented in our work may indicate the potential utilization of artificial intelligence in the education and practice of pediatric neurologists.
Disclosure: Nothing to disclose.

EPO-401 | Educational potential of the HealUA mobile app for peer-to-peer neurology consultations during wartime in Ukraine

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Background and Aims: The Russian invasion of Ukraine has significantly disrupted healthcare, including specialized fields such as neurology. To address healthcare delivery, HealUA, a mobile app developed with Ukrainian physicians, enables verified doctors to engage in remote, peer-to-peer consultations, fostering both education and clinical support.
Methods: HealUA was created by the Global Medical Knowledge Alliance and Empat. The software enables verified doctors to submit clinical cases, obtain expert advice, and share their knowledge for education. The free app was distributed via app markets as well as marketed through physician networks, social media, and medical associations. Data from the app were evaluated using descriptive statistics.

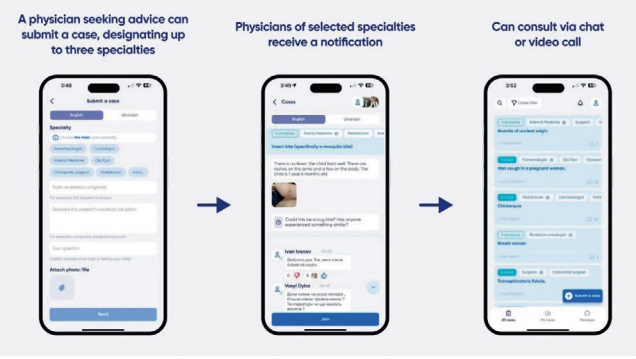

FIGURE 1 How does HealUA work?

Results: Between May 2022 and January 2025, 4282 physicians joined HealUA, included 327 neurologists and 123 neurosurgeons 95% ($n=4038$) came from Ukraine, 2% ($n=91$) from the United States, and 3% ($n=113$) from 33 different countries. Since May 2022, 577 requests have been sent using the app, with 55 categorized as "neurology" and 13 as "neurosurgery," all of them have gotten answers. International specialists consulted on 24 (43.6%) of the neurological cases presented.
Conclusion: This study demonstrates the potential of the HealUA mobile app as a valuable tool for peer-to-peer neurology consultations and education during the war in Ukraine. The platform offers a significant wealth of clinical cases, including neurology and neurosurgery, facilitating international knowledge exchange and highlighting case-based learning experiences. This innovative approach not only educates specialists in Ukraine, but also offers a model that can be repurposed in other countries facing crisis situations.
Disclosure: Nothing to disclose.

EPO-402 | Advancing cannabinoid delivery through nanotechnology and its implications for neurology

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Background and Aims: In the evolving landscape of cannabinoid-based medicine, neurologists must develop an understanding of cannabinoids to effectively incorporate them into treatment plans. Delivery method selection is critical for optimizing pharmacokinetic (PK) profiles, therapeutic efficacy, and patient outcomes. Cannabinoid therapies are available in oral, sublingual, inhalation, transdermal, and injectable modalities, each with unique strengths and limitations. Self-NanoEmulsifying Drug Delivery Systems (SNEDDS) and nanoemulsion technologies offer promising solutions to overcome poor solubility and bioavailability challenges of lipophilic cannabinoids. This abstract highlights PK and permeation data from two studies: one evaluating an oral SNEDDS cannabis product versus an oil-based tincture and another examining cannabidiol (CBD) dermal delivery using Capsoil Technology.
Methods: The first study was an open-label crossover trial in nine subjects administered an oral SNEDDS formulation (8 mg THC, 8 mg CBD) or an oil-based tincture with a 30-day washout. The second study used an in vitro Franz cell diffusion model with human skin to evaluate CBD absorption of a Capsoil Nanoemulsion versus a conventional CBD oil (10 mg/g CBD).
Results: The SNEDDS formulation demonstrated significantly higher Cmax values for THC (47.05 ng/mL vs. 12.66 ng/mL), CBD (10.62 ng/mL vs. 4.02 ng/mL), and their metabolites compared to the tincture. Bioavailability improvements ranged from 278.8% to 495.6%, supporting faster onset and prolonged therapeutic effects. The Capsoil Nano-emulsion achieved a four-fold increase in skin permeation and enhanced penetration across all layers, suggesting potential for effective transdermal applications.
Conclusion: These findings may support the use of SNEDDS-based cannabinoid products in headache medicine and inform neurologists in developing effective treatment plans.
Disclosure: Laszlo Mechtler, MD, has served on advisory boards for, consulted for, and/or been a speaker for AbbVie, Allergen (now AbbVie), Amgen, Biohaven (now Pfizer), Currax Pharmaceuticals, Electrocore, Impel Pharmaceuticals, H.S. Lundbeck, Novartis, Promius Pharma, Teva, Theranica Bio-electrics, Tonix

Pharmaceuticals. Dr. Mechtler serves on the Board of Directors for the International Headache Society and Genomate Health and serves as an advisory board member for NeurodiscoveryAI, Craniometrix, and the New York State Athletic Commission. The institution of Dr. Mechtler has received research and/or educational support from Abbvie, Aeon BioPharma, Alder, Allergan (now AbbVie), American Migraine Foundation, Amgen, Alpheus Medical, Biohaven (now Pfizer), Boston Biomedical, Charlotte's Web, Currax Pharmaceuticals, Delmar Pharmaceuticals (now Kintara Therapeutics), Eli Lilly, H.S. Lundbeck, Miles for Migraine, Novartis, Orbis Pharma, Shiratronics, Teva, The Harry Dent Family Foundation, Inc, and Theranica.

EPO-403 | Uncovering knowledge and practice gaps in focal epilepsy amongst European neurologists

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Background and Aims: Focal epilepsy poses diagnostic and therapeutic challenges due to varied clinical presentations, limited standardization, and evolving treatment paradigms. To identify and assess patterns relating to attitudes, knowledge and practice gaps, we conducted an educational survey among European neurologists.
Methods: A 27-question online CME survey assessed knowledge (disease burden, predictors, clinical data) and case-based competence. Conducted from April to December 2024, responses were de-identified and aggregated. Two questions mirrored a 2021 Medscape survey, allowing result comparisons.
Results: A total of 135 neurologists completed the survey. A difference was observed between performance on knowledge-based and competence-based questions, with better results on case-based clinical practice (Table 1). Comparing 2021 to 2024, similar results were seen on the same questions (Table 2). For a case of uncontrolled focal epilepsy on one ASM, 44% showed flexibility in choosing between two appropriate strategies, while 56% showed a definite preference: 39% for add-on therapy and 17% for switching. Regarding 3rd generation ASMs, 61% opted for use after failure of 2 therapies, 13% after 3, and 16% based decisions on the specific ASM. Physicians demonstrated poor understanding of SUDEP risk factors and clinical trial data supporting current practice. However, management of focal epilepsy and comorbidities appeared stronger although half demonstrate inflexibility in their approach.

Type	Knowledge questions (13)	Competence questions (7)
Percentage correct	49.7%	68.7%

Table 1: Comparison of outcomes for knowledge vs competence questions

Survey Year	Risk factors for SUDEP	Association of aetiology and seizure freedom
	% correct (n)	
2021 N = 164	29% (47)	70% (114)
2024 N = 135	33% (45)	71% (96)

SUDEP: Sudden unexpected death in epilepsy

Table 2: Comparison of 2021 survey results with 2024 survey

Conclusion: Whilst case-based questions may have been easier or more intuitive to answer, this study uncovered persistent and significant gaps in knowledge and clinical practice. These findings highlight an urgent and targeted need for sustained knowledge-based education to bridge critical gaps and enhance decision-making.
Disclosure: Developed through independent educational funding from Angelini Pharma.

EPO-404 | Promoting brain health and awareness of brain-related disorders among young people in Cameroon

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Background and Aims: The burden of brain-related disorders in Cameroon has been growing steadily, and brain health has been deteriorating among young people, mostly driven by increased substance abuse and a low level of public awareness of the importance of brain health. The objective of our project was to promote brain health and awareness of brain-related disorders so as to destigmatise brain-related disorders, leading to early detection and treatment.
Methods: We designed and implemented a peer-led awareness-raising initiative involving 25 young peer educators with healthcare and non-healthcare backgrounds who were trained and empowered with knowledge on common neurological disorders and brain health. These trained peer educators subsequently organise awareness-raising activities and workshops in schools and other public places using brain models and posters.
Results: Over a period of 24 months, we have reached over 15,000 young people in both rural and urban communities, engaging over 200 school authorities on brain health and establishing strong partnerships with local stakeholders. There has been an increase in the level of awareness of brain health and brain-related disorders with growing interest in neurology and neuroscience among students and increased engagement from school authorities.
Conclusion: Youth-led initiatives are important and feasible strategies to improve awareness of brain health and brain-related disorders among young people in resource-limited settings.
Disclosure: Nothing to disclose.

EPO-405 | Clinical profile of migraine in South Asian countries: A systematic review

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Background and Aims: Migraine, a condition causing moderate to severe headaches, ranks as the second most burdensome neurological disorder among Asians regarding disability-adjusted life years (DALYs). The paucity of knowledge from South Asia regarding migraine profiles made the commencement of this study imperative.
Methods: We conducted a systematic review per PRISMA guidelines. We screened English articles on descriptive studies done in the South Asian population with diagnosed adult migraine patients. The final review contained 36 articles.

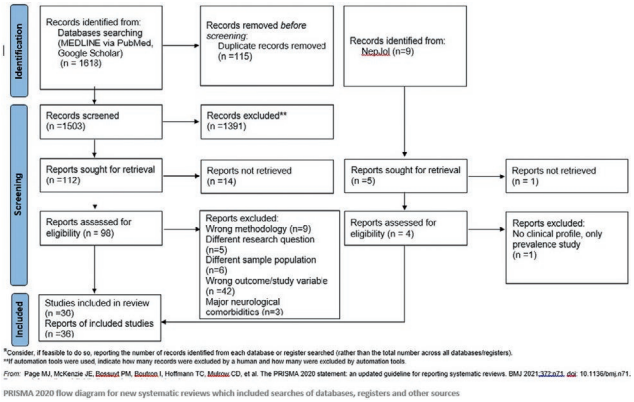

FIGURE PRISMA 2020 flow diagram of included studies.

Results: Migraineurs are mostly in their 30s, urban dwellers, with high female preponderance and family history. The commonest triggers were lack of sleep, stress, missed meals, specific smells/foods, and menstruation. Unilateral pulsatile headaches in the morning, and usually resolving within a day were found to be the most common occurrences. Migraine without aura was more commonly reported, with visual aura being the most prevalent. The most frequently associated features were photophobia, phonophobia, nausea, vomiting, vertigo, dizziness, neck pain, and vision problems. Most studies reported that medications like NSAIDs, acetaminophen, triptans, opioids, or combinations of these aid in relieving symptoms. While adequate sleep/rest and staying in a quiet room were commonly accepted non-pharmacological relievers, few studies revealed patients found solace after vomiting, food intake, and a change in posture.

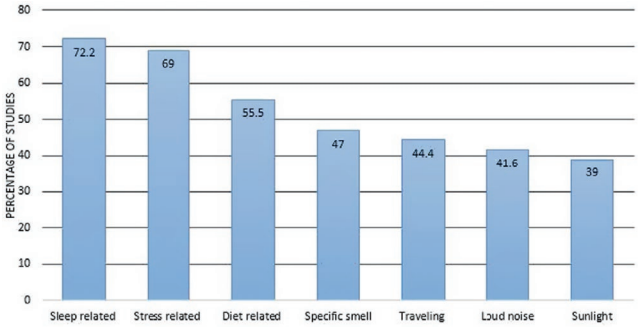

FIGURE Bar graph of common trigger factors of migraine.

Conclusion: As young females and urban dwellers are the common demographics, it highlights the role of genetics and environment in the etiology of migraine. Behavioral elements like stress, lack of sleep, fatigue, and diet habits being common triggers underscore the importance of identifying and preventing acute attacks with multispecialty care.
Disclosure: Nothing to disclose.

EPO-406 | The correlation between vitamin B12 serum levels and migraine: A case-control study

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Background and Aims: Migraine represents the prevailing form of primary headache with no fully described aetiology and pathophysiology. This study aimed to assess the association between vitamin B12 serum levels and both chronic and episodic migraine.
Methods: This study was conducted as a case-control study, including 90 migraineurs, divided into 48 with episodic migraine and 42 with chronic migraine as the case group, and 90 matched healthy participants as the control group. The serum level of vitamin B12 was measured using enzyme-linked immunosorbent assay (ELISA) for all subjects. Its association with the Migraine Disability Assessment (MIDAS) scale and migraine attack severity, measured using the Visual Analog Scale (VAS), was analyzed.
Results: Migraineurs exhibited a notable reduction in serum vitamin B12 levels compared to the control group (243.97 ± 124.85 pg/mL vs. 302.69 ± 143.69 pg/mL, $p = 0.014$). Furthermore, chronic migraine patients had significantly lower serum vitamin B12 levels when compared to episodic migraine patients (202.7 ± 75.62 pg/mL vs. 269.17 ± 143.31 pg/mL, $p = 0.026$). A significant negative correlation was found between serum vitamin B12 levels and the severity of migraine attacks, as measured by the VAS ($r = -0.407$, $p = 0.036$).
Conclusion: The current study highlighted that vitamin B12 deficiency is highly associated with migraine and its severity. Further interventional research is highly recommended to investigate the potential causality of this association.
Disclosure: Nothing to disclose.

EPO-407 | Non-pharmacological approaches to migraine management: Assessing the efficacy of repetitive transcranial magnetic stimulation

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Background and Aims: In recent years, the potential neuromodulatory effect of Repetitive transcranial magnetic stimulation (rTMS) has been investigated as a therapeutic tool in migraine. We aim to assess the impact of unilateral rTMS targeting the dorsolateral or dorsomedial prefrontal cortex, performed according to protocols for treatment-resistant major depression (TRMD) or obsessive-compulsive disorder (OCD) respectively, on migraine control.
Methods: Clinical characterization of a cohort of patients who underwent rTMS in the last 10 months for TRMD or OCD, with a concomitant diagnosis of migraine. We conducted a questionnaire regarding migraine frequency, pain intensity, use of rescue analgesia, before and after rTMS.
Results: We included 8 female patients, including 5 patients with frequent episodic migraine and 3 with chronic migraine The median time elapsed since the last session was of 2 months (IQR:1–9.25). Half of our sample perceived a positive/very positive overall change after rTMS regarding migraine, including 3 patients with TRMD and one patient with OCD. Four patients reported simultaneous reduction in migraine frequency and the need for rescue analgesia, of whom 3 also reported a decrease in maximum pain intensity. Prior to rTMS the mean days-per-week with migraine was 3, which was significantly reduced to 1.7 days-per-week ($p = 0.03$). Worsening of migraine was observed in one patient, in terms of frequency and intensity of pain. Transient peri-procedural headache was associated with lack of efficacy of rTMS regarding migraine ($p = 0.071$).
Conclusion: This preliminary investigation suggests a potential sustained benefit of rTMS in reducing the number and the severity of attacks in migraine.
Disclosure: Nothing to disclose.

EPO-408 | The Nordic chronic migraine trial of CGRP monoclonal antibody and onabotulinumtoxin A dual therapy (NorMig)

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Background and Aims: There is tremendous evidence demonstrating the efficacy of calcitonin gene-related peptide

monoclonal antibodies (CGRP mAbs) in migraine patients. However, patients with chronic migraine considered as responders may still experience substantial disease burden. For this patient group, a combination of CGRP mAbs and onabotulinumtoxin A, might be beneficial. Although there are real-world data supporting this combination therapy, evidence from randomized controlled trials is lacking. The aim of the NorMig trial is to assess the efficacy of dual therapy with CGRP mAbs and BTA compared to single therapy with CGRP mAbs in chronic migraine patients.

Methods: NorMig is an ongoing randomized placebo-controlled, double-blind multi-centre phase III trial of CGRP mAbs and onabotulinumtoxin A versus treatment with CGRP mAbs and placebo in patients with chronic migraine. The trial is conducted in compliance with Guidelines of the International Headache Society for controlled trials of preventive treatment in chronic migraine. Primary outcome is the reduction of Monthly Migraine Days over 12 weeks of treatment with the study medication. Patients with chronic migraine aged 18-70 years with indication for CGRP mAbs or onabotulinumtoxin A and no previous use of CGRP mAbs or onabotulinumtoxin A are included after 4-week baseline registration.

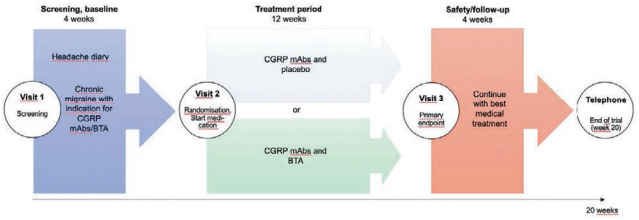

FIGURE 1 Timeline for the trial. Duration 20 weeks.

Results: The trial is starting at Norwegian sites and is planned to be extended to centres in the Nordic countries to reach the sample size of 450 patients. Updated numbers of inclusions will be presented at the congress.

FIGURE 2 Brain Twin app. Migraine tracker & headache diary.

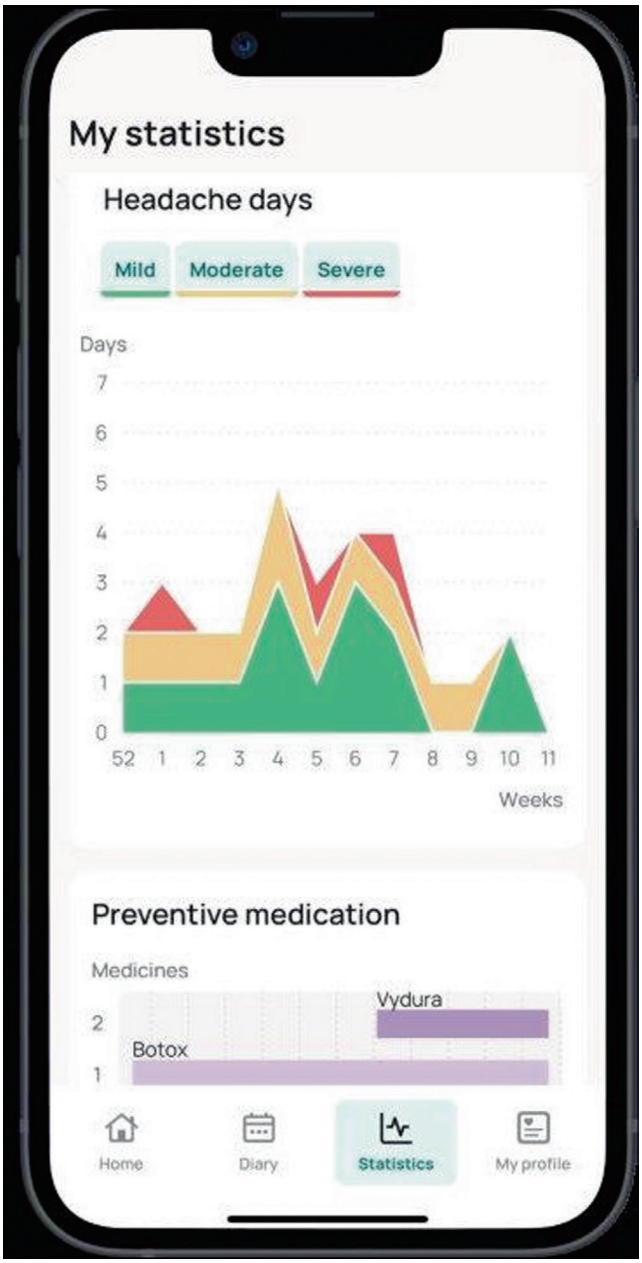

FIGURE 3 Brain Twin app. Migraine tracker & headache diary.

Conclusion: The NorMig trial has the potential to change current treatment practice for chronic migraine and reduce migraine related disability.

Disclosure: Lecture presentations for Lundbeck and Abbvie. Attended Nordic Migraine Symposium arranged by Teva.

EPO-409 | Identification of barriers in migraine care: A national survey of primary care physicians in Singapore

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Background and Aims: Despite the high prevalence and disability burden of migraine globally, it remains underdiagnosed and management is suboptimal. This study aimed to identify clinical gaps and educational needs for migraine care in the primary care setting in Singapore.

Methods: A national cross-sectional survey of primary care physicians in Singapore was conducted. The questionnaire evaluated confidence in diagnosing migraine and initiating prophylaxis, the frequency of addressing the impact of migraines on patients' lives, comorbid conditions, counseling on medication overuse, and the top reasons for referring patients to neurologists.

Results: A total of 94 primary care physicians participated. Of these, 58.5% (55/94) were confident in diagnosing migraine, 29.8% (28/94) were somewhat confident, and 10.6% (10/94) were not confident. Confidence in initiating prophylaxis was lower, with 29.8% (28/94) confident, 35.1% (33/94) somewhat confident, and 31.9% (30/94) not confident. Regarding the impact of migraine, 36.2% (34/94) inquired often about burden of migraine, 40.4% (38/94) did so occasionally, and 22.3% (21/94) rarely. Physicians Inquired about comorbidities associated with migraine often in 41.5% (39/94), sometimes in 34% (32/94), and rarely in 21.3% (20/94). Counseling on medication overuse was provided often by 38.3% (36/94), occasionally by 31.9% (30/94), and rarely by 28.7% (27/94). Neurologist referrals were mainly for concerns about secondary headaches (51.1%), treatment-resistant headaches (50%), patient preference for specialist opinions (39.4%) and diagnostic uncertainty (39.4%).

Table: Summary of results

	Total (n=94)
Confidence in diagnosing migraine	
Confident	55 (58.5%)
Somewhat confident	28 (29.8%)
Not confident	10 (10.6%)
Blank	1 (1.1%)
Confidence in initiating preventive medication for migraine	
Confident	28 (29.8%)
Somewhat confident	33 (35.1%)
Not confident	30 (31.9%)
Blank	3 (3.2%)
Impact and burden of migraine	
Always	34 (36.2%)
Sometimes	38 (40.4%)
Rarely	21 (22.3%)
Blank	1 (1.1%)
Comorbid conditions related to migraine	
Always	39 (41.5%)
Sometimes	32 (34%)
Rarely	20 (21.3%)
Blank	3 (3.2%)
Medication overuse counselling	
Always	36 (38.3%)
Sometimes	30 (31.9%)
Rarely	27 (28.7%)
Blank	1 (1.1%)
Reasons for neurologist referral	
(Multiple options allowed, maximal 3 options)	
Concerns of secondary headaches	51.1%
Treatment resistant headache	50%
Patient is keen for specialist opinion	39.4%
Diagnostic uncertainty	39.4%
Access to brain imaging	27.7%
Uncertainty regarding medication titration	5.3%
Uncertain about treatment options to initiate	4.3%

Conclusion: Primary care physicians in Singapore exhibited variable confidence and inconsistency in managing migraines. Structured training, robust education, adherence to guidelines, and clear workflows are crucial to improve outcomes for migraine patients.

Disclosure: Nothing to disclose.

EPO-410 | Headache attributed to low cerebrospinal fluid fistula: A clinical description with therapeutic particularities

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[1]Headache Unit, Neurology Department, University Clinical Hospital, Valladolid, Spain; [2]Neurology Department, Rio Hortega Hospital, Valladolid, Spain

Background and Aims: Cerebrospinal fluid (CSF) fistula is one of the causes of headache attributed to low CSF pressure. We aim to describe a case managed with conservative treatment.
Methods: A 57-year-old woman with previous menstrually related migraine. Admitted to emergency room with a one-week history of cervical stiffness and occipital headache.
Results: She was an informal caregiver of a disabled person, and pain began in relation to a transfer. Headache was oppressive, accompanied by nausea and photophobia, with complete resolution in supine position. Anesthetic blockade with 2% lidocaine was performed with transient resolution of the pain. A brain magnetic resonance imaging (MRI) showed pituitary and dural enhancement, with descent of the cerebellar tonsils. An axial MRI revealed linear epidural enhancement in the thoracic region, which was confirmed as a CSF fistula at T9-T10, in a computed tomography myelography. Fistula was related to a herniated disc, tearing dural sac. Agreement was reached with neurosurgery and the patient, and conservative treatment with rest, hydration, and caffeine was offered. After 2 months, the patient remains paucisymptomatic.

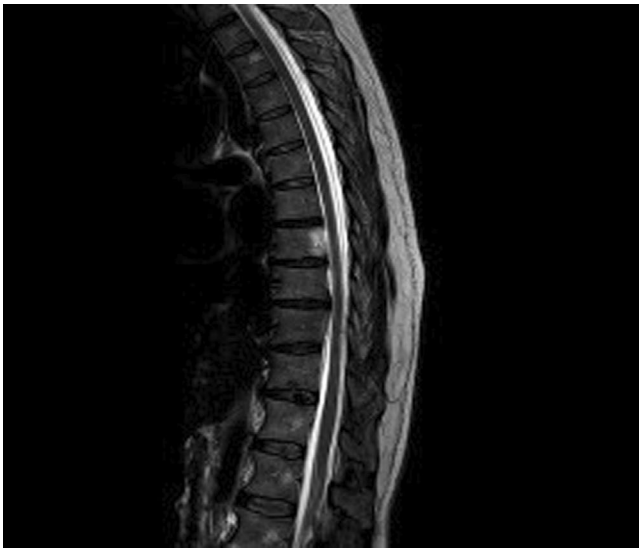

FIGURE 1 Dural detachment in sagital spinal cord MRI

Conclusion: CSF fistula headache is a rare condition, but it should be taken into account in middle-aged women carrying out physical activities without an adequate ergonomic approach. Conservative treatment may be enough for symptomatic control.
Disclosure: Nothing to disclose.

EPO-411 | Neuromodulation by transcranial direct current stimulation in the control of refractory neuropathic pain – Long effect

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Sarah Network of Rheabilitation Hospitals, Brasilia, Brazil

Background and Aims: Neuropathic pain is highly prevalent and often difficult to treat. TDCS is effective in controlling neuropathic pain, but the late effect remains unknown.
Methods: Serie of cases with neuropathic pain refractory to more than one medication, in the rehabilitation program at SARAH-BH. They underwent 2 cycles of 8 to 10 sessions of tDCS, anodal, daily, 20 minutes, 2mA in M1, with an interval of up to 6 months between cycles. They were assessed using the visual analogue pain scale (VAS). 22 patients who underwent two cycles of tDCS, with pain improvement, were interviewed at least 6 months after the last session to evaluate the late effect.
Results: TDCS sessions were performed in 50 patients; of these, 35 underwent 2 cycles. The diagnoses: traumatic (18)\ non-traumatic (4) tetraplegia, traumatic (18)\non-traumatic (8) paraplegia and peripheral neuropathy (2). In Cycle 1, 31 (62%) showed an improvement greater than 30% in VAS quantification (D1- average 6.97; D10- average 4.43). 35 underwent cycle 2: 21 (60%) maintained or increased the initial improvement. LATE EFFECT: 22 were evaluated after average of 13.6 months (6 to 22 months) from the last session: 12 (55%) maintained late benefit; 8 (36%) reported that the improvement lasted a few months and the pain returned as before; 2 (9%) reported that the pain became worse.
Conclusion: TDCS is effective, as adjuvant therapy, in multidisciplinary program to control refractory neuropathic pain. The benefit reduces over time after stopping sessions, but 55% of responsive patients still report benefit after average of 13.6 months since the last session.
Disclosure: Nothing to disclose.

EPO-412 | Prevalence, characteristics and risk factors of migraine among students in Horus University: A cross-sectional study

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Background and Aims: Migraine is a common neurological disorder with a significant disease burden. A number of different factors can trigger migraine attacks as anxiety, stress, skipped meals and irregular sleep pattern. This study was conducted to estimate the prevalence of migraine and to determine its characteristics in students of Horus University, Egypt.
Methods: A cross-sectional study was conducted using a self-administered questionnaire. The study included 1339 students. Migraine-related quality of life and disability were assessed using Migraine Specific Quality of life Questionnaire (MSQ) and Migraine Disability Assessment Scale (MIDAS) respectively
Results: The overall prevalence of migraine was 24%. The most frequent migraine triggers were mental stress, exertion, sleep disturbance and prolonged mobile use (74%, 72.7%, 68% and 55.8% respectively). Being a female, in the middle academic years and having low academic degrees were significant predictors of

migraine among university students. Regarding migraine students, disability was significantly higher among females and students who don't live with their families. Besides, their quality of life was significantly low among males, nonmedical students, students with low academic degrees and those with irregular physical exercise.

Students' characteristics	Migraine specific QOL score (n=319)	Test of significance	P value
Sex			
Male	43.37±12.63	t=3.02	**0.003**
Female	47.49±9.72		
Faculty			
Physical therapy	46.46±9.59		
Medicine	47.98±10.43		
Dentistry	44.20±11.50	F=2.95	**0.013**
Pharmacy	47.73±11.61		
Engineering	38.16±12.03		
Business	31.40±7.86		
Academic year			
First	47.70±10.05		
Second	45.51±11.14	F=1.256	**0.287**
Third	48.70±9.70		
Fourth	44.46±12.80		
Fifth	45.74±10.48		
Academic degree	44.92±10.01a		
A	48.16±10.42 b	F=4.547	**0.012**
B	42.80±12.59		
C	ab		
Living with family			
Yes	46.58±10.36	t=0.46	**0.644**
No	45.80±12.27	3	
Smoking habit			
Smoker	48.50±10.50	t=0.672	**0.502**
Non smoker	46.39±10.66		
Physical exercise	51.28±5.67a		
Regular	44.61±10.83	F=6.72	**≤0.001**
Irregular	ab		
No	47.73±10.85 b		

t: independent t teat, F: ANOVA test, similar letters indicate significant difference between groups y post hoc LSD test

Table (2): Association between Students' characteristics and Migraine specific QOL score (n=319)

Conclusion: Migraine is highly prevalent among university students with significant disability and negative impact on their quality of life.

Disclosure: Nothing to disclose.

EPO-413 | Gender differences in physical activity, sleep and personal care among armenian population with chronic back pain

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Background and Aims: Background: Chronic back pain has a profound impact on various aspects of daily life. The aim of this study is to investigate gender differences in physical activity, sleep patterns, personal care, and social life among patients with chronic back pain.

Methods: Methods: A cross-sectional study included 1562 patients diagnosed with chronic back pain (CBP), with no prior spine surgery, from 3 multidisciplinary medical centers. Participants completed the Oswestry Low Back Pain Disability Questionnaire. To assess gender differences, the mean and standard deviation (STDEV) of ODI scores for each domain were calculated. The statistical comparison between males and females for each category was performed using the Student's T-test with a two-tailed distribution and two-sample unequal variance (heteroscedastic).

Results: 967 women and 595 men were included. The overall total ODI% showed that men are significantly more affected than women (mean ODI% 40.1 + 20.32 in men versus mean 36.4+19 in women, $p=0.0005$). The independent *T*-tests conducted between two groups on all ODI criteria (pain intensity, ease of personal care, lifting, working, sitting, standing, sleeping, sex life, social life and traveling) showed no significant difference in pain intensity and social life, whereas personal care, physical activities, including sex life and travelling were more affected in men (see table 1&2).

TABLE 1

Patients per disability category

Row Labels	Count of patients per disability category	% of patients per disability category
Bed-Bound	19	3.20%
Crippled	83	13.97%
Minimal Disability	109	18.35%
Moderate Disability	221	37.21%
Severe Disability	162	27.27%
Grand Total	594	100.00%
mean ODI% males		40.1
standard deviation ODI% males		20.32104

Female patients per disability category

Row Labels	Count of patients per disability category	% of patients per disability category
Bed-Bound	18	1.86%
Crippled	106	10.95%
Minimal Disability	187	19.32%
Moderate Disability	447	46.18%
Severe Disability	210	21.69%
Grand Total	968	100.00%
mean ODI% females		36.4
standard deviation ODI% females		19.00
p-value=0.0002		

TABLE 2

Male vs Female difference in independent T-test p-value	
ODI categories	p-value
Pain intensity: male vs female independent T-test p-value	7,44623E-05
Personal care: male vs female independent T-test p-value	0,002621922
Lifting: male vs female independent T-test p-value	0,012548134
Walking: male vs female independent T-test p-value	0,000608708
Sitting: male vs female independent T-test p-value	0,001044473
Standing: male vs female independent T-test p-value	8,31592E-05
Sleeping: male vs female independent T-test p-value	0,000142794
Sex life: male vs female independent T-test p-value	0,034964457
Social life: male vs female independent T-test p-value	0,060586071
Travelling: male vs female independent T-test p-value	0,022471689
male vs female: total ODI%	0,000272163

Conclusion: Gender differences in chronic back pain disability are evident, with men being more severely affected. However, pain intensity and social life are equally affected in women and men. These findings highlight the importance of considering gender in the management of chronic back pain.
Disclosure: Nothing to disclose.

EPO-414 | Pharmacoepidemiology of idiopathic intracranial hypertension: An Austrian population based cohort study

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Background and Aims: Idiopathic intracranial hypertension (IIH) is a rare disorder characterized by headaches and papilledema. This case-control study utilized a large hospital-based database to investigate IIH prevalence and treatment patterns, invasive and non-invasive therapies
Methods: The Austrian health insurance register (>99% population coverage) was queried for patients discharged between 2016 and 2021 with ICD-10 code G93.2 and/or acetazolamide (AZM) prescription. IIH was considered confirmed if G93.2 was assigned ≥2 times and AZM was prescribed ≥ once. Five obese controls (OBC, ICD-10: E65/66/68) and five general population controls (GPC) were drawn from the register for each patient. Cumulative defined daily doses (cDDD) of prescribed medications and performed procedures were extracted.
Results: Of 5,969 patients identified, 114 met the criteria for confirmed IIH, yielding an estimated hospital-based prevalence of 0.78 per 100,000 discharges in total and 1.34 per 100,000 female discharges. Compared to 114 GPC and 114 OBC matched for age and sex, IIH patients had higher prescription rates of furosemide (18.4%, cDDD: 0.52 mg/d) and topiramate (39.5%, 0.26 mg/d). Invasive procedures were more frequent in IIH, with lumbar punctures in 13% (vs. 0%) and ventriculoperitoneal shunting in 18.4% (vs. 0%). Optic sheath fenestration was not observed. Bariatric surgery rates were lower (4.4%) than in OBC (31.6%) but higher than in GPC (0%).

TABLE 1 Demographics and frequency of invasive/non-invasive therapies SD = standard deviation, Md = Median, Q25 = lower quartile, Q75 = upper quartile, m = male, f = female, cDDD = cumulative defined daily dose.

	IIH patients	obese controls (OBC)	general population (GPC)	test statistic	ρ
N	114	114	114		
mean age in years (SD)	34.2 (10.9)	34.5 (10.9)	33.2 (10.9)		
sex (m:f) in %	12:88	12:88	12:88		
non-invasive treatments					
Acetazolamide (S01EC01)					
total prescription N (%)	114 (100%)	0 %	0 %		
> 1 package N (%)	102 (89.5%)	0 %	0 %		
Acetazolamide: cDDD (Md; Q25, Q75)	.67 (.37; 1.19)				
Furosemide (C03CA01)					
total prescription N (%)	21 (18.4%)	6 (5.3%)	1 (.9%)	$X_{(2)} = 25$	< .001
> 1 package N (%)	15 (13.2%)	4 (3.5%)	1 (.9%)		
Furosemide: cDDD (Md; Q25, Q75)	.52 (.25; .91)	.42 (.29; 1.6)		U = 40	1.0
Topiramate (N03AX11)					
total prescription N (%)	45 (39.5%)	3 (2.6%)	1 (.9%)	$X_{(2)} = 88$	< .001
> 1 package N (%)	33 (28.9%)	3 (2.6%)	1 (.9%)		
Topiramate: cDDD (Md; Q25, Q75)	.26 (.11; .40)	.22		U = 44	.79
Invasive treatments					
bariatric surgery (%)	5 (4.4 %)	36 (31.6 %)	0 %	$X_{(2)} = 63$	< .001
shunt surgery (%)	21 (18.4 %)	0 %	0 %	$X_{(2)} = 45$	< .001
lumbar puncture (%)	13 (11.4 %)	0 %	0 %	$X_{(2)} = 27$	< .001
number of lumbar punctures (Md; min, max)	1 (1; 3.5)				
optic nerve sheath fenestration (%)	0 %	0 %	0 %		

Conclusion: The estimated IIH prevalence is within the reported range for Middle Europe but likely underestimated due to reliance on hospital discharge data. Treatment patterns reflect guideline-based management, though the high frequency of invasive procedures suggests a bias toward more severe cases.
Disclosure: Funding There was no funding to this research. Competing interests Nina Müller[1,2], Nik Krajnc[1,2], Sina Zaic[1,2], Stefan Macher[1,2], Christian Wöber[1,2], Wolfgang Marik[2,3], Klaus Novak[2,4], Berthold Pemp[5], Berthold Reichardt[6], and Gabriel Bsteh[1,2] NM: declares no conflict of interest relevant to this study NK: has participated in meetings sponsored by, received speaker honoraria or travel funding from BMC/Celgene, Merck, Novartis, Roche and Sanofi-Genzyme. SZ: declares no conflict of interest relevant to this study SM: declares no conflict of interest relevant to this study CW: has received honoraria consultancy/speaking from Apomedica, Curelator, Eli Lilly, Grünenthal, Hermes, Novartis, Pfizer, Ratiopharm/Teva, and Stada WM: declares no conflict of interest relevant to this study. KN: declares no conflict of interest relevant to this study. BP: has received honoraria for consultancy/speaking from Chiesi, GenSight and Santen. BR: declares no conflict of interest relevant to this study. GB: has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene/BMS, Lilly, Merck, Novartis, Roche, Sanofi-Genzyme and Teva, and received honoraria for consulting Biogen, Celgene/BMS, Novartis, Roche, Sanofi-Genzyme and Teva. He has received unrestricted research grants from Celgene/BMS and Novartis.

EPO-415 | Preventive migraine treatment in primary care and headache clinic: A follow-up analysis in a Portuguese hospital

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Background and Aims: Migraine treatment has evolved. This study compares the management of migraine patients referred to a Portuguese tertiary hospital in 2023 and 2017, analyzing referral patterns, treatments, and follow-up.
Methods: Retrospective analysis. Data included referral sources, treatments, and follow-up duration. Inclusion criteria: age ≥18; managed in primary care pre-referral, no prior neurology follow-up.
Results: In a Portuguese tertiary hospital, 22/85 first consultations in 2023 and 32/136 in 2017 met the criteria. In 2023, the majority were women ($n=17$; 77.3%; mean age 41.6 years) as in 2017, ($n=31$; 96.9%; mean age 33.9 years). Patients in 2023 were significantly older ($p=0.018$). Preventive treatment criteria were met by 90.9% of patients in 2023 compared to 75% in 2017. The proportion of patients referred with prior preventive treatments increased in 2023 vs 2017 (77.3% vs 28.1%, $p<0.001$). Patients in 2023 initiated/tried significantly more preventive treatments before referral (2.0 vs 0.34; $p<0.001$). In primary care, the most prescribed preventives were topiramate (31.6%) and amitriptyline (26.3%) in 2023; propranolol (41.7%) and amitriptyline (25.0%) in 2017. In headache clinic, the mean number of preventive treatments attempted in 2023 was significantly higher compared to 2017 (1.3 vs. 0.7; $p=0.017$). In 2023, topiramate (18.75%) and galcanezumab (18.75%) were most prescribed, while in 2017, propranolol (36.4%) and topiramate (27.3%). The mean follow-up duration was longer in 2023 (452.0 vs 289.1 days; $p=0.004$).
Conclusion: Migraine management improved with more preventive treatments initiated in primary care, greater use of advanced therapies, and longer follow-up durations, reflecting significant progress in both primary and specialized care.
Disclosure: Nothing to disclose.

EPO-416 | Bilateral occipital nerve block in children with chronic migraine

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Background and Aims: Migraine is a common type of pain that has been recognized for thousands of years, yet its pathophysiology and morphological effects are not fully understood, and it can be remarkably resistant to treatments. Greater occipital nerve (GON) block is an effective and minimally invasive treatment option for primary headaches that can be used in patients older than 8 years, with relatively few side effects.
Methods: In this study, we retrospectively evaluated the efficacy of greater occipital nerve block in children and adolescents with migraine. We reviewed the medical records of patients aged 12 to 18 who had been diagnosed with migraine and treated with GON block. The GON block was performed bilaterally with 2 cc of 2% lidocaine weekly for 4 weeks, and monthly thereafter. Patients' headaches were assessed using a headache form, the PedMIDAS (Ped Migraine Disability Assessment) scale for evaluating migraine-related disability in children, and the Headache Impact Test (HIT) forms at both baseline and after GON application.
Results: A total of 22 patients were evaluated in the study, all of whom received their first GON block. The mean age of the patients was 14.2 years (range 11–18). 17 patients were female and 5 were male. GON block showed significant efficacy, with improvements in frequency, severity (measured by VAS), PedMIDAS, and HIT scales.
Conclusion: GON block is an effective and safe treatment option for children and adolescents with migraine, with minimal side effects, and should be considered as a first-line treatment option.
Disclosure: Nothing to disclose.

EPO-417 | Hemiplegic migraine attack misinterpreted as a stroke in postcoronarography – Case report

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Background and Aims: Hemiplegic migraine (HM) is a rare form of migraine with aura. The focal deficit can be misinterpreted as a stroke, making diagnosis challenging. This highlights the importance of a detailed patient history. However, obtaining this information can be difficult in the limited time available, as the benefit of brain reperfusion techniques is time-dependen
Methods: We present a case of a patient who developed right hemiplegia, aphasia, and somnolence immediately following coronary angiography. A CT scan and carotid angiography performed promptly showed no abnormalities. The initial diagnosis was an incidental post-coronary angiography ischemic stroke. However, a brain MRI performed a few days later revealed no evidence of stroke. The diagnosis of hemiplegic migraine (HM) was considered following a thorough history, provided by the patient's wife, which revealed multiple prior episodes and a history of migraines with aura that began at the age of 15. The patient had previously been hospitalized multiple times for motor deficits and coma of unknown origin, with numerous CT scans, brain MRIs, EEGs, and lumbar punctures consistently yielding no definitive findings.
Results: After admission, the motor deficit, aphasia, and somnolence fully resolved within 7 days. Cognitive assessments conducted during the acute phase and again 10 days later showed a remarkable improvement in test results. Genetic analysis identified a CACNA1A mutation (c.4523C>T/p.Ala1508Val)
Conclusion: Stroke mimics present a diagnostic challenge for all admissions to a stroke unit. Thorough investigations and a detailed patient history are crucial to avoid misdiagnosis, inappropriate medication prescriptions, and unnecessary tests
Disclosure: Nothing to disclose.

EPO-418 | Non-headache features in migraine as predictors of super-responders to prophylactic treatment

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Background and Aims: The non-headache symptoms in migraine (NHS) could be classified as hypothalamic, autonomic, psychiatric, or hypersensitivities. These symptoms may occur during premonitory, ictal, or postdrome phases and could represent manifestations of different pathophysiological pathways. We aimed to look for a relationship between the NHS and the degree of response to preventive treatment in migraine.
Methods: Retrospective, cross-sectional study included 58 migraine patients on prophylactic medication for at least one month. Data on demographics, headache characteristics, and non-headache symptoms were collected via patient interviews and medical records. Patients were categorized into super-responders (SR) if monthly headache days (MHD) decreased by at least 75% after preventive treatment. Statistical analyses were performed to identify associations between symptoms and treatment response.
Results: Among the 58 recruited patients (mean age 35 ±11, 84% females), 37 (63%) were SR. There was no difference in basal MHD between SR and the others (17.7 vs 22.1 *p* 0.2) treatment used (topiramate in 51% vs 52%), number of preventive treatments used (SR 2 [RIQ 1–3] vs others 1[RIQ 1–3] *p* 0.7). Premonitory osmophobia was more frequent in SR (35% vs 9%, *p* 0.03). Ictal conjunctival injection was also more prevalent in SR (24% vs. 0%, *p* 0.02). There were no differences in the prodromic phase.

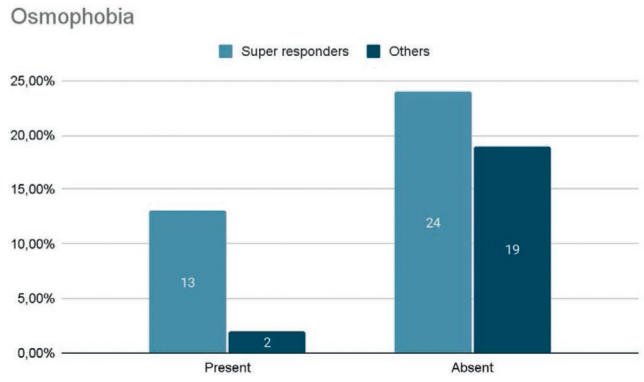

FIGURE 1 The relationship between premonitory osmophobia and super-response to migraine prophylaxis, with a treatment response rate of 75% or more ($p = 0.03$), highlighting its potential as a predictive factor.

Conclusion: The counterintuitive finding of conjunctival injection associated with a better response could be related to a predominantly peripherally sensitization, which could respond easily to treatment compared with central sensitization. Osmophobia was also associated with a better response rate.
Disclosure: Nothing to disclose.

EPO-419 | SS-31 alleviated nociception and restored mitochondrial function in a headache mouse model via the Sirt3/Pgc-1α loop

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Background and Aims: Migraine, the second leading cause of disability, imposes significant socioeconomic burden. Mitochondrial dysfunction has been implicated in migraine, and Szeto-Schiller peptide (SS-31), a mitochondria-targeted peptide, has shown promise in restoring mitochondrial function in various diseases. However, its potential effect on migraine remains unclear.
Methods: A headache mouse model was induced by repeated dural infusion of inflammatory soup (IS). The roles of the Sirt3/Pgc-1α positive feedback loop in mitochondrial function and headache pathogenesis were examined. SS-31 was administered, and mitochondrial function, ultrastructure, and nociceptive responses were assessed.
Results: IS infusion impaired mitochondrial function and homeostasis in the trigeminal nucleus caudalis (TNC). SS-31 reversed these impairments and alleviated IS-induced nociceptive responses. The effects of SS-31 were partially attenuated by a Sirt3/Pgc-1α inhibitor. Overexpression of Sirt3/Pgc-1α enhanced their protein levels, indicating their positive feedback loop.
Conclusion: SS-31 restores mitochondrial function and alleviates nociceptive responses in an IS-induced headache model through the Sirt3/Pgc-1α positive feedback loop.
Disclosure: Nothing to disclose.

Movement disorders 4

EPO-420 | A novel variant in GNAO1 causes epilepsy and movement disorder with a variable phenotypic spectrum in the same family

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Background and Aims: We describe a family with a novel pathogenic variant in the GNAO1 gene and its phenotypic variability.
Methods: A 56-year-old woman with moderate intellectual disability since childhood and generalized convulsive epilepsy starting at 47, well controlled with levetiracetam, complained of tremor, beginning at 47. Physical exam showed short stature (135 cm), dysmorphic features, a characteristic voice, bilateral intentional tremor (+/- myoclonus), and cervical dystonia

(Video 1A). Cranial MRI was normal. Genetic analysis revealed a heterozygous c.649G>T variant in GNAO1, likely pathogenic.
Results: The family includes 11 siblings with non-consanguineous parents (figure 1). A 50-year-old sister (II.4) had mild intellectual disability, anxiety, and her first generalized seizure at 49. Examination showed short stature (135 cm), a characteristic voice, hyperreflexia, mild chorea, and mild cervical dystonia (Video 1B). The 91-year-old mother had mild intellectual disability, subtle orolingual chorea, mirror movements, short stature (139 cm), and no epilepsy (Video 1C). Another brother (II.3) and sister (II.12) were reportedly affected by intellectual disability, psychiatric disorders, and, in the case of the latter, epilepsy, but they were unavailable for evaluation. The affected sister and mother carried the GNAO1 variant, whereas two unaffected sisters (II.6, II.8) did not. The c.649G>T variant is a nonsense mutation causing a premature stop codon at position 217. Loss-of-function variants in GNAO1 are associated with neurodevelopmental disorders, epilepsy, and movement disorders. This variant is absent from dbSNP and gnomAD databases, with a high pathogenic CADD score (40.0).

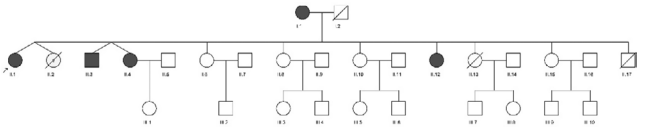

FIGURE 1

Conclusion: The c.649G>T mutation in GNAO1 is pathogenic, causing intellectual disability, epilepsy, and movement disorders with variable phenotypes.
Disclosure: Nothing to disclose.

EPO-421 | Safinamide significantly improves motor complications, motor and non-motor symptoms in Parkinson's disease patients

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Background and Aims: Chronic levodopa treatment is associated with motor complications and non-motor symptoms. Glutamate, besides other neurotransmitters, has been implicated in their development. Safinamide is multimodal drug with a dual mechanism of action, dopaminergic and glutamatergic, and has therefore the potential to improve these phenomena.
Methods: The effects of safinamide on motor complications, motor and non-motor symptoms were investigated using the data from eight interventional, double-blind, placebo-controlled clinical trials performed in Caucasian and Asian patients. Outcomes included OFF time, ON time without troublesome dyskinesia, UPDRS III motor scores, PDQ-39 mood and pain scores.
Results: Safinamide, compared to placebo, significantly improved ON time without troublesome dyskinesia ($p < 0.0001$), OFF time ($p = 0.0001$), motor symptoms ($p < 0.0010$), mood ($p < 0.0009$) and pain ($p = 0.0014$) with a good safety profile and without requiring any change in the concomitant dopaminergic therapy. These benefits were maintained also after a long-term treatment (up to 2 years).
Conclusion: Safinamide, administered as add-on therapy in fluctuating PD patients, improved motor symptoms, motor complications, mood, and pain without increasing troublesome dyskinesia. These effects may be explained by the modulation of glutamatergic hyperactivity. Further prospective studies are needed to fully explore its therapeutic potential.
Disclosure: Carlo Cattaneo is an employee of Zambon SpA.

EPO-422 | Treatment preferences in advanced Parkinson's disease: A discrete-choice experiment subgroup analysis

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Background and Aims: Preferences for advanced Parkinson's Disease (aPD) treatments are often influenced by an individual's characteristics. This study aimed to identify which characteristics of people with aPD (PwaP) impact treatment preferences. Care partners (CPs) reported proxy preferences for PwaP.
Methods: A discrete-choice experiment was conducted with 304 participants, requiring respondents to choose between pairs of hypothetical PD treatments with varying attribute levels (Table 1). Attribute Relative Importance (RI) was calculated using random-parameter logit estimates. Four subgroups were assessed (Table 2).

Table 1. Treatment attributes and levels.

Treatment Attributes	Attribute Levels
ON Time without troublesome dyskinesia **(ONwoTD)**	• 3 hours • 6 hours • 10 hours • 13 hours
Early morning OFF Time **(EMO)**	• Occasionally: once a week • Sometimes: 3 times a week • Very often: 7 times a week
Risk of mild to moderate skin reactions **(Skin reactions)**	• 5 out of 100 • 30 out of 100 • 60 out of 100 • 90 out of 100 patients
Risk of severe side effects requiring hospitalization **(Severe side effects)**	• 1 out of 100 patients • 10 out of 100 patients • 20 out of 100 patients
Route of Administration **(ROA)**	• Only oral pills • Device for infusion under the skin (subcutaneous); No surgery r • Device for infusion in the intestine; Stomach surgery required, • Device for electro stimulation of the brain; Brain surgery require
Frequency of pill regimen **(Pill burden)**	• No need to take pills • Pills 4 times in a day • Pills 8 times in a day
Device maintenance	• None • Once every 3 days • Once per day

Table 2. Subgroup definitions.

Subgroups	Sample size	Subgroup description
Type of participant		
Caregiver	81	The subgroup contains care partners who served as proxies to PwaP
PwaP	223	The subgroup contains PwaP
Age		
<65 (Younger)	126	The subgroup contains PwaP aged less than 65 years
≥65 (Older)	178	The subgroup contains PwaP aged 65 and older
Frequency of daily doses of oral pills		
< 5times/day of pills (Low Frequency)	167	The subgroup contains PwaP taking less than 5 times a day of pills
≥ 5 times/day of pills (High Frequency)	137	The subgroup contains PwaP taking 5 or more times a day of pills
Daily OFF time hours*		
< 2.5 hours OFF time (Low OFF)	78	The subgroup contains PwaP reporting less than 2.5 hours of OFF time
≥ 2.5 hours OFF time (High OFF)	226	The subgroup contains PwaP reporting 2.5 or more hours of OFF time

PwaP = People with advanced Parkinson's Disease.
*Threshold based on common PD clinical trial inclusion criteria for OFF time.

Results: PwaP had a mean age of 65.7 years (SD = 8.6), were diagnosed 10.0 years ago (SD = 4.2), and reported 4.0 OFF hours/day (SD = 2.4). PwaP received 29.6 (SD = 22.2) hours of CP support weekly. Across all subgroups, ON time without troublesome dyskinesia (ONwoTD) and route of administration (ROA) were main priorities. CPs valued ONwoTD significantly more than PwaP (RI = 35.9 vs. 22.8), while PwaP gave greater importance to risk of skin reactions (RI = 14.6 vs. 6.9) and ROA (RI = 36.6 vs. 30.5) than CPs. No statistically significant preferences linked to age, although younger participants emphasized ROA more than older participants (RI = 37.8 vs. 34.3). Conversely, older participants valued ONwoTD more (RI = 29.4 vs. 25.6). Those with higher pill frequencies prioritized ONwoTD more than those with lower frequencies (RI = 32.4 vs. 19.5). Self-reported daily OFF time had no significant influence on preferences.

Conclusion: Treatment preferences for PwaP are diverse, with ROA and ONwoTD as key attributes. These insights can guide healthcare providers in understanding unique PwP and CP priorities, enabling more personalized and effective PD management, and enhancing adherence to treatment regimens.

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EPO-423 | Clinical impact of nigrosome MRI–PET discrepancies on motor complications in Parkinson's disease

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Background and Aims: Accurate imaging markers for Parkinson's disease (PD) are key to both diagnosis and disease tracking. While FP-CIT PET (a dopamine transporter scan) typically confirms nigrostriatal degeneration, MRI-based nigrosome imaging has emerged as a useful complementary modality. Occasional discrepancies between these modalities—namely, cases in which FP-CIT PET is abnormal but nigrosome imaging appears normal—have not been thoroughly characterised.

Methods: In this retrospective study, we analyzed 88 consecutive patients with clinically diagnosed PD, all showing abnormal FP-CIT PET findings, who underwent MRI nigrosome imaging at nearly the same time as PET. Among them, seven cases showed discrepant findings between MRI and PET (MRI-PET discrepant). Demographic and clinical data, including LEDD (levodopa equivalent daily dose) at baseline and follow-up, wearing-off events, levodopa-induced dyskinesia (LID), and Unified Parkinson's Disease Rating Scale (UPDRS) scores, were collected. Kaplan–Meier analysis compared time to wearing-off or LID onset between patients with consistent and discrepant findings.

Results: The MRI-PET discrepant group had a shorter mean follow-up duration (46.11 vs. 66.17 months, $p = 0.044$). No differences were found in baseline or follow-up LEDD, wearing-off incidence, or UPDRS scores. LID did not occur in patients with discrepant findings, though the small sample size limits conclusions. Kaplan–Meier curves showed no significant difference in time to wearing-off or LID onset ($p = 0.27$).

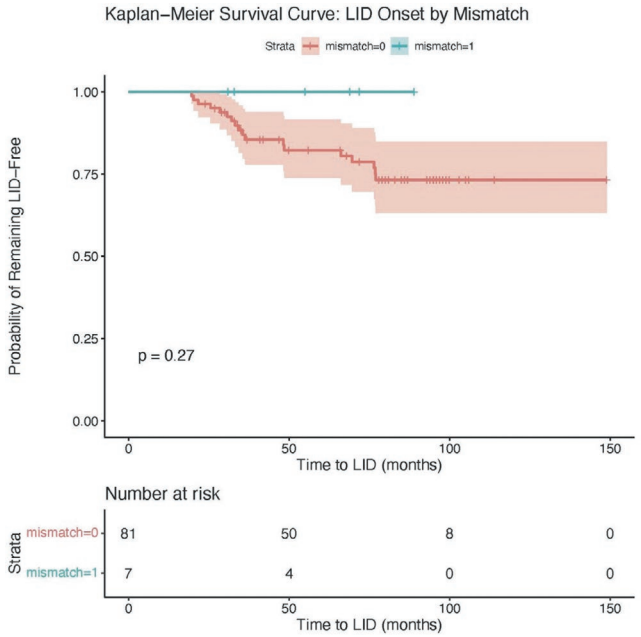

FIGURE 1 Kaplan-Meier curves comparing time to levodopa-induced dyskinesia (LID) between MRI-PET consistent (mismatch = 0, $n = 81$) and discrepant (mismatch = 1, $n = 7$) groups ($p = 0.27$). Shaded areas represent 95% confidence intervals.

Conclusion: MRI-PET discrepancies are uncommon and suggest minimal clinical impact on wearing-off or dyskinesia risk, though larger studies may help clarify the underlying physiology and prognostic significance.
Disclosure: Nothing to disclose.

EPO-424 | Women with Parkinson's disease – Menopause and the role of hormonal replacement therapy

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Background and Aims: Women spend 40% of their lives in the postmenopause. Hormonal replacement therapy (HRT) substantially eases the postmenopausal symptom burden. In Women with Parkinson's disease (WwPD), the impact of HRT on the risk of developing PD and the rate of PD progression remains unclear. This systematic review (PROSPERO ID 636960) investigates 1) the impact of menopause-related hormonal changes on the natural history of PD and 2) the impact of HRT on health-related quality of life (HRQoL), motor and nonmotor symptoms (NMS) in WwPD in peri-and postmenopausal period.
Methods: Eligible studies were identified through an electronic search of MEDLINE, Embase, and CENTRAL databases from inception to October 2024, hand-search of the EAN and MDS abstract books (2019 to 2024) and cross-checking of references. The titles and abstracts were screened, selected full texts will be assessed and the risk of bias evaluated (RoB2, ROBINS-I, or JBI checklist for case series) independently by two authors. Disagreements will be resolved through consensus or by a third reviewer. Data extraction will follow using a pre-established form, designed and pilot-tested by the authors. Thematic coding, summary and descriptive statistical analysis will be conducted.
Results: The search returned 4799 records, 1705 duplicates were removed. After title and abstract screening, 141 articles were selected for full-text screening. We synthetize available evidence on the impact of menopause/HRT on HRQoL, PD progression and burden of motor and NMS in WwPD.
Conclusion: Large RCTs are urgently needed to clarify the effects of HRT in women with Parkinson's disease and inform clinical decision-making.
Disclosure: Nothing to disclose.

EPO-425 | Cluster analysis of patient characteristics associated with up to 100% "off" time improvement from two phase 3 trials

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Background and Aims: As Parkinson's disease (PD) progresses, patients experience motor fluctuations at varying rates. Foslevodopa/foscarbidopa (LDp/CDp) is a soluble formulation of levodopa/carbidopa (LD/CD) prodrugs, administered as a 24-hour/day continuous subcutaneous infusion. In randomised controlled and open-label phase 3 trials, LDp/CDp demonstrated sustained "Off" time reductions. Given the heterogeneous nature and progression of PD, treatment responses also vary among patients. This analysis aimed to explore the baseline characteristics of patients who achieved "Off" time responses, including up to 100% improvement.
Methods: This post hoc analysis utilized cluster analysis to examine pooled patient demographics and baseline disease characteristics from two phase 3 trials: the 12-week active-controlled trial comparing LDp/CDp vs oral LD/CD (NCT04380142) and the 52-week open-label trial assessing LDp/CDp safety/efficacy

(NCT03781167). Patients with non-missing "Off" time data at baseline and Week 12 or Week 13 in their Hauser diaries (active-controlled and open-label trials, respectively) were grouped into clusters based on "Off" time improvement ranging from 0%–100%.

Results: Cluster analysis in the baseline population of 158 patients showed the largest cluster corresponded to those with 100% improvement (27% of patients; Table 1). Across clusters, most patients were aged > =60–80 years with <1800 mg levodopa equivalent daily dose. The 100% improvement cluster was characterised by patients with <10 years PD duration and <5 hours/day "Off" time.

Table 1: Baseline Demographics and Disease Characteristics in the Pooled Active-Controlled and Open-Label LDp/CDp-Treated Analysis Population Based on Patient Diary Reported "Off" Time Percent Improvement[a]

Parameter, N=158 (n [%])	0%[b] Improvement (30 [19.0])	1 – 25% Improvement (11 [7.0])	26 – 50% Improvement (22 [13.9])	51 – 75% Improvement (29 [18.4])	76 – 99% Improvement (24 [15.2])	100% Improvement (42 [26.6])
Sex, n (%)						
Female	11 (36.7)	7 (63.6)	5 (22.7)	14 (48.3)	12 (50.0)	10 (23.8)
Male	19 (63.3)	4 (36.4)	17 (77.3)	15 (51.7)	12 (50.0)	32 (76.2)
Age Category, n (%)						
< 50 years	4 (13.3)	0 (0)	0 (0)	2 (6.9)	1 (4.2)	4 (9.5)
50 – < 60 years	4 (13.3)	2 (18.2)	2 (9.1)	6 (20.7)	8 (33.3)	11 (26.2)
>= 60 – 80 years	21 (70.0)	8 (72.7)	20 (90.9)	19 (65.5)	15 (62.5)	27 (64.3)
> 80 years	1 (3.3)	1 (9.1)	0 (0)	2 (6.9)	0 (0)	0 (0)
PD Duration since Onset, n (%)						
< 10 years	12 (40.0)	6 (54.5)	7 (31.8)	7 (24.1)	12 (50.0)	22 (52.4)
10 – 14 years	11 (36.7)	4 (36.4)	7 (31.8)	13 (44.8)	7 (29.2)	11 (26.2)
> 14 years	7 (23.3)	1 (9.1)	8 (36.4)	9 (31.0)	5 (20.8)	9 (21.4)
LEDD, n (%)						
< 1800 mg	19 (63.3)	10 (90.9)	19 (86.4)	21 (72.4)	22 (91.7)	40 (95.2)
>= 1800 mg	11 (36.7)	1 (9.1)	3 (13.6)	8 (27.6)	2 (8.3)	2 (4.8)
Baseline "Off" Time, n (%)						
< 5 hours	12 (40.0)	2 (18.2)	4 (18.2)	9 (31.0)	4 (16.7)	20 (47.6)
5 – 7 hours	9 (30.0)	3 (27.3)	12 (54.5)	11 (37.9)	11 (45.8)	13 (31.0)
> 7 hours	9 (30.0)	6 (54.5)	6 (27.3)	9 (31.0)	9 (37.5)	9 (21.4)
Average Normalized Baseline "On" Time with nTSD, hours, mean (SD)	2.80 (2.50)	2.67 (2.25)	3.13 (3.09)	2.78 (2.49)	1.88 (2.66)	2.56 (3.02)
Average Normalized Baseline "On" Time with TSD, hours, mean (SD)	0.82 (1.41)	0.60 (0.85)	0.64 (1.00)	0.88 (1.55)	0.57 (1.31)	0.49 (0.94)

Abbreviations: %, percent; CDp, foscarbidopa; LDp, foslevodopa; LEDD, levodopa equivalent daily dose; n, number of patients included in the analysis subgroup or parameter; nTSD, non-Troublesome Dyskinesia; PD, Parkinson's disease; TSD, Troublesome Dyskinesia; SD, standard deviation

[a] Only patients with non missing values for both the Baseline and Week 12 (in the Active Controlled Trial) or Week 13 (in the Open Label Trial) were included in the calculation of "Off" Time percent Improvement, based on the prespecified study visit and assessment schedule (ie, timepoints) in each trial
[b] Patients in the '0% Improvement' subgroup demonstrated either no improvement or worsening

Conclusion: Cluster analysis identified patient profiles with 100% "Off" time improvement, characterised by shorter PD duration and less baseline "Off" time. These results highlight the potential for personalised approaches to optimise outcomes with LDp/CDp continuous infusion therapy in PD.

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EPO-426 | Hospitalisation rates of people with Parkinson's disease in Austrian districts are associated with agricultural exposure

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Background and Aims: Occupational exposure to pesticides is a known risk factor for Parkinson's disease. Previous studies have suggested that working in agriculture or living in rural areas may increase the risk of Parkinson's disease due to pesticide exposure, but the evidence remains inconsistent. This study explores whether there is an association between the hospitalization of people with Parkinson's disease and the proportion of individuals employed in agriculture and forestry across Austrian districts.

Methods: We acquired data on hospitalization rates of people with a main or secondary diagnosis of Parkinson's disease (ICD 10 G20-G22) between 2015 and 2023 from the national hospital discharge register of the Gesundheit Oesterreich GmbH. The agricultural index, which indicates the proportion of the working population employed in agriculture and forestry in the respective districts, was obtained from Statistik Austria. We performed regression analysis to estimate whether hospitalisation rates could be predicted by the agricultural index in Austrian districts.

Results: We found that the cumulative agricultural index for the years 1981, 1991 and 2001 significantly predicted the rate of hospitalized patients with a main and secondary diagnosis of Parkinson's disease (ICD 10 G20-G22) in the years 2015–2023 ($p = 0.01$).

Conclusion: The results indicate that the globally observed association between Parkinson's disease cases and agricultural employment may also be reflected within Austrian districts. Furthermore, the presented results suggest that the effects of agricultural by-products may impact not only those employed directly in agriculture but also residents of rural areas with generally high agricultural employment rates.

Disclosure: Nothing to disclose.

EPO-427 | N-acetyl-L-leucine for ataxia-telangiectasia: A multinational double-blind randomized placebo-controlled crossover study

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Background and Aims: Ataxia-telangiectasia (A-T) is a rare autosomal-recessive cerebellar ataxia. The modified amino acid N-acetyl-L-leucine has been associated with positive symptomatic and neuroprotective, disease-modifying effects

in observational clinical case studies and multinational clinical trials for various cerebellar ataxias and related lysosomal diseases. Most recently, N-acetyl-L-leucine (NALL) demonstrated a significant improvement in neurological manifestations in Niemann-Pick disease type C (NPC) in a Phase III double-blind, randomized, placebo-controlled crossover study (Study Code IB1001-301). Here, we describe the implementation of this master study protocol for the treatment of adult and pediatric patients with A-T (Sponsor Code IB1001-303).

Methods: The IB1001-303 protocol will enroll patients with a genetically confirmed diagnosis of A-T patients aged 4 years and older across 11 trial sites. Patients are assessed during a baseline period and then randomized (1:1) to one of two treatment sequences: IB1001 followed by placebo or vice versa. Each sequence consists of a 12-week treatment period.

Results: The primary efficacy endpoint is based on the Scale for the Assessment and Rating of Ataxia, and secondary outcomes include cerebellar functional rating scales, clinical global impression, and quality of life assessments.

Conclusion: The IB1001-301 clinical trial served as the basis for the FDA approval of IB1001 (AQNEURSA) for the treatment of NPC. Utilizing the same master protocol, the IB1001-303 placebo-controlled cross-over trial will evaluate the risk/benefit profile of IB1001 for A-T to give information about the applicability of IB1001 as a therapeutic paradigm for other rare neurological disorders and potential label expansion of IB1001 for patients with A-T.

Disclosure: Michael Strupp received speaker's honoraria from Abbott, Actelion, Auris Medical, Biogen, Eisai, Grünenthal, GSK, Henning Pharma, Interacoustics, MSD, Otometrics, Pierre-Fabre, TEVA, UCB, Viatris. Consultant for Abbott, Actelion, AurisMedical, Decibel, Heel, IntraBio and Sensorion. Shareholder of IntraBio. Marc Patterson, Janelle Raymond, Bethany Zanrucha, and Asante Hatcher are employees of IntraBio. Tatiana Bremova-Ertl received speaker's honoraria and consultancy fees from Actelion, Sanofi-Genzyme and Zevra as well as blinded video-rater fees from Intrabio.

EPO-428 | Current perspectives for wearable devices for Parkinson's disease: A systematic review

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Background and Aims: Wearable devices have emerged as valuable tools for monitoring and managing symptoms of Parkinson's disease (PD). These technologies offer objective data to assess motor symptoms such as tremor, bradykinesia, and gait abnormalities. This systematic review aims to summarize the wearable devices currently available for PD management, and overview their prevalence and applications in clinical practice.

Methods: We conducted a systematic search of PubMed, Embase, and Cochrane Library databases to identify relevant studies. Initial screening included 3660 articles, of which 178 were selected based on inclusion criterea. Further evaluation 43 excluded studies that did not involve patient data or solely described the technology without clinical application.

Results: In total, 5,250 patients were included. The most commonly used devices were (e.g., accelerometer-based sensors, gyroscopes, or smartwatches), primarily employed for continuous monitoring of gait and tremor. Most studies evaluated Gait abnormalities (51/135) 37%, followed by tremor (27/135) 20%, dyskinesia (17/135) 12%, and bradykinesia (16/135) 11%. These devices demonstrated significant potential for improving symptom tracking and treatment personalization. However, challenges such as device usability, cost, and integration into routine clinical workflows remain barriers to widespread adoption.

Conclusion: Wearable devices offer a promising avenue for enhancing the management of PD by providing objective, real-time data on motor symptoms. Neurologists should familiarize themselves with these tools to integrate them into clinical practice, ultimately benefiting patient care and improving outcomes. Further research is warranted to standardize device use and optimize their utility in PD management.

Disclosure: Nothing to disclose.

EPO-429 | Deep brain stimulation in the mesencephalic locomotor region of the rat induces behaviours beyond just locomotion

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Background and Aims: Deep brain stimulation (DBS) in the cuneiform nucleus (CnF), a subregion of the mesencephalic locomotor region (MLR), has been suggested for treating gait disturbances in severe Parkinson's disease (PD). However, recent studies observed no significant clinical effect of CnF-DBS, but instead reported increased anxiety. This raised the question about neurobiological connections of the CnF to motor centres and neural circuits for fear and anxiety.

Methods: Here, we applied DBS to the CnF of rats and analysed acute DBS-induced behaviour in an inversed open field. Unbiased behavioural analysis was conducted with DeepLabCut. Neural activity mapping was performed after DBS by quantifying de novo expression of the activity marker cFOS. Finally, we developed viral fibre tracers expressing plasma membrane-bound green fluorescent protein (GFP) in glutamatergic neurons to visualize the ascending input and output matrix of the CnF area.

Results: DBS in the CnF induced acute behaviour at frequencies of 80-130 Hz but not at 20-60 Hz. DBS initiated gait within a second, but also induced subsequent periods of different behavioural states like running, tail rattling, rearing, and freezing. Neurons in the stimulated area expressed cFOS within 90 minutes. Fibre mapping of CnF neurons identified ascending

projections to the substantia nigra, the subthalamic nucleus, different thalamic areas and the central amygdala.

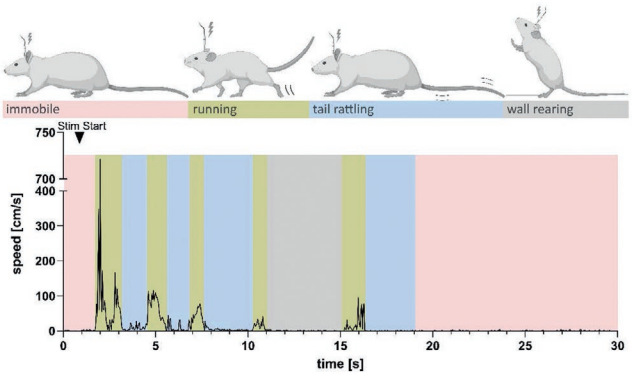

FIGURE 1 Categorization of acute behaviour after HF-DBS in the CnF.

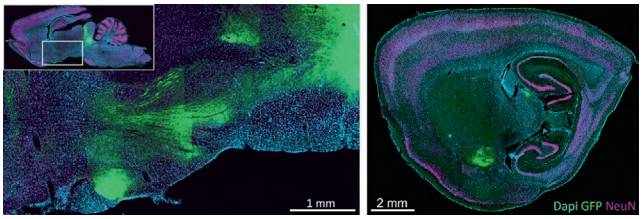

FIGURE 2 Anterograde tracing visualizes ascending projections to higher order motor centres and brain areas involved in defensive behaviours.

Conclusion: Our study suggests that the CnF in the MLR integrates behaviours beyond just locomotion by ascending, glutamatergic projections to higher order motor centres and brain areas involved in defensive behaviours.

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EPO-430 | Predictors of cognitive impairment and gait disorder after subthalamic deep brain stimulation in Parkinson's disease

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Background and Aims: Cognitive impairment and gait disturbances are the most common complications after subthalamic nucleus stimulation (STN-DBS) surgery, and the question of predisposing factors to these symptoms progression during STN-DBS remains controversial.We aimed to determine the predictors of cognitive decline and gait disorder after STN-DBS in PD.

Methods: A total of 22 PDpatients aged 45-60 years were examined. MRI voxel-based morphometry and tractography was applied before surgery. Neuropsychological testing was performed to identify frontal-striatal, posterior cortical, and mixed subtypes of mild cognitive impairment (MCI) preoperatively and to assess cognitive function over the next 3–5 years after STN-DBS surgery in PDpatients. The FOGQ assesses freezing of gait severity was used.

Results: In a retrospective analysis, PDpatients with preoperative frontostriatal or mixed MCI had greater cognitive decline in subsequent years compared with patients with posterior cortical MCI. These patients, along with a decrease in the density of the tracts connecting the frontal cortex with the caudate nucleus and putamen, had a more pronounced decrease in the volume of the orbitofrontal and ventromedial prefrontal cortex. The frontostriatal and/or mixed subtype MCI was also detected in patients who developed gait disturbances. A correlation was determined between the FOGQscore and the cortical areas volume related to the dorsal and ventral visual information processing system ($p<0.03$), as well as the frontal cortical areas ($p < 0.02$) responsible for planning and programming movements.

Conclusion: Thus, to select candidates for STN-DBS surgery, it is necessary to take into account MRI morphometry and tractography data, as well as MCI subtypes prior to surgery.

Disclosure: Nothing to disclose.

EPO-431 | Genetically determined dystonic syndromes associated with elevated alpha-fetoprotein

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Background and Aims: Alpha-fetoprotein (AFP) is a liver-produced glycoprotein with an unknown function. Elevated levels are linked to autosomal recessive cerebellar ataxias, where atypical forms may primarily present with dystonia. The most common example is ataxia telangiectasia (AT) caused by ATM gene mutation.

Methods: We aimed to identify patients with dystonia and pathogenic mutations linked to AFP elevation and evaluate whether AFP could serve as a suitable biomarker for dystonia patients.

Results: The study included 669 patients diagnosed with dystonic syndromes who underwent whole-exome sequencing. Pathogenic mutations associated with elevated AFP levels were identified in nine patients (five men). Among these were six cases of ATM gene mutations, two cases of SETX gene mutations, and one of an NGLY1 mutation. Dystonia was the only or dominant symptom in five patients, while ataxia was present in four patients. AFP-level testing was performed in eight of nine patients with the pathogenic mutation, revealing increased levels in seven patients. In one patient with an ATM mutation, the AFP plasma level was within the normal range on repeated

measurements, which is rare, but possible even with a diagnosis of ataxia telangiectasia.
Conclusion: We found a pathogenic mutation linked to AFP elevation in over 1 % of the patients, which we believe is significant enough to support the use of AFP as a biomarker for early-onset dystonia. Supported by the grant: AZV Czech Republic: NW24-04-00067 and EU programme EXCELES: LX22NPO5107.
Disclosure: Nothing to disclose.

EPO-432 | Systematic review and meta-analysis of neutralising antibodies to botulinum neurotoxin type A in multiple indications

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Background and Aims: Botulinum neurotoxin type A (BoNT-A) is a biological treatment for cervical dystonia (CD), spasticity, and blepharospasm. Its biological nature means some patients can develop anti-BoNT-A neutralising antibodies (NAbs), which may reduce efficacy and, in some cases, cause secondary treatment failure. This meta-analysis investigated the incidence of NAb-positivity after treatment with commercially-available BoNT-A formulations.
Methods: A systematic review was conducted in April 2024, and meta-analysis was performed of publications reporting data on immunogenicity after first-line treatment with abobotulinumtoxinA, incobotulinumtoxinA or onabotulinumtoxinA (excluding original formulation) in patients with CD, spasticity or blepharospasm
Results: In total, 29 publications reporting 28 unique studies were identified. The proportion of patients with CD developing NAbs was significantly higher after treatment with abobotulinumtoxinA (2.1%; $p=0.02$) versus incobotulinumtoxinA (0%). There was no difference in NAb positivity after onabotulinumtoxinA (1.5%) versus abobotulinumtoxinA ($p=0.72$) or incobotulinumtoxinA ($p=0.07$). The proportion of patients with spasticity developing NAbs after onabotulinumtoxinA (1.2%; $p=0.01$) was significantly higher than with incobotulinumtoxinA (0%); there was no difference between abobotulinumtoxinA (0.5%) versus onabotulinumtoxinA ($p=0.84$) or incobotulinumtoxinA ($p=0.12$). Based on only three identified studies, the proportion of patients with blepharospasm developing NAbs was significantly higher after abobotulinumtoxinA (16.7%) than onabotulinumtoxinA (0%; $p<0.001$) or incobotulinumtoxinA (0%; $p=0.002$).
Conclusion: No patients exclusively treated with incobotulinumtoxinA developed persistent NAbs, supporting the low antigenicity of this BoNT-A formulation. Clinicians must consider the potential effects of cumulative exposure to different BoNT-A formulations for different indications. We recommend incobotulinumtoxinA to avoid developing immunogenicity, particularly for patients requiring higher doses and repeated treatments.
Disclosure: This study was funded by Merz Therapeutics GmbH.

EPO-433 | Secondary treatment failure with botulinum neurotoxin type A: A systematic review and meta-analysis

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Background and Aims: Botulinum neurotoxin type A (BoNT-A) treatment is recommended for cervical dystonia (CD) and spasticity. Since it is a biological therapy, some patients can develop anti-BoNT-A neutralising antibodies (NAbs). NAbs reduce efficacy and, in some cases, cause secondary treatment failure (STF). This meta-analysis aimed to investigate the incidence of STF after treatment with commercially-available BoNT-A formulations for which long-term data are available.
Methods: A systematic review identified publications reporting NAb-induced STF after first-line treatment with abobotulinumtoxinA, incobotulinumtoxinA or onabotulinumtoxinA (excluding original formulation) in patients with CD or spasticity. STF occurrence was analysed in a meta-analysis using the DerSimonian-Laird random-effects method with Freeman-Tukey double arcsine transformation. Differences in STF occurrence between the three formulations were evaluated through heterogeneity testing.
Results: In total, 18 studies assessed STF in CD or spasticity. Meta-analysis showed that the proportions of patients with CD developing STF were significantly higher after treatment with abobotulinumtoxinA (9%; $p<0.001$) or onabotulinumtoxinA (3%; $p=0.03$) than with incobotulinumtoxinA (0%). There was no difference between the proportions of patients developing STF after abobotulinumtoxinA versus onabotulinumtoxinA ($p=0.08$). The proportion of patients with spasticity developing STF after treatment with abobotulinumtoxinA (5%; $p=0.01$) was also significantly higher than with incobotulinumtoxinA (0%). No patients treated exclusively with incobotulinumtoxinA developed NAb-induced STF, irrespective of the treatment indication.
Conclusion: IncobotulinumtoxinA was associated with a significantly lower risk of developing STF compared with abobotulinumtoxinA (CD and spasticity) and onabotulinumtoxinA (CD). IncobotulinumtoxinA is recommended to avoid developing NAb-induced STF, particularly for patients who require higher doses and repeated treatments.
Disclosure: This study was funded by Merz Therapeutics GmbH.

EPO-434 | Six-month comparison of DBS-STN, LCIG, CSCI and LECIG in advanced Parkinson's disease patients

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Background and Aims: Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by motor and non-motor symptoms. In advanced stages, individualized treatment strategies are needed to manage motor fluctuations and dyskinesias. This study compares the efficacy of deep brain stimulation of the subthalamic nucleus (DBS-STN), levodopa/carbidopa intestinal gel (LCIG), levodopa/entacapone/carbidopa intestinal gel (LECIG), and continuous subcutaneous infusion (CSCI) with foslevodopa/foscarbidopa in advanced PD over six months.
Methods: We analyzed 51 PD patients treated at the Clinic of Neurology, Clinical Hospital Center Rijeka, between 2022 and 2024. Patients were assessed at baseline and after six months, using Unified Parkinson's Disease Rating Scale (UPDRS) part III and IV scores.
Results: After six months, DBS-STN showed the highest efficacy, with a 51% improvement in UPDRS III and 53% in UPDRS IV scores. CSCI and LCIG demonstrated 30% improvement in both UPDRS III and IV scores, while LECIG improved UPDRS III by 29% and UPDRS IV by 22%.
Conclusion: These findings highlight DBS-STN as the most effective option for managing motor symptoms and complications in advanced PD. While CSCI, LCIG, and LECIG offer viable alternatives, their efficacy is lower, particularly in motor complication management. CSCI, being the least invasive, is an important option influencing patient decisions. DBS should be prioritized for eligible patients, with subcutaneous and intestinal gel therapies reserved for those unsuitable for surgery. This study continues prospectively to further evaluate long-term treatment outcomes.
Disclosure: Nothing to disclose.

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EPO-435 | Genetic control of enzymatic reactive oxygen species formation may influence idiopathic Parkinson's disease progression

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Background and Aims: The NOX2 enzyme is highly expressed by microglia and generates reactive oxygen species (ROS) to eliminate pathogens. While excessive NOX2 activation has been linked to neurodegenerative diseases, the role of NOX2 in Parkinson's disease (PD) is not fully understood. We aimed to determine the impact of variation in genes encoding NOX2 activity on long-term progression in patients with idiopathic PD. Single nucleotide polymorphisms (SNPs) at rs4673 and rs1049254 in CYBA, encoding the NOX2 subunit p22phox, influence NOX2 activity and impact on progression in multiple sclerosis and recovery from Guillain-Barré syndrome.
Methods: We genotyped 93 patients with idiopathic PD for these SNPs. Blinded investigators reviewed patient records to determine time from motor onset to the occurrence of 25 disease progression milestones. The impact of CYBA SNP genotypes on PD progression was assessed using individual milestones and a composite measure of all milestones. Data were censored when 50% of events within each milestone had occurred to reduce the contribution of normal aging.

TABLE 1 Patient characteristics.

		Number of low-ROS alleles[1] at rs4673 and rs1049254				
	All patients	0	1	2	3	4
Number of patients, N	93	14	20	30	16	13
Female sex, N (%)	35 (38)	5 (36)	9 (45)	12 (40)	5 (31)	4 (31)
Age at motor onset, years (range)	58 (27-79)	57 (27-79)	61 (39-77)	59 (31-76)	59 (44-75)	53 (30-65)
Median follow-up time[2], years (range)	18 (2-58)	17 (7-58)	16 (6-42)	19 (2-30)	17 (4-31)	24 (10-40)
Median age at death, years (range)	79 (57-94)	76 (57-88)	79 (64-91)	79 (55-86)	76 (65-94)	73 (45-92)
Has smoked[3], N (%)	36 (40)	5 (36)	6 (30)	15 (52)	5 (33)	5 (38)
PD progression milestones	Dose fractionation, dyskinesia, device-aided therapy, walking aids, repeated fall trauma, freezing of gait, fracture from falls, wheelchair, speech difficulties, referral to speech therapist, unintelligible speech, dysphagia, drooling, aspirations, drug-treated urinary problems, full incontinence, measured orthostatism, drug-treated orthostatism, hallucinations/illusions, other signs of cognitive impairment, established dementia, drug-treated new psychiatric symptoms, severe psychiatric symptoms with need for hospitalization or ECT, need for in-home care, need for institutional care					

[1]Low-ROS alleles denotes the combined number of rs1049254 G and rs4673 A alleles.
[2]Time from motor onset to death or lost to follow-up.
[3]Missing data from two patients.

Results: Patients carrying low-ROS genotypes showed a delayed onset of several individual milestones and a reduced accumulation of clinical milestones over time (Figure 1-2). These effects on milestone accumulation remained significant after adjusting for potential confounders ($p=0.006$ for rs1049254 and $p=0.001$ for low-ROS alleles). Ten years after motor onset, patients with a homozygous high-ROS genotype had acquired nearly three times as many clinical milestones as patients with a low-ROS genotype.

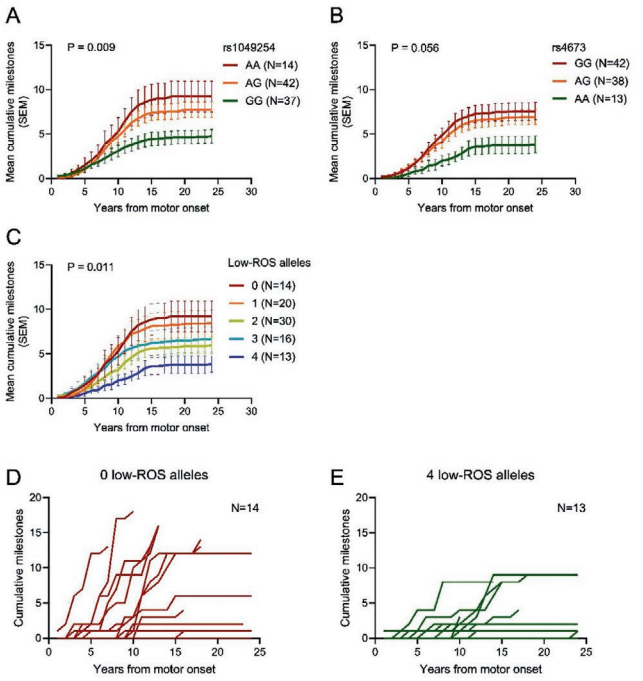

FIGURE 1 (A–C) Mean cumulative milestones within each genotype group. (D, E) Cumulated events for individual patients (lines) with (D) 0 or (E) 4 low-ROS alleles. (C–E) Combined rs1049254 G and rs4673 A alleles. Statistics by linear mixed-effects model.

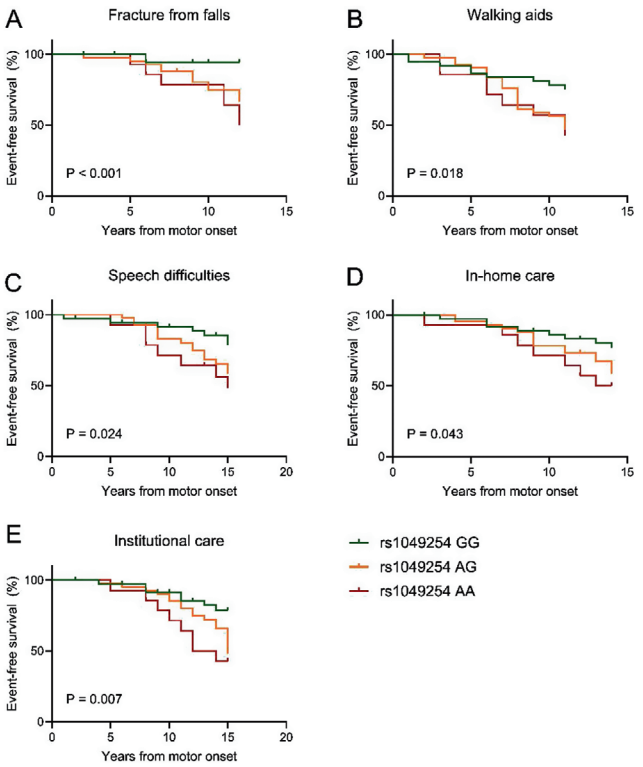

FIGURE 2 Time from PD onset to reach the milestones (A) fracture from falls, (B) need for walking aids, (C) speech difficulties, (D) in-home care or (E) institutional care. Patients grouped by rs1049254 genotype. Statistics by log-rank test for trend.

Conclusion: These results suggest a role for NOX2 in PD progression and highlight the potential of pharmacologically targeting NOX2 to reduce neurodegeneration.

Disclosure: Nothing to disclose.

EPO-436 | Motor symptoms and stigma in Parkinson's disease

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Background and Aims: Different motor symptoms have been described as being stigmatizing by Parkinson's disease (PD) patients. However, to date, findings are mainly based on qualitative research. Our aim was to address the association of motor symptoms and stigma by using the newly validated Parkinson's Disease Stigma Questionnaire (PDStigmaQuest).
Methods: This is a multi-center prospective study. We compared felt stigma domain scores to other PDStigmaQuest domain scores using Wilcoxon signed-rank tests. PDStigmaQuest domain scores and the total score were compared between early PD patients (disease duration ≤3 years) and other patients using Mann-Whitney *U* tests. Spearman correlations between PDStigmaQuest total score and the following clinical characteristics were calculated: Hoehn and Yahr (HY), MDS-UPDRS II, III, and IV, and PDQ-39 SI.
Results: In total, 201 PD patients (34.3% female, mean age 64.4, median HY 2.0) were included. Felt stigma scores were higher than hiding ($p < 0.001$), rejection ($p < 0.001$), and patronization scores ($p < 0.001$). Early PD patients showed significantly higher scores in the hiding domain ($p = 0.035$) and substantially lower rejection domain scores than other PD patients ($p = 0.004$). PDStigmaQuest total score correlated significantly with the following clinical characteristics: HY ($r = 0.15$, $p = 0.033$), MDS-UPDRS II activities of daily living ($r = 0.29$, $p < 0.001$), MDS-UPDRS IV dyskinesia score ($r = 0.23$, $p = 0.008$), and PDQ-39 SI ($r = 0.61$, $p < 0.001$).
Conclusion: These data provide evidence that stigma is a critical aspect for quality of life in PD. In particular, dyskinesia and impairment of ADLs were associated with stigma. This ongoing study is essential for a deeper understanding of stigma in PD and its management in the future.
Disclosure: Nothing to disclose.

EPO-437 | Subacute onset progressive gait disorder with recurrent falls: A case report

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Background and Aims: A 72-year-old male with a history of microcytic anemia, obstructive sleep apneas, arterial

hypertension, hypercholesterolemia, and nocturia, presented with progressive gait imbalance over the past year, worsening significantly in the last four months.

Methods: The patient reported recurrent falls, primarily backward and sideways, marked slowness in daily activities, and occasional non-formed visual hallucinations. Neurological examination revealed prominent antecollis, significant hypomimia, mild hypophonia, dysarthria without palilalia, bilateral grasp reflexes, and slowed saccades without ophthalmoplegia. Motor findings included rapid hypokinesia and rigidity, brisk reflexes, normal muscle strength, and absent tremors. Postural reflexes were significantly impaired, requiring a walker for ambulation. MDS-UPDRS III score was 56, with Hoehn & Yahr stage 4.

Results: Cognitive testing showed an MMSE score of 25/30, with deficits in verbal memory retrieval, visual naming, and psychomotor speed. Polysomnography confirmed central and mixed OSA. Laboratory findings included microcytic hypochromic anemia and folate deficiency. Brain MRI demonstrated marked mesencephalic atrophy, whereas the DAT scan was unremarkable. CSF analysis, autoimmune panels, and onconeural antibodies were negative; however, IgLON5 antibodies were detected in both serum and CSF.

Conclusion: A diagnosis of Anti-IgLON5 antibody disease presenting as an atypical parkinsonism of progressive supranuclear palsy (PSP) phenotype was established. Anti-IgLON5 disease is a rare autoimmune encephalopathy that bridges neurodegeneration and autoimmunity, often linked with tau-related pathology. Clinical features are diverse, encompassing parasomnias, cognitive and psychiatric symptoms, atypical parkinsonism with falls, bulbar dysfunction, and autonomic failure. This case underscores the importance of considering Anti-IgLON5 disease in patients with atypical parkinsonism and diagnostic inconsistencies.

Disclosure: Nothing to disclose.

EPO-438 | When phenotype outweighs genotype: Deep brain stimulation in ATP1A3-related dystonia

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Background and Aims: ATP1A3-related movement disorders are often severe, resistant to pharmacological treatments, and thus present a considerable therapeutic challenge. Historically, patients with ATP1A3 mutations have shown poor responses to deep brain stimulation (DBS) targeting the globus pallidus internus (GPi). Here, we describe a patient with an ATP1A3 mutation who achieved a remarkable therapeutic improvement with GPi DBS.

Methods: We evaluated a 24-year-old woman with a genetically confirmed ATP1A3 mutation (p.Arg756Leu), presenting with refractory myoclonic jerks and segmental dystonia, which significantly impaired her quality of life. She also had mild cerebellar ataxia but no intellectual impairment. Brain MRI was normal except for mild cerebellar atrophy. Polygraphic EMG recording showed subcortical myoclonus and mobile dystonia. Following a multidisciplinary evaluation, bilateral GPi DBS was implemented.

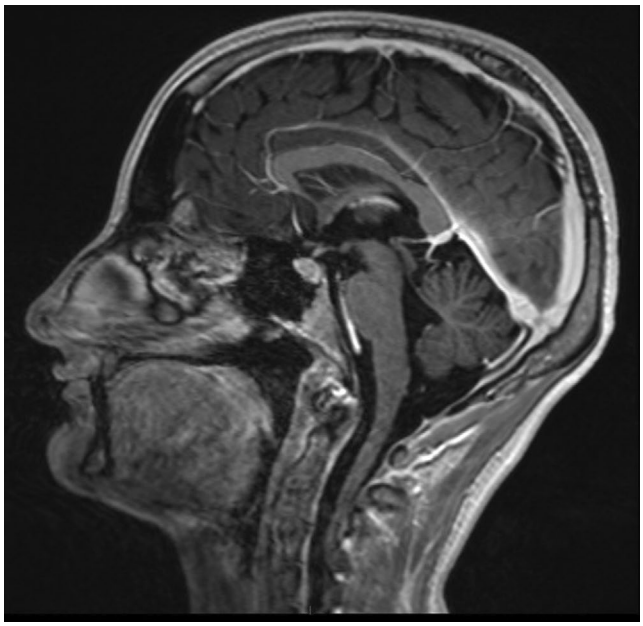

FIGURE 1 Preoperative Brain MRI

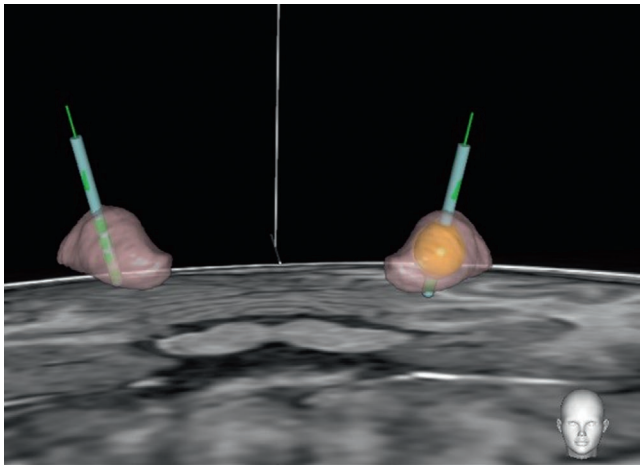

FIGURE 2 VOLUME OF TISSUE ACTIVATED (VTA) LEFT

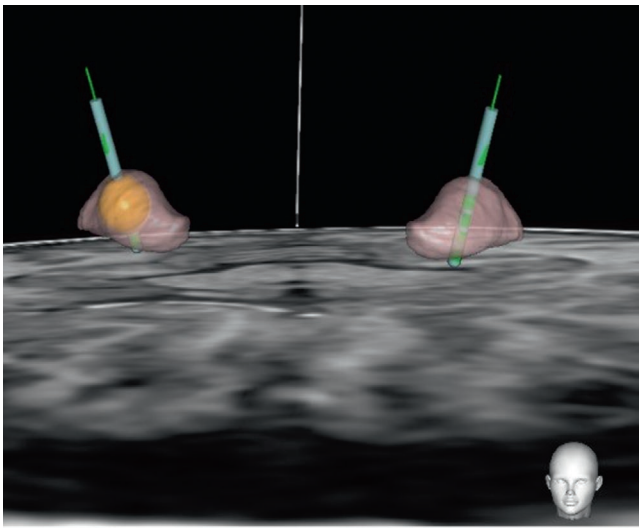

FIGURE 3 VOLUME OF TISSUE ACTIVATED (VTA) RIGHT

Results: The patient exhibited a profound and sustained reduction in myoclonus and dystonic postures following DBS, with significant functional and motor improvement. At last follow-up one year after surgery, clinical global impression improvement (CGI-I) was rated 2/7 (much improved) by both the patient and clinicians. The patient did not have any side effects from DBS.
Conclusion: This case highlights two key insights. First, the clinical spectrum of ATP1A3 mutations extends beyond established syndromic classifications, necessitating careful phenotypic characterization for personalized management. Second, we emphasize the importance of considering phenotype first when evaluating a patient for GPi DBS, even when the genotype generally suggests a poor response. Patients with prominent myoclonus without fixed dystonia and without significant lesions on brain MRI may respond well to GPi DBS, regardless of the underlying etiology.
Disclosure: Nothing to disclosure.

EPO-439 | Staged bilateral MR-guided focused ultrasound pallidothalamic tractotomy for Parkinson's disease

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Background and Aims: Since 2011, pallidothalamic tractotomy (PTT) has been employed as a therapeutic intervention for Parkinson's disease (PD) using magnetic resonance-guided focused ultrasound (MRgFUS). We aimed to investigate the Safety and Effectiveness of Staged Bilateral PTT-MRgFUS for PD.
Methods: Thirteen consecutive patients suffering from chronic (mean disease duration 9.0 years) and therapy-resistant PD were treated unilaterally with PTT MRgFUS. Eleven received operation of the second side. The primary endpoints comprised Unified Parkinson's Disease Rating Scale (UPDRS) scores assessed during both on- and off-medication states, along with adverse events recorded at baseline, 1 week, 1 month, 3 months, 6 months, and 12 months post-treatment.
Results: The mean duration between baseline UPDRS score and 1 year after the second side was 13.5 months. The UPDRS Part III score off-medication at 1 year after the first PTT was reduced by 37% ($p = 0.0002$) compared to that at baseline on-medication and 16% after the second PTT ($p = 0.02$). Percentage reductions of the mean scores comparing 1 year off- with baseline on-medication examinations were 83% for tremor, 63% for rigidity, and 57% for hypobradykinesia. Adverse events such as hypophonia (29%) and fatigue (29%) were mild and improved in post-treatment 3 months.
Conclusion: Our results suggest MRgFUS PTT was a safe and effective intervention for PD patients, in varying symptoms.Additional large-scale studies and long-term outcomes evaluation are needed.
Disclosure: Nothing to disclose.

EPO-440 | Aperiodic spectral component as a potential new marker and input signal for aDBS

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Background and Aims: New stimulation devices enable to record and analyze the local field potentials (LFPs) anytime, even during the deep brain stimulation therapy (DBS). The aim of our work was to study individual differences in LFPs, their evolution in time and to evaluate the influence of DBS on parameters of aperiodic spectral component.
Methods: LFP were recorded from the subthalamic nucleus (STN) in Parkinson´s disease patients (PD) ($n = 23$) during a simple experimental paradigm that included 5 minutes of resting state and a short gait during DBS "off" and "on" conditions ("off" medication). Classical spectral analysis was performed using Fast Fourier Transform (FFT). Progression in time could be already evaluated analyzing control measurement after one year ($n = 15$). Finally, the analysis of the aperiodic component was performed by fitting oscillations and one-over-F (FOOOF) approach.
Results: Typical beta power peaks, that represent a well-known correlate of PD main motor symptoms could be detected in the majority of our group of patients. Moreover, the frequency slowing of beta peak was detected in some cases comparing baseline and control measurement. Aperiodic slope and offset were significantly modified by DBS ($p = 0.0003$ and $p = 0.001$) tested by Wilcoxon signed rank test.
Conclusion: Beta power sensing is a well-established method in the DBS field, but has its limitations in the clinical practice. Evaluation of the aperiodic component in LFPs has the potential to better reflect the pathological activity of the neuronal network and might serve as a new clinical marker for adaptive DBS.
Disclosure: Nothing to disclose.

EPO-441 | Preliminary outcomes of MRgFUS thalamotomy or subthalamotomy for Parkinson's disease: A retrospective study

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Background and Aims: Tremor-dominant Parkinson's disease (TDPD) responds only partially to levodopa. Unilateral thalamotomy and subthalamotomy using magnetic resonance-guided focused ultrasound (MRgFUS) have shown improvements in motor symptoms and it could be an alternative to deep brain stimulation (DBS). We present our initial experience of TDPD patients treated with MRgFUS.
Methods: This is a retrospective study (2023–2024) of patients TDPD treated with MRgFUS-STN or MRgFUS-VIM which were evaluated at 1 and 6 months post-treatment. Change MDS-UPDRS motor part III score for the treated hemibody and total MDS-UPDRS III score. Treatment parameters were collected. All adverse events occurring during were documented. Data were analyzed with SPSS.
Results: Among 11 patients who underwent thalamotomy (mean age: 72.1 years; disease duration: 5.9 years), MDS-UPDRS III improvement for the treated hemibody was 63.3%, and MDS-UPDRS-III total score improvement was 34.09%; 5 patients experienced side effects at one month, of which 1 was permanent. In 10 patients with subthalamotomy (mean age: 68.6 years; disease duration: 7.5 years), improvements were 38.6% for the treated hemibody and 23% overall MDS-UPDRS-III; 8 patients experienced side effects at one month, of which 2 were permanent. SDR mean was 0.50. The mean coordinates of the subthalamus are: ML 12 mm; AP 7.83 mm; SI −3.83 mm and for thalamotomy are: ML 14.71 mm; AP: 6.25 mm and SI 1mm. Mean of sonications in thalamus was 7.5 and 9.62 in subthalamus.
Conclusion: Thalamotomy appears to be slightly more effective in controlling motor symptoms with fewer side effects than subthalamotomy. Further studies with longer follow-ups are needed.
Disclosure: Nothing to disclose.

EPO-442 | Hyperkinetic movement disorders expand the phenotypic spectrum of OPA1 variants: Case reports and literature review

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Background and Aims: Mutations in optic atrophy protein 1 (OPA1) gene are rare and are associated with dominant optic atrophy (DOA), They encompass multisystemic phenotypes, termed "DOA-plus" syndromes, often involving a constellation of neurological symptoms. Nevertheless, hyperkinetic movement disorders (HMDs) have been very rarely reported. We herein report two cases of HMDs linked to OPA1 variant.
Methods: Two patients presenting with HMDs underwent comprehensive multimodal evaluations, including genetic testing, within a long-term follow-up.
Results: Patient n. 1 (66 years old, male) presented with a long history of left-predominant intentional tremor in the upper-limbs, musician's dystonia and writer's cramp. Patient n. 2 (38 years old, female) had longstanding perioral dyskinesias, dystonic postures of both hands, and subtle bradykinesia. Electrophysiological studies revealed sensorineural deafness in case 1 and axonal sensory neuropathy in case 2. In both cases, genetic testing showed a heterozygous OPA1 variant, c.1149A>G (p.lle383Met), that was classified as pathogenic according to the American College of Medical Genetics (ACMG) criteria. A complete ophthalmological examination was then performed, although in the absence of subjective visual complaints.
Conclusion: Recognition of atypical presentations, such as HMDs, and the absence of visual symptoms in OPA1 mutation carriers emphasizes the importance of broader genetic testing in patients with HMDs. Early identification may facilitate management, enabling timely interventions to patients and their children to address emerging complications like optic atrophy or other systemic manifestations.
Disclosure: The authors have nothing to disclose with regard to the present research.

EPO-443 | Subclinical gait and postural changes are associated with a "malignant" phenotype in early Parkinson's disease patients

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Background and Aims: The presence of autonomic dysfunction, REM sleep behaviour disorders (RBD) and cognitive/behavioural symptoms has been associated with a so-called "malignant" phenotype in patients with Parkinson's disease (PD), according to the evidence of a more rapid disease progression. These symptoms have been also consistently associated with increased risk of falls. We aimed at investigating the association between severity of these symptoms and the presence of subtle gait and postural alterations in early non-demented PD patients.
Methods: Fifteen early PD patients (disease duration <5 years, Hoehn & Yahr ≤2.5) and 15 age and sex-matched healthy controls (HC) were consecutively enrolled. Gait and balance parameters were acquired using six Opal V2R wearable sensors during the Timed up and go in single/dual task (TUG-ST/DT) conditions. Motor symptoms was evaluated using the Unified Parkinson's disease Rating scale part III (UPDRS-III). Nonmotor symptoms were assessed by means of the Scales for Outcomes in Parkinson's Disease - Autonomic Dysfunction, Beck Depression

index and RBD single question. A II-level neuropsychological assessment was also performed. A "malignant" composite score (MCS) was created as numeric indicator of global nonmotor symptoms severity.
Results: Higher MCS significantly correlated with worse sit-to-stand performance at TUG-ST detected by wearable sensors. No correlations have been found between the MCS and UPDRS-III.
Conclusion: Our findings revealed that wearable sensors could provide useful information for the characterization of early PD patients. These subclinical changes are already associated with presence of autonomic dysfunction, RBD, cognitive and behavioural symptoms, suggesting a potential role to predict worse clinical outcome.
Disclosure: Nothing to disclose.

EPO-444 | Effects of subcutaneous foslevodopa-foscarbidopa on motor and nonmotor symptoms in Parkinson's disease

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Background and Aims: Foslevodopa/foscarbidopa is a new combination administered 24-hour/day continuous subcutaneous infusion (CSCI) for patients with fluctuating Parkinson's disease (PD).
Methods: We analyzed the effect of switching from oral L-dopa to CSCI on motor and nonmotor symptoms over a 3-month treatment period. From April to December 2024, 28 PD patients were implemented on CSCI in our site. Longitudinal data were available for 20 PD patients. At baseline and after 3 months, we evaluated motor symptom severity using the Unified Parkinson's Disease Rating Scale (UPDRS) part III; nonmotor symptoms burden with the NonMotor Symptom Scale (NMSS); treatment-related motor and nonmotor complications with the UPDRS part IV and Nonmotor Fluctuation Assessment questionnaire (NoMoFa), respectively; sleep quality with the Parkinson's Disease Sleep Scale 2 (PDSS-2); patient-reported quality of life using the Parkinson's Disease Questionnaire 8 (PDQ-8). At each visit, the total levodopa equivalent daily dose (LEDD) was calculated. Within-subject longitudinal differences on demographic and clinical variables between the two timepoints were assessed by means of one-way repeated-measures ANOVA analyses.
Results: Compared to baseline, significant changes were found in NMSS, PDSS-2 and PDQ-8 after 3 months of treatment with CSCI. Significant increase in total wake-up time spent in OFF state without troublesome dyskinesia was also observed at follow-up. No significant changes were observed in total LEDD (oral vs CSCI). Infusion site adverse events were common and generally well-tolerated after 3 months of treatment.
Conclusion: Our data reveal that, along with motor fluctuation stabilization, treatment with CSCI may significantly improve nonmotor symptoms burden in PD patients.
Disclosure: Nothing to disclose.

EPO-445 | Neuroacanthocytosis: Clinical and genetic heterogeneity in a cohort of 11 cases

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Background and Aims: Neuroacanthocytosis (NA) is a rare disease with approximately 1,000 cases reported worldwide. It encompasses a heterogeneous group of disorders characterized by neurological and psychiatric manifestations. This study describes the clinical and genetic characteristics of a cohort of 11 NA patients followed at the Movement Disorders Unit of Hospital Sant Pau.
Methods: Demographic, genetic, clinical, and neuroimaging data were analyzed. Descriptive statistics were calculated for age at symptom onset, age at diagnosis, and diagnostic delay.
Results: The cohort included 10 males (91%) and 1 female (9%), with a mean age at diagnosis of 41.4 years (SD ± 11.5) and a mean age at symptom onset of 34.8 years (SD ± 13.2). The average diagnostic delay was 4.8 years (SD ± 7.6), ranging from 0 to 22 years. The most frequent genetic diagnoses involved variants in VPS13A and XK. Initial symptoms included chorea (27%), tics (27%), and behavioral disorders (18%). Self-injurious behaviors and oromandibular dystonia were observed in 8 of the 11 patients (73%). Most patients exhibited psychiatric features, such as anxiety and depression, while one-third demonstrated cognitive impairments. Neuroimaging findings frequently showed caudate volume reduction. Two patients underwent deep brain stimulation (DBS) with good clinical response.
Conclusion: This study highlights the clinical and genetic heterogeneity of NA, emphasizing the importance of early diagnosis to optimize clinical management. The high prevalence of self-injurious behaviors and oromandibular dystonia emerges as a key distinguishing feature The positive outcomes observed with DBS in two cases suggest it may be a valuable therapeutic option in selected patients.
Disclosure: Nothing to disclose.

EPO-446 | Is there body district-specificity in sequence-specific implicit motor learning in Parkinson's disease?

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Background and Aims: Motor learning alterations are associated with Parkinson's disease (PD). Body district-specificity remains unexplored and could have implications for rehabilitation. We investigated sequence-specific implicit motor learning (iML) differences in alternative task movements in PD patients vs age-matched controls (HCs).
Methods: Thirty PD participants (67.6 ± 8.0 years, 1.9 ± 0.7 H&Y) and 30 HCs (69.6 ± 5.2 years) performed three Serial Reaction Time Tasks (SRTTs) differing for the adopted body part: Hands,

Arms, Feet. Visual-motor reaction time (RT) was recorded in response to visual stimuli. Eight blocks consisting of 4 repetitions of 12-stimuli sequence were presented: random sequence order was practiced in block one and eight (R1, R8); a fixed 12-stimuli sequence was performed in blocks from 2 to 7 (S2-S7). RTs were corrected for Errors (cRT) and reprocessed as percentage, where the mean RT of R1 represented 100% (cRTR1%). The responses curve (cRTR1-R8Curve), General Practice (GP, cRT% different from R1), Sequence Learning (SLcRT% from R8), and iML (% difference between R8 and S7) were compared among groups and body districts by two-way RM-ANOVA.
Results: PD patients showed slower cRTs for each test ($p < 0.05$), but both groups completed the repeated sequence faster than the random trials ($p < 0.05$), indicating that GP, SL, and iML did not differ across testing modalities and groups.
Conclusion: PD patients are able to gain an iML level comparable to HCs. The iML acquired in PD is consistent across different body regions. Therefore, SRTT could be a tool for studying iML in PD and may be used as neurorehabilitation outcome.
Disclosure: Nothing to disclose.

EPO-447 | Short-term heart rate variability recordings as a marker of Parkinson's disease severity

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Background and Aims: Heart rate variability (HRV) reflects autonomic function and can be easily assessed using short-term recordings. Despite their practicality, few studies have evaluated HRV in PD, and none have explored its relationship with disease severity. This study aimed to investigate the association between short-term HRV measures and PD severity.
Methods: We conducted a cross-sectional study, recruiting consecutive PD patients from outpatient clinics. A 5-minute ECG recording was performed in the supine position after 10 minutes of rest, fasting, and medication abstinence overnight. HRV analysis was conducted in time and frequency domains using Kubios software.
Results: The patients ($n = 40$) had a mean age of 70.5 ± 7.5 years, disease duration of 6.5 ± 5 years, and a UPDRS III score of 29.1 ± 14.4. Significant inverse correlations were observed between UPDRS III scores and mean RR interval ($\rho = -0.457$; $p = 0.021$), standard deviation of NN intervals (SDNN, $\rho = -0.436$; $p = 0.035$), low-frequency power ($\rho = -0.428$; $p = 0.042$), and total power ($\rho = -0.454$; $p = 0.028$), even after Bonferroni adjustment. Linear regression identified UPDRS III as an independent predictor of mean RR ($\beta = -0.388$; $p = 0.008$), SDNN ($\beta = -0.304$; $p = 0.05$), and SD2 ($\beta = -0.309$; $p = 0.046$) when adjusted for age. Patients were stratified by Hoehn and Yahr (H&Y) stage (≤2: $n = 20$; >2: $n = 20$). The more severe group had significantly lower RR ($p = 0.032$), SDNN ($p = 0.014$), low-frequency power ($p = 0.019$), high-frequency power ($p = 0.045$), total power ($p = 0.013$), and SD2 ($p = 0.012$), even after adjusting for age.
Conclusion: Short-term HRV recordings may provide a simple method to assess dysautonomia in PD. Reduced HRV measures were observed in patients with greater disease severity, highlighting autonomic impairment.
Disclosure: Nothing to disclose.

EPO-448 | Biocollection effort in Parkinson's disease, parkinsonism and neurodegenerative disorders: The PADUA-CESNE cohort

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Background and Aims: Recently, the potential role of fluid and tissue-based biomarkers in Parkinson's disease (PD) and neurodegenerative disorders has emerged; further work is needed to integrate them with other clinical and instrumental data, and translating them into clinical practice. We describe PADUA-CESNE biocollection program aimed at studying disease mechanisms and aiding in diagnosis-prognosis-therapy definition.
Methods: Standardized assessment and biocollection protocol.
Results: Patients undergo neurological evaluation to confirm clinical diagnosis of PD, parkinsonism or other neurodegenerative disorder. Biocollection program includes: - clinical data (motor and non-motor scales, extensive neuropsychological assessment), - genetic testing (NGS Illumina NextSeq550 custom gene panel, CNV, MLPA) to define genetic diagnosis and select patients for target-therapy trials, - skin/tissue biopsy (immunohistochemistry: phosphorylated alpha-synuclein pSyn SER129, alpha-synuclein oligomers Clone 5G4, phosphorylated Tau pTau Clone AT8, inflammatory markers; RT-QuIC assay), to define disease pathology at biological level, - fluid biomarkers collection (SIMOA test: serum GFAP, NFL, pTau181; chemiluminescence: plasma pTau217 and CSF 1-42/1-40 beta-amyloid, pTau181 and total Tau; RT-QuIC assay for synuclein in serum, CSF and plasma) to monitor disease progression, - structural and functional neuroimaging (MRI, fMRI, DAT-Scan, PET), - neurophysiology evaluation (HD-EEG) to measure cortical connectivity. 204 serum samples, 165 plasma samples, 66 skin biopsies, 22 fibroblast cultures, 203 MRIs, 135 EEG, 400 DNA samples were collected so far from patients and healthy controls.
Conclusion: Biocollection effort is a fundamental approach to study PD and neurodegenerative disorders, obtaining cohorts with integrated multimodal data and comprehensive biomarker

profiles for each patient, to improve diagnosis, prognosis and personalized medicine.
Disclosure: Nothing to disclose.

EPO-449 | Amantadine ER tablets for treatment of drug induced extrapyramidal reactions: A phase IV multicenter, single-arm study

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Background and Aims: This subset analysis of a phase IV study was performed to assess the safety and efficacy of amantadine extended-release (ER) tablets in Indian patients with drug-induced extrapyramidal reactions.
Methods: A subset of 22 patients from this single-arm, multicenter, phase IV study (CTRI/2023/04/051973), with drug-induced extrapyramidal reactions was analyzed for safety and efficacy of amantadine ER tablet. The starting dose was 129 mg orally once; further uptitrated at weekly intervals to a maximum daily dose of 322 mg (administered as 129 mg and 193 mg tablets) as per patient's response and tolerability. Treatment duration was upto 8 weeks depending on dose uptitration. Primary objective was safety assessment. Efficacy endpoints were change from baseline in Extrapyramidal Symptom Rating Scale (ESRS) total score and ESRS part I, II, III and IV subscores.
Results: A total of 8 treatment-emergent adverse events (TEAEs) occurred in 6 patients. The most common TEAE was hyperchlorhydria. All the TEAEs were non-serious and were resolved without sequelae at the end of the study. The total mean (±SD) ESRS score decreased significantly ($p < 0.0001$) from 38.52 (±13.14) at baseline to 19.62 (±11.83) end of treatment (EOT). Also, the mean (±SD) ESRS part I, II, III and IV sub scores significantly decreased gradually from baseline till EOT ($p < 0.05$).
Conclusion: Amantadine ER tablet was safe and efficacious in Parkinson disease with the convenience of once-daily dosing.
Disclosure: The study was funded by Sun Pharma Laboratories Limited (SPLL).

MS and related disorders 3

EPO-450 | Biosimilars education in neurology: Knowledge gains through online CME

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Background and Aims: We developed an online Continuing Medical Education (CME) activity titled: "Biosimilars 101: From Neurologists, for Neurologists". We hypothesized that participation in this education would lead to improved knowledge of the key features of biologic and biosimilar medicines and the similarities and differences between them.
Methods: Neurologists participated in a 30-minute video discussion between 3 experts with accompanying slides (https://www.medscape.org/viewarticle/996834). Educational effect was assessed using a repeated-pair design with pre-/post-assessment. Three multiple choice questions assessed knowledge and 1 question (Likert-type scale) assessed confidence. A paired samples t-test was conducted for significance testing on overall average number of correct responses and for confidence rating, and a McNemar's test was conducted at the learning objective level (5% significance level, $p < .05$). Cohen's d with correction for paired samples estimated the effect size of the education on number of correct responses (<.20 modest, .20-.49 small, .59-.79 moderate, ≥.80 large). The CME activity launched on 9/27/2023, and the data were collected through 2/27/2024.
Results: A total of 621 neurologists participated, of which 33 completed all the pre- and post-activity questions during the study period. Overall, 45% improved their knowledge of biosimilars ($p < 0.001$) indicating a considerable effect of the education (Cohen's $d = 0.73$) (see Table). Overall, 42% had a measurable improvement in confidence in their knowledge about biosimilars.

Learning Objective	Q	Aggregated Data		Linked Learning Results [a]	
		Average % correct pre- vs post-education	P-value	% Improved pre- vs post-education [b]	% Reinforced pre- vs post-education [c]
Increased knowledge regarding the key features of biologic medicines and their inherent variability	Q1	42% vs 64%	<.05	24%	39%
Increased knowledge regarding the basic biosimilar terminology (e.g., interchangeability, switching, totality of evidence)	Q2	0% vs 15%	<.05	15%	NA
Increased knowledge regarding the regulatory approval process of biosimilars	Q3	15% vs 36%	<.05	24%	12%
Confidence		Mean pre- vs post-education on 1-5 scale[d]		% Increased pre- vs post-education	% Maintained pre- vs post-education
Increased confidence in their ability to differentiate between biosimilars and generic medication	Q4	1.97 vs 2.52	<.01	42%	55%

[a] Each individual learner tracked pre- and post-education
[b] Incorrect answer pre-education, correct answer post-education
[c] Correct answer pre-education, correct answer post-education
[d] 1 – not confident to 5 – very confident

FIGURE 1 Impact of education on' knowledge of biosimilars

Conclusion: This online CME activity significantly improved neurologists' knowledge of biosimilars, however substantial gaps remain which should be addressed in future medical education.
Disclosure: Nothing to disclose.

EPO-451 | Probiotics supplementation for information process speed in multiple sclerosis

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Background and Aims: Probiotic supplementation, through the gut-brain axis, is suggested to enhance clinical outcomes in patients with Multiple sclerosis (MS) and also found to improve cognitive function. This study investigated the effects of probiotic supplementation on information process speed (IPS) in minimally disabled relapsing-remitting MS (RRMS) patients.
Methods: In this parallel, randomized, double-blind, placebo-controlled trial, 90 RRMS patients, with Expanded Disability Status Scale (EDSS) <4, received either the probiotics supplementation (Lactocare®) or a placebo twice daily for four months. Visual IPS was assessed using the Symbol Digit Modalities Test (SDMT), and the three-second version of the Paced Auditory Serial Addition Test (PASAT-3) was utilized to assess auditory IPS. Analysis of covariance (ANCOVA) -adjusted based on before values- was conducted using the SPSS software with 95% confidence intervals and 0.05 level of significance for *p*-value.
Results: Sixty participants completed the trial (29 in the probiotics group, 31 in the placebo group). Median disease duration was 60 [IQR: 93] and 48 [IQR: 63] in the probiotics and placebo groups, respectively and most of the participants were females (72.4% and 80.6% in the probiotics and placebo groups, respectively). Based on the ANCOVA, the estimated mean and standard error for SDMT in probiotics was 46.80 ±1.20 and in the placebo group, it was 47.47 ±1.12 (*p*-value: 0.68). For the PASAT-3, these values were 47.97 ±1.38 and 46.78 ±1.25 in the probiotics and placebo groups, respectively (*p*-value: 0.53).
Conclusion: Supplementation with a seven-strain probiotics supplementation does not result in a significant improvement in IPS in minimally disabled RRMS patients.
Disclosure: Nothing to disclose.

EPO-452 | Radiological isolated syndrome: Models for predicting multiple sclerosis

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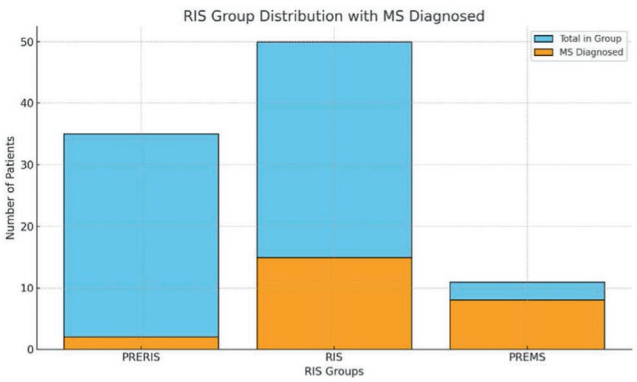
Background and Aims: Radiologically isolated syndrome (RIS) represents a preclinical stage of Multiple Sclerosis (MS) identified by incidental MRI findings in individuals without neurological symptoms. According to the criteria proposed in 2023, fewer lesions in typical spaces are sufficient for diagnosis. This study aims to characterize asymptomatic individuals with MRI-detected demyelinating lesions and proposes two additional terms: "preRIS" and "preMS."
Methods: A retrospective analysis of patient records identified 96 individuals with demyelinating MRI lesions typical for MS. These were classified into three groups: preRIS, RIS, and preMS. PreRIS denotes lesions insufficient for dissemination in space and time criteria, while preMS fulfills these criteria. Demographic and clinical features were analyzed.
Results: Among 96 patients (67 females, 69.8%; mean age: 37.3 ±10.6 years), 35 were classified as preRIS, 50 as RIS, and 11 as preMS. During a mean follow-up of 3.97 ±3.26 years, 26 patients (27%) converted to MS, with the preMS group showing the highest conversion rate and preRIS the lowest ($p < 0.001$). The mean time from RIS to MS diagnosis was 26.59 months (median: 12.67 months; range: 1.2–87.7 months). Common initial attacks included cerebellar symptoms and optic neuritis.



Conclusion: As a result of the study, preMS group demonstrated a significantly higher risk of MS conversion. Subgrouping RIS patients may refine risk stratification, improve monitoring, and inform early intervention strategies.
Disclosure: Nothing to disclose.

EPO-453 | Neuropsychological differences between NMOSD, MOGAD and MS

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Background and Aims: Neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) are rare inflammatory diseases. While cognitive involvement in Multiple Sclerosis (MS) is well-established, cognitive disability in NMOSD and MOGAD remain underexplored.
Methods: We enrolled 11 NMOSD (7 NMOSD + 4 MOGAD) and 11 SM patients (clinic-demographic data of the patients are reported in Table1). Patients were assessed clinically with EDSS, cognitively with BICAMS (from which we obtained the total cerebral functional score, CFS), and for depression with the Beck Depression Inventory II (BDI-II). SM patients were matched to NMOSD patients for age, education, sex and EDSS. Comparisons between-groups for Symbol Digit Modalities Test (SDMT), California Verbal Learning Test (CVLT), Brief Visuospatial Memory Test (BVMT) and BDI-II were performed through the Student's *t*-test.

TABLE 1 Clinical characteristics of patients with NMOSD, MOGAD, MS and in the combined NMOSD + MOGAD group.

	NMOSD	MOGAD	NMOSD+ MOGAD	MS
Number of patients, N	7	4	11	11
Sex				
Male, N (%)	2 (28.5)	3 (75)	5 (45)	5 (45.4)
Female, N (%)	5 (71.5)	1 (25)	6 (54)	6 (54.6)
Age, mean (SD) (years)	56.5 (14)	46.0 (13)	52.7 (14.6)	52 (15)
Schooling, mean (SD) (years)	10.9 (3.6)	14.2 (4.1)	12.1 (4.2)	11.1 (3.8)
DD, median (Range) (years)	8 (1.9-30)	2 (1.1-8.9)	7.0 (1.1-30)	13 (1.6-21.5)
EDSS, median (Range)	4 (3-7)	2 (1.5-2.5)	3 (1.5-7)	4 (1.5-5.5)

Abbreviations: EDSS= Expanded disability status scale; SD= Standard Deviation; MS= Multiple Sclerosis; N=Number, DD= disease duration.

Results: MS and NMOSD patients were similar for age, sex, education and EDSS. Disease duration was longer in MS patients vs NMOSD+MOGAD group (median = 13, range = 1.6–21.5 vs median = 7.0, range = 1.1–30; $p = 0.02$). SM patients had worse SDMT, BVMT and CFS scores while there was no difference for CVLT and BDI-II. Comparing MS to NMOSD patients confirms the significant difference for SDMT and BVMT scores, whereas no differences were reported comparing MS to MOGAD patients.
Conclusion: Patients with MS show greater deficits in visuospatial memory and attention/information processing speed domains than patients with NMOSD or MOGAD. This finding can be explained by the greater cortical involvement and cerebral white matter diffuse abnormalities more frequently affecting MS compared to NMOSD and MOGAD.
Disclosure: A.E. has received honoraria from Novartis. M.M. has received research grants from ECTRIMS-MAGNIMS, the UK MS Society, and Merck, and honoraria from Biogen, BMS Celgene, Ipsen, Janssen, Merck, Novartis, Roche, and Sanofi-Genzyme. M.P. has received research grants from the Italian MS Foundation and Baroni Foundation, honoraria from Health & Life and Biogen, and sponsorship for travel/meeting expenses from Novartis, Roche, and Merck. R.L. has received honoraria from Biogen, Merck, Novartis, Roche, and Teva. V.B.M. has received research grants from the Italian MS Society and Roche, and honoraria from Bayer, Biogen, Merck, Mylan, Novartis, Roche, Sanofi-Genzyme, and Teva. A.C. has received research grants from Almirall, research grants from ECTRIMS-MAGNIMS, and honoraria from Almirall, Biogen, Roche, Sanofi-Genzyme, Merck, Ipsen, and Novartis. None of the other authors has any conflict of interest to disclose.

EPO-454 | Ocrelizumab efficacy, safety, adherence, and retention in cypriot multiple sclerosis patients

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Background and Aims: We retrospectively evaluated real-world efficacy, safety, adherence, and retention of ocrelizumab (OCR) in adult cypriot multiple sclerosis (MS) patients.
Methods: Data from forty-five patients, encompassing two years prior and two years following OCR introduction, were analyzed. Thirty patients (67%) had Relapsing Remitting (RR) MS, whereas fifteen (33%) Primary Progressive (PP) MS.
Results: In RRMS patients (mean age at time of OCR initiation 42, mean MS duration 10 years, mean EDSS 3.7), mean Annual Relapse Rate (ARR) during the two years before OCR was 0.9 and mean EDSS progression 0.4. Two years after OCR, mean ARR was 0.1 and mean EDSS progression was 0.1, signifying reductions of 89% ($p = 0.003$) and 75% ($p = 0.017$) respectively compared to baseline. In PPMS patients (mean age at time of OCR initiation 51, mean MS duration 4 years, mean EDSS 5), the mean EDSS progression during the two years before OCR was 1.3. Two years after OCR, mean EDSS progression was 0.6, signifying a reduction of 54% compared to baseline ($p = 0.134$). Two patients (4%) discontinued OCR, one due to family planning and another due to disease progression. Forty-one patients (95% of completers) adhered to treatment, completing five or six OCR infusions in 24 months. Most frequent Adverse Drug Reactions (ADRs) were infections (11%), infusion-related reactions (4%) and gastrointestinal events (4%).
Conclusion: Ocrelizumab significantly reduced relapse rates and delayed disease progression in RRMS patients and considerably delayed disease progression in PPMS patients. ADRs were

generally mild and transient, leading to high adherence and retention to therapy.
Disclosure: Nothing to disclose.

EPO-455 | Bruton tyrosine kinase inhibitors in relapsing multiple sclerosis: A systematic review and meta-analysis

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Background and Aims: Bruton tyrosine kinase (BTK) inhibitors are oral drugs now being developed for the treatment of relapsing multiple sclerosis (RMS), offering potential benefits by targeting both B-cells and innate immune responses.
Methods: This systematic review and meta-analysis included three studies with four groups analyzing BTK inhibitors for RMS. A comprehensive search of PubMed, Embase, and Cochrane databases was conducted following PRISMA guidelines. Risk of bias was assessed, and a meta-analysis was performed using Review Manager 4.1.
Results: A total of 2,687 patients were included, with BTK inhibitor dosages ranging from 25 mg to 150 mg per day. BTK inhibitors significantly reduced relapse rates compared to placebo and standard treatment, with a pooled rate ratio of 0.50 (95% CI: 0.44–0.57, $p < 0.00001$) and minimal heterogeneity ($I^2 = 0\%$), indicating a consistent 50% reduction in relapse risk across studies. It also reduced T2 lesion volume compared to placebo and standard treatment (MD: −1.10, 95% CI: −1.83 to −0.37, $p = 0.003$, $I^2 = 26\%$). However, there was no significant effect on T1 gadolinium-enhancing lesion reduction (MD: 0.10, 95% CI: −0.13 to 0.33, $p = 0.39$), with high heterogeneity observed ($I^2 = 73\%$). Evobrutinib, tolebrutinib, and remibrutinib were all well tolerated, with manageable side effects.

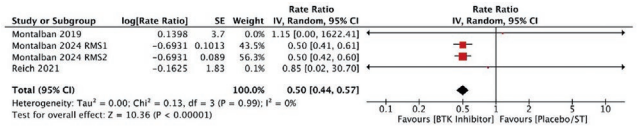

FIGURE 1 BTK – Relapse Rate

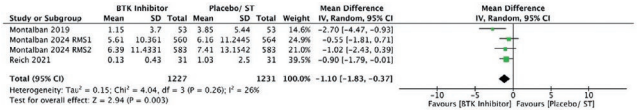

FIGURE 2 BTK – T2 lesion

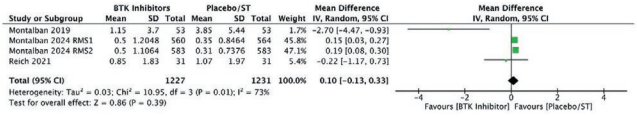

FIGURE 3 BTK – T1 lesions

Conclusion: This meta-analysis shows that BTK inhibitors reduce relapse rates and MRI-detected T2 lesion volume, suggesting potential benefits for RMS control. However, further research is needed to confirm long-term efficacy.
Disclosure: Nothing to disclose.

EPO-456 | Impact of treatment change on long-term disease outcomes in multiple sclerosis

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Background and Aims: Disease-modifying therapies (DMTs) alter the course of MS through immunosuppression or immunomodulation. Despite considerations of the side effect profiles and effectiveness of DMTs during clinical follow-up, determining the right medication at the right time can still be challenging for clinicians.The aim of this study was to compare relapse rates among people with MS who switched DMTs due to side effects with those who switched DMTs for other reasons, such as lack of efficacy, pregnancy, or scheduled stop.
Methods: A retrospective analysis was conducted on a cohort of 337 people diagnosed with MS who had undergone treatment changes and were followed up for 10 years. Patients were divided into two groups based on the reason for treatment discontinuation: side effects ($n = 253$, 75%) and lack of efficacy/pregnancy/scheduled stop ($n = 84$, 25%). Demographic and clinical characteristics were compared between the two groups using the Mann-Whitney U test. The primary outcome measure was the number of relapses after treatment discontinuation.
Results: There were no significant differences in sex, age, disease duration, disease type, or Expanded Disability Status Scale (EDSS) scores between the two groups ($p > 0.05$). However, patients who discontinued DMT due to side effects experienced significantly more relapses after switching medications [median = 2, interquartile range (IQR) = 0–3] compared to those who discontinued due to pregnancy or inefficacy (median = 1, IQR = 0–2) ($p < 0.001$).
Conclusion: Patients who discontinued DMTs due to side effects experienced a higher number of relapses after switching medications compared to those who discontinued due to pregnancy or inefficacy. This highlights the importance of careful consideration of treatment decisions, especially when managing adverse effects, to optimize patient outcomes.
Disclosure: Nothing to disclose.

EPO-457 | Dual diagnosis of multiple sclerosis and Parkinson's disease

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Background and Aims: This case report describes two patients with a rare dual diagnosis of MS and Parkinson's disease. Both were initially diagnosed with MS, but later developed Parkinsonism. A dopamine transporter scan confirmed reduced uptake, highlighting the need for ongoing clinical surveillance.
Methods: This case report contains two patient reports of such a dual diagnosis. In both cases, the patients had been diagnosed clinically with MS, and this was supported by MRI and CSF analysis.
Results: Case 1: A 58-year-old woman with MS developed Parkinson's disease (PD) 15 years later. Treatment with IFN-β, Levodopa, and Gabapentin improved symptoms but posed challenges with fatigue and worsening PD. Case 2: A 62-year-old man with MS and a family history of PD developed PD 2 years post-MS diagnosis. Ofatumumab and PD treatment yielded good outcomes with no MS progression.
Conclusion: The two cases highlight the rare co-occurrence of MS and PD, posing diagnostic and treatment challenges due to overlapping symptoms. Neuroinflammation and immune dysregulation may link both diseases. DaTSCAN aids diagnosis, and future therapies like NLRP3 inhibitors hold promise.
Disclosure: Nothing to disclose.

EPO-458 | Switching from fingolimod to B cell-depleting therapy in multiple sclerosis: A systematic review and meta-analysis

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Background and Aims: MS is a chronic disorder with a relapsing-remitting phenotype (RRMS). Fingolimod reduces relapse frequency, but a switch to ATZ, RTX, OCR, or cladribine may be needed if relapse prevention is insufficient.
Methods: MEDLINE, Embase, and Cochrane Library were searched. HR and RR were calculated using a random-effects model, both with 95% CI. Heterogeneity was assessed with the I^2 test.
Results: Switching from fingolimod to each B cell-depleting therapy reduces the annual relapse rate (ARR), with an effect of 0.2806 (95% CI 0.1356 to 0.4255; $p=0.15$). Furthermore, the risk of experiencing a first relapse after switching from fingolimod to a B cell-depleting therapy was significantly higher compared to patients who were treatment-naive (HR 5.2384; 95% CI 2.6839 to 10.2243; $p<0.001$). Expanded Disability Status Scale (EDSS) reduction was observed in the pooled analysis with an effect of 2.2932 (95% CI 1.4141 to 3.1723; $p=0.20$).

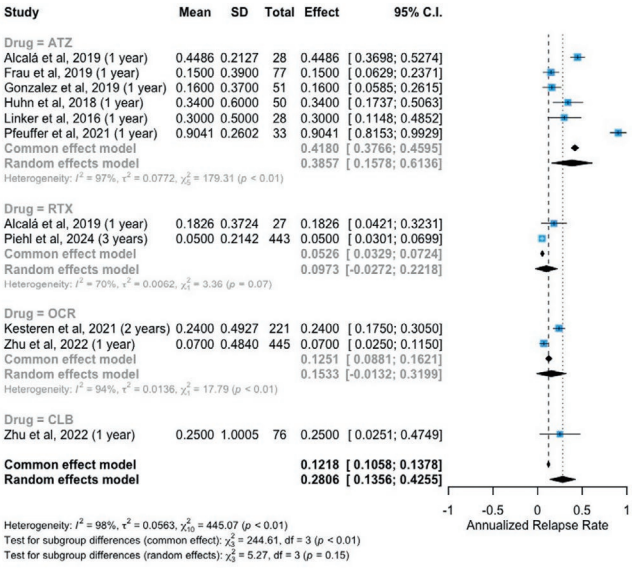

FIGURE 1 Annualized Relapse Rate

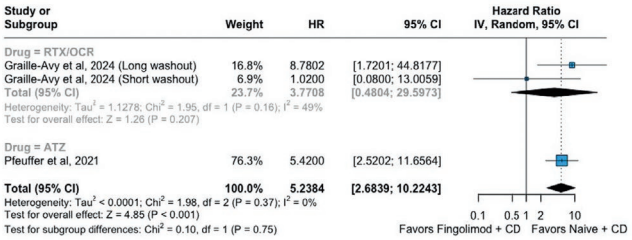

FIGURE 2 Time to First Relapse

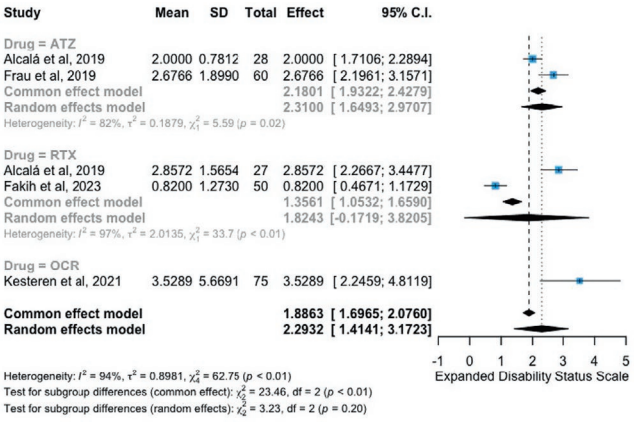

FIGURE 3 Expanded Disability Status Scale

Conclusion: ATZ most effectively reduces relapse rates and improves disability in patients switching from fingolimod, while the others therapies provide limited benefit.
Disclosure: Nothing to disclose.

EPO-459 | Social determinants of health in multiple sclerosis in Italy: A scoping review

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Background and Aims: Social determinants of health (SDH) can influence outcomes related to multiple sclerosis (MS) and the relationship between SDH and MS is complex, due to the interplay between a wide range of factors and to potentially bi-directional associations. Inequities can be also seen in countries with an universal health-care system such as Italy. This scoping review aims to identify and synthesize the existing and emerging literature on SDH in MS Italian population, exploring a wide range of determinants (sex, gender and sexuality; race and ethnicity; education; employment; socioeconomic status; domestic abuse; health-care access; food access; air pollution; social support).
Methods: This review followed the methodological guidelines for scoping reviews. Eleven PubMed search strings were defined and works exploring SDH in MS Italian patients over the past decade were included, together with emerging literature from the ECTRIMS congress.
Results: A total of 214 works (284 SDH findings) were included. More than one-third of the works focused on sex and gender while just one on domestic abuse; articles often presented results on several SDH simultaneously, especially for education and employment ($N=14$) and health-care access and social support ($N=10$). This work showed associations between a wide range of SDH and MS and revealed several unmet needs and disparities in the Italian MS population.

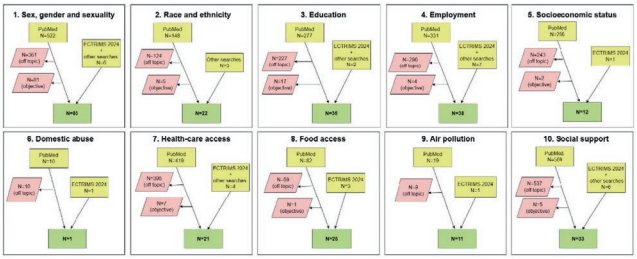

FIGURE 1 Flow diagram – study selection process

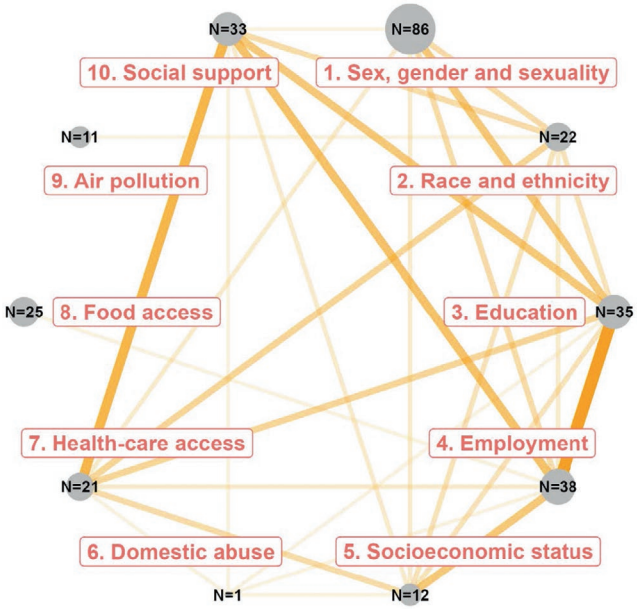

FIGURE 2 Relationship between the included studies

Conclusion: Disproportionality in thematic areas of research was observed and some gaps were identified. Findings from this review demonstrate the importance of accounting for SDH in the health context and can potentially guide future interventions from the Italian sociopolitical perspective.
Disclosure: Nothing to disclose.

EPO-460 | Reasons for switching initial disease modifying therapies in early relapsing MS: Lateral vs. escalation strategies

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Background and Aims: The number of treatment options for relapsing multiple sclerosis (MS) has increased considerably in recent years. Switches within disease-modifying therapies (DMTs) are common clinical practice. This study analyses reasons for switching from DMT of mild/moderate efficacy (MME-DMTs) either lateral (within the same efficacy category) or through escalation (to highly effective therapies, HE-DMTs).

Methods: Data from the German MS Register (as of 1-Sep-2024) included patients with relapsing-remitting MS (RRMS) on initial MME-DMT switching their DMT. Inclusion criteria were MS diagnosis ≥2016, initial DMT ≥2018 and discontinuation of the initial DMT. In the absence of a reported reason for DMT discontinuation, a surrogate for lack of therapy efficacy was used to evaluate switch reasons.

Results: The study population included 622 MS patients (73.6% female). Of these, 389 switched laterally to another MME-DMT and 233 escalated to HE-DMTs (Figure 1). The median age at start of the first DMT was 32.7 [25% quartile; 75% quartile: 25.8; 40.2] years. Median time to switch was 0.75 years for lateral and 1.25 years for escalation switch, with most switches occurring within the first two years (Figure 2). A lack of DMT efficacy was the primary reason for escalation switches (71.5%), while adverse events dominated lateral switches (53.8%). Patient requests and pregnancy-related reasons were more common in lateral switches (Table 1).

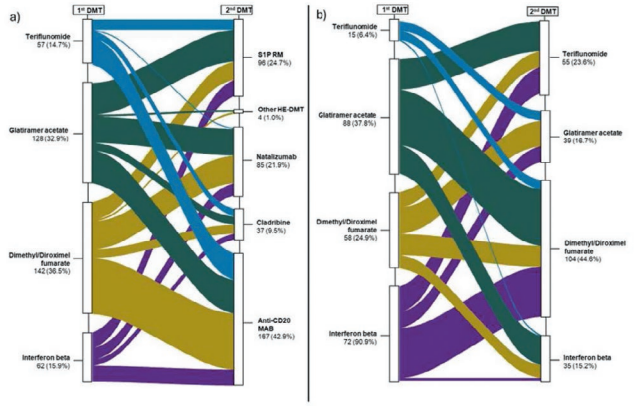

Figure 1: Characterisation of switches from initial DMT to immediate subsequent DMTs. Alluvial (a) represents the escalation switch to HE-DMT, while alluvial (b) shows the lateral switch to MME-DMT. The boxes on the left side represent the proportion of patients stratified by the initial DMT usage. Complementary to this, the boxes on the right-hand side show the immediate subsequent DMTs. The colored connecting lines between the boxes indicate the proportions of patients switching between the respective DMTs, with the thickness of the lines corresponding to the patient proportions.

Anti-CD20 MAB - anti-CD 20 monoclonal antibodies (ocrelizumab/ofatumumab/rituximab/ubituximab); DMF - dimethyl fumarate; DMT - disease-modifying therapy; S1P RM - sphingosine-1-phosphate receptor modulators (fingolimod/ozanimod/ponesimod/siponimod).

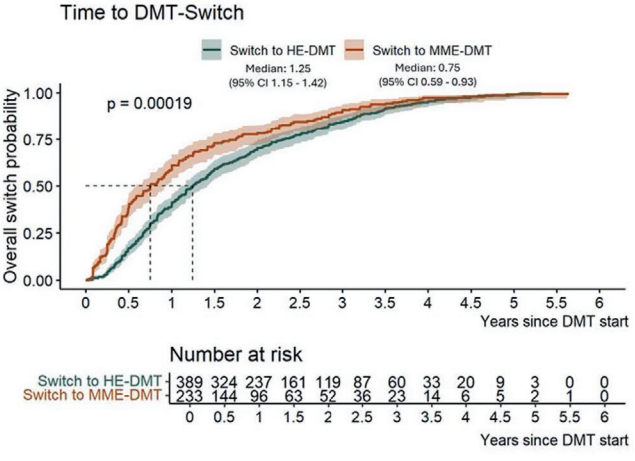

Figure 2: Time to switch from initial DMT. The Kaplan-Meier curve shows the probability of switching from the initial DMT over time. Patients switching to HE-DMT (green) had a median switch time of 1.25 years (95% CI: 1.15–1.42), while those switching to MME-DMT (orange) had a median switch time of 0.75 years (95% CI: 0.59–0.93). The p-value of <0.001 indicates a significant difference between the two groups. The shaded areas represent 95% CIs, and the table below shows the number of patients at risk over time.

CI - confidence interval; DMT - disease-modifying therapy; HE - high efficacy; MME - mild to moderate efficacy; MS - multiple sclerosis; N - number of patients; p - log-rank p-value.

Table 1: Reasons for discontinuation of the initial DMT by switch type

Reasons for first DMT discontinuation, N (%)	Escalation Switch (N=330)	Lateral Switch (N=199)
Lack of therapy efficacy (reported + surrogate):	236 (71.5)	43 (21.7)
Lack of therapy efficacy (reported)	194 (58.8)	19 (9.6)
Lack of therapy efficacy (surrogate)*	42 (12.7)	24 (12.1)
Adverse events	41 (12.4)	107 (53.8)
Patient request	20 (6.1)	25 (12.6)
Physician's decision	19 (5.8)	0 (0.0)
Pregnancy /Wish to have children	5 (1.5)	17 (8.5)
Other	9 (2.7)	7 (3.5)

If the reasons for the first DMT discontinuation was not available or previously unknown, it was excluded from this table.

** Lack of therapy efficacy indicated by fulfilling ≥1 of the following criteria: any relapse, increases in EDSS, MRI activity, increase in symptom load, or conversion to SPMS within half a year before the end of therapy (surrogate was only used in patients who discontinued the first DMT without providing a reason).*

DMT - disease-modifying therapy; EDSS - Expanded Disability Status Scale; MRI - magnetic resonance imaging; MS - multiple sclerosis; N - number of patients; SPMS - Secondary Progressive Multiple Sclerosis.

Conclusion: Reasons for escalation switches are primarily disease activity and progression (lack of efficacy). Escalation switches occur later compared to lateral switches. The findings highlight the differing clinical contexts and patient priorities influencing therapy decisions.

Disclosure: MP, DE, and FF have nothing to disclose. KH, AS, NF, PF, FP and HT have received speaking fees, travel support, honoraria from advisory boards and/or financial support for research activities from industry sponsors.

EPO-461 | Pseudocoloring and homomorphic filtering of product of T2 and weighted SWAN registered MRIs for CVS visualization

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Background and Aims: Revision of McDonald criteria'2024 takes into account recent advances in imaging of multiple sclerosis (MS). Revisions are likely to be published, new diagnostic markers include the central vein sign (CVS). CVS is studied only during study in-depth because either specialized routine as T2*, or analysis of multimodal magnetic resonance imaging (MRI). Visualization enhancement, especially, express method without need in both artificial intelligence and hardware-based MRIs, is very actual.

Methods: The golden standard of CVS visualization is hardware-based T2* MRI, but very similar result can be obtained by means of T2 and SWAN (magnitude and phase) processing (fig. 1). The set of MRIs (1.5 T and 3.0 T) was collected for 18 patients with diagnosed MS.

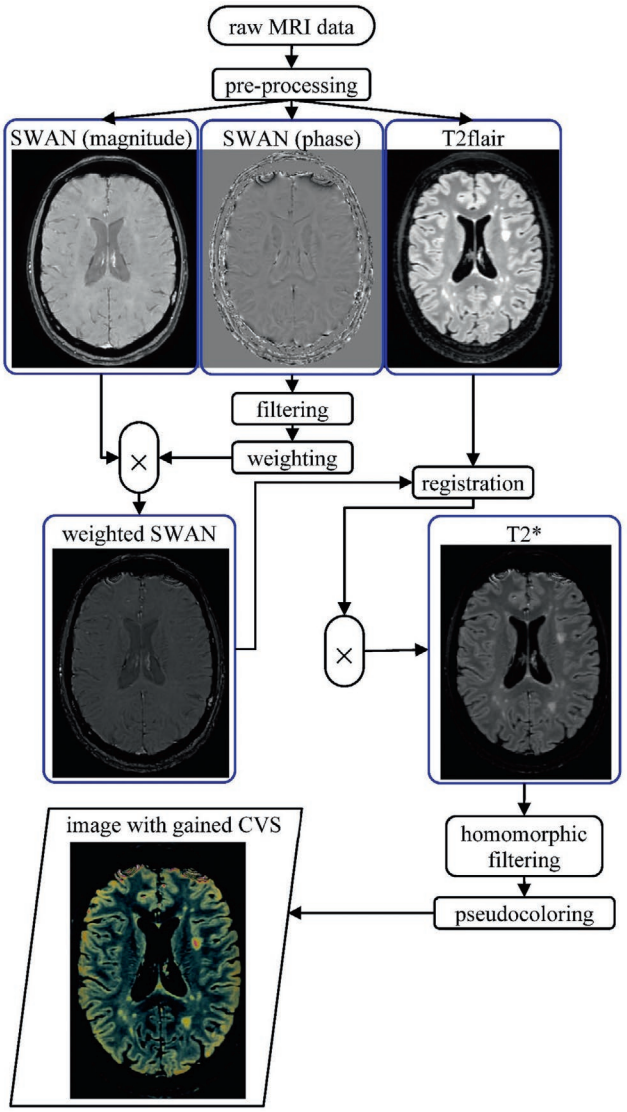

FIGURE 1 T2 and SWAN (magnitude and phase) processing scheme

Results: Each MRI is performed for 120–272 slices of both T2FLAIR and SWAN. Low-frequency fluctuations are filtered from SWAN phase simultaneously with local correction algorithms to reduce artifacts. The magnitude is multiplied by the filtered phase. Result image contains both magnitude and phase information, after it is registrated (SPM12) with T2 one and they are multiplied on order to form T2*. Homomorphic filtering of T2* allows to simultaneously normalize the brightness across an image and increase contrast, after non-monotonic pseudocoloring is applied. This allows to enhance visualization of "coffee bean", "central dot" and classical CVS patterns (fig. 2).

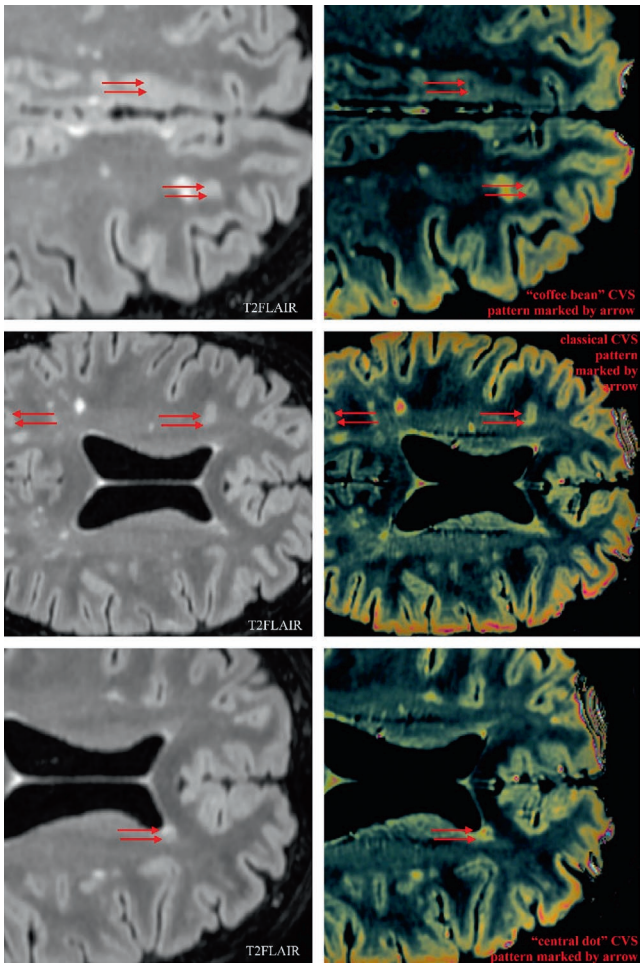

FIGURE 2 Improved visualization of "coffee bean", "central dot" and classical CVS patterns

Conclusion: This method enhances CVS visualization for both 1.5 and 3.0T MRIs, the approach is verified by direct comparison with registrated SWAN images.
Disclosure: Nothing to disclose.

EPO-462 | Application of phase stretch transform to standard MRI protocol for central vein sign visualization enhancement

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Background and Aims: The revision'2024 of McDonald criteria demonstrates the shift towards considering the pathomorphological basis of multiple sclerosis (MS). In patients with typical lesions in one topography, the presence of 6 lesions with central vein sign (CVS) plus dissemination in time is sufficient to diagnose MS. However, simplified magnetic resonance imaging (MRI) typically provide only T1/T2 routines. Especially, less than 3 T MRI, CVS is visualized poorly. In this paper, the image processing of phase stretch transform (PST) is adopted (with zero-learning approach) in order to enhance CVS visualization.

Methods: PST does not add additional info to image, it only gains valuable spatial frequencies. By so doing, "super-resolution" can be achieved by suppression of MRI-artefacts. Set of MRIs (34–272 slices of T2 each) was collected for 37 patients with diagnosed MS.
Results: MRIs are pre-processed in order to obtain T2flair images, after PST based on non-linear filtering of images phase in Fourier domain is applied. Before processing, the real-valued strength and warp of the phase profile are sweeped in order realize fine tuning of PST parameters, pre-learn nonlinear filter for "super-resolution" (fig. 1). PST gains valuable spatial frequencies for both 1.5 and 3.0T MRIs, it allows to enhance visualization of "coffee bean", "central dot" and classical CVS patterns (fig. 2).

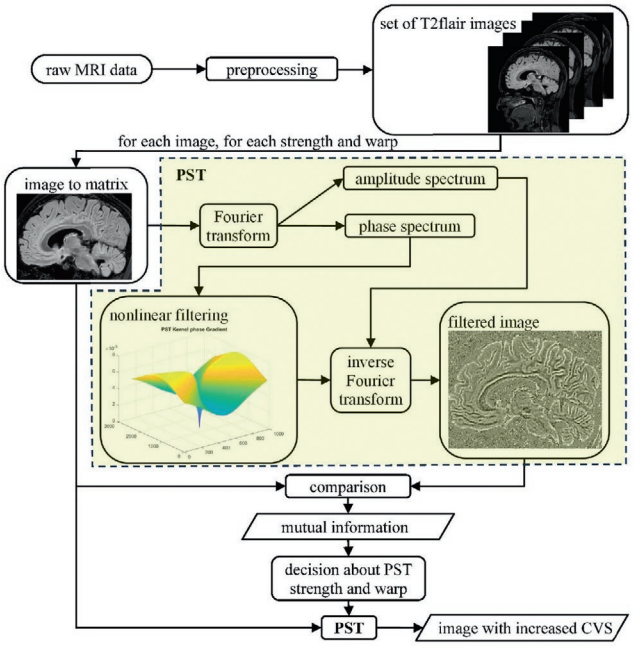

FIGURE 1 Image processing scheme

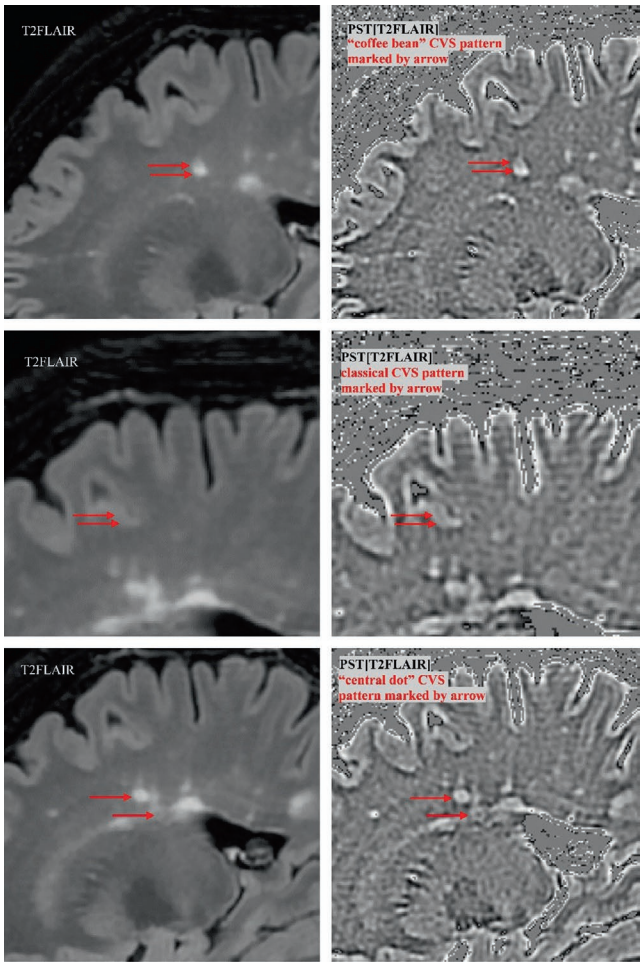

FIGURE 2 Improved visualization of "coffee bean", "central dot" and classical CVS patterns

Conclusion: PST visualization enhancement is verified by direct comparison with registrated SWAN for CVS. That allows to fulfil McDonald criteria'2024 even based on simplified MRI protocol.
Disclosure: Nothing to disclose.

EPO-463 | Lesions in critical brain regions increase the risk of migraine in multiple sclerosis

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Background and Aims: An increased prevalence of migraine in people with MS (pwMS) has been documented over the past decade, with one of the leading explanations being the presence of lesions within regions, critical for pain modulation.
Methods: PwMS fulfilling the 2017 Mc Donald criteria were recruited prospectively in the study from the outpatient MS clinic of Eginition University Hospital, Athens, Greece. Patients underwent a detailed neurological examination and assessment for primary headache disorders. Brain MRI scans were obtained

and assessed. Odd-ratios (ORs) were calculated to examine the potential association of lesions within pain-perceiving brain regions and primary headache disorders.

Results: A total of 96 participants were included in the study. PwMS with a lesion in the periaqueductal gray (PAG) were more than four times more likely to experience migraine compared to those without a lesion in this region (OR = 4.7; 95% CI: 1.62–13.57; $p < 0.05$). Although not statistically significant, thalamic or cortical lesions were also associated with migraine (OR = 6.9; 95% CI: 1.48–31.80; and OR = 5.8; 95% CI: 1.3–26.03; respectively).

Table 1. Patients' demographics and clinical data.

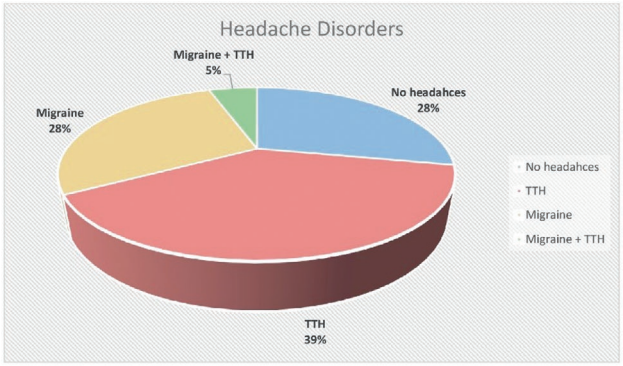
Demographical & Clinical Data	
Gender	
Female - n (%)	69 (71.9)
Male - n (%)	27 (28.1)
Age (years) mean ± SD	42.15 (12.81)
Disease subtype	
RRMS - n (%)	77 (77.1)
PPMS - n (%)	7 (7.3)
SPMS - n (%)	15 (15.6)
Disease duration (years) mean ± SD	8.57 (8.52)
EDSS mean ± SD	3.13 (1.88)
Disease modifying treatments - n (%)	
Ocrelizumab	41 (43.16)
Dimethyl-Fumarate	13 (13.68)
Glatiramer Acetate	10 (10.53)
Natalizumab	7 (7.37)
None	7 (7.37)
Fingolimod	6 (6.32)
Rituximab	3 (3.16)
Teriflunomide	3 (3.16)
Interferon beta-1a	2 (2.11)
Ofatumumab	1 (1.05)
Mycophenolate Mofetil	1 (1.05)

n:number of patients; SD: standard deviation; RRMS: relapsing remitting multiple sclerosis; SPMS: secondary progressive multiple sclerosis; PPMS: primary progressive multiple sclerosis; EDSS: Expanded Neurostatus Disability Scale.

Table 2. Association between key brain areas and prevalence of migraine and tension-type headache after adjusting for confounding factors.

Brain Regions	Migraine		Tension Type Headache	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Midbrain (PAG)	4.7 (1.62 to 13.57)	p < 0.05	1.5 (0.56 to 3.83)	p = 0.4
Pons (LC)	1.0 (0.20 to 5.55)	p = 2.6	0.77 (0.16 to 3.65)	p = 2.1
Thalamus	6.9 (1.48 to 31.80)	p = 1	0.3 (0.06 to 1.43)	p = 1.1
Cortex*	5.8 (1.3 to 26.03)	p = 1	2.1 (0.54 to 8.13)	p = 1.3

PAG: periaquadectal gray; LC: locus coeruleus
*Cortical regions include somatosensory cortex, cingulate gyrus, prefrontal cortex and insular cortex



TTH: tension-type headache

Figure 2. Prevalence of primary headache disorders across study participants

Conclusion: Lesions within critical brain regions are associated with migraine and are possibly the leading cause of the increased prevalence of migraine in pwMS.

Disclosure: Nothing to disclose.

EPO-464 | CIDP: A case series of 7 patients treated with Efgartigimod

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Background and Aims: Chronic inflammatory demyelinating polyneuropathy (CIDP) is a rare immune-mediated demyelinating disease of the peripheral nervous system, characterized by symmetrical proximal and distal limb weakness and sensory dysfunction. Efgartigimod, as a neonatal Fc receptor (FcRn) antagonist, has demonstrated potential therapeutic efficacy in some autoimmune diseases. Therefore, the aim of this study was to investigate the clinical application and efficacy of Efgartigimod in the treatment of CIDP patients.

Methods: We conducted a study on seven CIDP patients treated with Efgartigimod shock therapy. Prior to treatment, these patients underwent comprehensive neuroelectrophysiological assessments. The results revealed that all seven patients exhibited demyelinating changes combined with axonal injury, which met the diagnostic criteria for CIDP. Concurrently, the INCAT scores of these seven patients were meticulously recorded both prior to and following the treatment.

Results: Among the seven patients treated with Efgartigimod, five showed significant improvement in their INCAT scores. A paired *t*-test was employed, revealing a statistically significant difference in the scores before and after treatment ($t = 0.0214$, $p < 0.05$).

Conclusion: Efgartigimod appears to possess therapeutic potential for CIDP patients, especially in enhancing limb function and nerve conduction. This report provides preliminary clinical evidence for the application of Efgartigimod in CIDP treatment, offering a reference for further research and clinical practice.

Disclosure: Nothing to disclose.

EPO-465 | Mexiletine paediatric investigation plan, PIP4 study: Efficacy findings in children aged 0–

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Background and Aims: The PIP explores mexiletine use in children with myotonic dystrophy (DM) or non-dystrophic myotonia (NDM). Here, efficacy findings in PIP4 are presented.
Methods: PIP4 (EudraCT2019-003757-28): 12-week, open-label, non-comparative study of mexiletine in sequential cohorts. Cohort 1: 12–<18 years; Cohort 2: 6–<12 years. Study design: 4 weeks' screening; 4 weeks' mexiletine 62, 83 or 167 mg once-daily titrated to maximum 3-times-daily; 4 weeks' maintenance (best-tolerated dose). Efficacy endpoints (baseline to end of study): relaxation time measured by handgrip dynamometer; patient-reported visual–analogue scale [VAS] 0–100 scores [stiffness, pain, weakness/fatigue]); Myotonia Behavioural Scale (MBS); Pediatric Quality of Life InventoryTM (PedsQL); Clinical Global Impression (CGI).
Results: PIP4 Cohort 1 ($N=7$): 2 with DM1, 5 with NDM (mean age 13 years; 4 female; max dose range 186–500 mg). Cohort 2 ($N=5$) with NDM (mean age 8 years; 3 female; max dose range 186–249 mg). Mexiletine treatment improved relaxation time (all cohorts, Figure 1). PIP4 VAS scores ($n=10$): stiffness, 33.7–78.5% improvement; pain improvements, 85.4% (Cohort 1); 61.3% (combined cohort); weakness/fatigue, 43.2–60.2% improvements. MBS scores improved ($n=8$; 67%), were stable ($n=3$; 25%) or worsened ($n=1$; 8%) Overall, MBS scores decreased across cohorts (Figure 2). Improvements were observed for PedsQL (Figure 3), especially physical domain (most impacted at baseline) and among older children. PedsQL neuromuscular scores also improved, especially in Cohort 1. For CGI, mexiletine was rated very efficient (25%), good (58%), fair (17%) (all cohorts).

ANOVA table for RT

	DF	Sum of squares	Mean square	F-value	P-value	Lambda	Power
Subject	9	1346994.180	149666.020				
Category for RT	4	64126.080	16031.520	2.573	0.0541	10.292	0.663
Category for RT × Subject	36	224314.320	6230.953				

Means table for RT
Effect: category for RT

	Count	Mean	SD	SE
Baseline	10	348.900	207.485	65.613
V2	10	310.100	185.228	58.574
V3	10	303.300	228.987	72.412
V4	10	269.300	187.166	59.187
V5	10	244.500	98.814	31.248

Interaction bar plot for RT
Effect: category for RT
Error bars: ± 1SD

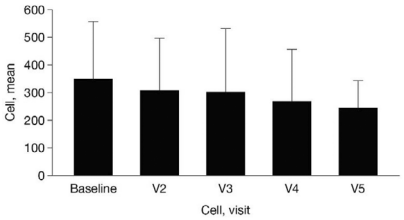
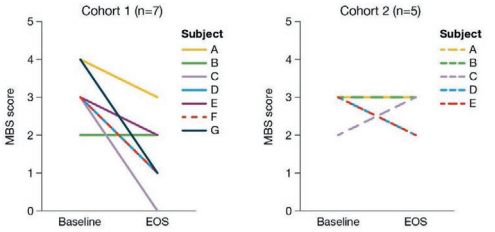


Figure 1: Change in handgrip relaxation time (RT) in PIP4, measured by dynamometer from baseline to end of study



MBS scoring: 0=No stiffness; 1=Some stiffness exists, which can be ignored; 2=Some stiffness exists, which can be ignored at times, but doesn't impair daily activities; 3=Stiffness exists, which demands a higher level of mental awareness when performing some duties and activities; 4=Severe stiffness exists, which impairs every duty and activity; 5=Incapacitating stiffness exists, which demands constant moving not to be totally locked up, with regard to movement. EOS, end of study; MBS, myotonia behaviour score.

Figure 2: Overall, myotonia behaviour scale (MBS) scores decreased across cohorts in PIP4, baseline to end of study (EOS)

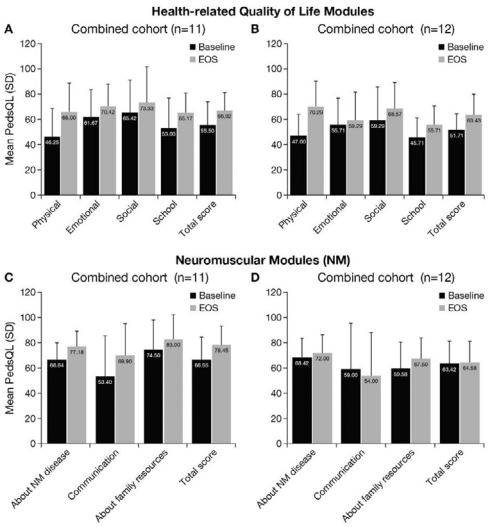


Figure 3: Improvements were observed in PedsQL scores, Health-related quality of life (HRQoL) and Neuromuscular (NM) Modules

Conclusion: PIP4 confirms that mexiletine is efficacious treatment for myotonia in children aged 6-<18 years. PIP4 completers are being followed for ≥2 years in PIP7.

Disclosure: CB; AI; J-YH; NA: consultancy fees from Lupin AZ-W: Lupin employee.

EPO-466 | Mexiletine paediatric investigation plan, PIP4 study: Safety and pharmacokinetic findings in children with myotonia

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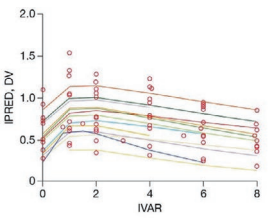
Background and Aims: The PIP explores safety of mexiletine treatment in children with myotonic disorders.
Methods: PIP4 (EudraCT2019-003757-28) was a 12-week open-label exploration of mexiletine in sequential cohorts. Cohort 1: 12–<18 years; Cohort 2: 6–<12 years. Design: 4 weeks' screening; 4 weeks' mexiletine 62, 83 or 167 mg once-daily titrated to maximum 3-times-daily; 4 weeks' maintenance (best-tolerated dose). Primary endpoints: Safety, pharmacokinetics (PK), tolerability, adverse-event (AE) profiling including ECG, baseline–end of study (EOS).
Results: Cohort 1: $N=7$ (mean age 13y; 4 female); cohort 2: $N=5$ (mean age 8 years; 3 female). Table 1 shows maintenance dose/body weight. Mexiletine exposure, ≥53 days (all subjects continue in PIP7 ≥24-month extension). ECGs were normal excluding one abnormal baseline assessment (not clinically significant). Mexiletine was well tolerated. All AEs and TEAEs were mild; most resolved without intervention and were unrelated. No subjects reported dose modifications. TEAEs were reported in $n=6$ (86%) Cohort 1, $n=1$ (20%), Cohort 2: overall $N=7$ (58%). No deaths, serious TEAEs, or TEAEs leading to study discontinuation were reported. Most frequent TEAEs: abdominal pain and nausea. Physical examinations and haematological, biochemical, and muscle-function assessments revealed no clinically significant changes. PK data confirm paediatric mexiletine exposure, consistent with well-established adult posology. PK modelling adequately described mexiletine concentration data, showing good agreement between observed and predicted concentrations. Paediatric doses required to achieve mexiletine concentrations are similar to adult doses (Figure 1). Bootstrap analysis indicates the model is robust (Table 2).



DV=observed mexiletine concentration, IPRED=individual predictions, IVAR=time in hours

Figure 1: Individual concentrations with individual predicted concentrations after oral administration of mexiletine in paediatric subjects (all subjects, N=12; PIP4) from the final model

Table 1: **PK modelling was used to determine appropriate mexiletine dosing. In paediatric patients, recommended mexiletine dose is dependent on body weight**

Body weight, KG	Approximate age group, years	Mexiletine dose*			
		Qnce-daily dosing (morning)	Twice-daily dosing (morning and evening)	Three-times daily dosing (morning, afternoon and evening)	Maintenance/ maximum total daily dose
20-30	6 to < 10	62 mg (1 x 62 mg capsule)	125 mg (2 x 62 mg capsules)	187 mg (3 x 62 mg capsules)	187 mg
30-40	10 to < 12	83 mg (1 x 83 mg capsule)	167 mg (2 x 83 mg capsules)	250 mg (3 x 83 mg or 4 x 62mg capsules)	250mg
40-60	12 to < 16	125 mg (2 x 62 mg capsules)	250 mg (3 x 83 mg or 4 x 62 mg capsules)	375 mg (6 x 62 mg capsules)	375 mg
≥ 60	16 to < 18	167 mg (1 x 167 mg or 2 x 83 mg capsules)	333 mg (2 x 167 mg or 4 x 83 mg capsules)	500 mg (3 x 166 mg or 6 x 83 mg capsules)	500 mg

*Allow for rounding; 62 mg capsule is 62.48 mg; 83 mg capsule is 83.31 mg; 167 mg capsule is 166.62 mg.

Table 2: Comparison of bootstrapped population PK parameters with final PK model

Comparison of bootstrapped population PK parameters with final PK model

Parameter	Final Model		Bootstrap (N=1000)	
	Estimate	95% CI	Estimate	95% CI
Ka (1/hr)	0.74	0.44–1.03	0.80	0.49–1.29
V (L)	38.76	24.00–53.52	41.10	27.58–61.98
V2 (L)	336.64	284.12–389.17	333.54	286.33–377.71
CL (L/hr/70kg)	28.21	18.94–37.47	26.88	18.34–38.72
Q (L/hr/70kg)	506.91	431.59–582.21	501.08	417.80–612.31
Residual variability	0.32	0.22–0.42	0.30	0.22–0.38

Conclusion: No unexpected safety findings were observed: safety profile was consistent with NaMuscla® SMPC. No events resulted in mexiletine discontinuation. PK analyses confirm paediatric mexiletine dosing.
Disclosure: CB; AI; HP; NA: consultancy fees from Lupin AZ-W: Lupin employee.

EPO-467 | Comprehensive analysis of efgartigimod: The real-world safety evaluation for myasthenia gravis from the FAERS database

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Background and Aims: Efgartigimod, a neonatal Fc receptor (FcRn) antagonist, is used to treat myasthenia gravis (MG). As the FDA's first approved FcRn antagonist for the treatment of MG, comprehending its post-marketing safety evaluation in the real-world context is essential.
Methods: This research collected data on efgartigimod in the real-world from the FAERS database from the fourth quarter of 2021 to the second quarter of 2024. To disproportionally analyze the adverse events (AEs) related to efgartigimod, we employed the methods of reporting odds ratio (ROR), proportional reporting ratio (PRR), multi-item gamma Poisson shrinker (MGPS), and Bayesian confidence propagation neural network (BCPNN). We used the Weibull distribution to model the risk of AEs over time.

Results: The study analyzed 12,757 AE reports related to efgartigimod. The dataset revealed a higher incidence of reports from females compared to males, with the peak reporting observed in the 65 to 85 years age cohort. Some adverse reactions were documented in the instructions, such as Dyspnea, Urinary tract infection, Headache, Feeling abnormal, and Respiratory tract infection. In the meantime, we also identified some potential adverse reactions which were not mentioned in the instructions, including Nausea, Diarrhea, Nasopharyngitis, Arthralgia, Herpes zoster, Influenza, and so on.
Conclusion: Our study found some new AE signals of efgartigimod and might enhance clinical surveillance and risk detection. However, because of the limitations of the data sources and analysis methods, these results require additional validation through extensive data analysis and ongoing research to further investigate and confirm.
Disclosure: Nothing to disclose.

EPO-468 | Efficacy of nusinersen treatment in type 1, 2, and 3 spinal muscular atrophy: Real-world data from a single-center study

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Background and Aims: Spinal muscular atrophy (SMA) is a genetic neuromuscular disorder caused by the absence of the SMN1 gene, leading to muscle weakness and atrophy. It is classified into types 0-4, based on symptom onset and severity. Recent treatments, including nusinersen, onasemnogene abeparvovec, and risdiplam, have significantly improved SMA prognosis. This study evaluated the safety and efficacy of nusinersen in pediatric SMA types 1, 2, and 3 in a real-world setting.
Methods: His prospective, observational, single-center study involved 23 pediatric patients with genetically confirmed SMA over a 22-month period. Participants received intrathecal nusinersen loading doses followed by maintenance doses. Functional assessments were made using the CHOP-INTEND scale, and clinical data were collected during routine visits. Adverse events were also recorded.
Results: Of the 37 initial patients, 23 were analyzed due to treatment changes. Significant improvements in CHOP-INTEND scores were seen, with an average increase of 4.2 points at 6 months, rising to 17.8 points at 22 months. By study end, all patients showed stabilization or improvement, with significant clinical progress in several. Nusinersen was well-tolerated, with post-lumbar puncture headache and back pain as common adverse events.
Conclusion: Nusinersen significantly improves motor function in pediatric SMA types 1, 2, and 3. Early and ongoing treatment is crucial for sustained improvements, supporting nusinersen as an effective therapy. Further research is needed to optimize long-term outcomes.
Disclosure: The authors declare no conflicts of interest.

EPO-469 | Abstract withdrawn

EPO-470 | Sustained minimal symptom expression in generalised myasthenia gravis: A 120-week post hoc analysis of RAISE-XT

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Background and Aims: Minimal symptom expression (MSE), defined as a myasthenia gravis activities of daily living (MG-ADL) score of 0 or 1, is a rigorous measure of therapeutic efficacy in myasthenia gravis (MG). This post hoc analysis of RAISE-XT (NCT04225871), a Phase 3, open-label extension study of the complement component 5 inhibitor zilucoplan, assessed the durability of MSE response.
Methods: Adults with anti-acetylcholine receptor antibody-positive generalised MG who completed a qualifying double-blind, placebo-controlled study (NCT03315130/NCT04115293 [RAISE]) could opt to enter RAISE-XT and self-administer once-daily subcutaneous injections of zilucoplan 0.3 mg/kg. The cumulative proportion of patients who achieved MSE (MG-ADL score of 0 or 1 without rescue therapy) at any time during zilucoplan treatment up to Week 120 and the proportion of time spent in MSE up to Week 120 were assessed post hoc (interim data cut-off: 11 November 2023).
Results: Of 200 patients enrolled in RAISE-XT, 183 received zilucoplan 0.3mg/kg or placebo in the double-blind studies. The cumulative proportion of patients who achieved MSE at any time from the start of zilucoplan treatment up to Week 120 in the zilucoplan 0.3 mg/kg/zilucoplan 0.3 mg/kg and placebo/zilucoplan 0.3mg/kg groups was 61% and 64%, respectively. After first achieving MSE during zilucoplan treatment, patients maintained their MSE response for a median (range) of 80.8% (0.8–100.0%) of their remaining time in the study up to Week 120. Treatment-emergent adverse events were experienced by 97.0% ($n = 194/200$) of patients; most were mild or moderate.
Conclusion: Zilucoplan demonstrated sustained efficacy, as shown by maintenance of MSE response up to 120 weeks of treatment.

Disclosure: This study was funded by UCB. Babak Boroojerdi, Fiona Grimson and Natasa Savic are employees and shareholders of UCB. Full disclosure of all industry relationships will be made during congress presentation if accepted.

EPO-471 | Real-world and recent clinical trials in NDM show consistent myotonia improvements with mexiletine

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Background and Aims: Studies evaluating mexiletine treatment for myotonia are generating a growing body of patient-reported evidence: data encompass subjective parameters of physical health/-quality-of-life (QoL) that inform real-world mexiletine use. However, individual studies contain low participant numbers and use different methodologies. To investigate signals of mexiletine efficacy, we reviewed key outcomes reported in three datasets evaluating treatment of adults with non-dystrophic myotonia (NDM): MYOMEX (N = 25), MEND (N = 60) and the Post Authorisation Safety Study (PASS; *N* = 53).

Methods: Study characteristics were compared (Table 1). Spearman correlations between baseline and post-mexiletine treatment data for myotonia-associated symptoms (stiffness [VAS/daily IVR]; locking and pain [INQoL, SF-36, respectively]; myotonia behaviour scale, MBS] were investigated. Changes were tested using the Wilcoxon signed rank test.

Results: Despite between-study methodological differences, including absence of/variation in comparator arms, consistent benefits were observed in patients receiving mexiletine. Reduction in patient-reported stiffness (on VAS/IVR) and improved QoL (e.g. reduction in locking/pain [INQOL] or bodily pain [SF-36]) were seen across the studies: (Tables 2, 3). Notably, MYOMEX data showed that although patients still reported locking at study end, its overall impact on QoL significantly reduced. Some PROs strongly correlated with baseline VAS stiffness assessment. Statistical changes were observed following mexiletine treatment e.g. VAS and INQoL locking domain; $p = 0.0249$ and $p = 0.0154$, respectively (PASS).

Table 1: **Characteristics of three different studies investigating mexiletine treatment in adults with non-dystrophic myotonia**

Study	MYOMEX[1]	MEND[2]	PASS[3]
Design (N)	Double-blind, crossover RCT (N=26)	Double-blind crossover RCT (N=60)	Non-interventional, prospective, observational (N=53)
Mexiletine Dosage	600 mg/day max mexiletine hydrochloride	600mg /day max mexiletine hydrochloride	334 mg/day mean; 501 mg/day max mexiletine
Comparator	Mexiletine vs Placebo	Mexiletine vs Lamotrigine	None
Primary Endpoints/Outcomes	VAS, stiffness score	PRO stiffness score based on IVR[a]	Safety, tolerability, efficacy (TEAEs SAEs), dose reductions, treatment discontinuations
Secondary Endpoints/Outcomes	Functional time up and go INQoL	MBS[b] SF-36	AEs, SAEs or AEs of specialist interest VAS, INQoL MBS
Tx Duration	18 days	8 weeks	36 months (interim analysis, 12 months)
Trial period	2011–2014	2021-2024	2020-2025
Countries	France	UK	Germany, UK, France

[a]Interactive voice response diary. Participants reported symptom severity on scale from 1 (minimal) to 9 (worst ever experienced). No symptom, 0 for analysis.
[b]Myotonia behaviour scale: range 1 (no stiffness) to 6 (incapacitating stiffness).

1. Vicart S et al. Neuromuscul Disord. 2021;31(11):1124-35.
2. Vivekanandam V et al. Lancet Neurol. 2024 Oct;23(10):1004-1012.
3. Rosenbohm A et al. 728LBP. Presented at 29th Annual Congress of the World Muscle Society, October 2024, Prague, Czechia.

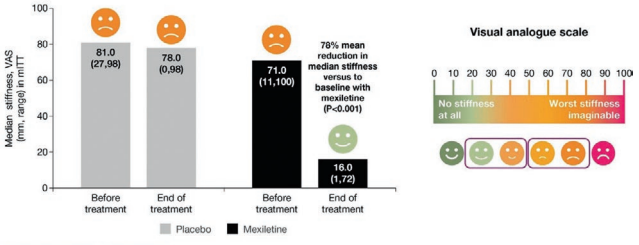
Table 2: **Core data from MYOMEX study (N=25)[1]**

Outcome	Baseline		After treatment	
	Placebo	Mexiletine	Placebo	Mexiletine
Primary				
Stiffness score, VAS, mm, median (range)	81 (27,98)	71.0 (11,100)	78 (0,98)	16.0 (1,72)
Secondary				
Patients with symptoms, n (%)				
Locking	24 (96.0)		23 (92.0)	24 (96.0)
Pain	15 (60.0)		18 (72.0)	8 (32.0)
INQoL, Symptoms, mean (SD)				
Locking	69.1 (22.9)		66.1 (30.8)	30.5 (20.3)[a]
Pain	38.5 (31.5)		46.3 (34.3)	12.9 (22.8)[a]

INQoL, Individualised Neuromuscular Quality of Life scores before and after treatment (mITT population). Although patients still reported locking after treatment, the impact of locking reduced significantly following mexiletine treatment.

1. Vicart S et al. Neuromuscul Disord. 2021;31(11):1124-35.

Evolution of stiffness (VAS scores before and at end of treatment [mITT])[a]



[a]Effect of treatment (mixed-effect linear model).
mITT, modified intention to treat; NDM, non-dystrophic myotonia; VAS, visual analogue scale.

Table 3: **Core data from (A) MEND study (mexiletine group only)[1]; (B) PASS study[2]**

A: MEND study: N=60 adults[1]

Outcome	Total cohort, Baseline, mean	Mexiletine mean after treatment (95% confidence interval)
Primary		
Interactive voice response-diary, stiffness score	5.30	2.54 (1.98 to 3.10)
Secondary		
Myotonia Behaviour Scale score	2.93	1.67 (1.33 to 2.01)
Medical Outcomes Study Short Form-36[a] Questionnaire subscale, Bodily pain	53.3	68.9 (61.6 to 76.2)

[a]Higher scores denote more favourable health states vs. lower scores.

B PASS study: N=53 adults taking NaMuscla® 167 mg average 2x daily[2]

Outcome		Baseline	Change from baseline, Month 12
Secondary efficacy endpoints			
VAS score, mean (SD)	Muscle stiffness	39.2 (27.31) n=42	−13.5 (25.77) n=34
	Pain	42.9 (29.14) n=15	−5.8 (27.55) n=9
INQoL, domain, mean (SD)	Locking	55.1 (23.61) n=32	−17.6 (24.01) n=28
	Pain	40.9 (25.27) n=17	−7.2 (24.37) n=11
MBS score, mean (SD)	MBS Score	2.69 (0.973) n=45	−0.25 (0.840) n=40

1. Vivekanandam V et al. Lancet Neurol. 2024 Oct;23(10):1004-1012
2. Rosenbohm A et al. 728LBP. Presented at 29th Annual Congress of the World Muscle Society, October 2024, Prague, Czechia.

Conclusion: Together, evidence from 3 studies ($N=138$ adults with NDM) illustrate the consistent impact of mexiletine on myotonia-associated patient-reported outcomes, especially stiffness and locking. Data strengthen the evidence base for mexiletine treatment, further validating the meaningful QoL benefits that symptom improvements bring to people with myotonia.
Disclosure: EM, SV, VV, SS, AR, CT, DJ, CS-GG, J-YH: Consultancy fees from Lupin AZ-W: Employee of Lupin.

EPO-472 | Glial fibrillary alfa protein level as a potential biomarker in patients with myasthenia gravis

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[1]Rīga Stradiņš University, Latvia; [2]Rīga Stradiņš University, Latvia; Pauls Stradiņš Clinical University Hospital, Department of Neurology, Latvia; [3]Department of Psychiatry and Neurochemistry, Institute of Neuroscience and Physiology, the Sahlgrenska Academy at the University of Gothenburg, Mölndal, Sweden; Clinical Neurochemistry Laboratory, Sahlgrenska University Hospital, Mölndal, Sweden

Background and Aims: At present, no reliable biomarkers are available that correlate with myasthenia gravis (MG) disease severity, highlighting the need for novel biomarkers to evaluate both disease progression and treatment efficacy. Plasma glial fibrillary acidic protein (GFAP) is a protein that is not only expressed in central nervous system, but also in denervated neuromuscular junctions by terminal Schwann cells. This study aims to investigate GFAP concentration in the MG patient group and compare it to the control group.
Methods: The study included 48 patients diagnosed with MG and 40 healthy controls. The disease clinical classification was based on the MGFA classification. The blood samples from both groups were taken during outpatient visits in 2024 and measured with a Simoa.
Results: There were 15 males and 33 females with mean age 46.0(SD ±10.8) years, mean disease duration 102.8 (SD ±96.1) months in the MG patient group. Control group consisted of 11 males and 29 females with mean age 41.5 (SD ±11.1) years. Median sGFAP concentration was 87.0 pg/mL (IQR=61.5 pg/mL) in MG patient group and 87.5 pg/mL (IQR=48.5) in control group. There was no significant difference between both groups ($U=870.500$, $p=0.668$). Analysing the association between sGFAP ($H=9.452$, $p=0.150$) and severity score MGFA no correlations were found.
Conclusion: There is no significant difference in sGFAP levels between patient group and control group. No correlation was observed between sGFAP levels and disease severity. Therefore, sGFAP could not serve as a potential biomarker also it does not appear to be effective for assessing disease severity or monitoring treatment efficacy.
Disclosure: Nothing to disclose.

EPO-473 | Myasthenic crisis – 15-years' single neuromuscular center experience

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Background and Aims: Myasthenic crisis (MC) is a life-threatening episode developing in 15–20% MG patients.
Methods: Retrospective analysis of all MC patients between 2009 and 2024.
Results: There were 89 MCs in 77 MG patients (F 48.3%); 14% had >2 MCs. Mean age at MC was 63.6 + 18.3 years, 73% had late onset MG. 62.9% had AChR-MG, 5.6% MuSK-MG, 10.1% had history of thymoma. Mean MG duration before MC was 50.7 + 72.3 months. In four (4.8%) MC was the initial MG presentation. 18 (20%) of cases had previous MC; they were younger at MG onset, had longer ICU stay ($p<0.05$) and MG duration ($p<0.01$). Before MC, 60.7% of patients were treated with glucocorticosteroids, 25.8% with nonsteroidal immunosuppressants. 48.3% patients received IVIg, 34.8% PLEX, 11.2% both. Mean length of mechanical ventilation (MV) was 12.9 + 8.6 days. Mean length of ICU stay was 24.6 + 18.5 days, longer in treated with IVIG (28.6 + 24), IVIG+PLEX (30.8 + 14.8) than with PLEX (18.5 + 6.8), $p<0.05$. In 38.2% MC was preceded by infection, 13.5% therapy change. CRP and WBC were increased at admission in 50.6 and 41.6% respectively; 22.5% had anaemia, 22.5% bacteriuria. MC was complicated by pneumonia 33.7%, urinary infections 19.1%, myocardiac infarct (9%), pulmonary embolism (7.9%), critical care neuropathy (5.6%). In 3.4% PEG, 4.5% tracheostomy, 4.5% nasogastric tube were maintained after extubation. Mortality was 4.5% ($N=4$), age at death 77.5 + 4.8 years. Higher WBC count at admission predicted longer MV.
Conclusion: MC in gMG patients is most often triggered by infection or therapy change, with 4.5% mortality in our cohort.
Disclosure: Nothing to disclose.

EPO-474 | Myasthenia gravis activities of daily living and myasthenia gravis quality-of-life questionnaires: Estonian versions

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Background and Aims: Evaluation of quality of life and impact of the disease on the daily life has become essential in healthcare. The aim of the study was to translate, adapt and validate the myasthenia gravis-specific activities of daily living (MG-ADL) scale and the 15-item myasthenia gravis quality-of-life (MG-QOL15) questionnaire into the Estonian language.
Methods: Translation and adaption of the questionnaires were performed. The validation protocol included the MG-QOL15, MG-ADL, myasthenia gravis composite score (MGCS) and quantitative myasthenia gravis (QMG) score. We used the Cronbach α to test internal consistency of the questionnaires, Cohen's weighted kappa to test short-term test–retest reproducibility, and Spearman's correlation between the questionnaries and MGCS and QMG score for construct validity.
Results: Twenty-six patients were enrolled into the study. The mean MG-ADL score was 5.9 ±3.5, with $\alpha = 0.76$ and test–retest scores 0.52–0.87. The mean MG-QOL15 score was 22.2 ±15.4, with $\alpha = 0.97$ and test–retest scores 0.57–0.89. The MG-ADL showed strong correlation with the MG-QOL15 ($r = 0.77$, $p < 0.0001$), the MGCS ($r = 0.82$, $p < 0.0001$) and moderate with the QMG score ($r = 0.64$, $p = 0.0002$). The MG-QOL15 had moderate correlation with the MGCS ($r = 0.63$, $p = 0.0003$) and the QMG score ($r = 0.56$, $p = 0.002$).

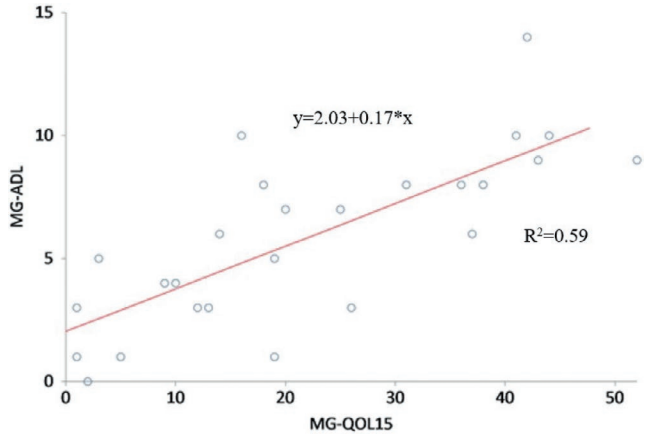

FIGURE 1 Correlation between MG-ADL and MG-QOL15.

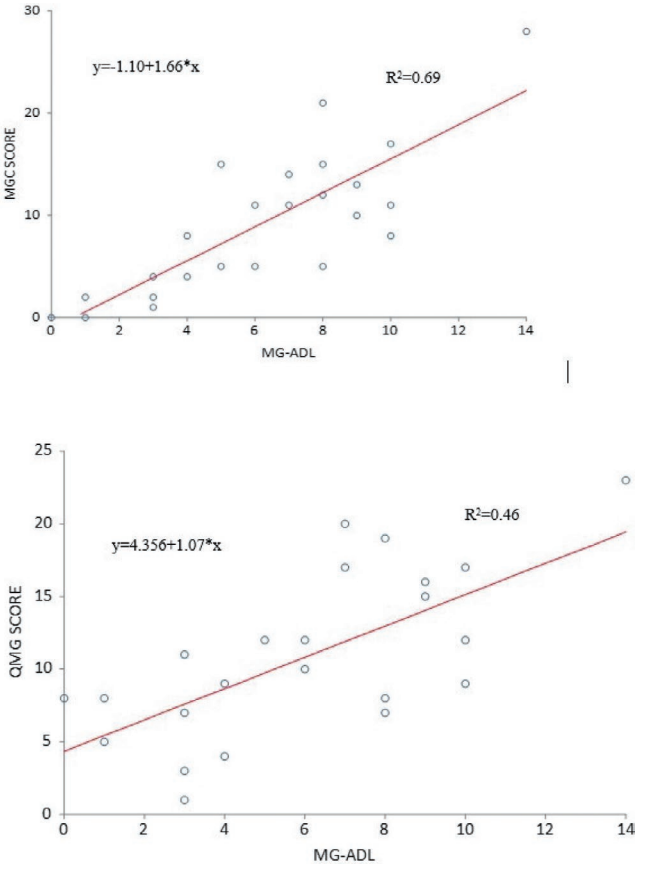

FIGURE 2 Relationships between (a) MG-ADL and myasthenia gravis composite (MGC) score and (b) MG-ADL and quantitative myasthenia gravis (QMG) score.

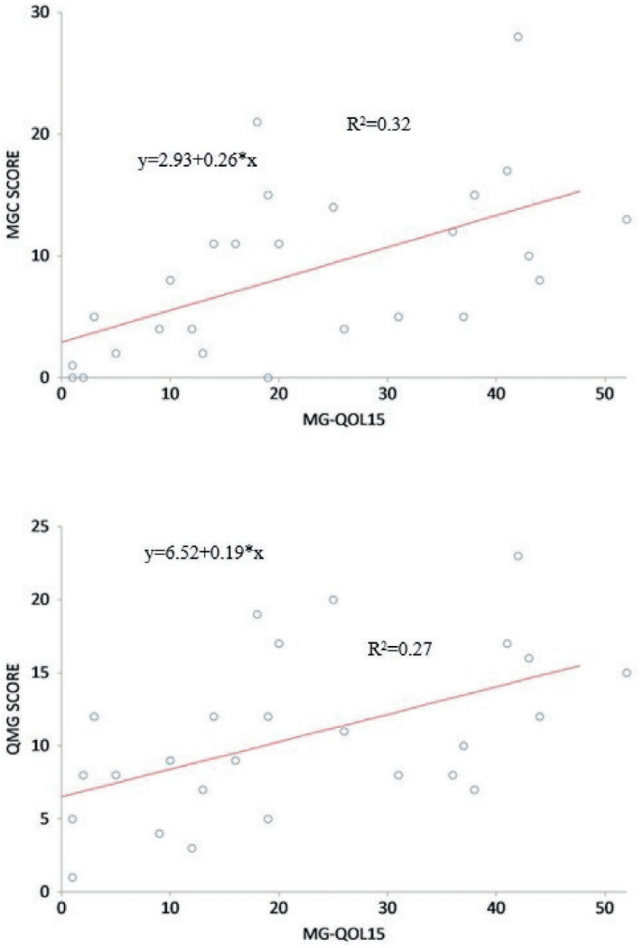

FIGURE 3 Relationships between (a) MG-QOL15 and myasthenia gravis composite (MGC) score (b) MG-QOL15 and quantitative myasthenia gravis (QMG) score.

Conclusion: The Estonian versions of the MG-ADL and MG-QOL15 are valid and reliable self-reported scales for monitoring patients in clinical practice, their disease severity and the impact of the disease on their lives.
Disclosure: Nothing to disclose.

EPO-475 | Effect of zilucoplan on rescue therapy use in patients with generalised myasthenia gravis: RAISE-XT post hoc analysis

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Background and Aims: In the Phase 3 RAISE study (NCT04115293), zilucoplan, a complement component 5 inhibitor, demonstrated clinically meaningful improvements in myasthenia gravis (MG)-specific outcomes versus placebo in patients with anti-acetylcholine receptor antibody-positive generalised MG (gMG); improvements were sustained during long-term use in the ongoing open-label extension study, RAISE-XT (NCT04225871). This post hoc analysis assessed rescue therapy use with long-term zilucoplan treatment.
Methods: Adults who completed a qualifying double-blind, placebo-controlled study (Phase 2 [NCT03315130] or RAISE) could enter RAISE-XT to self-administer daily treatment.subcutaneous zilucoplan 0.3mg/kg. If the investigator deemed rescue therapy necessary, patients could receive intravenous immunoglobulin or plasma exchange concomitantly with zilucoplan. A cycle of rescue was defined as > =1 treatments within a 7-day period. Incidence of rescue therapy per 100 patient-years at risk (PYAR) was assessed post hoc. The primary endpoint was incidence of treatment-emergent adverse events (TEAEs; data cut-off: 11 November 2023).
Results: During the double-blind periods, rate of rescue therapy use was 31.19 and 78.16 events per 100 PYAR for patients who received zilucoplan 0.3mg/kg (n=4/101) and placebo (n=13/103), respectively. During RAISE-XT (median [range] exposure: 2.2 [0.1–5.6] years; N=200), rate of rescue therapy use was 22.64 events per 100 PYAR. Overall, 17.2% (n=16/93) of patients who received zilucoplan 0.3mg/kg and 20.0% (n=18/90) of patients who received placebo in the double-blind studies received rescue therapy during RAISE-XT. TEAEs occurred in 97.0% (n=194/200) of patients.
Conclusion: Rescue therapy use was lower with zilucoplan versus placebo in the double-blind studies. Improvement in gMG disease fluctuations requiring rescue therapy was sustained with long-term zilucoplan treatment.
Disclosure: This study was funded by UCB. Babak Boroojerdi, Fiona Grimson and Natasa Savic are employees and shareholders of UCB. Full disclosure of all industry relationships will be made during congress presentation if accepted.

EPO-476 | A phase 1/2 study design to assess safety and efficacy of YTB323 in treatment-resistant generalised myasthenia gravis

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Background and Aims: Generalised myasthenia gravis (gMG) is an IgG autoantibody-mediated chronic autoimmune disorder affecting the neuromuscular junction, leading to fatigable muscle weakness variably involving ocular, bulbar, respiratory and limb muscles. B-cells are implicated in gMG pathophysiology as they produce IgG autoantibodies. YTB323 is an investigational, autologous CD19-directed chimeric antigen receptor (CAR)-T cell therapy which targets a broad population of the B-cell lineage. Here, we report the design of a phase 1/2 study to assess the safety, efficacy, and cellular kinetics of YTB323 in treatment-resistant gMG patients.
Methods: This is an open-label, multicentre, non-confirmatory study, with a single-dose design and a sentinel cohort of 3 patients, followed by an expansion cohort of 12 patients. The study will enrol patients aged 18–65 years, diagnosed with gMG (Myasthenia Gravis Foundation of America disease class III–IVa) who are either acetylcholine receptor positive (AChR+), or muscle-specific kinase positive (MuSK+), with a Myasthenia Gravis Activities of Daily Living (MG-ADL) score ≥6, and persistent MG symptoms despite adequate treatment courses with at least two different non-steroidal immunosuppressive drugs. The primary endpoint is the frequency and severity of adverse events and the change from baseline in safety parameters. Key secondary endpoints include an assessment of the MG-ADL and Quantitative MG (QMG) scores, and the pharmacokinetics of YTB323.
Results: Approximately 15 participants with gMG will be treated with YTB323. Following a 2-year core study, there will be a long-term follow-up study for 13 years.
Conclusion: This study will provide the scientific evidence needed for further development of YTB323 in treatment-resistant gMG patients.
Disclosure: Matthew Meriggioli, Martin Stangel and JoAnn Whittle are Novartis employees. Prof. James Howard Jr. has received honoraria/consulting fees from AcademicCME, Alexion AstraZeneca Rare Disease, Amgen, Biohaven Ltd, CheckRare CME, CoreEvitas, Curie.bio, Medscape CME, Merck EMB Serono, Novartis Pharma, PeerView CME, Physicians' Education Resource (PER) CME, PlatformQ CME, Regeneron Pharmaceuticals, Sanofi US, TG Therapeutics, Toleranzia AB, UCB Pharma, and Zai Labs. Prof. Howard has also received personal compensation for participating on advisory boards with Alexion AstraZeneca Rare Disease, argenx, Novartis, UCB (Ra Pharma), Merck EMB Serono, Amgen, Sanofi, Toleranzia AB.

EPO-477 | Real-world utilization of myasthenia gravis treatments and the influence of demographics on therapy selection

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Background and Aims: Treatment approaches for myasthenia gravis (MG) vary based on provider preferences, healthcare access, and disease severity. However, demographic factors such as age, gender, race, and ethnicity may also impact treatment selection. Understanding these trends is essential for identifying disparities and optimizing care.
Methods: A retrospective chart review was conducted using electronic medical records from the MedStar Neurology and Neurosurgery network. Data included the use of corticosteroids, intravenous immunoglobulin (IVIG), C5 inhibitors, FcRn inhibitors, B-cell depleting therapies, and antimetabolites.
Results: Corticosteroids were the most prescribed therapy, followed by IVIG, while C5 and FcRn inhibitors were used less frequently. Older patients were more likely to receive corticosteroids and antimetabolites, while younger patients were more likely to receive C5 and FcRn inhibitors. Women were more frequently treated with multiple therapies. White patients had higher IVIG utilization and were more likely to receive combination therapies. Hispanic and Black patients were less likely to receive advanced therapies.
Conclusion: Real-world MG treatment utilization shows significant demographic disparities. Corticosteroids remain the most widely used therapy, while IVIG, C5 inhibitors, and FcRn inhibitors were prescribed less frequently in Hispanic and Black patients, raising concerns about healthcare access. White and non-Hispanic patients had greater access to IVIG and combination therapies. The influence of age and gender was also evident, with older patients more likely to receive corticosteroids and younger patients more likely to receive newer biologic treatments. These findings highlight the need to investigate the causes of these disparities and develop strategies for equitable MG treatment.
Disclosure: Nothing to disclose.

EPO-478 | Overlap syndrome: Myositis, myocarditis, and myasthenia gravis secondary to checkpoint inhibitor treatment: Case series

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Background and Aims: Checkpoint inhibitors (ICP) are now standard therapy for advanced cancers, but can trigger autoimmune adverse effects. A rare but severe overlap of myositis, myocarditis, and myasthenia gravis (MG), termed the "3M Triad," has been reported, carrying a poor prognosis.
Methods: We describe 2 clinical cases of patients who developed myositis, myocarditis, and MG following ICP infusion.
Results: Patient 1: A 73-year-old man receiving durvalumab for advanced squamous cell lung cancer. Following the initial injection, he suffered left eyelid ptosis, pain, neck muscle weakness,

and dyspnea 27 days later In suspected ICP-related myasthenic syndrome, he received 2 mg/kg immunoglobulin and 1 mg/kg prednisone. He was admitted to the ICU for symptoms and lab results (CPK 1800, troponins 380, and fresh third-degree atrioventricular block). Myocarditis suspicions led to a temporary pacemaker and greater corticosteroid doses. Intubation and forced breathing killed him 14 days after admission from bacterial and cardiac issues. Patient 2: A 76-year-old pembrolizumab-treated advanced ductal breast cancer patient. 23 days after the injection, she suffered right eyelid ptosis, pain, lower limb weakness, and dyspnea. The ECG indicated ST-segment depression and elevated troponins. Coronary angiography removed significant obstructions. Symptom progression sent her to the cardiac ICU. Strong corticosteroids and 2 mg/kg immunoglobulin were given for five days. Despite treatment, her fragility and troponin levels increased, requiring mycophenolate and plasmapheresis. She died 25 days after admission.
Conclusion: Overlap syndrome of myositis, myocarditis, and myasthenia gravis is rare with ICP immunotherapy. Early diagnosis is essential for complete therapy due to its high mortality.
Disclosure: Nothing to disclose.

EPO-479 | Clinical implications of a very late presentation in myasthenia gravis – Real world experience in a tertiary center

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Background and Aims: Myasthenia Gravis (MG) is an immune-mediated disease with a bimodal incidence: early-onset (<50 years) and late-onset (>50 years). Recently, a subgroup with very late-onset (≥65 years) was described; however, its clinical relevance concerning disease course and prognosis remain uncertain.
Methods: We conducted a retrospective cohort study comprising all patients diagnosed with MG currently followed in the neuromuscular disorders unit consultation of a tertiary center. Clinical and paraclinical parameters were evaluated.
Results: Ninety-two patients were included, of which 51 (55.4%) were female, with a current mean age of 59.9 ± 18.0 years. Concerning the age of onset, 23 (25.6%) patients were classified as very late-onset. Gender distribution and number of patients with minimal manifestation status or better did not statistically differ between the late and very late onset subgroups. Myasthenic crisis and refractoriness were more frequent in the late-onset subgroup versus the very late-onset, but no statistical difference was found ($p = 0.221$ and $p = 0.650$ respectively). We did not find statistically significant differences in acetylcholine receptor antibody titers between the groups. No significant difference was observed in the prevalence of autoimmune co-pathology among the subgroups.
Conclusion: Our study suggests that the recently established subgroup of very late-onset may not be clinically distinct from late-onset MG, as these patients seem to exhibit a similar clinical trajectory.
Disclosure: All authors: No conflicts of interest to report.

Neuroimmunology 2

EPO-480 | Correlation of serum cytokines in patients with epilepsy of unknown etiology as a marker of neuroinflammation

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Background and Aims: Interest in epilepsy associated with autoimmunity (EAA) and the underlying immune-mediated mechanism is increasing, given the possibility that, in these patients (often resistant to antiepileptic drugs), immunotherapy (IT) may offer a therapeutic opportunity. Additionally, aspects of immunity not mediated by antibodies, such as the role of cytokines in these patients, are starting to be studied.
Methods: A total of 119 patients were recruited between January and November 2023 in a multicenter study conducted in Andalusia. Serum levels of 5 cytokines related to neuroinflammation in epilepsy patients (IL1b, IL4, IL6, IL10, and TNF-alpha) were measured using SIMOA, an ultrasensitive ELISA technique for analyzing molecules in biological samples.
Results: In patients with epilepsy associated with anti-GAD 65 antibodies, a higher median of TNF-alpha was observed compared to the rest of the sample (any anti-GAD 65-negative epilepsy), as well as compared to epilepsy cases without immunoreactivity (in which no antibodies were found in serum using advanced techniques such as indirect immunofluorescence on murine tissue). No differences were found in the median levels of cytokines in relation to drug resistance or absolute drug resistance (defined as failure of more than 6 antiepileptic drugs).
Conclusion: In patients with anti-GAD65-associated epilepsy, a significant increase in circulating TNF-alpha was observed compared to other patients, suggesting a potential target for treatment. Further studies and analysis of other subgroups are needed to determine differences that will allow for better characterization of neuroinflammation and EAA.
Disclosure: Nothing to disclosure.

EPO-481 | Frequency of LRP4 antibodies in a consecutive cohort of suspected myasthenia gravis patients

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Background and Aims: Autoantibodies to the lipoprotein receptor-related protein-4 (anti-LRP4) have been reported in a minority of patients with Myasthenia Gravis (MG), with potential pathogenic role and uncertain clinical relevance. However,

LRP4 antibodies frequency varies substantially according to the type of assay used for their detection. We aim to investigate the prevalence of anti-LRP4 in a consecutive cohort of patients with suspected MG.

Methods: A consecutive cohort of 333 suspected MG, compared to 68 disease controls (38 ALS and 30 NPH) and 55 healthy controls were tested. We implemented and validated both fixed and live cell-based assays (CBA) expressing full-length LRP4. All samples were tested in parallel with validated AchR and MUSK fixed and live-CBA. Seronegative MG (SNMG) diagnosis was assessed through clinical history, electromyography and pyridostigmine response.

Results: The LRP4-CBAs were validated by demonstrating their surface expression by staining of the live cells with a commercial antibody targeting extracellular epitopes of LRP4. Overall, 32% ($n=108$) were positive for either anti-AChR/MuSK, while 0/333 were positive for LRP4 as well as in the control groups. Among 225 triple-negative patients, a diagnosis of SNMG was established in 11% ($n=26$). The median age of SNMG at sampling was 63 years (range: 32–80), and 46% ($n=12$) were female. Thirty percent ($n=8$) of SNMG patients were collected at disease onset, and 58% ($n=15$) had generalized MG.

Conclusion: Using our implemented and validated CBA, LRP4 antibodies seem to be exceedingly rare, thus questioning their clinical relevance in routine clinical practice. Standardization studies are warranted to understand the actual clinical impact of requesting LRP4 testing.

Disclosure: Nothing to disclose.

EPO-482 | Distinguishing NMOSD and MOGAD: A systematic review and a meta-analysis of clinical and imaging differences

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Background and Aims: This study systematically compares the clinical and imaging characteristics of neuromyelitis optica spectrum disorder (NMOSD) and myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) to identify distinguishing features that enhance diagnostic accuracy and inform therapeutic strategies.

Methods: A systematic review of PubMed was conducted, selecting studies with NMOSD and MOGAD patient cohorts ($n > 5$ per group). Data extraction focused on clinical and imaging parameters. Random-effects models calculated odds ratios and standardized mean differences, with heterogeneity assessed using the I^2 statistic.

Results: A total of 2859 articles were screened, of which 131 provided relevant clinical data. NMOSD patients exhibited older age of onset and female predominance. MOGAD patients more frequently presented with bilateral optic neuritis and infectious prodromes, whereas NMOSD was associated with more frequent myelitis relapses, area postrema symptoms, and co-existing autoimmune disorders. Ethnic differences were observed, with MOGAD patients being more likely Caucasian, while NMOSD had a higher proportion of African-descendent patients. Imaging differences included a higher prevalence of area postrema and medulla lesions in NMOSD, whereas cerebellar and pontine lesions were more common in MOGAD. Juxtacortical lesions were predominant in MOGAD, while NMOSD showed a trend toward periventricular lesions.

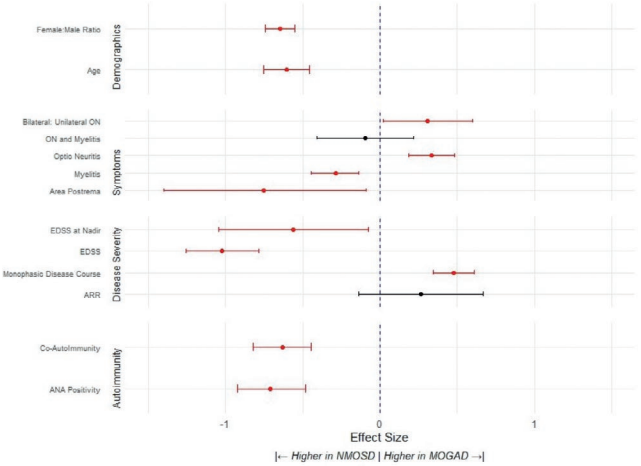

FIGURE 1 Clinical Differences between MOGAD and NMOSD patients

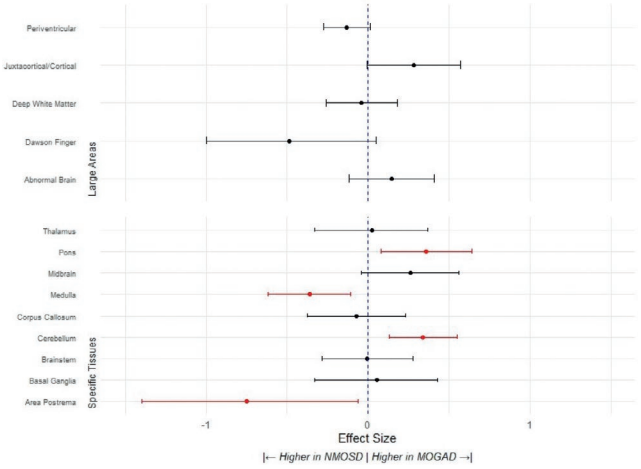

FIGURE 2 Imaging Differences Between MOGAD and NMOSD patients

Conclusion: This meta-analysis highlights distinct clinical and imaging patterns in NMOSD and MOGAD, reflecting significant differences in disease pathogenesis. These findings emphasize the need for tailored diagnostic and therapeutic approaches to address the unique characteristics of each disorder. A deeper understanding of these differences could provide valuable insights into the underlying pathophysiology, ultimately contributing to improved management and treatment strategies for both conditions.

Disclosure: Nothing to disclose.

EPO-483 | Clinical and serological characteristics of MOGAD: A retrospective single center cohort study

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Background and Aims: Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disorder (MOGAD) is a rare inflammatory demyelinating disease of the central nervous system. This study aims to address gaps in knowledge by examining the relationship between anti-MOG IgG titers, demographic characteristics, and clinical variables in MOGAD patients.
Methods: A retrospective study was conducted with 61 MOGAD patients, diagnosed per the 2023 consensus criteria, monitored at the Neuroimmunology Clinic of Sancaktepe Research and Training Hospital. Associations between age, gender, anti-MOG antibody levels (measured using an in-house flow cytometric live cell-based assay), cerebrospinal fluid (CSF) parameters, serological markers, and clinical features were analyzed.
Results: The cohort included 61 patients (32 females, 29 males) with a mean diagnosis age of 41.60 ±13.21 years (excluding those under 18). Presentations included optic neuritis (ON) in 25 patients, myelitis in 17, and other subtypes in 19. Fourteen patients had at least one relapse. Anti-MOG titers showed no significant associations with gender, age, relapse rates, or attack types. Male patients had significantly higher CSF protein levels ($p = 0.013$). ON relapsed in 80% of ON cases, and all myelitis relapses presented as myelitis. Tocilizumab had higher seroconversion rates to seronegativity compared to azathioprine and rituximab ($p = 0.040$).
Conclusion: This study highlights the heterogeneity of MOGAD and the potential role of tocilizumab as a superior therapeutic option. The relapse patterns suggest consistent clinical trajectories, particularly in ON and myelitis. However, the higher CSF protein levels in males may indicate gender-related differences. The retrospective design and single-center cohort limit generalizability, emphasizing the need for larger, multi-center studies to validate these findings.
Disclosure: Nothing to disclose.

EPO-484 | Combined central and peripheral demyelination study and the relationship with neurofascin antibody and mog antibody

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Background and Aims: This study aims to determine the rate of combined central and peripheral demyelination (CCPD), compare its clinical, radiological, and electrophysiological features with CNS demyelinating diseases and CIDP, and assess the role of Neurofascin-155 (NF-155) and myelin oligodendrocyte glycoprotein (MOG) antibodies.
Methods: We analyzed CNS demyelinating and CIDP patients, identifying CCPD cases. Neuroradiological imaging, laboratory findings, and electrophysiological exams were assessed. Hughes scores measured disability and treatment response in CCPD and CIDP groups, while EDSS was used for CNS cases. NF-155 and MOG antibodies were tested using a live cell-based assay. Statistical analysis was performed using SPSS.
Results: Among 122 patients, 10 had CCPD. While no significant age difference was found between CCPD and CNS groups, CCPD was more common in younger patients than CIDP ($p < 0.05$). CCPD showed distinct clinical features, with myelitis as the most frequent CNS involvement and variant CIDP as the most common PNS diagnosis. CCPD patients had higher spinal T2 lesion prevalence, elevated CSF protein, and OCB negativity ($p < 0.05$). Steroid/IVIG unresponsiveness was also significant ($p < 0.05$). Hughes scores improved post-treatment ($p < 0.05$). MOG antibodies were detected in four CCPD patients and NF-155 in two, linking them to CCPD.
Conclusion: CCPD presents unique yet overlapping features with CNS demyelinating diseases and CIDP. Anti-MOG and anti-NF-155 antibodies contribute to its pathogenesis, highlighting the need for targeted diagnostic and therapeutic approaches.
Disclosure: Nothing to disclose.

EPO-485 | Assessment of a commercial tissue-based assay for detecting neural surface antibodies in autoimmune encephalitis

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Background and Aims: The diagnosis of autoimmune encephalitis (AE) relies on the detection of neural surface antibodies (NSAbs). The recommended diagnostic strategy includes a combination of tissue-based assays (TBAs) and cell-based assays (CBAs). While specialized centers use in-house TBAs, many clinical laboratories rely on commercial TBAs, whose accuracy remains undetermined.
Methods: We included 92 CSF and 99 serum samples from AE patients with NSAbs (20 AMPAR, GABAAR, GABABR, IgLON5, LGI1, NMDAR, CASPR2; 19 mGluR5, 17 DPPX, 15 mGluR1) confirmed by in-house TBAs and CBAs, along with 50 CSF and 50 sera from negative controls. We evaluated the performance of a commercial indirect immunofluorescence (IIF)-TBA (EUROIMMUN). Slides were evaluated (positive/negative) by two experienced investigators (FG, JD); if discordant, an interrater discussion was conducted.
Results: The two raters were concordant in classifying 94% (133/142) of CSF and 88% (131/149) of sera. For CSF samples, 75% (106/142) were correctly identified, while 19% (27/142) were misclassified. Among sera, 66% (98/149) were correctly identified, while 22% (33/149) misclassified. The poorest performance was observed in detecting NMDAR, GABAAR, and mGluR5 Abs (not identified in 5/10, 6/10, and 5/9 sera and in 4/10, 5/10, 5/10 CSF samples, respectively). The sensitivity of the commercial IIF-TBA was 84% for CSF and 76% for serum; the specificity was 72% for CSF and 73% for serum.
Conclusion: The diagnostic performance of EUROIMMUN IIF-TBA for NSAbs is suboptimal. NMDAR-Abs can be missed in 50% of cases. Our findings suggest that this commercial TBA should not be used alone to screen for NSAbs.
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EPO-486 | Ublituximab and CD 19+ B cells rapid depletion after the first infusion: An early real-world experience

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Background and Aims: Ublituximab, a third-generation glycoengineered-chimeric monoclonal antibody, targets a unique epitope on the CD20-antigen and has a great antibody-dependent-cellular-cytotoxicity.
Methods: A monocentric, real-world Italian experience on three patients undergoing the first ublituximab infusion. The treatment protocol included an initial dose of 150/mg on day 1, followed by a second-dose of 450/mg two-weeks later. Blood samples were obtained before and at the end of the first split infusion (PRE/POST T0), after 7 days (T1), and after the second split dose (14 days) (POST-T2). Lymphocytic count and immunophenotype were collected.
Results: Three patients were enrolled, median age 49 years (Q1:Q3; 46–54.5); median Expanded-Disability-Status-Scale score 3.5 (Q1:Q3; 3.0–4.0). All patients were naïve to disease-modifying therapies and had high active disease course. Blood samples 'results are reported below. Patient 1: PRE-T0-absolute-lymphocyte-count 0.83 103/μL, CD19+B-cells-count 100 cells/μL; POST-T0-absolute-lymphocyte-count 0.40 103/μL, CD19+B cells-count 3 cells/μL, T1-absolute-lymphocyte-count 0.85 103/μL, CD19+B-cells-count 0 cells/μL, POST-T2absolute-lymphocyte-count 0.60 103/μL, CD19+B cells-count 1 cells/μL. Patient 2: PRE-T0-absolute-lymphocyte-count 1.83 103/μL, CD19+B-cells-count 191 cells/Ul; POST-T0-absolute-lymphocyte-count 0.14 103/μL, CD19+B-cells-count 0 cells/μL;T1-absolute-lymphocyte-count 1.57 103/μL, CD19+B-cells-count 0 cells/μL; POST-T2-absolute-lymphocyte-count 0.54 103/μL, CD 19+ B cells count 0 cells/μL. Patient 3: PRE-T0 absolute lymphocyte count 2.34 103/μL, CD 19+ B cells count 197 cells/μL; POST-T0 absolute lymphocyte count 0.24 103/μL, CD 19+B cells count 0 cells/μL; T1 absolute lymphocyte count 1.83 103/μL, CD19+B-cells-count 0 cells/μL; POST-T2 (not still available).
Conclusion: This study provides the first immunological profiling of CD19+ B cells depletion in patients receiving ublituximab after initial infusion. Further data are needed to validate them in larger cohorts.
Disclosure: Nothing to disclose.

EPO-487 | Real-world experience of efgartigimod in juvenile myasthenia gravis in China: A multicenter retrospective study

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Background and Aims: Therapeutic decisions for juvenile myasthenia gravis (JMG) rely mostly on pediatric retrospective studies or adult MG guidelines. Here, we investigated the effectiveness and safety of efgartigimod in JMG.
Methods: In this multicenter, retrospective study involving 12 centers in China, participants with JMG (<18 years old) who received at least one dose of intravenous efgartigimod were enrolled. The clinical status was analyzed using MG-related Activities of Daily Living (MG-ADL) scores, Quantitative Myasthenia Gravis (QMG) score, and MG composite (MGC) scales.
Results: Seventeen JMG patients (3 male, 14 female) were included with some refractory JMG, seronegative MG, ocular MG, and myasthenic crisis. The average age pre-efgartigimod treatment was 13.41 ± 2.96 years, with a median disease duration of 23 months (range, 1.5–166 months). At baseline, most of the patients (88.2%) were classified as MGFA classes II to V. Fifteen patients (88.2%) were anti-AChR antibody-positive. Most patients (16/17) received at least one immunomodulatory treatment. Following efgartigimod administration, 70.6%

showed therapeutic progress at V1. By V2, 73% achieved significant improvement; 91.7% had remission, and 8 (66.7%) achieved minimal symptom expression at V4. Compared to baseline, the MG-ADL and QMG scores decreased on average by 30% and 30.1% respectively at V1 and increased to 87.6% and 71.8% by V4. Efgartigimod improved symptoms across all muscle groups. No medication-associated allergic reactions, infections, or serious adverse events were reported.
Conclusion: Efgartigimod is safe and rapidly effective in managing JMG patients, especially in some refractory JMG and seronegative MG, while providing more proof for treatment options.
Disclosure: No conflicts of interest

EPO-488 | Reactive pleocytosis after repeated lumbar puncture – Implications for clinical practice

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Background and Aims: Lumbar puncture (LP) is a routine clinical procedure and in some cases repeatedly performed for diagnostic or therapeutic reasons. The impact of repeated LP on cerebrospinal fluid (CSF) findings is not clear.
Methods: Patients with non-inflammatory neurological disease (NIND) and at least two consecutive lumbar punctures (LP) were included. Longitudinal changes in CSF white blood cell count (WBC), CSF total protein (TP) and CSF/serum albumin quotient (Qalb) were assessed depending on the time interval between the LP.
Results: A total of 73 patients with a median age of 35 years (25th–75th percentile: 25–45) and a female predominance of 75% had second LP after 6 (3–19) days. Twenty (27%) patients developed pleocytosis with an increase of WBC count to 8 (6–15) with a maximum of 30. Patients with pleocytosis had the follow-up LP significantly earlier than patients without pleocytosis, 3.5 (3–7) versus 7 (3–28) days. The majority of patients (90%) with CSF pleocytosis had the second LP within 10 days. Further repeated LP in a subgroup of patients revealed similar findings. CSF TP and Qalb slightly increased in patients with pleocytosis.
Conclusion: Mild "reactive" CSF pleocytosis occurs in approximately one third of patients after repeated LP mostly when performed within 10 days.
Disclosure: Nothing to disclose.

EPO-489 | Comparative the efficacy of efgartigimod and intravenous immunoglobulin on AQP-4 IgG positive NMOSD during acute attacks

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Background and Aims: The aim of our study was to evaluate the efficacy of efgartigimod and intravenous immunoglobulin (IVIG) on Aquaporin-4 (AQP4) IgG positive Neuromyelitis optica spectrum disorders (NMOSD) patients during acute attacks.
Methods: A retrospective case-control study was designed to compare the clinical outcomes of 13 NMOSD patients treated with efgartigimod at a dose of 20 mg/kg on the first and fifth day and 20 NMOSD patients treated with IVIG at 0.4 g/kg/day for 5 days. Follow-up outcome information for patients is documented at 6 months post-discharge.
Results: Compared with IVIG, efgartigimod could improve NMOSD patients' symptoms at acute attacks, the Expanded Disability Status Scale (EDSS) scores were significantly improved from 3.0 at admission to 2.5 at discharge ($p < 0.001$). The serum IgG levels were obviously decreased in NMOSD patients treated with efgartigimod ($p < 0.001$). AQP-4 antibody in five NMOSD patients were found to turn negative after efgartigimod treatment.
Conclusion: The efficacy of efgartigimod is comparable to IVIG therapy in improving acute symptoms of AQP4-IgG-positive NMOSD. Efgartigimod could be an elegant alternative to IVIG therapy, and no serious adverse events were observed during infusion.
Disclosure: The authors declare that they have no competing interests

EPO-490 | Characteristics of recently diagnosed MS patients treated with ofatumumab in Switzerland: The KOSMOS study population

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Background and Aims: Real-world data evaluating the effect of ofatumumab on people with multiple sclerosis (pwMS) in a routine medical setting are still missing, especially for recently diagnosed pwMS. The goal of KOSMOS (Kesimpta® [Ofatumumab] in Swiss Multiple sclerosis patients – an Observational Study) is to close this evidence gap.
Methods: KOSMOS (COMB157GCH01/NCT05285904) is a non-interventional study aiming to investigate the impact of ofatumumab on an early RMS population under routine medical care. The study recruited adult patients within 5 years of RMS diagnosis who had received ofatumumab under Swiss Kesimpta label for 3 months or longer prior to inclusion. Patients had to be willing and able to participate and provide written informed consent. The primary endpoint of KOSMOS is NEDA-3 ("no

evidence of disease activity" defined as lack of relapses, MRI lesions, and disability worsening) at 12 months, as compared to the standard-of-care arm of a phase-3b study, STHENOS (COMB157G3301/NCT04788615). Other endpoints include adherence and persistence to ofatumumab, patient-reported outcomes, and immune cell population dynamics and serum biomarkers.

Results: A total of 107 pwMS were included across 18 centres (3 university hospitals, 3 other hospitals, 12 private practices). Here, we will present baseline data including demographic characteristics, medical history, previous disease-modifying therapies, clinical and MRI parameters, as well as patient-reported physical and psychological impact of MS (MSIS-29).

Conclusion: This baseline analysis will characterize data of an early Swiss RMS population under routine medical care with ofatumumab. Results from the KOSMOS study will provide insights into the effectiveness of ofatumumab in a real-world scenario.

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EPO-491 | Five-year outcomes in MS patients based on Type 2 and Type 3 oligoclonal band patterns

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Background and Aims: Oligoclonal bands (OCBs) are essential biomarkers in multiple sclerosis (MS), providing insights into disease activity and progression. However, the clinical significance of different OCB patterns, particularly Type 2 and Type 3, remains unclear. Understanding their impact on long-term outcomes may help refine prognostic assessments in MS. The study aims to compare the clinical characteristics and five-year outcomes of multiple sclerosis patients with Type 2 and Type 3 oligoclonal band positivity.

Methods: This retrospective cohort study included 1,090 MS patients with Type 2 OCB positivity and 180 with Type 3 OCB positivity. Clinical variables, including age of onset, gender, Expanded Disability Status Scale (EDSS) scores, relapse rates, and transition to secondary-progressive MS (SPMS), were analyzed at years two and five.

Results: At year two, the mean EDSS score was significantly lower in the Type 3 OCB group (1.11 ± 1.51) compared to the Type 2 group (1.51 ± 1.67; $p < 0.05$). By year five, EDSS scores increased in both groups (Type 3: 1.38 ± 1.83; Type 2: 1.7 ± 1.91), but the difference was no longer statistically significant. No significant differences were observed in relapse rates or SPMS transition.

Conclusion: Type 3 OCB positivity was associated with lower disability at year two, but this difference was not sustained at year five. Further studies incorporating cognitive and motor outcomes are needed to clarify the long-term prognostic value of OCB patterns in MS.

Disclosure: Nothing to disclose.

EPO-492 | Antineuronal antibody screening in the absence of neurological involvement in high-risk oncological patients

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Background and Aims: The incidence of paraneoplastic neurological syndromes (PNS) has significantly increased due to the widespread administration of immune checkpoint inhibitors (ICIs), inducing the production of antineuronal autoantibodies. The aim of this study is the detection of antineuronal autoantibodies in patients with small cell lung cancer (SCLC) in the absence of neurological signs and/ or symptoms.

Methods: 10 patients were included in this study. For the detection of antineuronal autoantibodies, tissue-based assay (TBA), line immunoassay (LIA), and enzyme-linked immunosorbent assay (ELISA) using patients' blood sera were performed.

Results: The male: female ratio was 7:3, the mean age of participants was 69.8 years (SEM $\pm$ 2.98 years), and the mean disease duration was 7.6 months (SEM $\pm$ 2.13 months). 70% of patients were diagnosed with extensive SCLC, whereas 30% were diagnosed with limited SCLC. 50% of patients were treated with ICIs and 30% of patients had received ICIs for ≥6 months. Antibody screening with TBA revealed the presence of antineuronal autoantibodies in 50% of patients. The presence of anti-GAD65 antibodies was identified using LIA, whereas anti-GAD65 titers were measured using ELISA (102.8 IU/mL). The presence of low-titer anti-GAD65, prior to ICIs initiation, was attributed to diabetes mellitus type 2, according to the patient's medical history.

Conclusion: Antineuronal autoantibodies were detected in the serum of a significant proportion of patients with SCLC in the absence of neurological signs and/ or symptoms. According to the currently available literature, the association between the presence of antineuronal autoantibodies and the development of PNS remains elusive.
Disclosure: Nothing to disclose.

EPO-493 | Clinical disability in coexisting NMOSD and systemic autoimmune diseases

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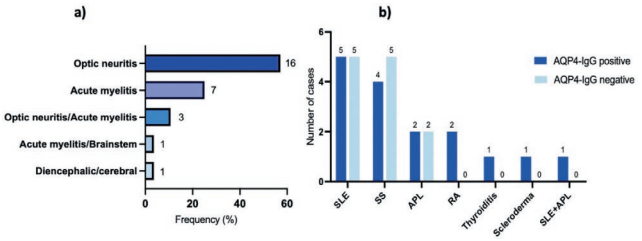
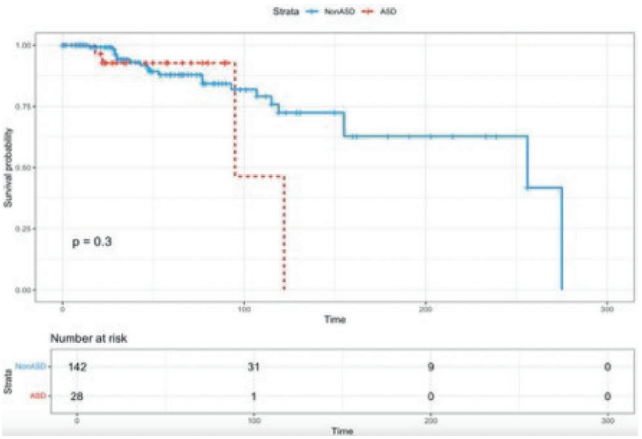
Background and Aims: Neuromyelitis optica spectrum disorder (NMOSD) is an autoimmune central nervous system disease that leads to significant clinical disability with each relapse. Its association with other autoimmune systemic diseases (ASD) is recognized, but the impact on clinical disability remains unclear.
Methods: Methods: A cross-sectional study was conducted on NMOSD patients diagnosed by the 2015 criteria, with follow-ups from January 2002 to December 2023. ASD was diagnosed by rheumatologists, and sociodemographic and clinical data were collected. Multivariate Cox regression identified factors associated with reaching an Expanded Disability Status Scale (EDSS) score of 6 or higher. Objective: To assess clinical disability in patients with coexisting NMOSD and ASD.
Results: Among 170 patients, 28 (16.5%) had coexistent-ASD. The clinical course was relapsing in 75% and monophasic in 25%. The most prevalent ASDs were systemic lupus erythematosus (35.7%) and Sjögren's syndrome (32.1%). Factors associated with higher clinical disability included AQP4-IgG positivity (HR = 2.82, $p < 0.05$*), age at NMOSD diagnosis (HR = 1.06, $p < 0.05$*), coexistent-ASD (HR = 1.68, $p = 0.36$), and first-attack neurological symptom (HR = 1.16, $p = 0.44$).

Variables	HR (95%CI)	p-value
Coexistence with ASD	1.68 (0.54 – 5.19)	0.36
Neurological symptom on first attack	1.16 (0.79– 1.70)	0.44
Age at NMOSD diagnosis	1.06 (1.02 – 1.10)	<0.05*
AQP4-IgG positive	2.82 (0.93- 8.59)	<0.05*

HR, hazard ratio; CI, Confidence intervals, *p<0.05.

Table 1. Multivariate Cox regression model of variables associated with the follow-up time to reach an EDSS of ≥ 6.0 in NMOSD





Conclusion: The coexistence of NMOSD and ASD impacts clinical disability, making early identification and evaluation crucial for effective therapy and reducing long-term disability.
Disclosure: Nothing to disclose.

Neurogenetics

EPO-494 | The effect of melatonin MTNR1A and MTNR1B receptor gene mutations in chronic insomnia

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Background and Aims: Insomnia is a common sleep disorder characterized by symptoms such as difficulty in falling asleep, maintaining sleep, or waking up early. When these complaints occur at least three times a week for three months and cause functional problems, it is called chronic insomnia. Our study aims to investigate genetic factors in the etiology of chronic insomnia by examining rs2119882 and rs4753426 mutations in the MTNR1A and MTNR1B genes.
Methods: 100 patients diagnosed with chronic insomnia and 100 healthy controls were included in our study. DNA isolation was performed from peripheral venous blood samples. Mutations rs2119882 in the MTNR1A gene and rs4753426 in the MTNR1B gene were investigated by real-time polymerase chain reaction method.
Results: 200 participants (100 patients, 100 controls) were examined. While no significant difference was found between the

groups in the rs2119882 polymorphism, the homozygous mutant (CC) genotype was more frequent in the patient group. In the rs4753426 polymorphism, the homozygous mutant genotype was found only in the patient group and was statistically significant ($p<0.001$). Additionally, when allele distributions between patient and control groups were compared, a statistically significant difference was found for the C allele in the rs4753426 polymorphism in the patient group ($p<0.05$).This result, showing a similar outcome to the higher presence of the CC genotype in the patient group, suggests that the C allele may predispose to the formation of insomnia.

Conclusion: Our study suggests that the rs4753426 mutation in the MTNR1B gene, particularly the CC genotype, may predispose to insomnia. This study may guide gene therapy studies.

Disclosure: Nothing to disclose.

EPO-495 | Mitochondrial ataxia: The Italian experience

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Background and Aims: This retrospective study assessed the prevalence and characteristics of ataxic syndrome in 764 patients genetically or clinically diagnosed with late-onset (age >16) primary mitochondrial disease (PMD).

Methods: Data from the Italian database of mitochondrial diseases were analyzed including clinical, neurophysiological, neuroimaging, and genetic information.

Results: Ataxia was observed in 63 patients (33 females), with a mean PMD onset age of 36.38 and ataxic syndrome onset at 39.86. Ataxia preceded PMD diagnosis in 7 cases and coincided with it in 28 cases. We observed cerebellar ataxia in 26 patients, pure sensory ataxia in 10 and spinocerebellar ataxia in 27 cases. Electroneurography showed axonal sensory neuropathy in 24 patients, axonal sensory motor involvement in 12, and normal findings in 10. MRI findings included cerebellar (47.6%), brainstem (14.3%) and global cerebral atrophy (50.8%), white matter hyperintensities (42.9%), lactate peak on spectroscopy (17.5%), and basal ganglia abnormalities (22.2%). Genetic analysis identified mtDNA variants in 25 patients (mostly m.8344A>G in MT-TK and m.3243A>G in MT-TL1), single mtDNA deletions in 3 patients, and nDNA gene variants in the remaining cases (16 POLG1, 3 OPA1, 2 C10ORF2, 1 AARS2, 1 DARS2, 1 PMPCA).

Conclusion: As ataxic syndrome frequently occurs at the onset of PMD and given the increasing prevalence of PMDs, mitochondrial etiology should be included in adult-onset ataxia diagnostic flowchart. Early identification of this etiology can be crucial for addressing any concurrent medical conditions that may arise in PMDs patients, as well as for potential target therapies.

Disclosure: Nothing to disclose.

EPO-496 | Genetic mutations in early onset dementia

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Background and Aims: Early-onset dementia (EOD) is a heterogeneous group of neurodegenerative disorders with an important genetic component. This study aimed to assess the prevalence of genetic mutations in symptomatic patients and explore correlations with disease onset, clinical phenotype, and cognitive impairment severity.

Methods: We enrolled patients with dementia onset before 65 years, evaluated clinically, through brain imaging, and cerebrospinal fluid (CSF) biomarker analysis (Aβ42, t-tau, p-tau, Aβ42/Aβ40). Then, it was performed a genetic testing with 52 genes implicated in EOD. Fifty patients from our University Hospital's Center for Cognitive Disorders and Dementias (CCDD) were analyzed in 2023-24.

1. CAUSAL GENETIC VARIANTS STRICTLY RELATED TO THE DISEASE		2. GENETIC VARIANTS RELATED WITH MEDIUM TO LOW RISK	3. NEW CANDIDATE GENES				
APP	FUS	APOE	DCTN1	CCNF	HRPA2B1	TBK1	ELP3
PSEN1	CHMP2B	TREM2	JIP3	CHCHD10	NEK1	UBQLN2	EPB41L1
PSEN2	TARDBP	ABCA7	LRRK2	CHMP2B	OPTN	UNC13A	ERBB4
MAPT	DYNACTIN-1	SORL	BACE1	CTSF	PFN1	VAPB	LMNB1
GRN			VPS13C	FIG4	SIGMAR1	VRK1	PLD3
C9ORF72			ANO	GLE1	SQSTM1	CYP27A1	PRNP
VCP			BSCL2	HNRNPA1	EWSR1		
			SPG2	TARBDP	TAF1		

FIGURE 1 The genes' list with his subdivision in three categories is reported in the table

Results: Genetic testing identified pathogenic mutations in 15% of cases, consistent with literature data. These included autosomal dominant Alzheimer's disease (ADAD), frontotemporal dementia (FTD), behavioral variant FTD (FTDbv) and Cerebrotendinous xanthomatosis (CTX). No clear genotype-phenotype correlation emerged, likely due to the limited sample size. Among seven mutation-positive patients, two were women with a positive family history: a 38-year-old with PSEN1 and a 63-year-old with MAPT. The five men included a 67-year-old with GRN mutation and memory-executive dysfunction, a 54-year-old with MAPT and stuttering onset, a 59-year-old with C9ORF72 and severe psychiatric symptoms, a 47-year-old with CYP27A1 and progressive dementia, and a 55-year-old with TBK1

Conclusion: Genetic mutations were found in a minority of EOD cases, underscoring the need for further research. Advances in genetic testing, biomarkers, and therapies are crucial for improving diagnosis, prognosis, and patient management. Understanding EOD's genetic basis is key to precision medicine and targeted interventions.

Disclosure: Nothing to disclose.

EPO-498 | A case report of a de novo TAOK1 variant associated with childhood-onset action tremor

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Background and Aims: The aim of this study was to investigate the potential genetic basis of childhood-onset tremor in a 15-year old patient.
Methods: We conducted a clinical and genetic evaluation of a 15-year-old patient with symptoms of essential tremor. The patient was assessed through neurological examination, electromyography and magnetic resonance imaging as well as metabolic tests. Trio exome sequencing was performed on the patient and his parents to identify potential genetic etiology. The identified variant was further analyzed using available genomic databases.
Results: The patient presented with a bilateral upper limb postural and kinetic tremor, initially observed in early childhood and progressively worsening with age. The tremor was exacerbated by stress and emotions. Neurological examination revealed no other significant findings. EMG confirmed a kinetic tremor with a frequency of 6–7 Hz. Exome sequencing identified a de novo heterozygous frameshift variant in TAOK1 (NM_020791.4: c.952del, p.Gln318Argfs*9), classified as likely pathogenic based on ACMG criteria. This variant was absent in both GnomAD and ClinVar databases. The patient's tremor significantly improved with propranolol treatment.
Conclusion: This case supports the association between TAOK1 mutations and tremor, specifically childhood-onset, action tremor, even in the absence of other neurodevelopmental symptoms. Further studies involving larger patient cohorts are needed to explore the frequency of TAOK1 mutations in hereditary essential tremor.
Disclosure: Funding sources: This work was supported by funding from the EJP RD (EJP RD Joint Transnational Call 2022) and the German Federal Ministry of Education and Research (BMBF, Bonn, Germany), awarded to the project PreDYT (PREdictive biomarkers in DYsTonia, 01GM2302). This research was also supported by a "Schlüsselprojekt" grant from the Else Kröner-Fresenius-Stiftung (2022_EKSE.185). In addition, this study (M.Z.) has received funding from the Federal Ministry of Education and Research (BMBF) and the Free State of Bavaria under the Excellence Strategy of the Federal Government and the Länder, as well as by the Technical University of Munich - Institute for Advanced Study. M.Z. receives research support from the German Research Foundation (DFG 458949627; ZE 1213/2-1).

EPO-499 | Unraveling the genetic basis of heterogeneous neurologic and other phenotypes through genomic data reanalysis

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Background and Aims: Next Generation Sequencing (NGS), particularly Whole Exome Sequencing (WES), has revolutionized rare disease diagnostics by enabling earlier and more precise molecular diagnoses. As genomic databases expand and analytical tools improve, regular reanalysis of NGS data in undiagnosed Mendelian disorders is strongly recommended, as it can lead to new diagnoses in previously unsolved cases. In this study, we aimed to evaluate the effectiveness of re-analyzing pre-existing whole-exome sequencing (WES) data from patients with rare diseases for whom a molecular cause has not yet been identified.
Methods: We analyzed WES data from 243 undiagnosed individuals using the Genome-Phenome Analysis Platform (GPAP) and in-house analysis pipelines. The study cohort included cases referred to the Neurology and Neurogenetics Lab (NNL) at the University of Crete between 2014 and 2024, which remained unsolved after previous analyses. All participants were Caucasians residing in Greece, presenting with diverse clinical features, primarily neurological (72.4% of cases) and developmental manifestations.
Results: A causative variant was identified in 29 patients, resulting in a diagnostic yield of 11.9%. Of the causative variants detected, 24 were novel. The remaining cases were classified into two groups for further analysis: those with a potential diagnosis (11.1%) and those without a diagnosis (76.9%), based on the strength of evidence supporting a genetic cause.
Conclusion: Our reanalysis provided a genetic diagnosis for 29 previously unsolved rare disease cases. We identified 24 novel pathogenic variants and uncovered two ultra-rare syndromes—Verheij and White-Sutton syndromes—each with approximately 60 and 100 reported cases in the literature, respectively.
Disclosure: Nothing to disclose.

EPO-500 | Prevalence of intronic repeat expansions in RFC1 in Slovak patients with idiopathic late-onset ataxia

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Background and Aims: Biallelic repeat expansions in RFC1 cause Cerebellar ataxia, neuropathy and vestibular areflexia (CANVAS) in multiple populations. Therefore, this study aims to investigate the frequency of CANVAS among Slovak patients with idiopathic late-onset spinocerebellar ataxia [1].

Methods: DNA samples from 51 cases from 2 tertiary movement disorders centres (Kosice and Zvolen, Slovakia) involved in the CEGEMOD consortium [2] were analysed with Flanking PCR and Repeat Primed PCR for (AAGGG)n, (AAAGG)n and (AAAAG)n RFC1 repeat expansions. Southern blot confirmed positive cases [3].

Results: We identified one patient positive for biallelic pathogenic (AAGGG)n repeat expansion (1/51 = 1.96%). The patient, an 82-year-old female, developed generalised chorea at 73y old, unresponsive to antipsychotic treatment changes (initiated for depression and anxiety). Within five years, she also developed dysarthria, slight dysphagia, nystagmus, slow vertical saccades, appendicular and gait ataxia, followed by EMG-verified sensory-motor axonal-demyelinating neuropathy and vestibular areflexia with abnormal HIT. Additionally, she complained about mild cough and memory issues. MOCA score was 24p. Brain MRI showed significant cerebellar atrophy. The family history was negative. Previous genetic testing for Huntington's disease, SCA1,2,3,6,7,17, C9orf72 and WES was negative. We did not identify any (AAAGG)n or (AAAAG)n repeat expansions in our study group.

Conclusion: Our data suggest that though rare, CANVAS should be included in the standard clinical genetic testing of patients with spinocerebellar ataxia in Slovakia, especially to prevent delayed diagnosis as initial symptoms may vary. To our knowledge, this is the first patient with CANVAS reported from Slovakia.

Disclosure: This project was supported by the Slovak Grant and Development Agency under contract APVV-22-0279 and by the EU Renewal and Resilience Plan "Large projects for excellent researchers" under grant No. 09I03- 03-V03-00007 References: 1. Dominik, N. et al. Normal and pathogenic variation of RFC1 repeat expansions: implications for clinical diagnosis. Brain 146, 5060–5069 (2023). 2. Ostrozovicova, M. et al. Central European Group on Genetics of Movement Disorders. Eur. J. Neurol. 31, e16165 (2024). 3. Ronco, R. et al. Truncating variants in RFC1 in cerebellar ataxia, neuropathy, and vestibular areflexia syndrome. Neurology 100, e543–e554 (2023).

EPO-501 | The complex molecular landscape of Parkinson disease in Turkey – Genotype-phenotype correlations in a genetic cohort

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Background and Aims: Parkinson Disease (PD) is the second most prevalent neurodegenerative disorder (NDD) characterised by its cardinal motor signs and non-motor symptoms. Due to its ancient history, Turkey's population is admixed. Also genetically underrepresented, it needs more thorough investigations.

Methods: A cohort comprising 209 PD patients with either family history or early age of onset and 21 patients with atypical PD was analyzed by WES and conventional methods. Seven unsolved patients were re-annotated to investigate candidate gene variants, not associated with any disease in OMIM.

Results: Ninety-three patients were identified with rare or novel variants in 27 different genes that are causative (12 PD- and 13 NDD-associated genes) and/or risk factors for PD (GBA1 and GLUD2) with a diagnostic yield of 40.4% (Figure 1,2). Fifteen and 23 patients were detected with heterozygous variants in the possible risk genes PRKN/PINK1 and TENM4, respectively. Further ten possible candidate genes were identified by re-annotating WES data and analysing AMP-PD and PPMI.

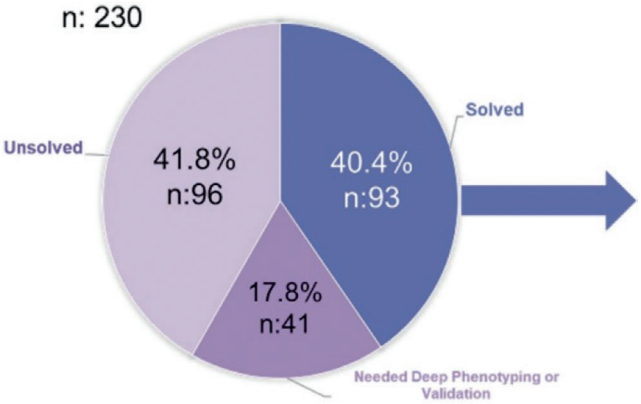

FIGURE 1 The diagnostic yield of the study cohort.

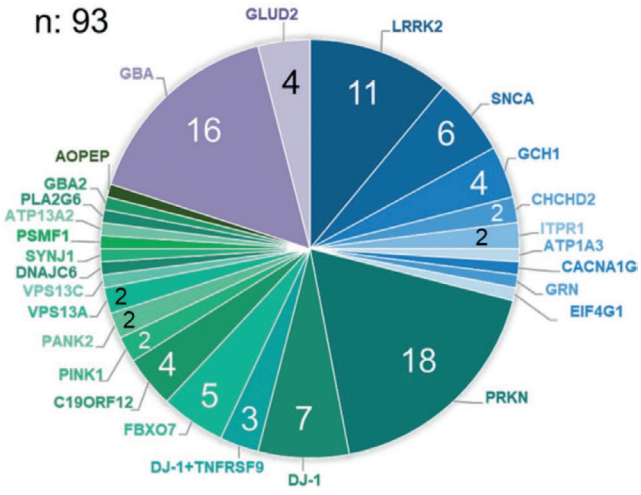

FIGURE 2 Genes with pathogenic variants identified in the patients solved. Autosomal dominantly inherited genes are in bluish colours, autosomal recessive genes are in greenish hues, and the risk factors are in purple.

Conclusion: To the best of our knowledge, this is the most comprehensive study on the molecular structure of PD in Turkey. The PRKN gene was identified as the most frequently mutated

gene in the predominantly genetic cohort under study. Detection of reported variants in genes associated with other NDD, points to the genetic heterogeneity within and overlap across these diseases. Our results are expected to contribute to new knowledge of the genetic and mechanistic factors underlying PD in Turkey.
Disclosure: This study was supported by Suna and İnan Kıraç Foundation and Koç University Research Center for Translational Medicine (KUTTAM).

EPO-502 | CANVAS: Not the usual pentanucleotide

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Background and Aims: Cerebellar Ataxia, Neuropathy, and Vestibular Areflexia Syndrome affects approximately 1 in 20,000 individuals (1). The most common cause is a biallelic expansion of the AAGGG pentanucleotide in the second intron of the RFC1 gene. In December 2023, a study suggested that additional pentanucleotides expansions beyond speciphic sizes can also be causative of the disease (2). Until then, expanded alleles other than AAGGG had only been found in control groups (3). Only isolated cases of this condition have been identified, no family studies having been reported.
Methods: A family of 6 siblings underwent neurological examination, electrophysiological assessment (ENG-EMG), and blood sampling for genetic investigations, at the Polo Pontino/ICOT of Rome Sapienza University. Pathogenic expansion of the (AAGGG)n, and the expansion of the (AAAGG) ≥600 was investigated.
Results: The 4 symptomatic patients exhibited cerebellar ataxia, nystagmus, hypoacusis, and sensory axonal neuropathy. The onset was late-onset, with a slowly progressive course. They showed compound heterozygosity with the pathogenic pentanucleotide expansion AAGGG and the AAAGG pentanucleotide expansion exceeding 600 repeats. The samples from healthy controls showed only the presence of the pathogenic AAGGG pentanucleotide in heterozygosity.

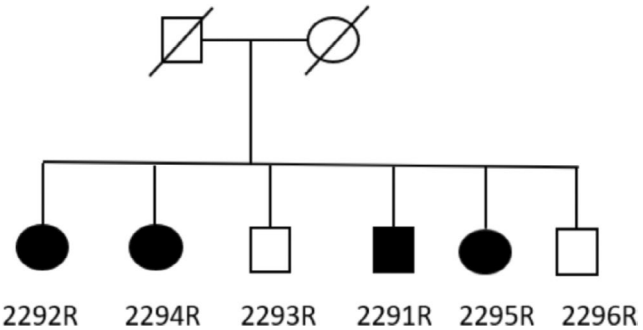

FIGURE 1 FAMILY TREE

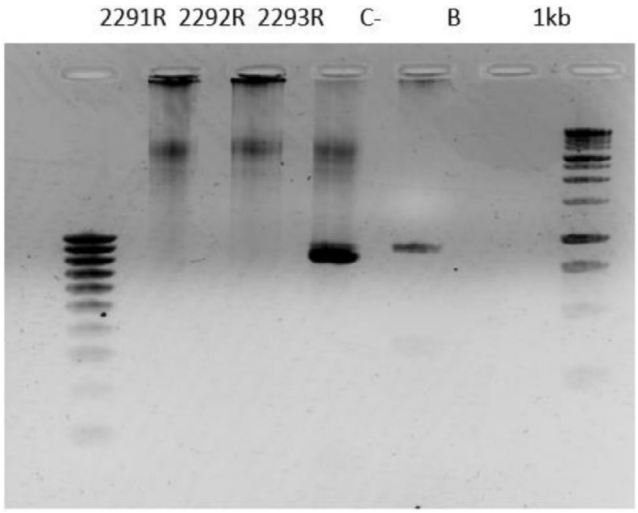

FIGURE 2 electrophoresis

	Allele 1	Allele 2
2291R (04/10/1942) S: C B	(AAGGG)exp	(AAAGG) ~700
2292R (09/01/1935) B: C B	(AAGGG)exp	(AAAGG) ~700
2293R (23/05/1940) V: A B	(AAAAG)~100	(AAAGG) ~700
2294R (03/10/1936) E: C B	(AAGGG)exp	(AAAGG) ~700
2295R (06/05/1946) G: C B	(AAGGG)exp	(AAAGG) ~700
2296R (23/08/1948) A : C A	(AAGGG)exp	(AAAAG) ~100

FIGURE 3 Alleles

Conclusion: CANVAS is usually diagnosed after reassessing ataxic patients with no family history, a late-onset and sensory axonal neuropathy, frequently accompanied by a cough. In our family the clinical presentation was similar with little intrafamilial variability and without clear vestibular issues and cough. This study presents an Italian family with four siblings affected by CANVAS caused by compound heterozygosity of the AAGGG pentanucleotide expansion and the AAAGG pentanucleotide expansion exceeding 600 repeats.
Disclosure: Nothing to disclose.

EPO-503 | Genetic landscape of primary dystonic syndromes: Insights from next-generation sequencing in a cohort of 65 patients

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Background and Aims: Dystonia, a movement disorder, can manifest in isolation or combination and involves various genetic causes. TOR1A (DYT1) was the first gene linked to primary dystonia, but advances in gene sequencing have identified

many other implicated genes [1,2]. This study aimed to examine the prevalence of genetic variants associated with dystonic syndromes and characterize their clinical phenotypes in 65 patients with primary dystonic syndrome.
Methods: We studied 65 patients with primary dystonic syndrome, analyzing their Next-Generation Sequencing (NGS) dystonia panel to identify mutations and assess their association with compatible clinical phenotypes.
Results: NGS panels of 26 of these patients (40%) were negative. In 39 patients (60%) variants were detected. A total of 62 variants were reported, among which 13 were classified as pathogenetic/likely pathogenetic, and 49 as variants of unknown significance (VUS). Six patients received a genetic diagnosis (ATM, PRRT2, TH, GNAL, GLB1 and SGCE). Four patients presented VUS in ANO3, CIZ1, TOR1A, ATP7B and had clinical signs and a segregation of the variants compatible with the related clinical phenotype. The remaining twenty-nine patients had inconclusive results.
Conclusion: Overall, 9% of patients achieved a definitive genetic diagnosis, with an additional 6% having probable diagnoses. Despite the modest diagnostic yield, the study highlights the role of genetic analysis in identifying atypical phenotypes and providing tailored patient care. The predominance of VUS underscores challenges in variant interpretation and family counseling. The increasing accessibility of NGS panels enhances diagnostic accuracy, yet pre-test counseling remains critical to prepare patients for possible inconclusive results.
Disclosure: Nothing to disclose.

EPO-504 | A presentation of PDGFRB-related parkinsonism without cranial CT calcifications

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Background and Aims: Mutations in PDGFRB are linked to Primary Familial Brain Calcification (PFBC), a neurodegenerative disorder marked by basal ganglia calcifications [1]. Tadic et al. provided a systematic review of neuroimaging in PFBC with known gene mutations, showing calcifications on cranial CT in all cases [2].
Methods: We present a 46-year-old man with young onset parkinsonism and likely pathogenic PDGFRB variants, but without CT-detected calcifications. Symptoms began at age 39 with asymmetric resting tremor and bradykinesia, minimally responsive to dopaminergic treatment. He had also developed anxiety and gambling issues prior to dopaminergic therapy, with a family history of hearing loss (father) and late-onset Parkinson's disease (paternal grandfather).
Results: Magnetic resonance imaging was normal. Genetic testing (Next Generation Sequencing) revealed a Variant of Uncertain Significance (VUS) in PDGFRB (c.2325C>G, shared with the father); a second PDGFRB VUS (c.763G>A) and a LRRK2 VUS (c.7337G>A), both shared with the mother. Neither the patient nor his parents exhibited calcifications on cranial CT. PDGFRB variants follow an autosomal dominant inheritance pattern with variable expressivity. The VUS PDGFRB:c.2325C>G, present in father and likely in the affected paternal grandfather, is a null variant in a gene where loss of function is a known disease mechanism, suggesting its pathogenicity. However, parkinsonism associated with PDGFRB mutations in the absence of cranial CT calcifications has never been described before [2].
Conclusion: This case could highlight a novel presentation of PDGFRB mutation-linked parkinsonism without CT calcifications, expanding the phenotypic spectrum of PDGFRB-associated disorders. Further studies are needed to clarify the pathogenicity of these variants and their clinical manifestations.
Disclosure: Nothing to disclose.

EPO-505 | Delineation clinical phenotype spectrum in autosomal recessive SLC9A1-related ataxia

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Background and Aims: Biallelic pathogenic variants in SLC9A1 gene have been linked to Lichtenstein-Knorr syndrome (LKS) based on the consecutive report of six affected individuals. In the current study we provide expanded clinical description with functional studies for a total of 35 patients from 23 families including updated data for previously reported patients.
Methods: We used the GeneMatcher platform and extensive worldwide data sharing. Clinical data was collected MRI was reviewed by a pediatric neuroradiologist. All subjects gave informed consent for the publication of clinical and genetic information according to the declaration of Helsinki.
Results: Our cohort (mean age 16 +/- 13 years (range 4–51)) predominantly presented moderate-to severe ataxia starting mostly in early childhood involving gait, trunk and limbs with dysmetria (97%) and tremor (60%). Intellectual disability (93%) was mainly mild to moderate. Amelogenesis imperfecta (91%), motor delay (91%), speech delay (76%) and cognitive impairment (86%) were particularly frequent. Sensory-neural hearing loss (69%) was mainly severe to profound with onset mostly before the age of one year. Other features included hyporeflexia (77%) and hypotonia (59%), Seizures (50%) Abnormal eye movements (36%), dyskinetic movements (31%), dystonia (24%). Cerebellar atrophy was observed in most patients. Of the 16 variants identified, 13 were novel and functional studies were performed in eight these variants and had deleterious effects.

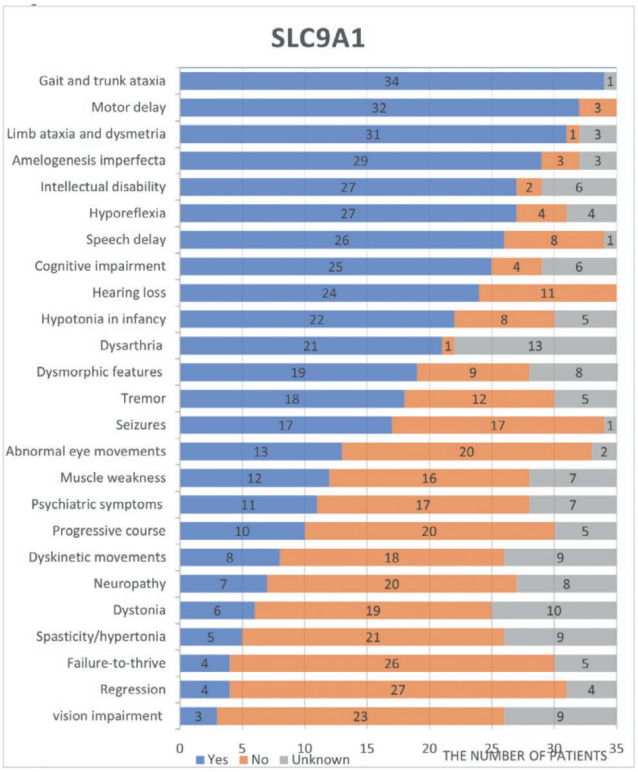

FIGURE 1 Clinical features of patients with SLC9A1-related ataxia

Conclusion: The association of hearing loss, amelogenesis imperfecta, intellectual disability, motor delay and cerebellar atrophy allow to suspect SLC9A1-linked ataxia.
Disclosure: Nothing to disclose.

EPO-506 | Vestibulo-ocular reflex gain and vestibular evoked potentials in patients with spinocerebellar ataxia

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[1]Department of Neurophysiology, Liverpool Hospital, Australia; [2]Institute of Clinical Neurosciences, Royal Prince Alfred Hospital, Camperdown, Australia; [3]Faculty of Medicine of Clinica Alemana, Universidad del Desarrollo, Santiago de Chile, Chile; [4]Concord Repatriation General Hospital, Department of Neurology, Concord, Australia

Background and Aims: The spinocerebellar ataxias (SCAs) are a genetically heterogeneous group of autosomal dominantly inherited progressive disorders characterised by loss of balance and coordination.
Methods: 16 patients (SCA3 $n=6$, SCA6 $n=4$, SCA7 $n=2$, SCA14 $n=2$, SCA34 $n=2$) with mean age 56.0 $\pm$11.1 years (5F/11M), were recruited from Outpatient Balance Neurology Clinic. Video Head-Impulse test was used to assess vestibulo-ocular reflex (VOR) function in all three canal planes and cervical and ocular-Vestibular-Evoked Myogenic Potentials (c- and oVEMP) were used to assess otolith function.
Results: Mean International Co-operative Ataxia Rating Scale (ICARS) was 30.1 $\pm$15.0 and Scale for the assessment and rating of ataxia mean (SARA) score was 10.2 $\pm$5.5. Saccadic pursuit was present in 13 (81%) patients, and loss of VOR suppression in 11 (69%) patients. Air-conducted cVEMPS were absent in 4 (25%) patients and bone-conducted oVEMPS were absent in 5 (31%) patients. Horizontal, anterior and posterior canal (HC, AC, PC) VOR-gains were 0.63 $\pm$0.2, 0.67 $\pm$0.3, 0.60 $\pm$0.3. HC, AC and PC VOR-gain were reduced in 12 (75%) patients, 10 (62%) and 11 (68%) patients. All patients with SCA3 had VOR-gain reduced in all six-canals. Patients with SARA scores ≥10 had significantly lower HC VOR-gain compared to the patients with mild disease severity (0.49 vs 0.76, $p=0.015$). There was a negative correlation between SARA score and HC VOR-gain ($r=$ -4.001, $p=0.034$).
Conclusion: In patients with SCAs reduction in the VOR-gain is common and is associated with higher degree of functional impairment.
Disclosure: Nothing to disclose.

Neuro-ophthalmology/neuro-otology

EPO-507 | Type III cryoglobulinemia presenting with acute cochleovestibular loss

A. Costa[1]; F. Bartolomeu[2]; M. Amorim[2]; D. Damas[3]; S. Matos[3]; A. Inês Martins[3]; A. Jorge[3]; J. Lemos[3]; J. Lemos[4]
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Background and Aims: Type III cryoglobulinemia is a mixed cryoglobulinemia involving polyclonal immunoglobulins that form immune complexes, depositing in small to medium-sized vessels and causing end-organ damage. Symptoms include purpura, arthralgias, weakness, and rarely, cochleovestibular loss.
Methods: We describe a type III cryoglobulinemia patient with sequential acute cochleovestibular loss.
Results: A 26-year-old female presented with sudden painless left-sided hearing loss and imbalance. The use of ototoxic agents was ruled out. Her medical history was notable for a previous episode of acute cochleovestibular loss on the right side 2 years prior (characterized by right moderate sensorineural hearing loss on audiogram, right gain reduction on VHIT and normal brain and inner ear MRI), without an established etiology. An audiogram confirmed acute left-sided sensorineural hearing loss, and VHIT demonstrated reduced gain values bilaterally, now indicating new-onset left vestibular nerve dysfunction. Brain and inner ear MRI were again unremarkable. Autoimmune assessment revealed the presence of cryoglobulins (polyclonal IgM), indicative of type III cryoglobulinemia. Other laboratory studies were unremarkable. She was treated with a 125 mg bolus of methylprednisolone and a 5-day course of 60 mg deflazacort and was putted on aspirin. Imbalance fully improved spontaneously, while the hearing loss remained unchanged after one month.
Conclusion: This case highlights inner ear dysfunction in type III cryoglobulinemia, manifesting as sequential cochleovestibular loss. Although audiovestibular symptoms are uncommon, they occur in up to one-third of mixed cryoglobulinemia patients, possibly due to cryoglobulin precipitation in inner ear

vessels causing vasculitis. Mixed cryoglobulinemia should be considered in unexplained cochleovestibular loss.
Disclosure: Nothing to disclose.

EPO-508 | Central positional downbeat nystagmus responsive to clonazepam in SCA3

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Background and Aims: Ocular motor phenotypes in spinocerebellar ataxias (SCA) have been progressively described, with some features predominating over others, depending on genotype. As an example, central positional nystagmus is extremely rare in SCA3, while being present in ~80% of SCA6 patients. The treatment of CPN poses a clinical challenge, as only a few drugs have been anecdotally reported to improve CPN in some (but not in others) SCA patients.
Methods: Case report of SCA3 patient with symptomatic CPN and positional square-wave-jerks with a striking response to clonazepam.
Results: A 28-year-old SCA3 male patient presented with 3-year positional vertigo. Exam in upright position showed square-wave-jerks and microflutter, gaze evoked nystagmus, impaired pursuit, hypometric saccades, impaired head impulses, partial upgaze restriction and divergence/convergence insufficiency. During positional testing, head-hanging maneuver showed after ~5sec latency, torsional square wave jerks ~5sec followed by paroxysmal downbeat nystagmus ~10sec, associated with intense vertigo and patient's unwillingness to repeat maneuvers. Positional central downbeat nystagmus and torsional square wave jerks were diagnosed and prescribed with oral clonazepam 0.5 mg once daily. Two months later, the patient reported complete resolution of positional vertigo. Head-hanging maneuver showed no nystagmus or saccadic intrusions, indicating optimal response to treatment.
Conclusion: Oral clonazepam might have abated central positional nystagmus in the current case by restoring cerebellar nodulus/uvula inhibitory output on vestibular nuclei, through GABA-related circuitry. Given the scarce literature, multicentric studies on SCA-related CPN are most needed to help guide treatment. Similar treatment efficiency on positional saccadic intrusions, a yet largely neglected entity, equally deserves further research.
Disclosure: Nothing to disclose.

EPO-509 | A diagnostic challenge: Differentiating thyroid orbitopathy from carotid-cavernous fistula

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Background and Aims: Carotid-cavernous fistula (CCF) is an abnormal connection between the internal carotid artery (ICA) and the cavernous sinus, affecting cranial nerves III, IV, V1, V2, and VI. It presents with vision-threatening symptoms like proptosis, blurry vision, chemosis, headache, and ophthalmoplegia. Early-stage CCF can mimic other conditions, such as thyroid-associated ophthalmopathy (TAO), presenting with diplopia, progressive proptosis, conjunctival congestion, and chemosis.
Methods: A 67-year-old male presented with left eye redness lasting three months, without trauma or significant medical history. Physical examination revealed left-sided proptosis, chemosis, restricted eye movements, and dilated episcleral vessels. Thyroid function tests showed mildly suppressed TSH and elevated thyroid antibodies, suggestive of thyroiditis. Thyroid ultrasonography identified a solid nodule and increased vascularity in a heterogeneous thyroid gland. Imaging findings included hyperintensity in the retrobulbar tissues on MRI, thickened medial and inferior rectus muscles, and a prominent ophthalmic vein. MR venography revealed narrowing and discontinuity in the superior sagittal sinus. Diagnostic angiography confirmed an indirect CCF originating from meningeal branches of the right ICA and external carotid arteries (ECA), draining into the left cavernous sinus.

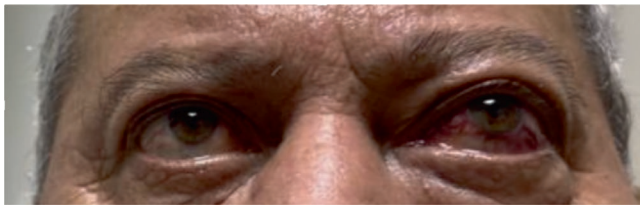

FIGURE 1 Bilateral exophthalmos, more pronounced on the left side, along with proptosis and chemosis

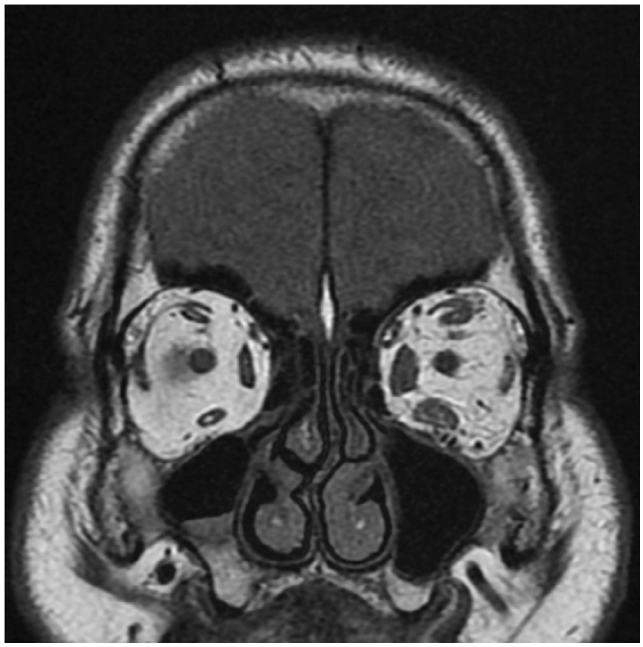

FIGURE 2 Orbital MRI demonstrated thickening of the medial and inferior rectus muscles in the left orbit

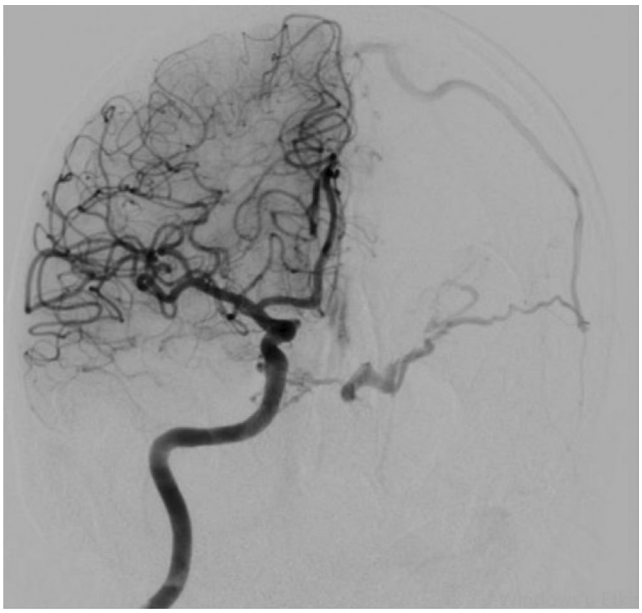

FIGURE 3 DSA confirmed an indirect CCF originating from meningeal branches of the right ICA and ECA, draining into the left cavernous sinus.

Results: This case highlights the diagnostic challenges of distinguishing CCF from TAO, emphasizing the importance of cerebral angiography as the gold standard for diagnosis. Endovascular intervention, the preferred treatment, successfully resolves most cases.
Conclusion: Clinicians should maintain a high index of suspicion for CCF in patients with atypical orbital symptoms to ensure timely and accurate management.
Disclosure: Nothing to disclose.

EPO-510 | Vestibular agnosia in elderly subjects with small vessel disease and imbalance – Perliminary results

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Background and Aims: Vestibular agnosia (VA) is a brain disconnection syndrome that manifests with imbalance and an altered sensation of self-motion perception despite an intact peripheral vestibular system. VA can be measured and quantified employing vestibular psychophysics. Only recently VA was described for the first time in acute traumatic brain injury. VA has been reported to occur in elderly patients in whom there is disconnection within the brain due to small vessel disease (SVD). In an ongoing exploratory prospective single-centre study we assess elderly patients with imbalance and dizziness for vestibular perceptual thresholds (VPTs) and balance control.
Methods: 4 patients with SVD (Fazekas 2–3) and imbalance/falls were assessed, 2 males, 2 females (age 75, 76, 81, 82 years). 4 elderly controls were assessed, 1 male, 3 females (age 72, 74, 79, 89 years). VPTs were determined for yaw-plane rotations with randomly presented half cosine stimuli (0.1 Hz). Peripheral vestibular function, balance control, handedness, reaction times, cognition and self-reported symptoms of dizziness, anxiety and depression were assessed.
Results: 4 patients with SVD and imbalance had elevated VPTs (range 6.3–19.9°/s; cut-off 5°/s for controls, mean age 42.3 years) despite intact peripheral vestibular function and abnormal balance control. 4 controls had VPTs within a low normal range (0.8–2.7°/sec). 3 patients indicated only slight handicap because of dizziness.
Conclusion: VPTs in elderly subjects over the age of 70. VPTs might be within normal ranges and severe as a biomarker for imbalance and risk of falls in elderly subjects.
Disclosure: HMR has received funding from Freiwillige Akademische Gesellschaft Basel (FAG), lecture fees from Forum für medizinische Fortbuildung (FomF) and Volkshochschule Basel CS has nothing to disclose BMS has nothing to disclose FH has nothing to disclose.

EPO-511 | Biomarkers in patients with optic neuritis: Demographic, clinic and prognostic features

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Background and Aims: The new optic neuritis (ON) classification leads to a change in how ON patients are grouped. Our aim is to appraise the clinical features and prognoses of patients with autoimmune ON not associated with MS.
Methods: Patients referred to our neuro-ophthalmology laboratory were enrolled to this retrospective study. Patients with ON associated with MS were excluded. The remaining patients were divided into three groups: aqauaporin-4 (AQP4) antibody ON group, myelin oligodendrocyte glycoprotein (MOG) antibody ON group, and seronegative ON group. The patients were examined on admission, one month after acute treatment, and at the third-year follow-up. We compared demographic, clinical, radiologic, laboratory data, and treatment responses among these three groups.
Results: The study included 92 patients with 120 eyes. The older age of onset, bilateral simultaneous involvement of the optic nerves, severe vision loss at onset, and need for aggressive treatment were more common in the AQP-ON and the MOG-ON groups than the seronegative ON group ($p=0.01$, $p=0.003$, $p=0.011$, $p=0.007$, $p<0.001$, $p<0.001$, respectively). The presence of optic disc edema was a significant feature of MOG-ON as well as long-length contrast enhancement on MRI ($p=0.003$, $p=0.002$). Additional autoimmune antibodies and CNS lesions outside the optic nerve were the features of AQP4-ON patients ($p<0.001$, $p=0.015$). Generalized estimating equations analysis revealed that the presence of AQP4 antibody, increased age and recurrence were associated with visual acuity over time ($p=0.014$, $p=0.002$, $p=0.016$, respectively).

TABLE 1 Baseline characteristics and treatments of the patients.

	AQP4-ON (*n*=19, eyes=28)	MOG-ON (*n*=17, eyes=26)	Seronegative ON (*n*=56, eyes=66)	P_1	P_2	P_3
Age, years (mean±SD)	40.58±10.50	42.41±11.93	32.45±11.86	0.638	**0.010**	**0.003**
Sex, female/male (rate)	15/4 (3.75)	10/7 (1.42)	33/23 (1.43)	0.190	0.116	0.993
Interval of onset to admission, days, median (IQR)	8 (3 to 12)	5.5 (4 to 9.75)	14 (7.5 to 27)	0.99	**0.012**	**0.006**
Bilateral simultaneous ON, *n* (%)	9 (47.3)	9 (52.9)	10 (17.8)	0.738	**0.011**	**0.007**
Orbital pain at ON presentation, *n* (%)	10 (52.6)	12 (70.5)	31 (55.3)	0.269	0.778	0.295
Disc edema, *n* (%)	7 (36.8)	13 (76.4)	20 (35.7)	**0.016**	0.929	**0.003**
RAPD, *n* (%)	12 (63.1)	5 (29.4)	25 (44.6)	0.042	0.163	0.263
Recurrent ON, *n* (%)	6 (31.5)	3 (17.6)	12 (21.4)	0.335	0.370	0.735
Length of optic nerve contrast enhancement, *n* (%)				0.195	0.155	**0.002**
Short (Less than ½ length of optic nerve)	14 (73.7)	9 (52.9)	49 (87.5)			
Long (More than ½ length of optic nerve)	5 (26.3)	8 (47.1)	7 (12.5)			
CNS lesion other than the optic nerve, *n* (%)	9 (47.3)*	4 (23.5)*	3 (5.3)	0.137	**<0.001**	0.025
Cortical/Juxta-cortical	0	2 (5.8)	1 (1.7)			
Subcortical	1 (5.2)	2 (5.8)	2 (3.6)			
Brainstem	2 (5.2)	0	0			
Spinal cord	7 (31.5)	1 (5.8)	0			
ANA/ANCA positive, *n* (%)	4 (26.6)	1 (5.8)	2 (3.5)	0.188	**0.015**	0.674
Plasma exchange, *n* (%)	7 (36.8)	2 (11.7)	7 (12.5)	0.082	0.181	0.935
Long term treatment, *n* (%)						
Slow taper of steroids	14 (73.6)	14 (82.3)	26 (46.4)	0.532	0.039	**0.009**
SSI or monoclonal antibody	18 (94.7)	10 (58.8)	7 (12.5)	**0.009**	**<0.001**	**<0.001**

ANA: antinuclear antibody, ANCA: antineutrophil cytoplasmic antibodies, AQP4: aquaporin-4, CNS: central nervous system, IQR: interquartile range, MOG: myelin oligodendrocyte glycoprotein, *n*: number, ON: optic neuritis, RAPD: Relative Afferent Pupillary Defect, SD: standard deviation, SSI: steroid-sparing immunosuppressant. P_1: P value AQP4-ON compared to MOG-ON, P_2: P value AQP4-ON compared to seronegative ON, P_3: P value MOG-ON compared to seronegative ON.

*: Overlap in some cases

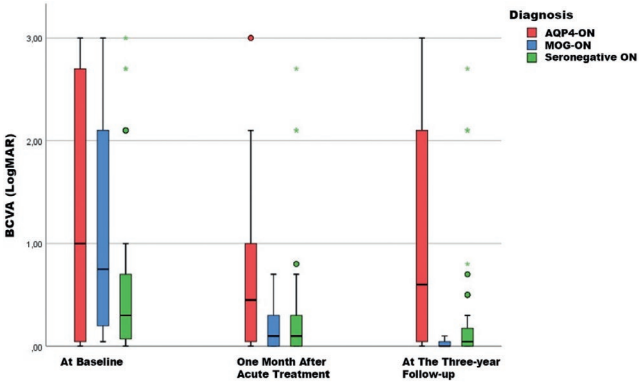

FIGURE 1 A clustered boxplot graphic showing patients' visual acuities. BCVA: best corrected visual acuity, LogMAR: Logarithm of the Minimum Angle of Resolution.

Table 2. Covariates and factors influencing LogMAR BCVA over time.

	B-Coefficient	Standard Error	*P*
Age, years	0.015	0.004	**0.002**
Sex, male	0.25	-0.121	0.826
Interval of onset to admission	-0.008	0.006	0.252
Bilateral optic neuritis	0.108	-0.116	0.395
Orbital pain	-0.122	-0.018	0.366
Optic disc edema	-0.008	0.111	0.946
RAPD	0.67	-0.117	0.569
Recurrent optic neuritis	0.280	-0.123	**0.016**
More than ½ length of optic nerve contrast enhancement	0.155	0.139	0.266
CNS lesion other than optic nerve	0.291	0.596	0.062
Positive serum ANA/ANCA	0.105	0.445	0.554
Biomarker status			
AQP4	R	R	
MOG	-0.449	0.171	**0.007**
Seronegative	-0.386	0.165	**0.014**

ANA: antinuclear antibody, ANCA: antineutrophil cytoplasmic antibodies, AQP4: aquaporin-4, CNS: central nervous system, IQR: interquartile range, MOG: myelin oligodendrocyte glycoprotein, R: reference, RAPD: relative afferent pupillary defect.

Conclusion: The association of serum biomarker status with demographic, clinical features, and visual outcomes indicate the importance of biomarker detection in these patients.
Disclosure: Nothing to disclose.

EPO-512 | Ocular dysmotility in orbital neoplasms

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Background and Aims: To analyze the pattern of ocular motility disturbances caused by orbital tumors, and investigate factors associated with the severity of misalignment or motility limitation.
Methods: The medical records of 68 patients with orbital neoplasm were retrospectively reviewed. The location, type, and size of tumor were noted. The limitation of extraocular muscle (EOM) movement was quantitatively scored for upgaze, downgaze, abduction, and adduction by the severity of limitation on a grading scale. The maximum range of abduction, adduction, supraduction and infraduction were measured by image analysis based on 9 gaze photographs using the 3D Strabismus Photo Analyzer.
Results: Twenty patients(29%) patients had extraconal orbital tumors (60%), while 8 had intraconal lesions(40%).The mean size of extraconal tumors was significantly larger than intraconal tumors ($p=0.010$), and there were no significant differences in tumor size between each four quadrants. In 75% of patients with extraconal neoplasms, ocular motility was limited towards the action of the adjacent EOM. Conversely, in cases with intraconal

neoplasms, ocular motility was limited towards the opposite direction of the nearest EOM action in 75% cases. Compared with the normal fellow eye, significant limitations of ocular motility were observed in adduction ($p=0.043$) and supraduction ($p=0.002$). The size of intraconal tumors was the only significant factor related to ocular motility limitation ($p=0.010$).
Conclusion: A significant movement restrictions in upgaze and adduction varied depending on whether the tumor was located extraconally or intraconally. The size of orbital tumor in the intraconal region was the only factor related to ocular motility limitation.
Disclosure: Nothing to disclose.

EPO-513 | Spatial orientation impairment in patients with bilateral vestibulopathy and persistent postural-perceptual dizziness

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Background and Aims: Spatial orientation abilities typically decrease with higher age, cognitive impairment or vestibular disorders. Bilateral vestibulopathy (BVP) is known to be associated with poorer performance in orientation and navigation tasks. Less is known about possible visuospatial deficits in persistent postural-perceptual dizziness (PPPD).
Methods: 32 patients with BVP (17 females), 43 with PPPD (25 females) and 32 healthy controls (HC, 15 females) participated in a clinical bedside test investigating spatial orientation abilities (3D real-world pointing task, 3D-RWPT). This test includes a cognitive (mental rotation) and a vestibular paradigm (passive whole-body rotation without visual feedback). All participants had normal cognitive testing results and were younger than 65 years. Participants additionally filled out self-reports of subjective spatial abilities and spatial orientation discomfort. PPPD and HC had normal peripheral-vestibular function.

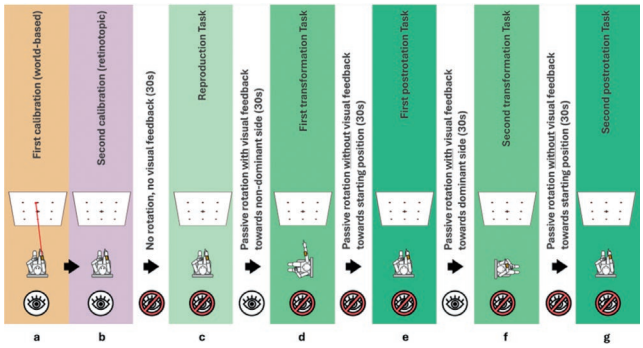

FIGURE 1 Overview of the 3D-RWPT. The full test consists of two calibration paradigms (a, b) and five test paradigms (c–f).

Results: Patients with BVP and PPPD showed substantially larger angular deviations (i.e., lower accuracy) in the 3D-RWPT compared to HC (BVP: 9.62 ± 3.21°, PPPD: 9.16 ± 3.85, HC: 7.77 ± 2.86°; p 0.03*), especially in the subtasks which rely on vestibular function (BVP: 8.11 ± 5.51°, PPPD: 6.62 ± 4.46, HC: 4.45 ± 2.33°; $p < 0.01$**). All cohorts had comparable levels of self-assessed spatial abilities, while both BVP and PPPD patients showed higher levels of spatial orientation discomfort.
Conclusion: PPPD patients exhibited measurable visuospatial deficits in the 3D-RWPT, although these deficits were not as pronounced as in BVP patients. Since especially the vestibular subtasks were affected, one might speculate that PPPD patients show a reduced use of vestibular input and rely more on visual input. Both PPPD and BVP patients reported spatial orientation discomfort.
Disclosure: Nothing to disclose.

EPO-514 | Downbeat nystagmus, symptom of a sensorimotor syndrome of vertical spatial disorientation

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Background and Aims: Downbeat nystagmus (DBN), the most common form of acquired central fixation nystagmus, causes vertical oscillopsia, imbalance and postural instability in the anterior-posterior direction. So far, DBN-related alterations of the internal representation of space have not been investigated.
Methods: 20 patients with DBN (13 females, mean age 69.97 ± 10.17 years) and 20 age-, sex-, handedness-, and cognition-matched participants (13 females, mean age 69.87 ± 9.52 years) without peripheral-vestibular deficits underwent a spatial orientation bedside test (3D real-world pointing task, 3D-RWPT)

based on whole-arm pointing at a target matrix. For both cohorts, the subjective haptic straight ahead (SHA) with eyes closed was measured. Additionally, quantitative (horizontal and vertical angular deviation) and qualitative performance markers (morphology of target matrix) were investigated. DBN intensity was measured using videooculography.

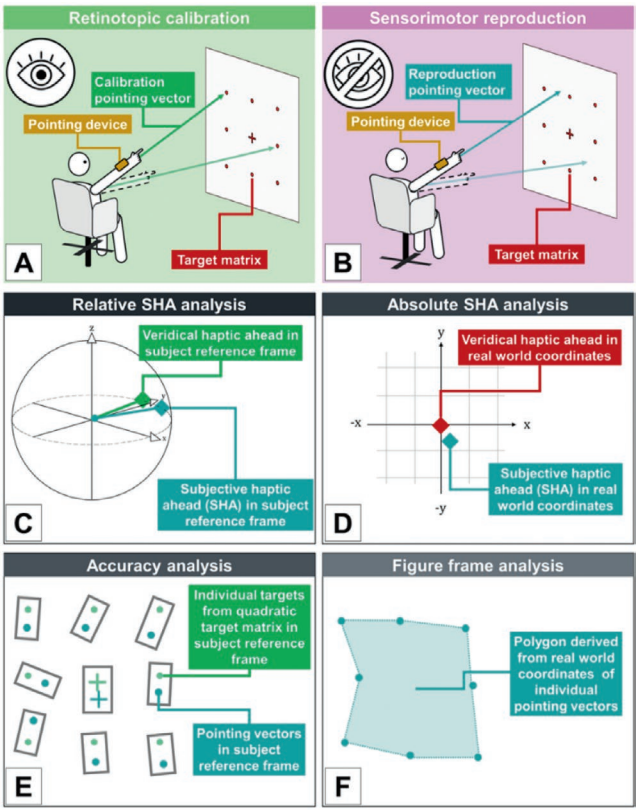

FIGURE 1 Depiction of the 3D-RWPT and the analyses performed in this study.

Results: Compared to the control cohort, the DBN cohort exhibited an absolute (real-world coordinates) and relative (subject reference frame) SHA downward shift. DBN patients showed vertically (but not horizontally) decreased pointing accuracy (Welch's *t*-test azimuth/horizontal deviation: n.s.; polar/vertical deviation: $t = 3.85$, $p < 0.001$***). DBN intensity was not robustly associated with 3D-RWPT performance or postural swaying patterns.
Conclusion: DBN is associated with a SHA downward shift in a pointing task performed without visual feedback. This is contradirectional to prior research investigating the subjective visual ahead, which is shifted upwards in DBN. These findings indicate that DBN-associated spatial impairment is not solely caused by oscillopsia and thus an ocular motor syndrome, but persists even without visual input, hinting at central-vestibular alterations of spatial perception of head and body in space.
Disclosure: Nothing to disclose.

EPO-515 | Unveiling dual diagnoses: Papilledema and pseudopapilledema in a series of patients

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Background and Aims: Papilledema indicates the presence of bilateral optic disc edema caused by intracranial hypertension (IH), and is potentially associated with sight- and/or life-threatening conditions. Pseudopapilledema consists of a disk elevation associated with underneath tilted disks/high myopia (TD), optic disk drusens (ODD) or other variants, which carries no relevant risk.
Methods: This study describes a retrospective series of patients demonstrating the rare instance of presenting with both pseudopapilledema and papilledema.
Results: We included 7 patients (4 males, mean age 34.5 ± 18.2 years). Presenting symptom/sign leading to neuro-ophthalmic assessment included: headache (2), transient monocular vision loss (2), pulsatile tinnitus (1), seizure (1) and incidental fundoscopic finding (2). Pseudopapilledema consisted of: OOD (4), TD (2) and ODD plus TD (1). OCT showed retinal nerve fiber layer thickening in 6, and ODD in 5 patients. The initial presumptive neuro-ophthalmic diagnosis was: definite papilledema and pseudopapilledema (3), definite pseudopapilledema and possible papilledema (2), definite pseudopapilledema (1), and definite papilledema (1). In the first two groups, CSF opening pressure and papilledema improvement after oral acetazolamide confirmed the concurrent presence of papilledema associated with idiopathic IH and pseudopapilledema. In the patient with presumptive pseudopapilledema (ODD and meningioma with apparently no imaging signs of IH), follow-up retinography clearly showed papilledema resolution while leaving unchanged baseline ODD. In the patient with presumptive papilledema, after complete resolution of the papilledema with oral acetazolamide for idiopathic IH, baseline TD were now apparent.
Conclusion: The presence of pseudopilledema should never preclude the active exclusion of papilledema, as both can occur simultaneously.
Disclosure: Nothing to disclose.

EPO-516 | Unrecognized benign paroxysmal positional vertigo in frail in-patients

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Background and Aims: Dizziness is a common complaint, its incidence increases with age and is often associated with

balance disorders and predispose the patient to falling. Benign paroxysmal positional vertigo (BPPV) is an important cause which can easily be treated but is frequently not recognized by professionals. We sought to determine the prevalence of unrecognized BPPV in hospitalized elderly patients.
Methods: Patients admitted to Department of Geriatrics were enrolled in the study. A questionnaire was used to obtain uniform and detailed history, patients with previous diagnosis of BPPV were excluded. A clinical neuro-otologic examination (including Romberg test, spontaneous and gaze nystagmus) was performed, as well as Dix-Hallpike and Supine-Roll test. Prevalence was tested with Fisher's exact test.
Results: We evaluated a sample of 77 patients (53 women) during 3-month period (mean 79.1 ±10.3 years). There was no statistically significant difference in age or sex between groups. 41 (53.2 %) of them reported a fall in the past six months and 38 (49.4 %) dizziness. Definite BPPV was found in 8 patients (10.1 %). Most (87.5%) referred symptom was dizziness during standing up and a sensation of spinning in general (all $p < 0.05$). Only half of them reported positional-related symptoms after head movement or rolling in the bed ($p < 0.05$).
Conclusion: These data indicated that unrecognized BPPV is quite common in elderly in-patient population. Only half of them reported positional related symptoms, but most of them nonspecific dizziness. Diagnostic maneuvers should be part of the essential examination algorithm and successful treatment of BPPV may reduce morbidity and mortality.
Disclosure: Nothing to disclose.

EPO-517 | Bedside assessment of square-wave jerks in movement disorders: Evaluating reliability with quantitative oculography

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Background and Aims: Square-wave jerks (SWJs) are clinically observable fixation intrusions that occur with increased frequency in various neurological conditions, particularly movement disorders. Although SWJs are included in the diagnostic criteria for progressive supranuclear palsy, the reliability of their clinical detectability at the bedside has never been formally evaluated.
Methods: Patients with various movement disorders were prospectively examined by a neurologist specializing in movement disorders. The number of SWJs during one minute of straight-ahead fixation was counted at the bedside. Each patient also underwent binocular video-oculography while fixating on a visual target in the primary position, with SWJs detected. Offline using custom-written MATLAB software. Physicians operating the oculography setup were blinded to the clinicians' SWJ counts, and vice versa.
Results: A total of 21 patients (17 female, mean age: 64 years, range: 36–78 years) with various movement disorders, including Parkinson's disease, Parkinson-plus syndromes, cerebellar ataxia and Stiff-Person Syndrome, were included in the study. The agreement between bedside and apparatus-based SWJ counts was poor, as indicated by an intraclass correlation coefficient (ICC) of 0.268 (95% CI: −0.900 to 0.709). Bedside counting underestimated SWJ counts in 17 patients and overestimated them in 4 patients. When using a threshold of >10 SWJ/min to define abnormality, the agreement between bedside assessment and oculography remained poor, with a Cohen's kappa of 0.106 ($p > 0.05$).
Conclusion: Counting SWJs at the bedside does not appear to align well with quantitative measurements obtained via videooculography. Clinical assessment tends to underestimate SWJ rates in most cases, though there are a few notable exceptions where it overestimates them.
Disclosure: Nothing to disclose.

EPO-518 | Unidirectional visual motion exposure does not modify cVEMP amplitude in vestibular migraine

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Background and Aims: Vestibular migraine (VM) is the leading cause of non-positional episodic vestibular complaints. It results from an altered state in the brain that disrupts sensory processing across various modalities. A reliance on clinical history alone for diagnosis dictates a need for bedside biomarkers for the early diagnosis of this condition, particularly in emergency settings where misdiagnosis rates are highest.
Methods: A cross-sectional study utilizing non-probabilistic sampling was conducted. Seventeen healthy controls (mean age = 34, age range = 21–55; 13 females) and seventeen patients (mean age = 38.7, age range = 20–64; 15 females) diagnosed with VM were recruited from acute vertigo clinics at the UCLH. The study protocol involved repeated cVEMP (cervical vestibular evoked myogenic potentials) measurements, before and after a Unidirectional Visual Motion Stimuli presented through VR (Virtual Reality) goggles.
Results: No significant differences in amplitude response (μv) were found between groups at baseline. A statistically significant difference in Right - Left cVEMP amplitude asymmetry between groups was noted. SPANOVA revealed no significant effects for maximum amplitude. No significant correlation was found between questionnaire-based symptom burden scores and changes in cVEMP amplitude following visual stimulation, in either group.
Conclusion: The study found that a prolonged unidirectional visual stimulation does not affect cVEMP responses in vestibular migraine patients, making it unsuitable as a bedside diagnostic biomarker for VM.
Disclosure: Nothing to disclose.

EPO-519 | Visual assessment in cerebral venous thrombosis: a prospective retinographic, perimetric and tomographic study

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Background and Aims: Papilledema has been reported in 30-80% of cerebral venous thrombosis (CVT) patients. Optical coherence tomography (OCT) and orbital ultrasound may be used to portray papilledema in CVT. We aim to quantitatively assess visual function of CVT patients at presentation.
Methods: CVT patients were prospectively recruited and separated based on the presence versus absence of papilledema. We analysed symptoms, visual function (OCT, automated perimetry, and retinography), affected sinuses (3T MRI), orbital and transcranial ultrasound.
Results: 39 CVT patients were recruited (9 male; mean age 40.21 ±13.17). Sigmoid (79.5%) and transverse (76.9%) sinuses were the most affected. Symptoms included headache (97.4%), tinnitus (23.1%), focal neurological deficits (20.5%), transient visual obscurations (5.1%), vision loss (2.6%), whereas no patient had diplopia. Confrontational visual fields were abnormal in 2 (5.1%), papilledema was present in 13 (30.8%), and no patient had 6th nerve palsy. Perimetry was abnormal in 8 (20.5%) patients. The presence of focal neurological deficits was significantly associated with papilledema ($p=0.029$) and the same trend was observed with tinittus ($p=0.066$). Intracranial pulsatility (IC) index positively correlated with RNFL thickness in the left eye (right IC, $r=0.376$, $p=0.020$; left IC, $r=0.501$, $p=0.001$). The extent of CVT, deep venous system involvement, and symptom duration did not predict the presence of papilledema.
Conclusion: Mild papilledema is present in around one-third of CVT patients and is not associated with relevant visual field loss. The presence of focal neurological deficits and increased IC predicted papilledema. Longitudinal assessment of CVT patients may further help evaluate the role of quantitative visual measures in predicting long-term outcomes.
Disclosure: Nothing to disclose.

EPO-520 | Individual disease trajectories in childhood-onset subacute/dynamic eyes by age at onset from the Case Record Survey-2

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Background and Aims: Childhood-onset Leber hereditary optic neuropathy (LHON) is a distinct form of LHON with varied clinical presentation and often better outcomes. Improved understanding of the clinical course of childhood-onset LHON is essential for optimising management in this patient subgroup. Here, we present individual visual acuity (VA) trajectories by age at symptom onset (OoS) in childhood-onset subacute/dynamic (S/D) eyes from the Case Record Survey-2 (CRS-2; NCT02796274).
Methods: Retrospective clinical data were extracted from case records of LHON patients. Eligibility: aged ≥12 years at enrolment, m.11778G>A, m.3460G>A, or m.14484T>C mitochondrial DNA mutation, OoS after 1999 and ≥2 VA assessments within 5 years of OoS and prior to idebenone use. Baseline (BL) was first VA assessment after OoS; S/D eyes were those with BL≤1 year after OoS.
Results: A total of 51 S/D eyes were aged <15 years at OoS with a mean (± standard deviation) follow-up time from BL of 48.0 ± 55.2 months. Distribution of age at OoS was: 6–<9 years: 27.5% ($n=14$); 9–<12 years: 33.3% ($n=17$); 12–<15: 39.2% ($n=20$). Individual VA trajectories by age at OoS are shown in Figure 1. High variability in VA trajectories was observed within and between age at OoS subgroups. Rapid VA decline in the first 6 months was infrequently observed, and many eyes with follow-up >1 year remained on-chart (<1.68 logMAR) throughout the chronic phase.

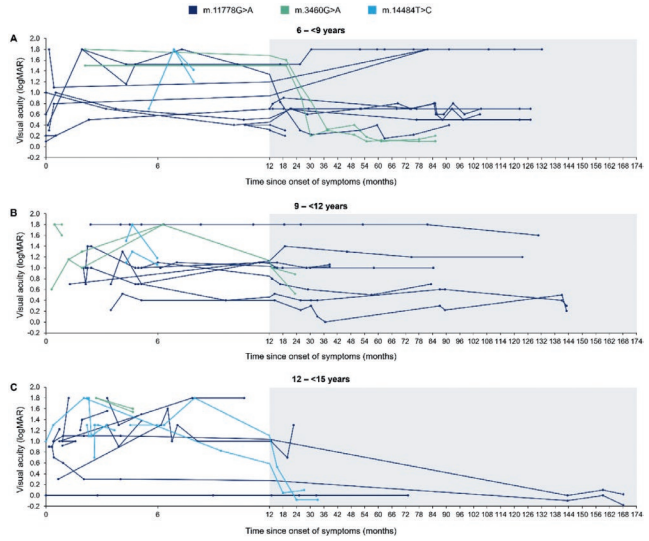

FIGURE 1 Individual VA trajectories after OoS in childhood-onset S/D eyes that were (A) 6.

Conclusion: High variability in the trend of vision loss over time in childhood-onset eyes from CRS-2, irrespective of age at OoS, emphasises the importance of regular follow-up and individualised management for patients with childhood-onset LHON.

Disclosure: The CRS-2 study was funded by Santhera Pharmaceuticals. TK, PYWM, and VC received research support and/or personal compensation from Santhera Pharmaceuticals, Chiesi Farmaceutici S.p.A., and GenSight Biologics. PYWM also received consultation fees from Neurophth. BPL received consulting fees and travel support from GenSight Biologics. JvE, MK and CL have nothing to declare. XL is an employee of Chiesi Farmaceutici S.p.A. Medical writing support was provided by nspm ltd, Switzerland, and funded by Chiesi Farmaceutici S.p.A.

Tuesday, June 24 2025

Clinical neurophysiology

EPO-521 | The role of lower motor neuron dysfunction in cutaneous silent period alterations in ALS

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Background and Aims: The aim of this study was to evaluate cutaneous silent period (CSP) in patients with amyotrophic lateral sclerosis (ALS), and investigate its correlation with lower motor neuron (LMN) dysfunction.

Methods: CSP was recorded from the abductor pollicis brevis (APB) muscle using strong electrical stimuli applied to the index finger of the least affected hand. LMN dysfunction was assessed using the compound muscle action potential (CMAP) and motor unit number index (MUNIX) in APB. Sixty patients with definite ALS, as defined by the El Escorial criteria (disease duration 15.5 [10; 24] months) were included, with 30 (50%) presenting with spinal-onset ALS and 30 (50%) with bulbar-onset ALS. The control group consisted of 48 age- and sex-matched healthy subjects.

Results: CSP onset latency ($p < 0.01$) and duration ($p < 0.05$) were significantly prolonged in ALS patients as compared to controls. No statistically significant differences in CSP parameters were found between subgroups with spinal- and bulbar-onset. CSP duration correlated positively with disease duration ($r = 0.63$, $p < 0.05$) but not with ALSFRS-R score. MUNIX and CMAP values in ALS patients were significantly lower than in controls ($p < 0.05$). CSP onset latency showed no correlation with CMAP or MUNIX of APB, though a weak positive correlation was observed between CSP duration and MUNIX ($r = 0.31$, $p < 0.05$).

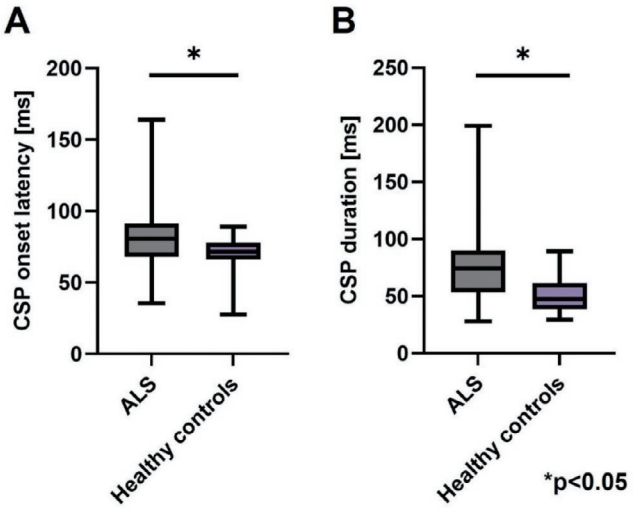

FIGURE 1 Comparison of CSP onset latency (A) and duration (B) between the ALS group and healthy controls.

Conclusion: Prolonged onset latency and duration of CSP in ALS has been previously reported, with some authors attributing this to upper motor neuron involvement. Our study suggests that LMN dysfunction may contribute to CSP alterations in ALS, although further research on CSP in patients with lower MUNIX values is needed,

Disclosure: The authors have nothing to disclose.

EPO-522 | Clinical, neurophysiological and imaging features of lissencephaly

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Background and Aims: Lissencephalies are a rare and heterogenous group of cortical malformations, defined by different MRI and EEG patterns. We aim to characterize a cohort of

lissencephaly patients of a tertiary center and explore potential associations between MRI findings, EEG patterns, and clinical presentation.

Methods: Retrospective analysis of clinical, imagiological and electroencephalographic data of a consecutive sample of lissencephaly patients followed at a tertiary center.

Results: Nineteen patients were included, 63.2% ($n=12$) female, with a median age at diagnosis of 11 months (IQR 3 years). Genetic mutations were confirmed in 68.4% ($n=13$), most commonly in the DCX gene (38.5%). The average time between imaging and genetic diagnosis was 6.3 ± 5.1 years. Seventeen patients developed epilepsy (89.5%) at a median age of 2 years (IQR 6.2 years), with tonic seizures being most frequent ($n=11$, 64.7%). The most common EEG pattern ($n=6$; 31.6%) was characterized by diffuse high amplitude alpha/beta activity. Patients with this pattern or with normal EEG had a better functional status ($p<0.001$) and more commonly had non-refractory epilepsy ($p=0.03$). Focal or multifocal epileptiform activity was observed in 11 patients (57.9%). The anterior gradient was the most frequent neuroimaging pattern ($n=9$, 47.4%) and was not associated with epilepsy severity or functional status.

Conclusion: Nearly all lissencephaly patients developed early-onset epilepsy. Despite the typically symmetrical cortical abnormalities, focal or multifocal epileptiform activity was common. In our cohort, the EEG pattern was associated with epilepsy severity and functional status. The neuroimaging pattern was independent of clinical or electroencephalographic aspects.

Disclosure: Nothing to disclose.

EPO-523 | Trigeminal reflex abnormalities distinguish between classical and idiopathic trigeminal neuralgia

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Background and Aims: Primary trigeminal neuralgia (TN) is a representative neuropathic facial pain condition classified into classical (associated with neurovascular compression), and idiopathic (unknown etiology). Differentiating between classical and idiopathic TN based on clinical and neurophysiological findings remains challenging. In this clinical and neurophysiological study, we aimed to identify predictive clinical and neurophysiological variables that may distinguish between the two types of TN.

Methods: We retrospectively analyzed clinical records and neurophysiological data from 114 patients with primary TN (84 classical TN, 30 idiopathic TN). We implemented a logistic regression model to identify predictive variables for classical and idiopathic TN.

Results: Thelogistic regressionmodel showed that a trigeminal reflex latency asymmetry longer than 0.5ms between the affected and unaffected sides was predictive of classical TN ($p<0.05$). Additionally, combined involvement of the second and third trigeminal divisions was predictive of idiopathic TN ($p<0.05$).

TABLE 1 Significant predictors of idiopathic TN according to the logistic regression analysis.

Predictors	Odds ratio	95% CI	*p*-value
V1-involvement*	3.44	[0.34,31.45]	0.263
V2-involvement*	1.81	[0.41,7.97]	0.423
V1V2-involvement*	1.79	[0.44,7.53]	0.410
V2V3-involvement*	6.96	[1.80,30.75]	**0.007**
V1V2V3-involvement*	1.17	[0.14,7.08]	0.869
With TR asymmetry >0.5 ms**	0.19	[0.03,0.80]	**0.045**
With remission, N (%)**	0.39	[0.14,0.99]	0.052*

*(vs V3); **(vs without)*

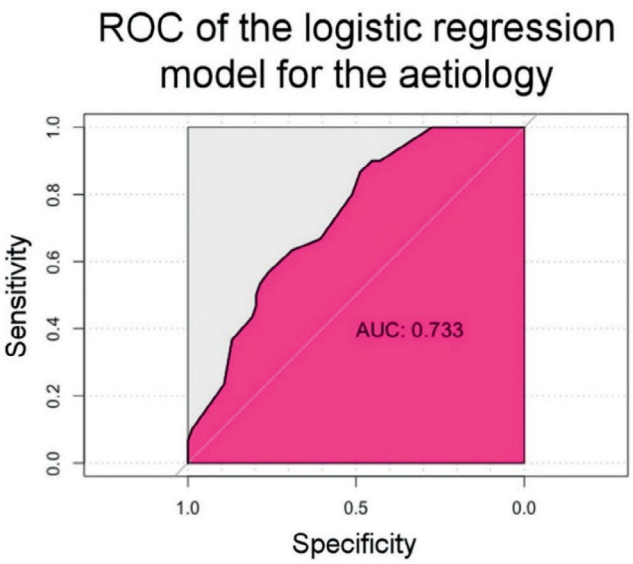

FIGURE 1 ROC of the logistic regression model for the aetiology

Conclusion: Our findings suggesting that latency asymmetry in trigeminal reflexes differentiate between classical and idiopathic TN probably reflects the association of classical TN with neurovascular compression, while idiopathic TN may involve other factors affecting trigeminal nerve fibers.

Disclosure: Nothing to disclose.

EPO-524 | Neurophysiological biomarkers in adults with type III spinal muscular atrophy

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Background and Aims: This study aimed to evaluate the feasibility and tolerability of MUSIX (Motor Unit Size Index) and MUNIX (Motor Unit Number Index) as potential biomarkers of disease progression in patients with spinal muscular atrophy

(SMA) and to identify the most reliable target muscle. It also sought to establish correlations between neurophysiological outcomes and changes in motor scores (RULM and HFMSE).
Methods: Four patients with SMA type III (mean age 35.5 ± 15 years) were enrolled. MUNIX and MUSIX were assessed in various limb muscles, and the results were compared to those from healthy controls. A potential correlation between neurophysiological measurements and functional motor scales was subsequently analyzed.

TABLE 1 Clinical data.

Clinical data	Patient 1	Patient 2	Patient 3	Patient 4
Sex	Male	Female	Male	Male
Age at the time of the study	36 years	30 years	64 years	20 years
Age at onset	4 years	3 years	15 years	2 years
Years of the disease	32 years	27 years	49 years	18 years
Stage of the disease	Walker	Sitter	Sitter	Walker
SMN2 copies	4 copies	3 copies	4 copies	3 copies
RULM score	R: 21, L: 27	R: 33, L: 31	R: 34, L: 24	R: 37, L: 33
HFMSE score	21	36	25	58

Results: MUSIX values were higher in SMA patients compared to healthy controls, suggesting greater neurogenic damage and active reinnervation, while the compound muscle action potential (cMAP) amplitude and MUNIX values were lower. The cMAP amplitude of less affected muscles approached the normal range, whereas MUNIX and MUSIX values did not, highlighting their greater sensitivity as neurophysiological parameters. A significant inverse correlation was observed between MUSIX values in the abductor pollicis brevis (APB) muscle and the ipsilateral RULM score ($p < 0.05$). Furthermore, MUSIX demonstrated an inverse correlation with muscle strength and the degree of disability, while MUNIX revealed a direct correlation.

TABLE 2 Neurophysiological parameters with pathological values in bold

	Patient 1			Patient 3			Patient 4			Range	
	cMAP µV	MUNIX	MUSIX	CMAP µV	MUNIX	MUSIX	cMAP µV	MUNIX	MUSIX	MUNIX	MUSIX
EDB R	**4040**	59	69	7489	82	**91**	7812	96	**81**	94.8±	64.5±
EDB L	**3308**	**45**	74	5095	60	**85**	6253	95	66	34.9	13.1
TA R	**1748**	**31**	**56**	**3841**	54	**71**	5260	54	**97**	59.3±	43.8±
TA L	**2207**	**25**	**82**	**2831**	**17**	**171**	6892	**95**	**74**	13.7	11.5
APB R	**5293**	**20**	**269**	6853	**57**	**121**	9847	**136**	**72**	191.0±	179.1±
APB L	8806	**79**	**112**	**5595**	**45**	**125**	8214	**98**	**84**	43.6	38.8
BB R	**762**	**7**	**115**	**1516**	**31**	49	8933	**81**	**111**	166.1±	60.4±
BB L	3800	**51**	**74**	**2363**	**42**	57	5369	**80**	67	40.7	12.5

Conclusion: In conclusion, this study utilized an innovative neurophysiological approach to assess a cohort of adult SMA patients. The findings suggest that these techniques, particularly MUSIX, hold promise as outcome measures in this population.
Disclosure: Nothing to disclosure.

EPO-525 | The long-term effects of repetitive magnetic stimulation in stroke hand rehabilitation depend on hemispheric dominance

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Background and Aims: This randomised, double-blind study investigated the long-term effects of 1Hz rTMS over the contralesional M1 in stroke patients with a moderate hand motor disability.
Methods: 40 stroke patients received 1 Hz rTMS/sham rTMS followed by motor training of the affected hand over three weeks. The hand motor function (Wolf Motor Function Test, Motor Evaluation Scale for Upper Extremity in Stroke Patients, Finger Tapping) and neural networks (Motor Evoked Potentials) were tested (i) immediately prior, (ii) immediately after, and (iii) six months after the intervention.
Results: Significant intervention-induced reduction of corticospinal excitability was detected after 1 Hz rTMS (in comparison to sham rTMS), independent of lesion location. The motor function of the affected hand improved after verum rTMS only in patients with lesioned dominant hemisphere ($n = 17$). Patients with the lesion within the non-dominant hemisphere ($n = 23$) did not benefit from this intervention.
Conclusion: The impact of hemispheric differences on rehabilitation-induced effects in stroke subjects was only insufficiently investigated up to now. Future studies should devote more attention to this relevant topic.
Disclosure: Nothing to disclose.

EPO-526 | Not everything that is rhythmic is a seizure: EEG characteristics during cognitive fluctuations of LBD

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Background and Aims: Lewy Body Dementia (LBD) is associated with EEG slowing, but its characteristics and relationship with the ictal-interictal continuum during cognitive fluctuations (CF) remain underexplored.
Methods: A comprehensive literature review was conducted on PubMed with the MeSH terms "Dementia with Lewy Body" and "Electroencephalogram." From 184 articles, studies addressing CF and EEG findings were selected. Additionally, two new case reports from our institution initially admitted for suspected NCSE/seizures were included.
Results: Nine studies involving 170 LBD patients consistently reported EEG background slowing during CF, with one case NCSE pattern. Three studies described cognitive impairment in LBD later diagnosed as seizures, successfully treated with antiseizure medications (ASMs). Four studies identified rhythmic patterns outside CF, including Frontal Intermittent Rhythmic Delta Activity (FIRDA) in 18 patients and Generalized Rhythmic Delta Activity (GRDA) in 14 patients. One study reported an increased prevalence of interictal epileptiform discharges in LBD. Personal cases: i) a 76-year-old woman presented with long-lasting episodes of altered mental status. Initially, NCSE was diagnosed and ASMs started. Long-term video-EEG monitoring of the episodes fulfilled EEG criteria for ictal-interictal continuum / possible NCSE according to ACNS terminology; ii) an 82-year-old woman with episodes of confusion underwent prolonged EEG monitoring showing bilateral frontotemporal slow-wave activity. Neither case showed a clinical or EEG response to ASMs. Both patients were later diagnosed with LBD.
Conclusion: EEG background rhythms during CF in LBD commonly show rhythmic theta/delta patterns. However, long-term video-EEG studies remain scarce. Our cases show how

EEG findings alone can be misleading, prompting misdiagnosis of NCSE.
Disclosure: Nothing to disclose.

EPO-527 | High-density surface electromyograms reveal the diffusion of the botulinum neurotoxin effect

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Background and Aims: The successful administration of Botulinum Toxin depends on the diffusion of its silencing effect rather than on its dispersion within the targeted tissue. Quantifying the distribution of muscle fibres responding to BT is therefore imperative if the muscle region under BT effect is to be assessed. Here we investigate the potential of assessing the diffusion of the BT effect based on surface electromyograms detected from multiple skin location: the HD-sEMG.
Methods: Grids with 64 electrodes were used to sample HD-sEMG, bilaterally from gastrocnemius medialis muscles. M wave were elicited through supramaximal stimulation of the tibial posterior nerve, before (T0), at four (T1), and at 12weeks post-injection. Our reasoning is that action potentials would not be triggered by nerve stimulation only in the muscle fibres under the BT effect. We hypothesise the amplitude of M waves detected on skin locations covering the silenced fibres would be sensitive to the BT. Contrarily, no change would be expected for the contralateral muscle.
Results: Figure 1 shows M waves at the three evaluation points for a single subject. A notable T0-T1 reduction in M wave amplitude was observed for the spastic though not for the control muscle. This difference was evident only for 12-grouped electrodes (Figure 2).

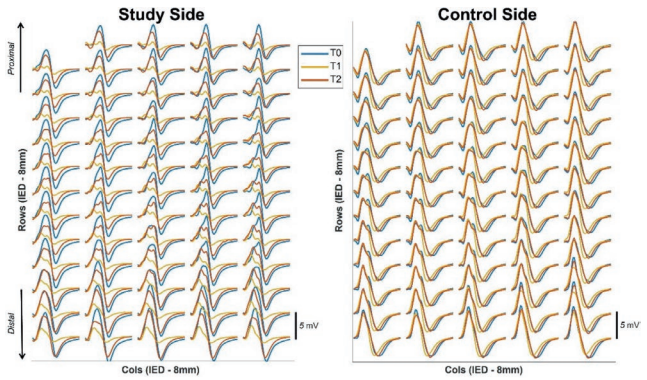

FIGURE 1 This figure shows the raw M-waves recorded with two 64-electrode grids at T0, T1, and T2. The left panel (study side) shows reduced amplitudes at T1 (BT peak effect) with partial recovery at T2. The right panel (control side) shows consistent amplitudes.

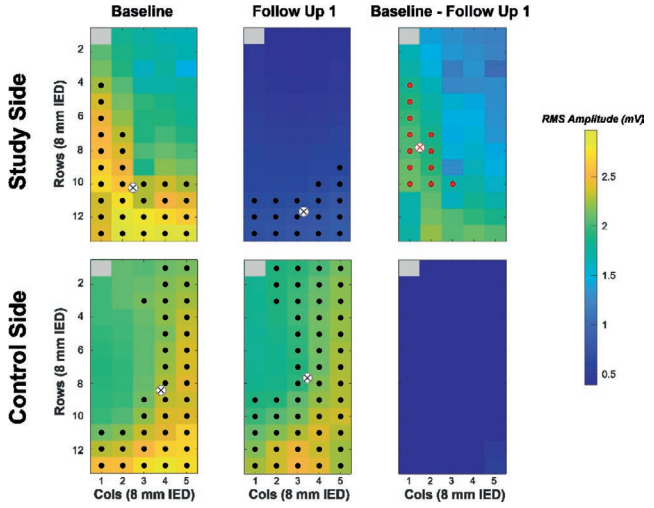

FIGURE 2 This figure shows RMS values as colormaps and segmented channels (>70% max amplitude) at T0, T1, and their difference. On the study side, 12 channels active at T0 disappear at T1, indicating BT's effect. Control side colormaps remain consistent.

Conclusion: HD-sEMG proved sensitive to the diffusion of the BT effect. Presumably, the electrodes providing M waves with reduced amplitude after injection reflect the location of the silenced fibres: we are collecting follow-up data from other subjects to further this possibility.
Disclosure: This study was carried out within the «BREAKing BONDS» project – funded by the Ministero dell'Università e della Ricerca – within the PRIN 2022 program (D.D. 104 – 02/02/2022). This manuscript reflects only the authors' views and opinions and the Ministry cannot be considered responsible for them.

EPO-528 | Posterior interosseous neuropathy secondary to parosteal lipoma: A case report and literature review

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Background and Aims: Parosteal lipomas are a relatively rare cause of compressive posterior interosseous neuropathy. The objective of this case report is to raise awareness of this highly treatable entity and underline the importance of neurophysiological assessment in localising the site of injury.
Methods: Case report and review of literature.
Results: A 58-year-old right-handed woman presented with a six-week history of progressive right arm pain, wrist drop and clawing of right hand. Examination revealed moderate weakness of right wrist extension and right finger extension and flexion with normal reflexes and sensory examination. Nerve conduction studies demonstrated absent right radial motor response and intact right superficial radial sensory response. Needle electromyography showed severe subacute partial denervation in right extensor digitorium communis and right extensor indicus, with occasional neurogenic units in her right triceps. MRI cervical spine showed severe narrowing of the exit

neural foramina bilaterally at C6-C7 level, with left nerve root abutment. MRI right forearm revealed a non-enhancing 5.2 x 6.5cm parosteal lipoma wrapping around the ulnar aspect of the proximal radius. She underwent surgical excision of the lipoma with resultant improvement in right upper limb function.
Conclusion: Posterior interosseous neuropathies due to lipoma are rarely encountered in clinical practice but important to recognise as they are eminently treatable with early surgical intervention. This case highlights the clinical utility of neurophysiological studies in temporally differentiating between a more indolent chronic right C7 radiculopathy and a symptomatic subacute compressive right posterior interosseous neuropathy.
Disclosure: Nothing to disclose.

EPO-529 | Multimodal transoperative neurophysiological monitoring in carotid surgery. Ten years of experience

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Background and Aims: Carotid surgery (CS) is a surgical procedure to treat carotid stenosis (CAS) and paraganglioma (PG). There is a high risk of stroke during carotid artery cross occlusion and secondary embolism when performing selective bypass (BS) as well as cranial nerve (CN) injury. The use of multimodal intraoperative neurophysiological monitoring (MNFIOM) using somatosensory evoked potentials and electroencephalography can be used to monitor cerebral perfusion during CC, is useful in determining the need and timing of BS. Locating and mapping NC VII (3 branches), IX and X and monitoring their function during surgery minimizes postoperative deficit.
Methods: Observational, retrospective, cross-sectional study of consecutive patients undergoing CS at ABC Medical Center from 2012 to 2023.

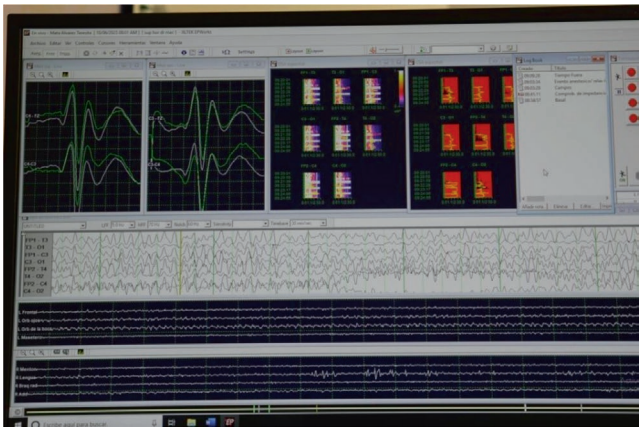

FIGURE 1 Top Left: PESS Top Right Center: EEG Frequency Scale Center: Short EEG Bottom: Free Cranial Nerve Needle EMG

Results: Eighty-eight patients were included, 51 (58%) male, median age 62.7 years. CC was performed in 43.18% (38) for CG and 56.82% (50) for symptomatic CAS (71) 80.68%, and 16 severe asymptomatic (18.18%). Fifty-six left carotid arteries (63.64%) were operated on using MNFIOM, with an average operative time of 82 minutes and an average clamping time of 21 minutes. Only one case presented with stroke, which was thrombolyzed with total recovery at 6 months. In addition, BS was performed in 10 cases by neurophysiological indication, the complications were transient facial paralysis (7) and swallowing problems in (7) patients.

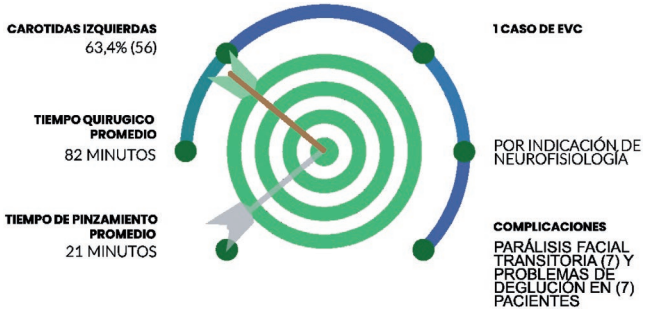

FIGURE 2 Left Carotids 63.4% (56) Average Surgery Time 82 minutes Average Clamping Time 21 minutes 1 Stroke Intraoperative Mechanical Thrombectomy 10 Carotid Bypasses Indicated by Neurophysiology Complications Transient Facial Paralysis (7) Swallowing Proble

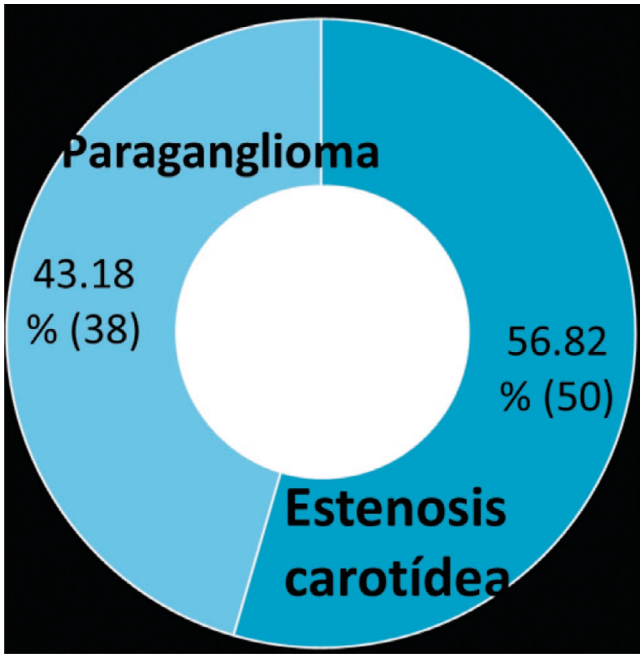

FIGURE 3 Here's the updated translation with the appropriate labels: Etiologies (Left Pie Chart): Paraganglioma: 43.18% (38) Carotid Stenosis: 56.82% (50) Symptoms (Right Pie Chart): Asymptomatic: 18.18% (16) Symptomatic: 80.68% (71)

Conclusion: This study stressed that the routine use of MNFIOM is sensitive and specific to prognosticate and minimize any postoperative neurological deficits. It helps to monitor cerebral perfusion during surgery, predict the need for BS after cross-occlusion and preserve NCs.
Disclosure: Nothing to disclose.

EPO-530 | Abstract withdrawn

EPO-531 | Analysis of intraoperative neurophysiological monitoring in neuromuscular and idiopathic scoliosis surgery

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Background and Aims: There are few comparative studies of intraoperative neurophysiological monitoring (IONM) between neuromuscular scoliosis (NS) and idiopathic scoliosis (IS). We made comparative analysis, especially in patients with no postoperative motor deterioration.

Methods: We reviewed 53 IONM records of scoliosis operation (NS: 25, IS: 28). The maximum percentage of amplitude decrement of MEPs (ΔMEPampMax) and SEPs (ΔSEPampMax), and the maximum percentage of prolonged SEPs latency (ΔSEPlatMax) compared to baseline value were analyzed. The preoperative motor score (Motorpre) of both lower extremities by the International Standards for Neurological Classification of Spinal Cord Injury were calculated using the MRC grade. Cobb's angle (Cobb'spre), corrected Cobb's angle (ΔCobb's) were measured. The maximum and minimum systolic BP (SBP) and diastolic BP (DBP) during surgery.

Results: NS showed significantly lower height, weight, and Motorpre, compared to IS. NS had larger Cobb'spre, longer fixation level and operation duration, and more bleeding amount than IS (Table 1). However, there were no significant differences of ΔMEPampMax, ΔSEPampMax, or ΔSEPlatMax between two groups. By Pearson's correlation analysis, ΔSEPampMax were significantly correlated with operation duration ($p=0.01$) in NS. In addition, ΔSEPampMax were correlated with DBPMin ($p=0.04$) and MEPampMax ($p=0.01$) in IS. The ΔSEPlatMax was correlated with SBPMax ($p<0.01$) and ΔSEPampMax ($p<0.01$) in NS. On the linear regression analysis, bleeding amount, SBPMax, and DBPMax were significant contributing factors for ΔSEPlatMax in NS (Table 2).

Table 1. Difference between neuromuscular and idiopathic scoliosis surgery

Scoliosis	NS (n=25)	IS (n=28)	*P* value
Age	15.7 ± 2.9	15.9 ± 2.6	0.79
Sex			< 0.01*
Male	20 (80.0)	3 (10.7)	
Female	5 (20.0)	25 (89.3)	
Diagnosis			
Adolescent idiopathic scoliosis		28 (100.0)	
Muscular dystrophy[a]	16 (64.0)		
Spinal muscular atrophy	4 (16.0)		
Other[b]	5 (20.0)		
Height	148.6 ± 13.7	162.9 ± 8.3	< 0.01*
Weight	37.7 ± 14.9	56.7 ± 15.9	< 0.01*
Preoperative motor score	22.0 ± 11.5	50.0 ± 0.0	< 0.01*
Simple plain image			
Cobb's$_{pre}$ (°)	63.7 ± 16.5	21.1 ± 3.8	< 0.01*
⊿Cobb's (°)	39.7 ± 16.8	50.4 ± 6.5	0.59
Fixation level (level)	16.0 ± 0.8	12.0 ± 1.8	< 0.01*
Operation duration (hr)	8.2 ± 2.0	7.1 ± 1.6	0.03*
Hemodynamics			
Bleeding amount (mL)	2,705.2 ± 1,550.2	1,687.1 ± 819.7	0.004*
SBP_{Max}	132.0 ± 19.9	136.3 ± 12.6	0.35
SBP_{Min}	76.0 ± 9.1	81.5 ± 5.8	0.01*
DBP_{Max}	81.6 ± 14.3	80.8 ± 10.1	0.82
DBP_{Min}	39.1 ± 4.9	41.1 ± 4.9	0.15
Changes in IONM			
⊿$MEPamp_{Max}$	0.1 ± 158.4	-11.4 ± 35.1	0.71
⊿$SEPamp_{Max}$	-33.6 ± 22.4	-37.7 ± 16.3	0.45
⊿$SEPlat_{Max}$	5.4 ± 8.5	5.5 ± 6.1	0.10

NS, neuromuscular scoliosis; IS, idiopathic scoliosis; Cobb's$_{pre}$, preoperative Cobb's angle; ⊿Cobb's, corrected Cobb's angle via scoliosis surgery; SBP_{Max}, Maximum systolic blood pressure; SBP_{Min}, Minimum systolic blood pressure; DBP_{Max}, Maximum diastolic blood pressure; DBP_{Min}, Minimum diastolic blood pressure; Δ$MEPamp_{Max}$, Maximum amplitude decrement of motor evoked potential compared to baseline; Δ$SEPamp_{Max}$, Maximum amplitude decrement of somatosensory evoked potentials compared to baseline; Δ$SEPlat_{Max}$, Maximum latency delay of somatosensory evoked potential compared to baseline.
a, 9 Duchenne muscular dystrophy, 5 progressive muscular dystrophy, 1 myotonic muscular dystrophy, 1 limb-girdle muscular dystrophy; b, 1 Lennox-Gastaut syndrome, 1 Dandy-Walker syndrome, 1 Cardiofaciocutaneous syndrome, 1 bacterial meningitis, 1 lipomeningomyelocele. *, *P* value < 0.05.

Table 2. Regression analysis for intraoperative MEPs and SEPs in neuromuscular and idiopathic scoliosis surgery.

Variables	ΔMEP_{Max}		Δ$SEPamp_{Max}$		Δ$SEPlat_{Max}$	
Scoliosis	NS	IS	NS	IS	NS	IS
Age	0.70	0.29	0.56	0.56	0.24	0.88
Height	0.37	0.67	0.50	0.20	0.26	0.91
Weight	0.83	0.66	0.50	0.98	0.70	0.66
Preoperative motor score	0.88		0.48		0.81	
Cobb's$_{pre}$	0.51	0.10	0.29	0.78	0.10	0.05
⊿Cobb's	0.72	0.86	0.44	0.33	0.33	0.13
Fixation level	0.15	0.08	0.23	0.54	0.24	0.75
Operation duration	0.83	0.15	0.05	0.27	0.78	0.41
Bleeding amount	0.52	0.19	0.13	0.77	0.04*	0.58
SBP_{Max}	0.50	0.83	0.26	0.66	<0.01*	0.50
SBP_{Min}	0.72	0.50	0.75	0.27	0.84	0.49
DBP_{Max}	0.63	0.54	0.65	0.59	0.01*	0.33
DBP_{Min}	0.44	0.09	0.94	0.07	0.21	0.89

NS, neuromuscular scoliosis; IS, idiopathic scoliosis; Cobb's$_{pre}$, preoperative Cobb's angle; ⊿Cobb's, corrected Cobb's angle via scoliosis surgery; SBP_{Max}, Maximum systolic blood pressure; SBP_{Min}, Minimum systolic blood pressure; DBP_{Max}, Maximum diastolic blood pressure; DBP_{Min}, Minimum diastolic blood pressure; Δ$MEPamp_{Max}$, Maximum amplitude decrement of motor evoked potential compared to baseline; Δ$SEPamp_{Max}$, Maximum amplitude decrement of somatosensory evoked potentials compared to baseline; Δ$SEPlat_{Max}$, Maximum latency delay of somatosensory evoked potential compared to baseline. *, *P* value < 0.05.

Conclusion: These results represent that the bleeding amount and the following hemodynamics are important factors to make the SEP latency prolonged in NS.

Disclosure: Nothing to disclose.

EPO-532 | Feasibility study of predicting functional outcome after cardiac arrest, evaluating the effects of trial-prognostication

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Background and Aims: This study aims to evaluate the safety of predicting functional outcome after cardiac arrest by evaluating the effects of trial-prognostication in the yet largest randomized cardiac arrest cohort.
Methods: Retrospective analysis of the prospective Targeted Hypothermia versus Targeted Normothermia after Out-of-Hospital Cardiac Arrest (TTM2)-trial. Patients with available functional outcome at six months were included. The prognostic accuracy of conservative TTM2-trial criteria and the effects of hypothermia were assessed.
Results: We included 1829/1861 (98.3%) patients (Fig. 1). Trial prognostication according to conservative TTM2-trial criteria was performed in 881 patients at median 110 (IQR: 98–133) hours with sedation weaned off for median 13 (IQR: 1–48) hours (Table 1). Withdrawal of life-sustaining therapy (WLST) was performed in 324/881 (36%) and 345/948 (36%) of the trial-prognosticated and non-prognosticated patients at median 141 (IQR: 109–195) and 53 (IQR: 21–86) hours, respectively. Neurological cause to WLST was more common and performed at later timepoints in the trial-prognosticated patients than in the non-prognosticated cohort, 270/324 (83%) at median 133 (IQR: 105–172) hours vs 78/345 (23%) at 90 (IQR: 74–112) hours, respectively ($p < 0.001$). Poor functional outcome was found in 476/811 (54%) and 509/948 (54%) in trial-prognosticated and non-trial prognosticated patients, respectively. TTM2-trial prognostication identified 47% (95% CI: 42–52%) of poor outcome patients (Table 1). Patients randomized to hypothermia woke up significantly later than normothermic patients, at median 72 (IQR; 47–119) hours vs 61 (IQR: 45–102) hours, respectively ($p = 0.00186$) (Fig. 1).

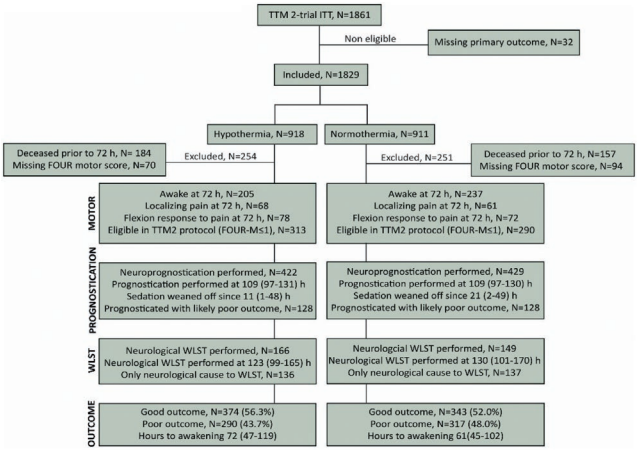

FIGURE 1

Table 1. Descriptive table of patient prognostication within TTM2-trial

	Trial prognostication performed, N=881	No trial prognostication, N=948
Motor response at prognostication[a]		
Awake	302/872 (34.6)	140/250 (56.0)
Localising pain	79/872 (9.1)	24/250 (9.6)
Flexion response	102/872 (11.7)	18/250 (7.2)
Extensor response	73/872 (8.4)	7/250 (2.8)
No response	316/872 (36.2)	61/250 (24.4)
Missing motor score	9	295
Dead		403 (35.9)
Prognostication and WLST		
Hours to prognostication	110 (98-133)	
Premature prognostications ≤96 h *count (min-max)*	12 (76-95)	
Hours without sedation at prognostication	13 (1-48)	
Likely poor neurological outcome	264 (30.0)	
WLST performed	324 (36.8)	345 (36.4)
Hours to WLST	141 (109-195)	53 (21-86)
Neurological WLST	270 (30.6)	78 (8.2)
Hours to neurological WLST	133 (105-174)	90 (73-110)
Outcome mRS		
Poor (4-6)	476 (54.0)	509 (53.9)
Dead prior to 96 h	41/420 (9.8)	403/491 (82.1)

Conclusion: Trial prognostication is associated with higher rate of neurological WLST and delayed WLST compared to non-prognosticated patients. Hypothermia is associated with longer time to awakening.
Disclosure: Nothing to disclose.

EPO-533 | A consensus conference on care pathways for individuals with post-anoxic disorder of consciousness (CaPIADoC)

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Background and Aims: Accurately evaluating the level of consciousness and promptly identifying neurological complications in intensive care settings are pivotal for proper prognostication and personalized treatment in patients with post-anoxic disorders of consciousness (DoC). This Consensus Conference, organized across multiple Italian scientific societies, aimed to tackle ongoing debates surrounding diagnostic and prognostic strategies.
Methods: Twelve working groups, comprising 22 professionals from diverse disciplines and representing 9 scientific societies along with 2 associations of patients' families, performed a systematic review of the literature to address 12 key questions - 5 focusing on diagnosis and 7 on prognosis. The included studies were assessed for quality of evidence using the Oxford Centre for Evidence-Based Medicine Levels of Evidence. Based on these findings and expert opinion, a jury comprising members

from scientific societies and family associations developed recommendations.

Results: Out of 1,219 articles initially identified, 21 were included in the analysis. Each working group provided insights into the strengths and weaknesses of the evidence addressing their specific question. A key recommendation was to adopt a multimodal approach, integrating validated clinical tools, neurophysiological tests, and neuroimaging techniques for diagnostic and prognostic evaluations, enabling tailored treatment plans. Additionally, the use of standardized terminology and diagnostic criteria was strongly encouraged to ensure uniformity and appropriateness in managing patients.

Conclusion: This multidisciplinary Consensus Conference has established the first set of operational recommendations to guide clinical practice for patients with post-anoxic DoC. Periodic updates will be required to incorporate new evidence and enhance the current guidelines over time.

Disclosure: No disclosures.

EPO-534 | Impact of fever prevention on acute cerebrovascular injury outcomes: A meta-analysis of randomized controlled trials

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Background and Aims: Fever occurrence in patients with acute vascular brain injury, may contribute to poorer outcomes. However, the effectiveness of the interventions in improving functional recovery and reducing mortality is still unclear.

Methods: A systematic search was conducted in the MEDLINE, Cochrane, Web of Science, and Embase databases for Randomized Controlled Trials investigating patients with Acute Vascular Brain Injury and the effects of fever prevention. Data were analyzed using the inverse variance method with 95% confidence intervals (CIs). Heterogeneity was assessed using the I^2 statistic. Statistical analysis was performed using RStudio, version 4.3.2.

Results: We included 9 studies and 9,687 patients. Compared with standard care, fever prevention achieved better rates of brain injury (45%–42%; OR 1.11; 95% CI 1.01–1.22; $p=0.029227$; $I^2=0\%$). The outcome of fever burden was statically desfavorable to the fever prevention group (MD = −0.63; 95%; CI −1.80 to 0.53; $p=0.285593$; $I^2=96\%$), while there was a lower incidence of sepsis (RR = 0.68; 95% CI 0.37–1.27; $p=0.65$; $I^2=0\%$). The outcome of pneumonia was statistically favorable to standard care group (RR = 1.10; 95% CI 0.90–1.34; $p=0.361892$; $I^2=0\%$). Also resulted of death was not statistically favorable for both groups (15% vs 17% RR = 0.96; 95% CI 0.81–1.12; $p=0.592765$; $I^2=46\%$).

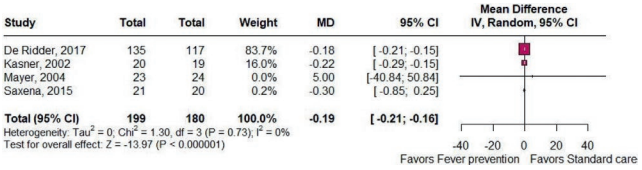

FIGURE 1 Temperature

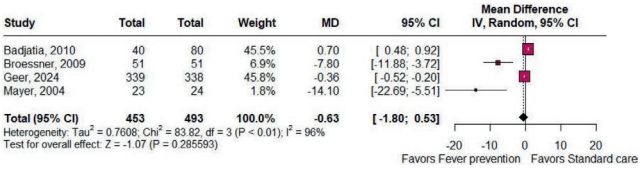

FIGURE 2 Ferver burden

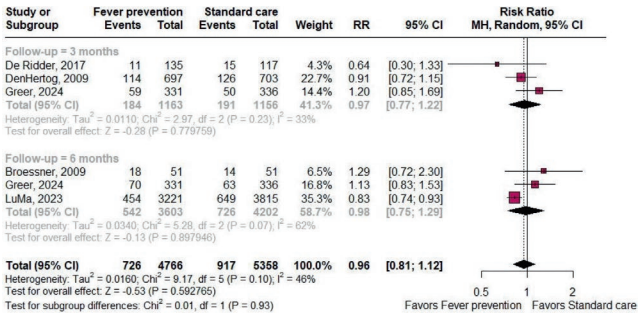

FIGURE 3 mRS = 6

Conclusion: This meta-analysis demonstrated that the use of antipyretics or temperature control devices for effective fever control resulted in decreased complications like sepsis and pneumonia in patients with acute vascular brain injury.

Disclosure: Nothing to disclose.

EPO-535 | Spontaneous eyes movement in comatose patients: radiological findings, etiology and outcome

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Background and Aims: Spontaneous eye movements (SEM) in comatose patients often signal a poor prognosis; they are usually classified as vertical (bobbing, dipping) and horizontal (ping pong, periodic alternating gaze). The aim is to assess neurological diagnosis, radiological correlations, and the outcome associated with SEM.

Methods: Observational study involving two cohorts of adult patients. One comprises patients prospectively collected from a community hospital's ICU (Sion, Switzerland) between 2016 and 2020. The second one is a retrospective cohort from a university hospital (Boston, USA) identified based on a keyword search in patients' medical files data. Patients with vertical and horizontal eyes movements were compared.

Results: We studied 85 patients (21 patients in the prospective and 64 patients in the retrospective cohort) (Table 1). Median age was 56.8 years (range: 18–92). The most frequent diagnoses were cerebral anoxia (41.2%), posterior fossa stroke (22.4%), and traumatic brain injury (7.1%); other conditions accounted for 29.3%. Vertical SEM were more common (82.4%) than horizontal. Multifocal/diffuse and posterior fossa lesions were more frequent in vertical movements, while anoxia was more prevalent in horizontal SEM. Imaging was unremarkable in 20% of cases in both groups. The overall prognosis was poor, with a median mRS of 6 (range 0−6) without difference between the two groups. Four patients only reached a mRS ≤2 at discharge.

		Total (85)	Vertical gaze (70)	Horizontal gaze (15)	
Age	Median, range	56.78 (18 – 92)	55.77 (22-85)	61.47 (18-92)	P = 0.215
Male	N (%)	51 (60)	45 (64.29)	6 (40)	P= 0.134
Imaging	N (%)				P = 0.010
- Diffuse/multifocal		36 (42.35)	31 (44.29)	5 (33.33)	
- Unremarkable		17 (20.00)	14 (20.00)	3 (20.00)	
- Focal posterior fossa		14 (16.47)	13 (18.57)	1 (6.67)	
- Cortical focal		8 (9.41)	7 (10)	1 (6.67)	
- n/a		10 (11.77)	5 (7.14)	5 (33.33)	
Diagnosis (in order of frequency)	N (%)				P= 0.012
- Brain anoxia		35 (41.18)	27 (38.57)	8 (53.33)	
- Posterior fossa stroke (incl. pontine hemorrage)		19 (22.35)	18 (25.71)	1 (6.67)	
- TBI		6 (7.06)	3 (4.29)	3 (20.00)	
- Autoimmune encephalitis		4 (4.71)	2 (2.86)	2 (13.33)	
- Metabolic encephalopathy		4 (4.71)	4 (5.71)	0 (0.00)	
- Other		17 (20.00)	16 (22.86)	1 (6.67)	
mRanking score at discharge	Median, range	6 (0-6)	6 (0-6)	5 (2-6)	P = 0.161

FIGURE 1 Comparison of comatose patients with vertical and horizontal spontaneous eyes movements. Other diagnostic includes 3 bacterial meningitis, 3 brain tumor; 2 SDH, 2 multifocal embolic strokes, 1 status epilepticus, 1 SAH, and 5 non available n/a.

Conclusion: Despite different movement axis and the more frequent correlation of vertical SEM with diffuse and posterior fossa lesions than horizontal SEM, both are strongly associated with extreme poor prognosis.

Disclosure: Nothing to disclose.

EPO-536 | Performance of four different EWS for predicting adverse outcomes in hospitalized patients with neurological conditions

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Background and Aims: Early warning systems (EWS) are crucial for detecting clinical deterioration. They reduce mortality rates and facilitate transfers to critical areas without requiring emergency procedures. No EWS has been specifically designed for hospitalized patients with neurological conditions. We aimed to evaluate different EWS and create a new EWS for neurological diagnosis.

Methods: We conducted a retrospective study. The sample was subdivided into neurological and neurosurgical. The performance of the EWS, was assessed at different times of hospitalization, in predicting the composite outcomes (urgent transfer to a critical area and in-hospital death). The AUC was calculated, and calibration was analyzed through probability plots. We developed a new predictive score; the sample was randomly divided into derivation and validation datasets. A multivariate logistic regression was applied to evaluate the association between physiological parameters and clinical outcomes. Subsequently we assess the discriminatory performance of the new EWS.

Results: The evaluated EWS performed below the levels reported in the literature. mREMS demonstrated the best predictive ability for composite outcomes. All patients, neurological and neurosurgical. AUC: 0.68 (0.602–0.758), 0.754 (0.649–0.86) and 0.646 (0.551–0.74) respectively. The proposed model was superior to all EWS to predict the composite outcome for neurological patients. AUC of new model 0.782 (0.611–0.953).

Prediction Timing	Outcome	NEWS-2	mREMS	RAPS	GCS
During hospitalization (predictors measured at admission)	*In-hospital mortality*	**0.777 (0.613-0.942**	**0.739 (0.665-0.812)**	0.434 (0.297-0.572)	0.533 (0.366-0.701)
	Urgent transfer to a critical care unit	0.566 (0.451-0.682)	**0.658 (0.581-0.735)**	0.597 (0.5-0.693)	0.524 (0.422-0.626)
	Composite outcome	**0.597 (0.488-0.706)**	**0.68 (0.611-0.748)**	0.572 (0.481-0.662)	0.52 (0.426-0.614)
During the next 8 hours	*In-hospital mortality*	**0.916 (0.84-0.992)**	**0.815 (0.723-0.908**	0.491 (0.359-0.623)	0.53 (0.363-0.696)
	Urgent transfer to a critical care unit	0.596 (0.478-0.715	**0.654 (0.567-0.741)**	**0.611 (0.528-0.694)**	0.535 (0.432-0.639)
	Composite outcome	**0.649 (0.54-0.757)**	**0.68 (0.602-0.758)**	0.582 (0.502-0.662)	0.529 (0.434-0.624)

Table 5. The areas under the ROC curve with 95% confidence intervals (CI) are shown. Highlighted values indicate tests that predict significantly better than chance (i.e., the 95% CI does not cross 0.5).

Table 5. Area Under the ROC Curve in Patients with Surgical and Non-Surgical Neurological Conditions.

Table. for the 4 EWS studied, with the area under the ROC curve for the composite outcome anda secondary outcomes, for all patients.

	Score					
Predictor	2	1	0	1	2	3
Type of patient			Women without surgical condition	All other patients		
Age (years)	≤39		40-59			≥60
Heart rate (bpm)		≤69	70-89		≥90	
Respiratory rate (rpm)			≤19	≥20		
Temperature (°C)		≤35.9	≥36.0			
Need for suplemental O2			No	Yes		
GCS	≤13		≥14			

Table 10. Scores of the new scale to predict adverse outcomes in patients with neurological conditions.

Prediction Timing	Outcome	New Score	NEWS-2	mREMS	RAPS	GCS
During hospitalization (predictors measured at admission)	*In-hospital mortality*	**0.787 (0.534-1)**	**0.806 (0.547-1)**	**0.773 (0.653-0.893)**	0.522 (0.261-0.783)	0.5 (0.237-0.763)
	Urgent transfer to a critical care unit	0.638 (0.299-0.977)	0.685 (0.307-1)	**0.69 (0.561-0.819)**	0.488 (0.161-0.815)	0.5 (0.165-0.835)
	Composite outcome	**0.787 (0.534-1)**	**0.806 (0.547-1)**	**0.773 (0.653-0.893)**	0.522 (0.261-0.783)	0.5 (0.237-0.763)
During the next 8 hours	*In-hospital mortality*	**0.832 (0.569-1)**	**0.853 (0.673-1)**	**0.782 (0.611-0.953)**	0.579 (0.375-0.783)	0.494 (0.235-0.753)
	Urgent transfer to a critical care unit	0.723 (0.325-1)	0.756 (0.497-1)	0.696 (0.473-0.919)	**0.669 (0.506-0.832)**	0.494 (0.163-0.825)
	Composite outcome	**0.832 (0.569-1)**	**0.853 (0.673-1)**	**0.782 (0.611-0.953)**	0.579 (0.375-0.783)	0.494 (0.235-0.753)

Table 11. Area under the ROC curve in patients with non-surgical neurological conditions

Table with the new proposed EWS score and table with the area under the ROC curve for the composite outcome anda secondary outcome, for neurological patients.

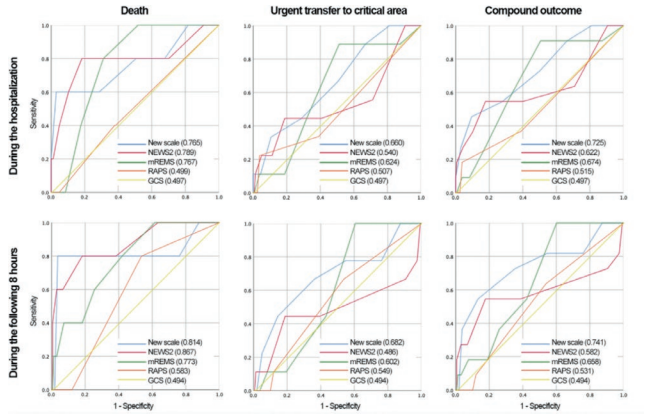

Figure with ROC curve for 4 EWS and new EWS proposed.

Conclusion: EWS in neurological diagnosis, can improve, if adjusted to include specific clinical variables. From the EWS use in today's practice; mREMS system is recommended for all neurological conditions due to its superior predictive power. For neurological patients they could benefit more from the new EWS score proposed in this paper.
Disclosure: Nothing to disclose.

EPO-537 | Neuroendoscopy is better than conventional cranitomy in treating intracranial hemhorrage

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Background and Aims: Intracranial Hemorrhage has high mortality and morbidity, and there's still doubts in the medical community about what should be the standard approach. When compared to conventional craniotomy, neuroendoscopy is less invasive and may be a viable alternative.
Methods: PubMed, EMBASE, and Cochrane databases were systematically searched for studies that compared craniotomy to neuroendoscopy in intracranial hemorrhage and reported: (1) surgery/anesthesia time; (2) hematoma drainage rate; (3) blood loss rate; (4) mortality rate; (5) complication/infection rate; (6) Modified Rankin Scale. Heterogeneity was examined with I2 statistics. P values of <0.05 were considered statistically significant.
Results: A total of 6 randomized controlled trials (RCTs) and 13 retrospective studies (non-RCTs) involving 1922 patients were included in the final analysis. Minimum follow up was 1 month post operation. Operation time (SMD −3.32; 95% CI [−4.08] to [−2.55]; $p<0.00001$), Evacuation rate (SMD 1.18; 95% CI 0.73–1.62; $p<0.00001$), Blood loss (SMD −3.34; 95% CI [−4.30] to [−2.39]; $p<0.00001$), Mortality (RR 0.69; 95% CI 0.53–0.90; $p=0.006$), Infection rate (RR 0.53; 95% CI 0.40–0.71; $p<0.0001$) were all in favour of the efficacy of neuroendoscopy when compared to craniotomy. Rebleeding (RR 0.62; 95% CI 0.37–1.07; $p=0.09$) and Modified Rankin Scale (SMD -0.44; 95% CI [−1.01] to [0.12]; $p=0.13$) were not considered statistically significant.
Conclusion: These findings suggest that neuroendoscopy has superior efficacy to conventional craniotomy as a drainage procedure in patients with intracranial bleeding.
Disclosure: Nothing to disclose.

EPO-538 | Clinical features of neurological disorders in Hatay after the February 6 earthquake

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Background and Aims: This study aimed to evaluate the clinical features, mood, and sleep quality of patients with Alzheimer's Disease (AD), Epilepsy, Multiple Sclerosis (MS), and Parkinson's Disease (PD) followed in the Neurology Outpatient Clinic at Hatay Mustafa Kemal University Hospital after the February 6 earthquake.
Methods: A total of 200 patients (50 from each group) participated. Depression, anxiety, and sleep quality were assessed using the Beck Depression Inventory (BDI), Beck Anxiety Inventory (BAI), and Pittsburgh Sleep Quality Index (PSQI).
Results: Among AD patients, 78% experienced clinical deterioration, with 84% showing depression, 90% anxiety, and all having poor sleep quality. A negative correlation was found between MMSE scores and sleep quality ($p=0.042$). In the epilepsy group, 54% had increased seizure frequency, with higher seizure

occurrence among those staying in containers ($p=0.041$). Depression and anxiety were present in 46%, and 60% had poor sleep quality. In the MS group, 62% reported seizures after the earthquake, and depression, anxiety, and poor sleep quality were found in 52%, 50%, and 70%, respectively. Low education levels were associated with higher depression and anxiety ($p<0.05$). For PD patients, 64% experienced clinical deterioration, linked to diagnosis duration, Hoehn-Yahr stage, and container housing ($p<0.05$). Depression, anxiety, and poor sleep quality were found in 56%, 68%, and 86%, respectively.

Conclusion: Clinical deterioration was observed across all groups, strongly associated with increased depression, anxiety, and poor sleep quality. These findings highlight the significant impact of the earthquake on the health and well-being of patients with neurological conditions.

Disclosure: Nothing to disclose.

EPO-539 | Sepsis associated encephalopathy-prevalence and related clinical factors

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Background and Aims: Sepsis-associated encephalopathy (SAE) is a common complication of sepsis, significantly increasing mortality among patients and potentially leading to long-term neurological deficits. The study aimed to determine the frequency and clinical factors related to development of SAE in acute phase of sepsis.

Methods: Sepsis was diagnosed based on a SOFA scale score ≥2. SAE was diagnosed in situations of acute worsening of cognitive functions and consciousness, temporarily related to symptoms of sepsis. Data on patients clinical course, mortality and laboratory tests were retrospectively collected.

Results: 443 cases of sepsis were identified with 240 cases of SAE. The most common neurological impairments were communicative disorders (97.6%), confusion (76.8%), and drowsiness (60%). 125 septic patients died, including 109 with SAE. Procalcitonin levels were higher in patients with SAE. Patients developing SAE were more severely burdened by comorbidities.

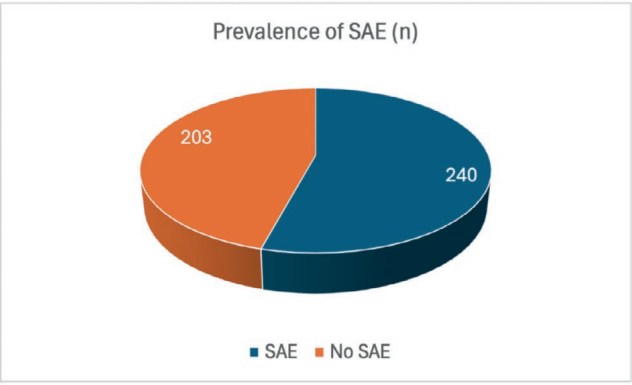

FIGURE 1 Prevalence of SAE in septic patients

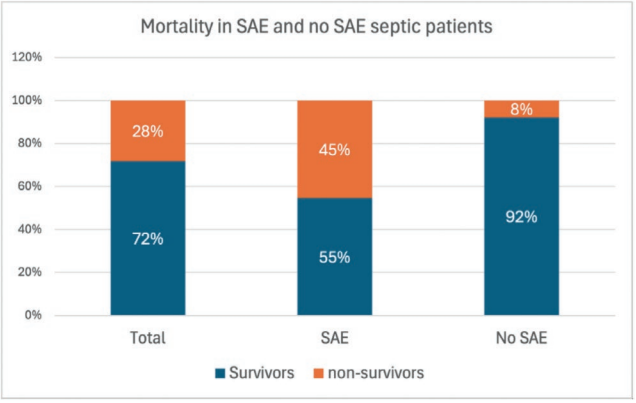

FIGURE 2 Mortality in SAE and Non-SAE groups of septic patients

Conclusion: SAE is a frequent but still under diagnosed neurological complication of sepsis strongly increasing probability of patient's death. Our data suggest that development of SAE is related to intensity of generalized inflammatory process measured with procalcitonin. Risk of SAE increases in parallel to burdens of comorbidities.

Disclosure: Nothing to disclose.

EPO-540 | Stimulants for disorders of consciousness in ICU patients: Randomized, placebo-controlled, cross-over trial

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Background and Aims: In the intensive care unit (ICU), there is a critical need for therapeutic strategies that promote consciousness recovery. We evaluated apomorphine and methylphenidate in brain injury patients with acute disorders of consciousness (DoC), hypothesizing that the stimulants would enhance consciousness biomarkers assessed by automated pupillometry (I) and improve clinical signs of consciousness (II).

Methods: We randomized 50 ICU patients with DoC (14 women; mean age 63 ±10 years; 48 with non-traumatic brain

injuries) into strata of three consecutive treatment sessions with apomorphine, methylphenidate or placebo. We administered 112 study medications: 36 apomorphine, 39 methylphenidate and 37 placebo. Automated pupillometry recordings ($n = 590$) from 48 (96%) patients were analyzed.

Results: Cognitive load during mental arithmetic was identified in 70 (12%) recordings. Seven (15%) patients fulfilled criteria for cognitive motor dissociation. Apomorphine (OR 1.35, 95% CI: 0.93–1.96) and methylphenidate (OR 1.29, 95% CI: 0.89–1.86) did not significantly increase cognitive load per pupillometry. In total, 10 (20%) patients showed improved clinical arousal at least once: 1 after placebo, 4 after apomorphine (OR 5.04, 95% CI: 0.56–120.7), and 7 after methylphenidate (OR 9.96, 95% CI: 1.36–235.8). Changes toward higher consciousness levels followed 1 placebo, 4 apomorphine (OR 5.67, 95% CI 0.63–169.46), and 3 methylphenidate doses (OR 3.41, 95% CI 0.34–88.00).

Conclusion: While pupillometry revealed no significant effects on covert cognition, stimulants may have triggered clinical arousal in some patients. Replication is needed. Our results should guide future pharmacological trials aimed at improving arousal and consciousness recovery. DoC patients may have cerebral reserves that can be activated in the ICU.

Disclosure: Nothing to disclose.

EPO-542 | Decompressive craniectomy versus conservative management for spontaneous intracranial hemorrhage: A meta-analysis

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Background and Aims: Spontaneous intracerebral hemorrhage (sICH) is a significant contributor to stroke-related morbidity and mortality worldwide. Despite recent advancements in pharmacological and surgical management, outcomes remain challenging. Recent studies suggest that decompressive craniectomy (DC) may offer benefits over best medical treatment (BMT) in certain sICH cases. This study aims to compare DC versus BMT with respect to neurological function, morbidity, and mortality in patients with sICH.

Methods: PubMed, EMBASE, Cochrane and Web of Science databases were searched for randomized and observational studies comparing DC with conservative management alone for treatment of patients with sICH. The outcomes analyzed were modified Rankin Scale (mRS), mortality at 30 days, overall mortality and length of hospital stay. Odds ratio (OR) and mean difference (MD) were calculated for binary and continuous outcomes, respectively.

Results: Of the 1182 studies initially identified, 8 met the inclusion criteria for quantitative analysis. These studies included 746 patients, with 345 undergoing DC and 375 receiving conservative management. BMT alone was associated to a poor neurological function (mRS of 5–6) (OR 0.44; 95% CI 0.24–0.78; p-value 0.005; $I^2 = 39{,}8\%$), higher mortality at 30-days and at last follow up (OR 0.36; 95% CI 0.19–0.66; p-value 0.001; $I^2 = 0\%$), (OR 0.33; 95% CI 0.21–0.52; p-value < 0.001; $I^2 = 34{,}8\%$), respectively. Length of hospital stay was superior in the DC cohort, but without statistical significance (MD 16.05; 95% CI −3.24 to 35.34; p-value 0.1; $I^2 = 92.9\%$).

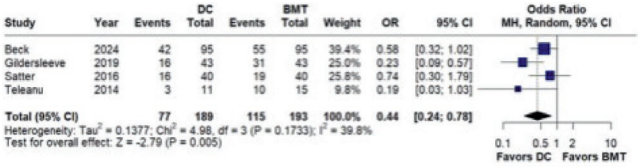

Figure 1: Forest plot for mRS 5-6 at last follow up.

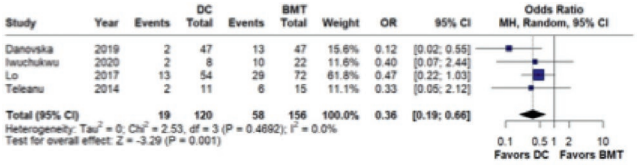

Figure 2. Forest plot for 30-days mortality.

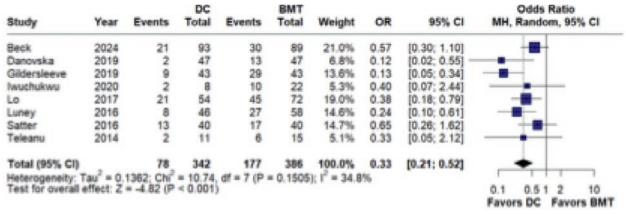

Figure 3. Forest plot for mortality at last follow-up.

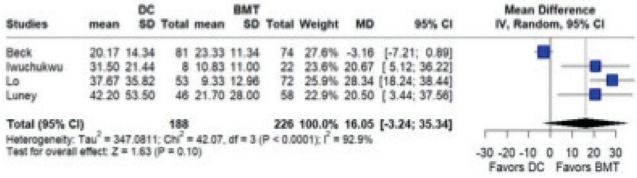

Figure 4. Forest plot for length of hospital stay.

Conclusion: In patients with sICH, DC is associated with a reduced mortality and better neurological function, despite superior length of hospital stay, when compared to best medical treatment alone.

Disclosure: Nothing to disclose.

EPO-543 | Intraoperative salvage red blood cell transfusion on total blood transfusion in spine surgery: A meta-analysis

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[1]Departament of Medicine, University of West of Santa Catarina, Joaçaba, Brazil; [2]Healthcare Institution of South Iceland, Selfoss, Iceland; [3]Faculty of Medical Sciences in Zabrze, Medical University of Silesia, Katowice, Poland; [4]Escola Superior de Ciências da Santa Casa de Misericórdia de Vitória, Vitória, Brazil; [5]Jinnah Medical and Dental College, Karachi, Pakistan; [6]Department of Neurosurgery, Hospital Nacional Edgardo Rebagliati Martins, Lima, Peru; [7]NOESC (Universidade do Oeste de Santa Catarina), Brazil; [8]Higher School of Sciences of the Holy House of Mercy of Vitória (EMESCAM), Vitória, Brazil

Background and Aims: Blood transfusion is a common practice in spine surgery, associated with potential complications. Intraoperative salvage red blood cell (SRBC) transfusion is a blood conservation technique that reinfuses a patient's own blood collected during surgery. This study aims to assess the impact of intraoperative SRBC transfusion on total blood transfusion volume in spine surgery.
Methods: PubMed, Embase, Web of Science, and the Cochrane Library were searched for randomized and observational studies evaluating the intraoperative use of SRBCs. Outcomes assessed included autologous transfusion rates, estimated blood loss, intraoperative allogeneic transfusion rates, operative time, postoperative allogeneic transfusion rates, and total transfusion requirements. Odds ratios (ORs) were calculated for binary outcomes, while mean differences (MDs) were calculated for continuous outcomes.
Results: A total of 14 studies involving 1,660 patients were included in the meta-analysis. 44% underwent ISRBC. No significant difference was seen between ISRBC and control for AT (MD 456.99 mL; 95% CI 369.90–564.58; $I^2 = 97\%$), IAT (MD -0.33; 95%CI -0.81 to 0.14; $p = 0.17$; $I^2 = 97\%$), PAT (MD -0.24; 95% CI -0.49 to 0.02; $p = 0.07$; $I^2 = 76\%$), PT (OR 0.57; 95% CI 0.30-1.11; $p = 0.1$; $I^2 = 67\%$) and TT (OR 0.92; 95% CI 0.43-1.98; $p = 0.836$; $I^2 = 83\%$). However, EBL (MD 150.76mL; 95%CI 36.62-264.9; $p < 0.01$; I2 = 87%) and OT (MD 19.87 h; 95% CI 3.02-36.73; $p = 0.02$; $I^2 = 87\%$) significantly favored control.
Conclusion: Our results suggest no significant reduction in allogeneic transfusion rates with ISRBC transfusion in spine surgery. However, ISRBC was associated with increased estimated blood loss and operative time. Further research is needed to determine the clinical significance of these findings.
Disclosure: Nothing to disclose.

Cerebrovascular diseases 4

EPO-544 | Prognostic factors in vascular motor aphasia after music therapy

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Background and Aims: Aphasia is a language disorder linked to brain damage or dysfunction, characterized by difficulties in expression and/or comprehension. Aphasia is common after a stroke and may require lengthy, costly, and sometimes inappropriate treatments, which can hinder the patient's socio-professional life. The use of self-administered rehabilitation methods, such as music therapy, could improve the functional outcomes of aphasic patients.
Objectives: To determine the prognostic factors of post-stroke motor aphasia treated with music therapy.
Methods: This was a prospective, bi-center cohort study including patients with verbal expression disorders of vascular origin, without a history of motor aphasia or cognitive disorders. Aphasia was assessed using the LAST score. Patients were randomly divided into three groups: GBI1 (speech therapy), GBI2 (music therapy), and GNBI (no rehabilitation). Sessions were conducted for up to 3 months, with assessments made at admission, at month 1, and at month 3.
Results: A total of 55 patients were included, predominantly male, with an average age of 61 years. Broca's aphasia accounted for 2/5 of the study population. The mean LAST scores at 1 month were 8.7 for GBI1, compared to 11.4 for GBI2 and 6.3 for GNBI. At 3 months, the scores were 10.55, 13.4, and 6, respectively. The prognostic factors for vascular motor aphasia treated with music therapy included the musical environment, the type of stroke, and the automatic series. These factors were associated with the LAST score dimensions of naming, repetition, and automatic series.
Conclusion: Music therapy improves aphasia of vascular origin.
Disclosure: Nothing to disclose.

EPO-545 | Evaluation of risk factors in stroke patients with paroxysmal atrial fibrillation (PAF) and development of a risk score

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[1]Department of Neurology, University of Health Sciences, Prof. Dr. Cemil Tascioglu City Hospital, Istanbul, Turkey; [2]Department of Cardiology, University of Health Sciences, Prof. Dr. Cemil Tascioglu City Hospital, Istanbul, Turkey

Background and Aims: Our study aims to develop a new scoring system to assess the risk of paroxysmal atrial fibrillation (PAF) in stroke patients, helping to identify the correct patient group and prevent recurrent strokes.

Methods: 940 stroke patients included and divided into two groups: 261 with PAF, 679 non-PAF. Logistic regression analysis was performed to assess risk factors.

Results: In our study, stroke history, temporal summation in the anterior/posterior circulation, gender, age, hypertension, dyslipidemia, ischemic heart disease, APC on ECG, MRS>2, NIHSS>5 were identified as risk factors for PAF. Infarction in the MCA and in multiple-vascular areas was more likely to be associated with PAF ($p < 0.001$). Infarction in the inferior division of the MCA and the isolated occipital/occipitotemporal areas increased the risk for PAF. All cortical borderzone ischemias were seen in the PAF group. The ischemic patterns associated with PAF were confluent-additional and small-scattered lesions ($p < 0.001$). Infarctions in the cortical, bilateral and anterior/posterior circulations, elevated T4, moderately reduced ejection fraction, left atrial enlargement, moderate/greater mitral insufficiency or accompanying mitral stenosis were additional parameters that increased the risk of PAF. Risk-reducing factors included smoking, basilar, lateral thalamic and internal borderzone infarction. After determining the parameters in the score, a user interface was designed using the free licensed Python language (v.3.9.0), creating a new risk scoring system for PAF.

Risk Parameters in Our Scoring System
Age
Gender (Female)
Hypertension
Dyslipidemia
Ischemic Heart Disease (Ref: None)
APC
MRS (Ref: ≤2) >2
NIHSS (Ref: ≤5) >5
Prior Ischemic Stroke
- In Anterior System
- Anterior and Posterior System Temporal Summation
- Number of Previous Strokes
Elevated T4
Moderately Decreased EF
LA Enlargement (mm)
- Mildly Dilated
- Moderately Dilated
- Severely Dilated
Aortic Valve Stenosis
Mitral Valve Characteristics
- Mild Mitral Insufficiency
- Mild-Moderate Mitral Insufficiency
- Moderate Mitral Insufficiency
- Severe Mitral Insufficiency
- Mitral Stenosis and Mitral Insufficiency
Vascular territory
Anatomical localisation
Pattern of Infarction
Cortical / Non-cortical
Bilateral / Unilateral
Anterior / Posterior circulation

FIGURE 1 Risk parameters in our scoring system

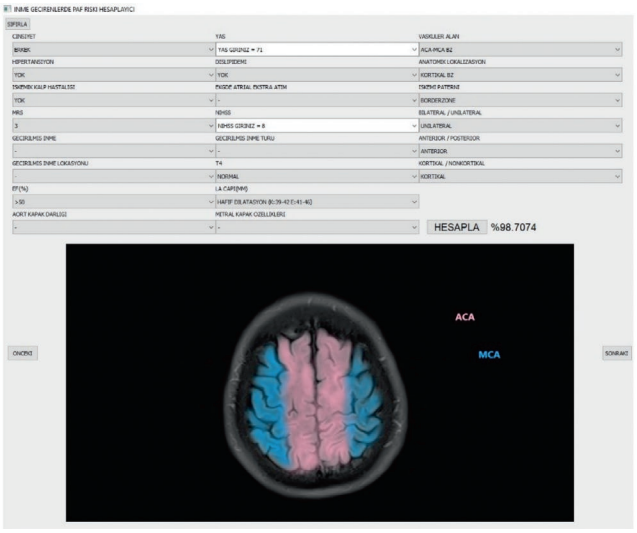

FIGURE 2 An example of PAF risk calculator

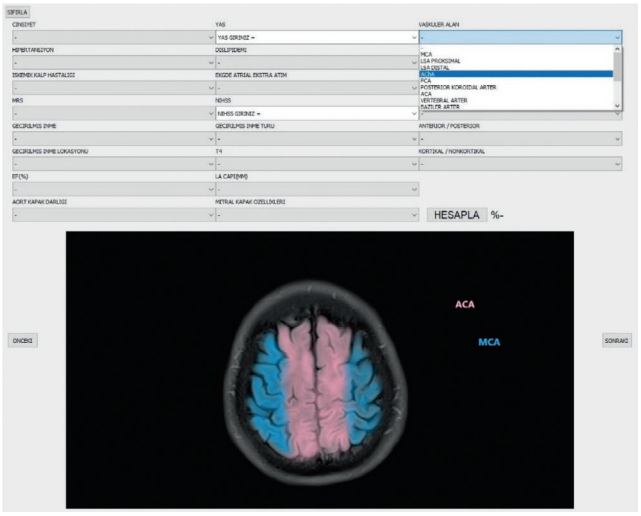

FIGURE 3 An example of PAF risk calculator

Conclusion: While existing scoring systems for PAF in ESUS patients are limited, our study introduces a novel approach by incorporating detailed topographical stroke features. Our scoring system can quickly identify patients who need advanced monitoring and anticoagulation, helping to prevent recurrent strokes.

Disclosure: Nothing to disclose.

EPO-546 | Differences in serum elabela-apelin levels in acute and chronic ischemic stroke patients with different etiologies

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Background and Aims: Apelin and elabela are components that play crucial roles in angiogenesis, with potential neuroprotective effects. This study aims to investigate serum apelin and

elabela levels in ischemic stroke patients of different etiologies in acute and chronic periods and compare them with healthy individuals.

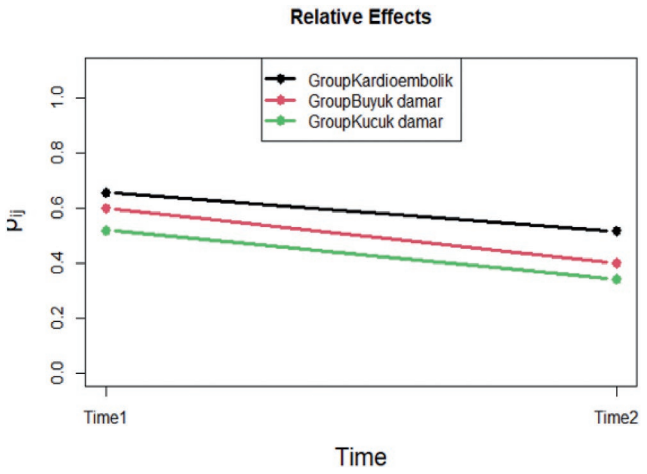
Methods: This study includes 126 patients diagnosed with ischemic cerebrovascular disease (ICVD) and 30 healthy controls. Patients were classified according to the TOAST classification into cardioembolic stroke (CES), large artery atherosclerosis (LAA), and small vessel occlusion (SVO) groups. Serum apelin and elabela levels were measured within 48 hours and at 6-month follow-up.

Results: Serum elabela levels were significantly lower in ICVD patients and subgroups during acute phase compared to healthy controls. In all patient groups, serum elabela levels significantly decreased over 6 months. Serum apelin levels didn't differ significantly between patient groups and healthy controls in acute phase. However, SVO patients had significantly lower apelin levels compared to other subgroups. Serum apelin levels decreased significantly in the LAA and CES groups, while no change was observed in the SVO group. In chronic phase, serum elabela levels were significantly lower in SVO compared to CES patients.

TABLE 1 Serum elabela comparison between patient and healthy control groups.

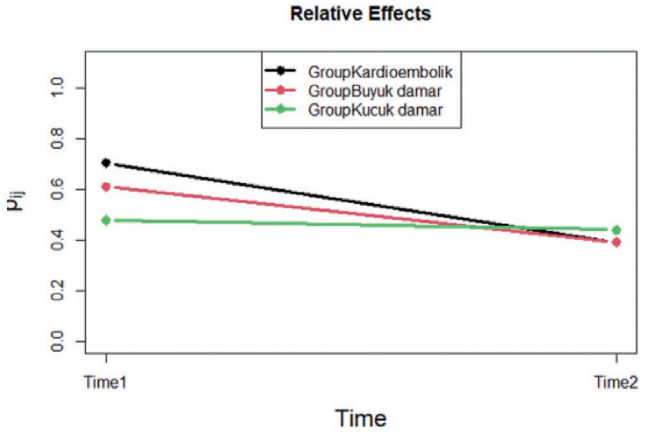
Group	Number (n)	Percentage (%)	Elabela Avg.	Sd	Med.	Min.	Maks.	p
Control	30	19,2	1.296,93	1.281,53	541,38	221,47	4.007,51	<0,001 Ω
Patient	126	80,8	464,44	459,25	361,43	53,05	3.774,91	
Control[a]	30	19,2	1.296,93	1.281,53	541,38	221,47	4.007,51	<0,001¥
CES[b]	39	25,0	527,96	590,02	364,26	86,17	3.774,91	
LAA[b]	43	27,6	430,68	195,14	366,14	157,51	1.193,54	
SVO[b]	44	28,2	441,12	512,74	354,39	53,05	3.706,94	
Total	156	100,0	624,53	765,31	384,59	53,05	4.007,51	-

Sd: Standart deviation, CES: Cardioembolic stroke,
LAA: Large artery atherosclerosis, SVO: Small vessel occlusion
ΩMann-Whitney U test
¥Kruskal-Wallis H test
[a,b]Post-hoc as a result of pairwise comparisons performed with the Mann-Whitney U test and Bonferroni correction, groups with statistically significant differences are indicated with different superscripts.



time 1: acute period, time 2: 6th month control
GroupKardioembolik: Group Cardioembolic stroke
GroupBuyuk damar: Group large artery atherosclerosis
GroupKucuk damar: Group small vessel occlusion

FIGURE 1 Temporal change of serum elabela level for each subgroup



time 1: acute period, time 2: 6th month control
GroupKardioembolik: Group Cardioembolic stroke
GroupBuyuk damar: Group large artery atherosclerosis
GroupKucuk damar: Group small vessel occlusion

FIGURE 2 Temporal change of serum apelin level for each subgroup

Conclusion: This study is the first to compare apelin and elabela levels in ICVD patients and examine their temporal changes. The fact that serum elabela levels are found to be lower in all ISVH subgroups compared to healthy controls and are related to temporal course of ISVH suggest that this parameter may be valuable for stroke.

Disclosure: Nothing to disclose.

EPO-547 | Two-year follow-up of bilateral spontaneous cervical carotid artery dissection with NOTCH1 mutation: A case report

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Background and Aims: Spontaneous cervical artery dissection (CAD) is a rare but significant cause of stroke, with genetic predispositions such as mutations in the NOTCH1 gene being even less common. NOTCH 1 mutations have been associated with arterial fragility, particularly in coronary and recurrent extracranial artery dissections. This report presents a case of bilateral cervical internal carotid artery dissection (ICAD) presenting with pulsatile tinnitus, exploring the potential role of a NOTCH1 mutation in vascular pathology.
Methods: A 46-year-old male presented with bilateral pulsatile tinnitus without ischemic symptoms. Audiometric evaluation revealed no evidence of hearing impairment.
Results: Magnetic resonance (MR) and cerebral angiography showed severe stenosis in the distal right internal carotid artery (ICA) and fusiform dilatation with intimal flaps in the left ICA with mild proximal stenosis. Next-generation sequencing (NGS) subsequently identified a heterozygous NOTCH1 mutation (p. Asn685Ile). Echocardiography ruled out coronary artery involvement. The patient was treated with dual antiplatelet therapy, and follow-up imaging over two years showed persistent but stable dissections bilaterally.
Conclusion: NOTCH1 related vascular dissections are exceedingly rare, with only a few cases documented in the literature. This case adds to the limited evidence of the mutation's role in arterial fragility and site-specific vascular involvement. Advanced imaging and genetic testing are crucial for the diagnosis and management of spontaneous CAD. This patient's stable vascular condition over two years implies that NOTCH1 mutations may predispose to dissection without rapid progression. Larger studies are needed to confirm the association and inform personalized management strategies.
Disclosure: Nothing to disclose.

EPO-548 | New discoveries in amyloid-related imaging abnormalities with hemorrhage and anti-amyloid beta monoclonal antibodies

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Background and Aims: Amyloid-related Imaging Abnormalities (ARIA) are adverse effects that occur during amyloid beta monoclonal antibody treatment for Alzheimer's disease, including edema-type ARIA and hemorrhage-type ARIA (ARIA-H). Few retrospective analyses have compared ARIA-H incidence among individual monoclonal antibodies, and a comprehensive comparison is currently lacking. After the approval of these antibodies, research has mainly focused on dosing frequency and drug dosage, leaving it unclear whether ARIA-H is associated with the specific characteristics of different monoclonal antibodies.
Methods: We compared the characteristics of 7 monoclonal antibodies marketed and under study. We chose five variables: (1) Types of Amyloid Beta Binding, (2) Polymer Affinity, (3) Binding Epitope, (4) Fc Subtype, (5) Amyloid Beta Clearance Rate.
Results: The risk of ARIA-H, from highest to lowest, is as follows: Donanemab, Aducanumab, Bapineuzumab, Lecanemab, Gantenerumab, Crenezumab, Solanezumab. Besides, ARIA-H is associated with the characteristics of monoclonal antibodies. (1) More mature Amyloid Beta clearance is associated with a higher risk of ARIA-H. (2) Lower clearance of Amyloid Beta oligomers is associated with a higher risk of ARIA-H. (3) Amyloid Beta clearance closer to the N-terminus is associated with a higher risk of ARIA-H. (4) Monoclonal antibodies with an IgG4 structure are more likely to cause ARIA-H than those with an IgG1 structure. (5) Faster achievement of Amyloid Beta clearance thresholds is associated with a higher risk of ARIA-H.
Conclusion: This research enhances our understanding of ARIA-H and may guide future monoclonal antibody drug development, which may improve the cognition and overall prognosis of Alzheimer's disease patients.
Disclosure: Nothing to disclose.

EPO-549 | Quantitative EEG can predict early functional stroke outcome after mechanical thrombectomy

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Background and Aims: Stroke caused by large artery occlusion (LAO) in the anterior circulation is a leading cause of morbidity and mortality, but mechanical thrombectomy (MT) improves functional outcomes. Quantitative electroencephalography (qEEG) allows objective assessment of functional damage and may predict clinical outcomes. This study aimed to evaluate qEEG parameters in predicting early functional clinical outcome in MT-treated anterior circulation LAO stroke patients.
Methods: We included consecutive LAO anterior circulation stroke patients treated with MT at the Neurology Clinic, University Clinical Center of Serbia, between July 20 and November 20, 2024. EEG was performed within 72h post-MT using cap electrodes (10-10 system) and NicoletOne software. Delta/alpha ratio (DAR) and (delta+theta)/(alpha+beta) ratio (DTABR) were calculated via Fast Fourier Transformation. Ischaemic volume was measured using computed tomography 24h post-MT. Early functional outcome was assessed on ex-mission using modified Rankin Scale (mRS), categorizing patients as having poor outcomes (mRS>2) or favourable outcomes (mRS< =2). Statistical analysis (SPSS V.26) included Mann-Whitney for group differences, logistic regression for predictive values, and Spearman's coefficient for correlation, with $p<0.05$ for significance.

Results: The study included 30 patients (Table 1). DTABR was significantly higher in patients with mRS>2 than mRS< =2 (0.14 vs. 0.03, $p=0.008$), while DAR showed no significant difference between groups. A DTABR cut-off at >0.1 had a positive predictive value of 83.3%, 95% CI [62.9-95.6%] for unfavourable outcomes at exmission, with odds ratio 7.0 95% CI [1.3-37.9]. No significant correlation was found between DAR, DTABR and ischaemia volume.

TABLE 1

Age [years]	68.0, 48.0-88.0 (median, interval)	
Male (%)	16 (53.3)	
Wake-up stroke (%)	5 (16.7)	
Preintervention imaging	Core volume [ml]	4.0, 0.0-68.0 (median, interval)
	Penumbra volume [ml]	167.0, 55.0-341.0 (median, interval)
	ASPECTS	10.0, 5.0-10.0 (median, interval)
Initial NIHSS score		12.0, 1.0-22.0 (median, interval)
Occlusion (%)	ACM M1 segment	23 (76.7)
	ACM M2 segment	5 (16.7)
	ACI terminal segment	2 (6.6)
TICI (%)	0	3 (10)
	1	0 (0)
	2	7 (23.3)
	3	20 (66.7)

TICI – Thrombolysis in Cerebral Infarction, ASPECTS – Alberta stroke programme early CT score, NIHSS – National Institutes of Health Stroke Scale, ACM – Middle cerebral artery, ACI – Internal carotid artery

Conclusion: qEEG is a promising tool for predicting functional outcomes in MT-treated stroke patients.
Disclosure: Nothing do disclose.

EPO-550 | A cryptogenic stroke associated with non-infectious Endocarditis and antiphospholipid syndrome

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Background and Aims: Ischemic stroke is the most common neurological complication of endocarditis. Cardiac myxoma (CM) is the most frequent type of cardiac neoplasm.The antiphospholipid syndrome (APS) occurs most commonly in the systemic lupus erythematosus.
Methods: Testing for thrombophilia, laboratory test, neurological exam, echocardiography, magnetic resonance tomography (MRI).
Results: We present a clinical case42-year old female admitted with weakness in the left foot. She weak up with difficulties in performing dorsal and plantar flexion evaluated3/5with manual muscle testing. No pathological reflexes were found.Firstly, peripheral nerve damaged was observed. After MRIof the head was performed showing ischemic stroke in the high right frontal parietal area (image 1, 2, 3, 4). After consultation with cardiologist and echocardiography, it was found endocarditis of mitral valve with mild mitral regurgitation. Patient was tested for thrombophilia with positive antiphospholipid antibodies (anticardiolipin antibodies (ACL)/+/-beta2Glicoprotein I antibodies/+/). Several sets with blood cultures were taken-all of them were negative and blood tests were negative for inflammation (normal levels for C-reactive protein, normal count for leucocytes). A surgery was performed for mitral valve with prosthesis. Biopsy of the tumor valve formation showed mitral valve myxoma (image 5). Only few clinical cases have described the coexistence of atrial myxoma and APS which was found in our patient. Interleukin-6 (IL-6) could be produced by myxoma and trigger an immunological reaction leading to the secondary APS.

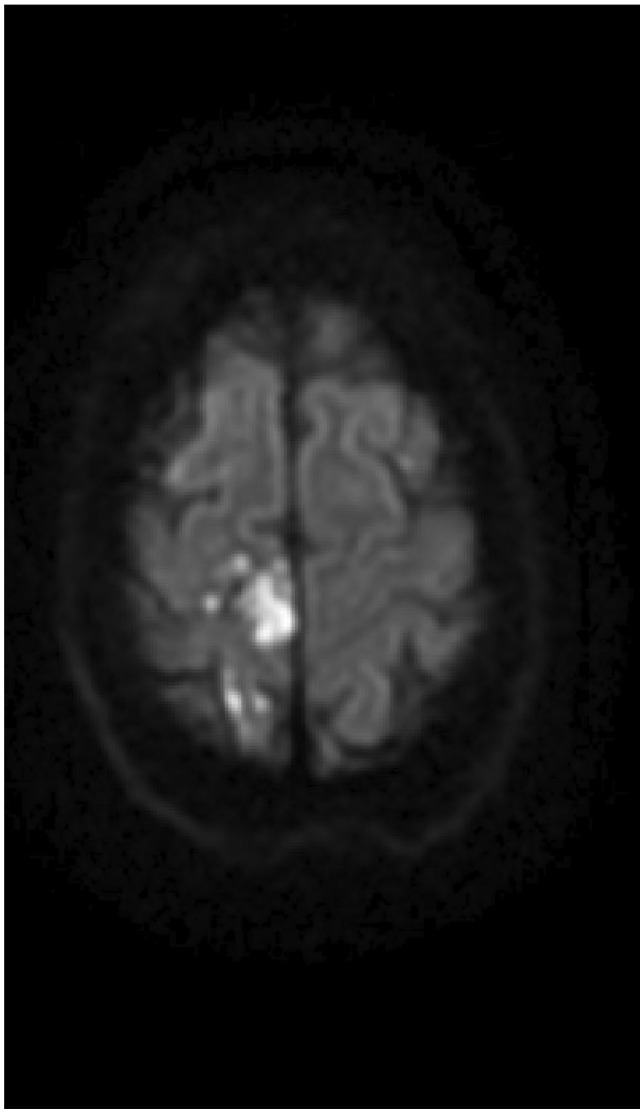
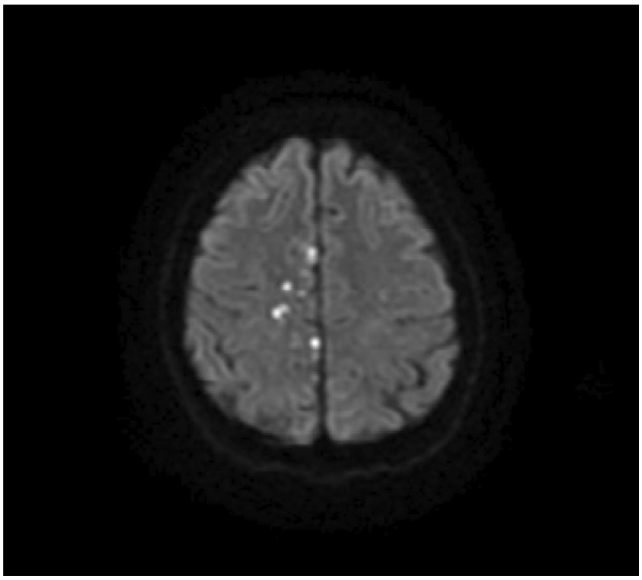


image 1



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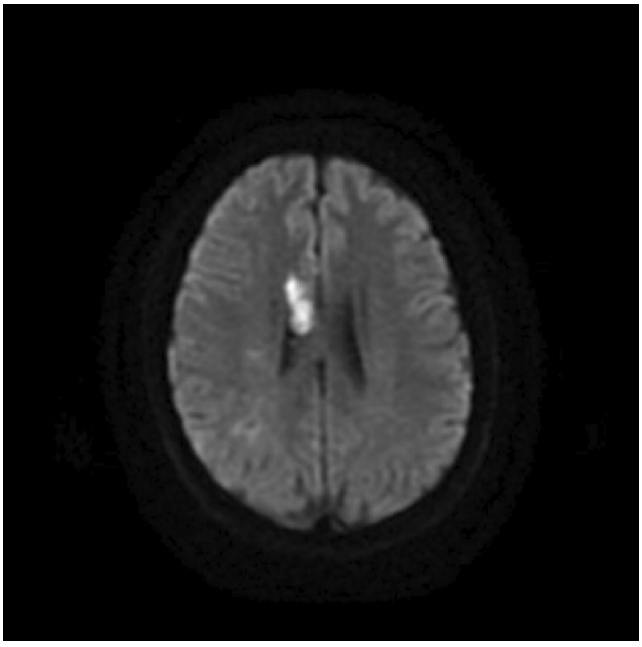

image 3

Conclusion: Endothelial injury from circulating cytokines such as tumour necrosis factor or interleukins in a hypercoagulable state patient causes platelets aggregation in the affected valves.It is mandatory to check them for underlying malignancy,systemic lupus erythematosus,antiphospholipid antibody syndrome.Non infectious endocarditis should be excluded in young adults with cryptogenic stroke.
Disclosure: Nothing.

EPO-551 | Risk factors for the epileptic seizures in cerebral venous sinus thrombosis

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Background and Aims: Cerebral venous sinus thrombosis (CVST) constitutes 0.5-1% of all strokes in all age groups. Epileptic seizures (ES) occur in 12-31.9% of patients with CVST, while up to 44.3% of patients may have ES in the early stage of the disease. Our objective is to determine the risk factors for ES in CVST.
Methods: A retrospective study from 2010-2024 in the Emergency Institute was performed. 50 patients were included in the study. The patients with a past history of epilepsy and structural lesions other than CVST were excluded.
Results: Our patients were divided into groups: with ES (14 patients with acute early seizures (28%)) and without ES (36 patients (72%)). The median age was 40 years. Females are more commonly (64.3%) involved in developing ES in CVST. ES group include-28.6% with Status Epilepticus (SE), and 71.4%-focal with secondary bilateral seizures. Sagittal superior sinus (57.2%), Galen Vein (28.6%), and cavernous sinus (14.3%) involvement were more common in the ES group. Sagittal inferior sinus (55.56%), transverse sinus (27.75%), and sigmoid sinus (16.67%) involvement were in the non-ES group. The altered state of consciousness (35.7%) presents a risk factor for the ES. Hemorrhagic infarction, in the frontal cortex was present in 35.7% of the ES group.
Conclusion: Risk factors for acute ES in CVST are sagittal superior sinus, Galen Vein, and cavernous sinus involvement. Galen Vein thrombosis was seen to be included in patients with SE. Altered state of consciousness, hemorrhagic infarction in the frontal cortex and female gender are predisposing factors for ES.
Disclosure: Nothing to disclose.

EPO-552 | Endovascular or medical treatment for acute stroke due to medium-vessel occlusion: Which is the best option?

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Background and Aims: Medium-vessel occlusion (MeVO) accounts for 30% of acute ischemic stroke cases. Deciding on treatment with mechanical thrombectomy (MT) remains a challenging task. This study aimed to compare three clinical strategies.
Methods: We conducted a retrospective analysis at a stroke center from April 2023 to April 2024. Patients with MeVO

involving occlusions in segments M2/M3/M4, A2/A3, or P1/P2 were included. Patients treated with endovascular thrombectomy (EVT), intravenous thrombolysis (IVT), or medical management were compared using multivariable logistic regression. The primary outcome was to assess functional independence, defined as a modified Rankin Scale (mRS) score of 0–2 at 3 months, and treatment safety.
Results: A total of 138 patients were included in the study. Thirty-one patients (22.5%) received medical management without reperfusion, 48 (34.8%) underwent IVT only, and 59 (42.8%) underwent MT with or without IVT. The mean age was 73 years. The most common occlusion site was M2 (42.8%), followed by M3 (15.9%). No significant differences were found in functional outcomes as measured by mRS at 3 months (P = 0.713). A lower baseline NIHSS score was significantly associated with favorable functional outcomes (OR 1.18, 95% CI 1.03–1.36) across all groups.
Conclusion: This study did not find significant differences in functional outcomes among patients with medium-vessel occlusions treated with EVT, IVT, or medical management. Larger registries are needed to define the optimal strategy for this patient group.
Disclosure: Nothing to disclose.

EPO-553 | The reliability of modified Rankin Scale assessed at discharge from the stroke unit for the actual functional outcome

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Background and Aims: This study aimed to evaluate the reliability of the mRS score obtained at discharge from the stroke unit (SU) compared to the assessment shortly after discharge when patients had already encountered challenges of home environment or more complex tasks in a neurological rehabilitation ward (NRW). Special emphasis was placed on distinguishing independence (mRS 0-2) from dependence (mRS 3-5) and no significant disability (mRS 0-1) from disability (mRS 2-5).
Methods: We enrolled 116 acute ischaemic stroke discharged from SU with residual deficits (mRS 1–4) from October 2020 to June 2022, assessed by a certified rater at discharge and 7–21 days later. The agreement was reported as Krippendorff's alpha.
Results: Of 109 analysed patients 61 (56%) were transferred to NRW. The agreement between mRS assessments at discharge from SU and shortly after was low overall (alpha 0.34) and in patients discharged home (alpha 0.41), while very low in patients transferred to NRW (alpha 0.10). At discharge home: 21% of patients initially assessed as mRS 0-1 turned out 2-5; 9% of those assessed as mRS 0-2 turned out 3-5; 35% of assessed as mRS 3-4 were scored 0-2. At discharge to NRW: none was initially assessed as mRS 0-1; 10% of those assessed as mRS 0-2 turned out 3-4; 35% of assessed as 3-4 turned out 0-2.
Conclusion: The agreement between mRS assessments at discharge from SU and shortly after is modest. This points to the risk of bias when SU-based mRS scores are used to represent long-term functional outcome.
Disclosure: Nothing to disclose.

EPO-554 | Newly diagnosed diabetes mellitus and prediabetes in a stroke unit

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Background and Aims: Diabetes mellitus and prediabetes are modifiable vascular risk factors for ischemic stroke that double the risk of stroke and are associated with poorer functional prognosis, and increased risk of recurrent cerebrovascular events. The objetives were to determine the prevalence of newly diagnosed diabetes and prediabetes in patients with acute ischemic stroke admitted to the stroke unit of a university hospital and to evaluate whether there is an association with stroke etiology.
Methods: Retrospective observational study of a prospectively included sample of adult patients admitted to a stroke unit due to ischemic stroke or TIA during the second semester of 2023. A chi-square test was performed to assess the association between newly diagnosed diabetes or prediabetes and stroke etiology according to TOAST classification.
Results: A total of 199 patients were included, 37 of whom had a prior diagnosis of diabetes. Among the included patients, 53.3% were newly diagnosed with diabetes (7.5%) or prediabetes (92.5%). Of the latter group, 51.4% showed a high risk of progression to diabetes. Regarding ischemic stroke etiology, the majority were cardioembolic, followed by large artery atherosclerosis and small vessel occlusion. No statistically significant association was found between new diagnosis of diabetes or prediabetes and a specific stroke etiology.
Conclusion: The high prevalence of newly diagnosed prediabetes and diabetes in our sample, corroborates data indicating that these conditions are frequently underdiagnosed in patients with acute ischemic stroke. Including glycated hemoglobin measurement in stroke unit protocols allows for better secondary prevention through tailored management of these vascular risk factors.
Disclosure: Nothing to disclose.

EPO-555 | The two most interesting polymorphic sites in the 9r21 chromosomal locus associated with arteriovenous malformations

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Background and Aims: An aberrant tangle of arteries and veins that diverts blood from the arterial bed into the venous, excluding the capillary network, is known as an arteriovenous malformation (AVM). The two most interesting polymorphic sites in the 9r21 chromosomal locus are rs7865618 in the CDKN2A gene and rs1333040 in the CDKN2B gene. The CDKN2A/B gene is involved in cell cycle regulation and affects a number of physiological processes, including aging, apoptosis, stem cell self-renewal, and tissue remodeling. In certain hereditary disorders, dysregulation of these genes has been connected

to aberrant vascular development. Theoretically, mutations in these genes may contribute to the creation of AVMs if they affect the integrity or repair of the normal vessel wall. This study aims to investigate the contribution of allelic polymorphisms of the CDKN2B and CDKN2A genes to the genetic susceptibility to the development of AVM in Uzbek citizens.
Methods: 95 individuals from Tashkent's clinical centers were included in the study group. Using competing TaqMan probes, polymorphic gene variants were identified by real-time PCR.
Results: According to data, patients with the GG genotype have a roughly two-fold increased risk of developing an AVM compared to those with the GA and AA genotypes for the polymorphic locus rs7865618 of the CDKN2A gene (OR = 1.915, CI = [1.158-3.167], $p = 0.01$).
Conclusion: Thus, for Uzbek citizens, genotype GG rs7865618 of the CDKN2A gene is a risk factor for the development of AVM.
Disclosure: Nothing to disclose.

EPO-556 | Prognostic impact of malnutrition assessed by bioelectrical impedence vector analysis in acute ischemic stroke

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Background and Aims: Until now, the assessment of nutritional status in stroke patients has been mainly based on laboratory-based composite scores. Bioelectrical Impedance Analysis (BIA) and Bioelectrical Impedance Vector Analysis (BIVA) are non-invasive, cost-effective, and rapid methods that accurately provide body composition, nutritional and hydration status. The aim was to compare the ordinal distribution of the mRS scores 90 days after an acute ischemic stroke, distinguishing between malnourished and non-malnourished patients according to the BIVA malnutrition parameter.
Methods: We conducted a single-centre prospective observational study on all patients admitted for acute ischemic stroke to our Centre between April 1st 2024 and September 30th 2024. We applied the IPW statistical technique and ordinal logistic regression to compare mRS scores in malnourished and non-malnourished patients.
Results: We analysed 195 ischemic stroke patients using the BIVA. Of these, 37 patients (19%) were malnourished at the time of admission to our Stroke Unit. The ordinal distribution of mRS scores 90 days after the ischemic stroke was higher in patients who were malnourished upon Stroke Unit admission according to BIVA parameters (cOR 3.34; $p = 0.001$). Even after accounting for relevant covariates, malnutrition remained an independent predictor of unfavourable outcomes (acOR 2.79; $p = 0.005$), along with NIHSS score at admission (acOR 1.19; $p < 0.001$), intravenous thrombolysis (acOR 0.28, $p < 0.001$), absolute lymphocyte count (cOR 1.01; $p = 0.027$), and albumin concentration (cOR 0.82; $p < 0.001$).
Conclusion: Malnutrition, assessed through BIVA at the time of admission to the Stroke Unit, is associated with worse clinical outcomes at 90 days following the ischemic cerebrovascular event.
Disclosure: Nothing to disclose.

EPO-557 | Eagle syndrome

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Background and Aims: Eagle syndrome is a rare condition characterized by elongated styloid processes or calcified stylohyoid ligaments that may impinge on adjacent anatomical structures, leading to diverse symptoms. It was first described in 1937 by Watt W. Eagle with classical symptoms of throat pain, dysphagia, and referred otalgia, typically exacerbated by head movement or palpation. This case highlights an unusual presentation with syncopal episodes resulting from elongated styloid process' pressure on internal carotid artery.
Methods: Case report.
Results: A 59-year-old man presented to the emergency department with recurrent syncopes which had increased in frequency, now presenting monthly. Episodes started with hazy vision, general weakness, sensory disturbances on left side of the head after which he lost conciousness for few seconds. He also reported occasionally hearing pulsating noise while falling asleep and occasional throat discomfort. Neurological and cardiovascular examinations were unremarkable. CT scan of the brain was normal, CT-angiography with 3D reconstruction revealed bilateral elongated styloid processes, the right one being in direct contact with right internal carotid artery in extracranial portion causing significant compression and ~50% narrowing of its lumen. Patient was referred to vascular surgeon for follow-up and additional testing. Repeat imaging after 3 months was without dynamics and at the moment patient remains on watchful waiting surveillance.

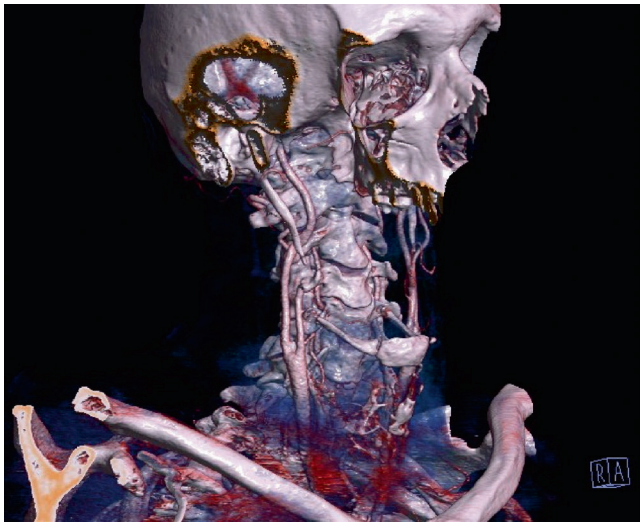

Image 1 3D reconstruction of CT angiography showing conflict of elongated styloid process and internal carotid artery on the right side.

Conclusion: This case underscores the need for heightened awareness of Eagle syndrome in patients presenting with atypical symptoms such as syncopal episodes. Early diagnosis and appropriate interventions can significantly alleviate symptoms and improve patient outcomes.
Disclosure: Nothing to disclose.

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EPO-558 | Shifting mortality trends in stroke patients: Analysis of U.S. national data from the CDC WONDER database

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Background and Aims: Stroke remains a leading cause of mortality worldwide, yet recent trends in stroke-related deaths have shown variation across time, gender, and stroke subtypes. This study aims to analyze national stroke mortality trends to identify temporal patterns and demographic disparities.
Methods: We conducted a retrospective analysis of stroke-related mortality in the U.S. from 1999 to 2020 using the CDC WONDER database. Joinpoint regression was employed to assess trends in stroke-related deaths, calculating the annual percent change (APC) with 95% confidence intervals (CIs).
Results: Mortality declined significantly from 1999 to 2013 in individuals <45 years (-1.88%/year) and from 1999 to 2012 in those 45–64 years (-2.29%/year), followed by an increase (2018–2020: +3.82%/year). In ≥65 years, a sharp decline (1999–2006: -7.24%/year) slowed, with a slight rise from 2012 to 2020 (+0.45%/year). Black individuals exhibited a significant decline from 2002 to 2012 (-4.70%, 95% CI: -5.44 to -4.36), followed by a subsequent rise (1.22%, 95%CI: 0.69 to 1.92). Stroke subtype analysis revealed a consistent decline in hemorrhagic stroke mortality, while mortality from cerebral infarction showed a sharp increase from 2014 to 2017 (37.43%, 95% CI: 26.78 to 44.51). Gender analysis indicated an early decline in stroke mortality for both males and females, but a significant reversal in recent years, particularly in males (Slope 4: 0.0421, $p < 0.0001$).

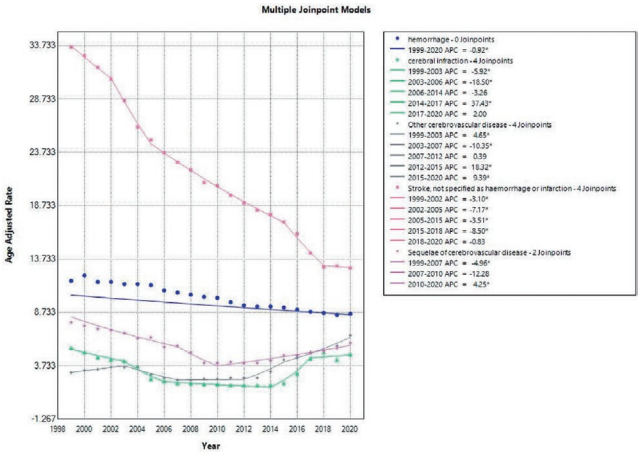

FIGURE 1 Trend analysis for stroke patients subgrouped by the Cause

Conclusion: While stroke mortality rates declined substantially between 1999 and 2012, recent data suggest a plateau or reversal in progress, particularly among middle-aged adults, Black populations, and those with ischemic stroke.
Disclosure: Nothing to disclose.

EPO-559 | Intracerebral hemorrhage in the young: Clinical characteristics and outcomes in a university hospital stroke registry

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Background and Aims: Intracerebral hemorrhage (ICH) is a severe stroke syndrome. While commonly encountered >60 years age, ICH is also occurs in younger individuals, with varied characteristics. We compared the clinical and outcome profiles of ICH among patients <50 and >50 years age in a University Stroke-Registry at Oman.
Methods: Hospital records were reviewed for demographics, risk-factors, cause, clinical characteristics and outcomes. Univariate and logistic regression analyses were utilized to compare profiles among younger (18-50 yr ICHy) and older (>50 yr ICHo) cohorts.
Results: Among 1483 patients with stroke over 10 years, 263 had ICH (17.7%) (age: 62+13 yrs; M:F::1.7:1). 79/263 (30%) had ICHy (age: 44.8+6 yrs; M:F::1.8:1) while 183/263(70%) were older (>50 yr; ICHo: age 65.5+10; M:F::1.6:1). Underlying causes of ICHy were hypertension or hypertensive-emergency (HTN) in 91%. Causes of ICHo were hypertension (73%), cerebral small-vessel-disease (15.8%) and cerebral-amyloid-angiopathy (5%). Altered sensorium, hemiparesis, aphasia were presenting symptoms in both. Mean ICH volumes (30.5 + 41 mL vs 27.7 + 34 mL) were similar. 22.8% of patients died. Good outcomes (MRS 0-3) were more prevalent in ICHy than ICHo (38% vs 26.6%, $p = 0.012$). Gender, age, altered sensorium and hemiparesis were

independent predictors of mortality ($p < 0.02$). We explored the utility of a modified ICH-score with lower age cut-offs for improved outcome predictability.
Conclusion: Up to 30% of all ICH patients are <50 years of age. Hypertensive crisis was the most common precipitating cause of ICHy. While ICH volumes and mortality are similar to older patients, good outcomes are higher in ICHy. Improved control of hypertension to prevent hypertensive crises may have higher impact for ICH prevention in young adults.
Disclosure: Nothing to disclose.

EPO-560 | Prevalence of post stroke delirium and associated risk factor, a multicenter prospective study, Addis Ababa Ethiopia

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Background and Aims: Post-stroke delirium is a frequent and significant complication of stroke. The impact of post-stroke delirium on stroke recovery is substantial. It leads to prolonged hospital stays, increased dependence and mortality rates. As a result, early identification and prompt treatment of post-stroke delirium are imperative for optimizing outcomes in stroke patients.
Methods: We performed a prospective observational cross sectional study, including all the stroke patients admitted to respective study areas during the study period. A total of 101 participants who fulfilled the inclusion criteria were involved in this study. Data was collected using interviewer administered Questionnaire with well tested and validated tool, Patients were assessed for Delirium within 48 hour of admission and subsequently screened every 12 hours.
Results: Out of 101 patients 26(25.7%) had Post stroke Delirium. Majority 56 (55.4%) of the patients were females. The mean (SD) age of the study participants was 56.05 ±15.38 years, the mean time in day's until the occurrence of delirium is 3 ±1 days. Multivariable logistic regression analysis showed that, Age greater than 60(AOR = 19.1, 95% CI (1.7-211) $p = 0.016$, Presence of Sepsis (AOR = 8.3, 95% CI (1.2-56) $p = 0.029$, Presence of Polypharmacy (AOR = 157, 95% CI (10.2-244) $p = 0.0001$, Presence of Electrolyte Derangement (AOR = 65.2, 95% CI (3.4-124.1) $p = 0.005$ were statistically significant risk factors.
Conclusion: Our Study showed that Post Stroke Delirium occurs in a quarter of patients admitted with Diagnosis of Acute Stroke, and the Identified risk factors were Age greater than 60, Polypharmacy, Presence of Sepsis and Electrolyte Derangement, Medical professionals responsible for caring for acute stroke patients should be vigilant in identifying those at higher risk of developing post-stroke delirium.
Disclosure: Nothing to disclose.

EPO-561 | Possible sleep quality factors predictors of wake-up strokes

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Background and Aims: Wake-up stroke (WUS) physiopathology is not completely understood but studies report a possible sleep association.
Methods: We conducted a prospective observational study including all patients admitted to the neurology department for acute stroke during a 4-month period. We excluded patients due to hemorrhagic stroke, impaired language or disagreement with the written consent. Selected 81 patients that were screened about vascular risk factors. Sleep quality was assessed using a self-fulfilled questionnaire, STOP-BANG Sleep Apnea Questionnaire, Epworth Sleep Scale, and Insomnia Severity Index. Clinical and demographic data was collected, and statistical analysis performed.
Results: The sample included 81 patients (43 men) with a mean age of 73.7 ±12.9 years at symptoms' onset; 18.52% patients ($n = 15$) had WUS. NIHSS score was higher in WUS than non-wake-up stroke (NWUS) patients (9.73 ±4.25 vs. 6.65 ±4.81, $p = 0.013$). Cervical perimeter showed a mean of 39.8 ±3.64 cm and was significantly higher in WUS patients (43.6 ±2.44 vs. 39.0 ±3.32, $p < 0.001$). Daytime sleepiness was significantly more frequent in WUS patients (53.3% vs. 25.8%, $p = 0.037$). Pre-stroke sleep characteristics demonstrated no statistically significant difference. Logistic regression analysis showed a significantly higher cervical perimeter in patients with WUS (OR = 1.586, 95% CI = 1.21-2.08, $p < 0.001$).
Conclusion: We found an association between WUS and cervical perimeter and daytime sleepiness, suggesting an underdiagnosis of sleep disorders. Understanding WUS physiopathology and risk factors might help optimize prevention strategies.
Disclosure: Nothing to disclose.

EPO-562 | Intravenous thrombolysis in patients with acute ischemic stroke: Clinical experience from two egyptian centers

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Background and Aims: We aimed to identify the barriers that prevent the utilization of rt-PA in a proper time for reducing delays for revascularization therapies.
Methods: This retrospective study was conducted on patients with acute ischemic stroke and were treated with Intravenous rt-PA within 4.5 hours of the onset. The data was collected from an archiving system of Stroke Units of Al-Azhar University and ALmaadi Military Hospital between May 2014 and April 2021.
Results: A total of 167 patients (mean age of 62.55 ±9.94 years) and included 94 males (56.2%) were included. 88 patients (52.6%) were treated within 0-3 hours and 79 patients (47.3%) within 3-4.5 hours from stroke onset. Lack of knowledge about emergency calling was reported in 46 patients (27.5%). Door-to-needle time

≤60 minutes was achieved by only 32.8% (42/128) of patients who arrived within 0-2 hours of their symptom onset compared to 48.7% (19/39) of those who arrived at the emergency department within 2-3.5 hours of their symptom onset. The reported complications included symptomatic intracerebral hemorrhage (10.7 %), asymptomatic intracerebral hemorrhage (2.9 %) and hematuria (2.3 %). However, pneumonia due to COVID-19 infection was the cause of death in 15 patients (8.9%) during the era of the COVID-19 pandemic.

Clinical Outcome of the patients 24 hours post-rt-PA infusion	
Early clinical improvement	127 (76.0%)
Early clinical deterioration	29 (17.3%)

Clinical characterstics

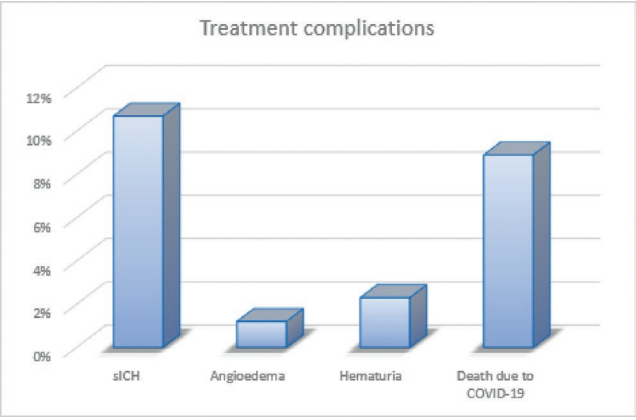

FIGURE 1 Complications

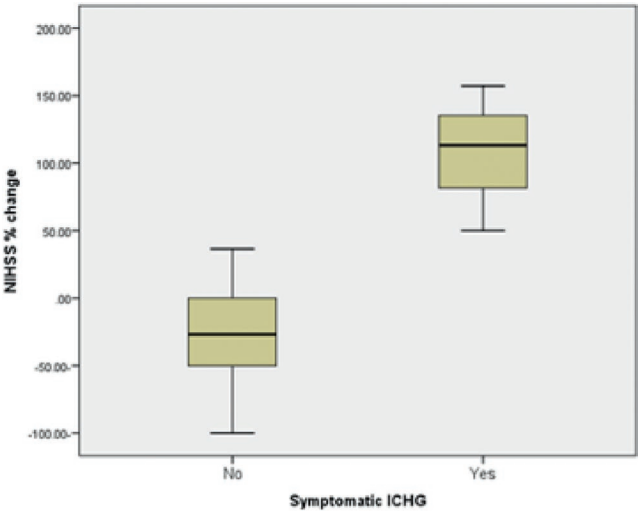

FIGURE 2 Complication

Conclusion: The extremely low number of stroke patients receiving rt-PA in developing countries was attributed to several barriers including a lack of public awareness, and Inaccessibility to emergency medical services especially restrictions and logistic rules of many hospitals during COVID-19 pandemic.
Disclosure: Nothing to disclose.

EPO-563 | Clinical features in the occlusion of artery of Percheron. A challenging diagnosis

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Background and Aims: Occlusion of the artery of Percheron (AOP) is a rare cause of bilateral thalamic stroke, posing significant diagnostic challenges due to its low incidence and diverse clinical-radiological presentations. This study aimed to improve the understanding and early recognition of AOP stroke by describing its clinical features, diagnostic approach, and outcomes.
Methods: A retrospective review was conducted on patients discharged from the Hospital General Universitario Santa Lucía de Cartagena (2013–2024) with a diagnosis of bilateral thalamic stroke or AOP occlusion confirmed by MRI. Demographic data, clinical presentation, imaging findings, and outcomes were analyzed.
Results: The study included 12 patients (66% male, median age 73.5 years). Cardioembolism was the predominant etiology (58.3%), and the main risk factors were atrial fibrillation (50%) and hypertension (33%). Median NIHSS at presentation was 4, with consciousness decline being the most prevalent symptom (91.6%), primarily somnolence (73%). Cognitive-behavioral impairment (66%) and vertical gaze palsy (50%) were common, although only 33% presented the classic triad. MRI revealed bilateral paramedian and anterior thalamic infarctions with midbrain involvement in 41.6%, correlating with more severe consciousness decline and triad prevalence. CT scans were initially normal in 75% but showed abnormalities on review in 50%. At six months, half of the patients had favorable outcomes (mRS ≤ 2), while 16.7% experienced fatal outcomes.

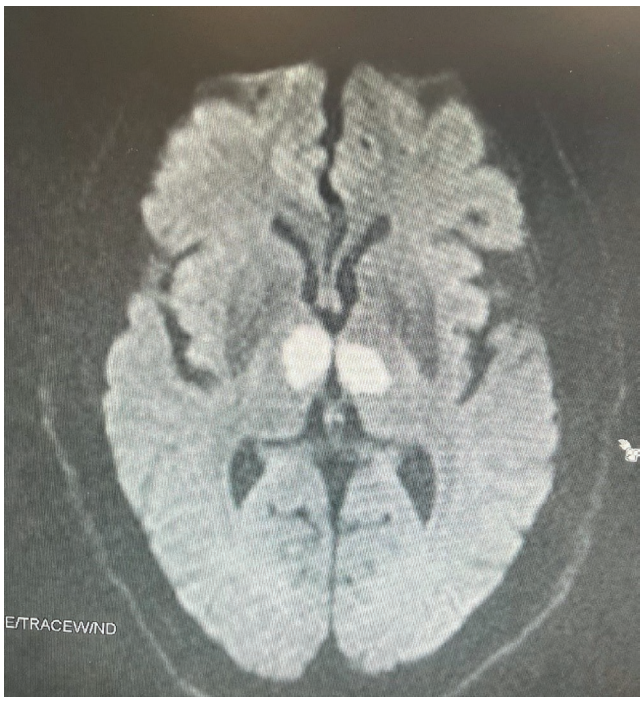

FIGURE 1 Bilateral paramedian and anterior thalamic infarction

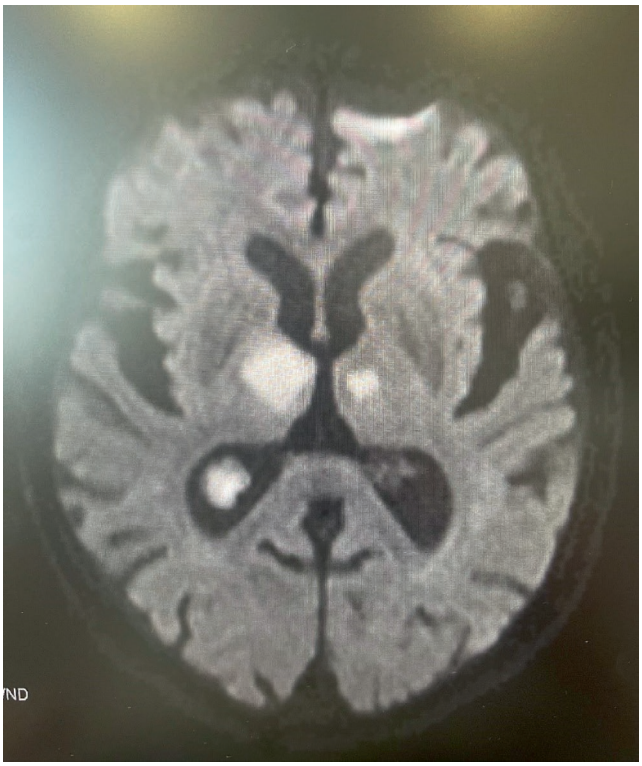

FIGURE 2 Bilateral paramedian and anterior thalamic infarction 2

Conclusion: AOP stroke requires high clinical suspicion, particularly in patients with unexplained consciousness decline and associated neurological deficits. Early MRI is critical for diagnosis, although early CT signs and clinical expertise may guide prompt recognition and management.
Disclosure: Nothing to disclose.

EPO-564 | Impact of adherence to key performance indicators (KPI) on acute stroke outcome in a tertiary hospital in Tanzania

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Background and Aims: Adherence to key performance indicators has been associated with shorter lengths of hospital stay, reduced medical complications and lower-case fatality among stroke patients. This study explored the impact of adherence to key performance indicators for acute stroke management in Aga Khan hospital, Dar es Salaam.
Methods: This was a prospective longitudinal observational study. Stroke patients, 18-years and above admitted via the accident and emergency unit of the hospital between February 2018 and January 2023 were evaluated. Patients' demographics, stroke types, and ten KPIs were profiled. KPI adherence and its relationship with prolonged hospital stay, in-hospital mortality and complication were analyzed. Analysis was performed using spss V22. Level of significance was set at $p \leq 0.05$.
Results: 155 acute stroke patients (M: F; 113:42) with mean age (SD) of 57.9 (13.63) were admitted via the ER within the study period. 121(78.1%) had ischemic stroke while 34 (21.9) patients had hemorrhagic stroke. Code stroke was activated in 143 patients (92.3%). 120 (77.45) had a brain CT within 25 minutes of arrival at ER. 80 (51.9%) had complete (100%) compliance with stroke KPIs. Intrahospital complication was noted in 23(14.8%), 7 days case fatality was 4 (2.6%). 46 (29.7%) patients had prolonged hospital stay (> 7 Days). Non-compliance with KPI was not associated with intrahospital mortality ($p = 0.948$) and prolonged hospital stay ($p = 0.134$) but was associated with intrahospital complications ($p = 0.006$).

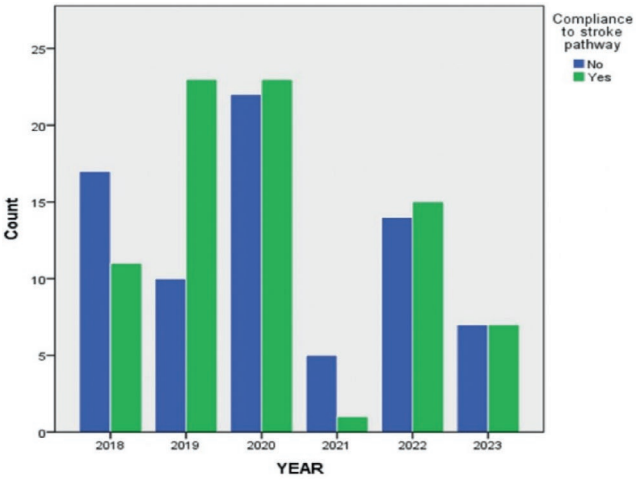

Figure 1- STROKE KPI Compliance Trend Between 2018-2023

Conclusion: Continuous quality measurement, education and improvement in stroke care delivery should be reinforced for optimal stroke outcomes.
Disclosure: Nothing to disclose.

EPO-565 | Cerebral venous congestion presented with aphasia in a hemodialysis patient

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Background and Aims: Cerebral venous congestion results from obstructed venous outflow, like thrombosis or dural arteriovenous fistulas (AVF). We report a rare case of an AVF in a dialysis patient causing reversed internal jugular vein (IJV) flow and aphasia from left hemisphere congestion.
Methods: A 54-year-old male presented to the emergency department with three days of language impairment. He had been on hemodialysis via an AVF in the left arm for 9 years without complications. Neurological examination revealed reduced speech fluency and impaired comprehension, but no other focal deficits. Brain MRI showed hemosiderosis and disseminated

microbleeds in the left hemisphere and left cerebellum, while TOF-MRA showed prominent flow in in the left transverse sinus and IJV. Left internal carotid artery DSA showed delayed venous drainage through the right transverse sinus into the right IJV, but no dural arteriovenous fistula. Duplex sonography revealed reversed blood flow in the left IJV, which normalized upon AVF compression. These findings led to a diagnosis of venous congestion in the left hemisphere due to IJV reflux.
Results: Angiography of the AVF revealed severe stenosis in the left brachiocephalic trunk, with predominant venous drainage into the left IJV. Angioplasty for severe stenosis in the left brachiocephalic trunk resolved the patient's language impairment.
Conclusion: Neurological issues in hemodialysis patients typically include stroke or uremic encephalopathy. Reversed IJV flow due to vascular stenosis in the hemodialysis access route resulting in cerebral venous congestion is rare. This condition was successfully managed through angioplasty of the brachiocephalic vein.
Disclosure: Nothing to disclose.

EPO-566 | Nurse detection of atrial fibrillation in stroke unit patients with suspected cardioembolic stroke on admission

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Background and Aims: Detecting atrial fibrillation (AF) is crucial for understanding stroke mechanisms and preventing secondary strokes. This study aims to evaluate the effectiveness of nurses' detection of AF in a stroke unit and its influence on the occurrence of subsequent cerebral infarctions.
Methods: Acute ischemic stroke patients admitted to ASU and diagnosed as embolic stroke of undetermined source (ESUS) was enrolled. Cardiac workups including cardiac rhythm monitoring during admission to the ASU was performed. Factors associated with detection of AF detection and AF detection by nurse in the ASU were investigated.
Results: Among 235 ESUS patients, 114 (48.5%) had AF. Hypertension (OR 1.913), admission heart rate (OR 1.016), and NIHSS score (OR 1.069) were significantly associated with AF detection. Nurses in the ASU identified 24 suspicious AF cases (10.2%), confirming 54.2%. Among them, higher Troponin I levels were associated with nurse detection (p = .005). Screening indicators such as premature atrial contraction (92.9% vs. 0.0%) and short runs of atrial tachycardia (28.6% vs. 8.0%, p=0.031) on holter monitoring were significantly more prevalent in the nurse-detected group. Of the 112 nurses, those with 10+ years of experience detected 48.9% of cardiac abnormalities (p=0.006), with 83.3% confirmed as AF (p = .044). Nurse detection led to shorter stays (7.38 vs. 10.12 days, p = .030) and lower costs ($217.40 vs. $462.60, p = .001), and avoided invasive tests like loop recorders.
Conclusion: Nurse detection of AF led to shorter hospital stays, reduced costs, and minimized invasive testing. Experience in neurology improved AF detection rates.
Disclosure: Nothing to disclose.

EPO-567 | Hypernatremia in the acute ischemic stroke undergoing endovascular thrombectomy and its influence on functional outcomes

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Background and Aims: The potential influence of hypernatremia, a known mortality risk factor in intensive care settings, on functional and neurological outcomes following acute ischemic stroke remains unclear. This study aimed to evaluate the association between hypernatremia and functional and neurological outcomes in patients with acute ischemic stroke.
Methods: This retrospective study investigated patients with acute ischemic stroke meeting all the followings: undergoing endovascular thrombectomy at our hospital from October 2018 to December 2023, achieving successful reperfusion, and premorbid modified Rankin Scale (mRS) 0–3. Hypernatremia was defined as peak serum sodium > =146 mmol/L during hospitalization. Patients were matched by the presence of hypernatremia using propensity-score matching. Primary outcome was mRS at 3 months.
Results: Following propensity score matching (n=152), compared to the non-hypernatremia group, the hypernatremia group exhibited significantly worse outcomes in mRS at both 3-month follow-up (median 4 [IQR 3–5] vs 3 [1–4], p <0.001) and discharge (4 [4–5] vs 3 [2–4], p <0.001), and higher National Institutes of Health Stroke Scale (NIHSS) score at discharge (13 [3–23] vs 4 [1–12], p <0.001). Shift analysis of mRS revealed that hypernatremia was independently associated with worse functional outcomes at 3 months (adjusted odds ratio 3.36 [95% confidence interval 1.86–6.15, p <0.001) and at discharge (2.93 [1.63–5.35], p <0.001).

	All (n=152)	Hypernatremia (n=76)	Non-hypernatremia (n=76)	P value
Age (years), median (IQR)	79 (71–87)	78 (71–88)	79 (71–86)	0.860
Female sex, n (%)	81 (53)	40 (52)	41 (53)	1
Premorbid mRS, median (IQR)	0 (0–2)	0 (0–2)	0 (0–2)	0.684
Initial NIHSS, median (IQR)	21 (15–26)	22 (14–26)	21 (16–25)	0.709
Baseline ASPECTS, median (IQR)	9 (7–10)	9 (7–10)	9 (6–10)	0.505
Large vessel occlusion, n (%) (CCA, ICA, M1, BA)	126 (82)	62 (81)	64 (84)	0.830
Etiology				
- Large artery atherosclerosis, n (%)	23 (15)	9 (11)	14 (18)	NA
- Cardioembolic, n (%)	102 (67)	51 (67)	51 (67)	NA
tPA administration, n (%)	63 (41)	31 (40)	32 (42)	1
Onset to reperfusion time (minute), median (IQR)	221 (156–472)	220 (141–407)	228 (159–477)	0.706
Hospitalization period (day), median (IQR)	22 (15–34)	27 (18–39)	18 (14–26)	<0.001

*: Covariates including age, sex, premorbid mRS score, initial NIHSS, occlusion site (LVO or not), tPA administration
Mann–Whitney U test for continuous variables
Fisher's exact test for categorical variables
Abbreviations: ASPECTS, Alberta Stroke Program Early Computed Tomographic Score; BA, basilar artery; CCA, common carotid artery; ICA, internal carotid artery; IQR, interquartile range; IVT, intravenous thrombolysis; LVO, large vessel occlusion; mRS, modified Rankin Scale; M1, middle cerebral artery M1 segment; NA, not available; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio; tPA, intravenous recombinant tissue plasminogen activator

Table 1 Baseline characteristics and treatment status after propensity score matching*

	All (n=152)	Hypernatremia (n=76)	Non-hypernatremia (n=76)	P value	Adjusted OR** (95% CI)	P value
Primary outcome						
mRS at 3-month, median (IQR)	4 (2–5)	4 (3–5)	3 (1–4)	<0.001	3.36 (1.86–6.15)	<0.001
Secondary outcome						
mRS at discharge	4 (3–5)	4 (4–5)	3 (2–4)	<0.001	2.93 (1.63–5.35)	<0.001
NIHSS at discharge	8 (1–18)	13 (3–23)	4 (1–12)	<0.001	NA	NA
Initial NIHSS - NIHSS at discahrge	9 (1–17)	6 (0–12)	12 (4–18)	0.010	NA	NA

*: Covariates including age, sex, premorbid mRS score, initial NIHSS, occlusion site (LVO or not), IVT administration
**: adjusted for age, premorbid mRS, initial NIHSS, rt-PA administration.
Abbreviations: IQR, interquartile range; IVT, intravenous thrombolysis; LVO, large vessel occlusion; mRS, modified Rankin Scale; NA, not available; NIHSS, National Institutes of Health Stroke Scale; OR, odds ratio.

Table 2 Functional and neurological outcomes after propensity score matching*

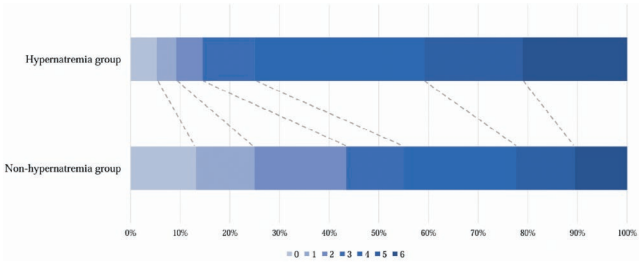

Figure 1 Distribution of modified Rankin Scale (mRS) scores at 3 months

Conclusion: These findings indicate that hypernatremia in acute ischemic stroke settings may be associated with poorer functional outcomes and negative influence on neurological status, suggesting the importance of appropriate sodium management in preventing possible secondary brain injury.
Disclosure: The authors declare that they have no disclosure.

EPO-568 | Exploring results of mechanical thrombectomy in nonagenarians with ischaemic stroke and anterior circulation occlusion

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Background and Aims: Data on very elderly patients treated with mechanical thrombectomy (MT) for acute ischemic stroke (AIS) is scarce. Our aim is to explore the safety and efficacy of MT in patients aged ≥90y who suffer AIS due to large vessel occlusion in the anterior circulation (LVO-AC).
Methods: Retrospective observational study of a series of consecutive patients aged ≥90y diagnosed of AIS admitted to a Comprehensive Stroke Centre (2020-2024). Patients with mRS ≤3, <24h from symptom-onset and LVO-AC (TICA/M1/M2/A1/Tandem) were included. MT was compared with best medical treatment (BMT), including intravenous thrombolysis (IVT). The primary efficacy outcome was 3-month mRS (favourable if ≤3), and safety outcomes included hemorrhagic transformation (PH2/symptomatic) and 3-month mortality. Analysis was adjusted just for baseline NIHSS to avoid overfitting.
Results: We included 31 patients (mean age 92+/-2.2y, 66.7% women). Median baseline NIHSS was 17 (IQR 8–20). 18 patients received MT and 9 IVT. Patients treated with MT had higher NIHSS (18 [IQR 17-22] vs.7 [IQR 5-16]) and more TICA/M1 occlusions (14 vs. 3). Among patients treated with MT, 38.9% achieved 3-month mRS≤3, compared to 66.7% in those receiving BMT. Adjusting for baseline NIHSS, no statistically significant differences were found ($p=0.725$). No significant differences were observed in hemorrhagic transformation (MT 5.6%, BMT 0%; $p=0.99$) or 3-month mortality (MT 44.4%, BMT 16.7%; $p=0.235$).
Conclusion: In our sample, nonagenarians with LVO-AC who received MT had worse basal NIHSS and more proximal occlusions. MT was safe, but considering the relevant differences in our cohorts we did not find differences on functional outcomes and further studies are needed.
Disclosure: Nothing to disclose.

EPO-569 | Central nervous system vasculitis as an etiology of stroke code activation: A case series

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Background and Aims: Central nervous system vasculitis (CNSV) may present as acute ischemic stroke, prompting stroke code activation. However, evidence regarding safety and efficacy of reperfusion therapies—such as intravenous thrombolysis and mechanical thrombectomy—in this context remains limited.
Methods: We report a series of five patients with CNSV (two women, aged 35-63 years old) who triggered stroke code activation, focusing on their initial management, complications related to reperfusion therapy, and clinical outcomes.
Results: All patients had an initial NIHSS scores of 2-6, and ASPECTS score of 10. One received intravenous thrombolysis, two underwent mechanical thrombectomy with intracranial stent placement followed by dual antiplatelet therapy, and the remaining two were managed with dual antiplatelet therapy alone. During hospitalization, four patients received intravenous methylprednisolone followed by immunosuppressive therapy (three with primary CNS angiitis and one with giant cell arteritis). The fifth patient was treated with intravenous penicillin and antiplatelet therapy for meningovascular syphilis. No reperfusion-related complications were observed. At three-month follow-up, three patients achieved functional independence.

TABLE 1 This table summarises the characteristics of five patients with CNS vasculitis who triggered stroke code activation. Three patients presented acute worsening during admission; new NIHSS and ASPECTS are reported using brackets.

Patient ID	1	2	3	4	5
Age, sex	59yo, male	63yo, female	51yo, male	35yo, male	59yo, female
Basal mRS score	1	1	0	0	0
Stroke Syndrome	Lacunar	Lacunar	Hemispheric	Lacunar	Hemispheric
NIHSS score at admission (worsening)	2	2	6 (14)	2 (8)	2 (13)
ASPECTS at admission (worsening)	10	10	10 (10)	10 (7)	10 (9)
CT Angiography	Left ICA and MCA stenosis	Unremarkable	Left ACA occlusion	Right MCA narrowing	Left MCA occlusion and ACA stenosis
Acute treatment	DAPT	DAPT	IVT, EVT + Stenting	DAPT	EVT + Stenting
V-W MRI	Concentric vascular enhancement	Concentric vascular enhancement	Concentric vascular enhancement	Concentric vascular enhancement	Concentric vascular enhancement
Final diagnosis	PACNS	PACNS	PACNS	Meningovascular Syphilis	Giant Cell Arteritis
Aetiological treatment	Immunosuppression	IV MTP + immunosuppression	IV MTP + immunosuppression	IV MTP + Penicillin	IV MTP + immunosuppression
NIHSS at discharge	2	1	3	5	1
mRS at discharge	2	3	4	4	1
NIHSS at 3-month	2	1	3	4	0
mRS at 3-month	2	3	3	3	2

Conclusion: CNSV is a rare cause of stroke code activation. In this series, reperfusion therapies showed a favorable safety profile. However, further studies are necessary to better define their role in CNSV-related stroke.
Disclosure: Nothing to disclose.

EPO-570 | Factors associated with carotid atheromatosis in asymptomatic population

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Background and Aims: Carotid atherosclerosis is the leading cause of atherothrombotic stroke, yet no screening guidelines exist for asymptomatic individuals. This study aimed to identify variables linked to carotid atheromatosis without stenosis (CAWS) and hemodynamically significant carotid stenosis >50% (HSCS) in an asymptomatic population regarding cerebrovascular and retinal events.
Methods: A retrospective observational study was conducted with prospective data collection from patients who underwent Echo-Doppler of the supraaortic trunks between 2021 and 2022 at a Spanish hospital. Patients with formal indications for the test due to cerebral or retinal ischemic symptoms were excluded. The association of HSCS and CAWS with medical history and analytical parameters was analyzed.
Results: Among 261 patients (mean age 70.9 ±12.4 years, 55.9% women), 16 (6.1%) had HSCS and 157 (60.2%) had CAWS. CAWS was associated with male sex ($p=0.012$), advanced age ($p<0.001$), hypertension ($p=0.002$), diabetes ($p=0.036$), smoking ($p=0.016$), ischemic heart disease ($p=0.018$), small-vessel cerebrovascular disease ($p=0.023$), and lower glomerular filtration rate ($p=0.007$). HSCS was linked to male sex ($p=0.040$), smoking ($p=0.001$), ischemic heart disease ($p<0.001$), peripheral vascular disease ($p=0.001$), and elevated triglyceride levels ($p=0.044$). Multivariate analysis independently associated CAWS with male sex ($p=0.029$), advanced age ($p<0.001$), and smoking ($p=0.007$), while HSCS was linked to smoking ($p=0.015$), ischemic heart disease ($p=0.001$), and elevated triglycerides ($p=0.030$).
Conclusion: These findings highlight known vascular risk factors for CAWS and HSCS. Future studies should evaluate their potential in developing screening systems for at-risk populations.
Disclosure: Nothing to disclose.

EPO-571 | Outcomes predictors in patients with basilar artery occlusion and NIHSS

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Background and Aims: Treatment of basilar artery occlusions (BAO) is controversial for patients presenting with a NIHSS<10. Current ESO recommendations favor best medical management (BMM) over mechanical thrombectomy (MT) in this subgroup of patients. Nonetheless, recent evidence suggests the potential benefit of MT over BMM. In this retrospective multicenter study, we analyzed a large cohort of BAO patients with a baseline NIHSS<10 that received MT, to identify variables influencing the 3 months outcome.
Methods: The prospective database of 10 European stroke centers were screened. Patients older than 18 years old, presenting with BAO and a NIHSS<10, treated with MT, were included. Patients were divided into two groups according to the dichotomized 90-day modified Rankin Scale score (mRS, 0-2 vs. 3-6) and univariate and binary logistic regression (BLR) analysis were performed.
Results: 116 patients were collected. Among them, 82 patients achieved a 90-day mRS of 0-2. Based on univariate analysis results and clinical reasoning, 9 variables were included in the BLR model. Among them, a distal occlusion site and a higher baseline pcASPECTS were independent predictors of 90-day mRS of 0-2. Conversely, higher pre-event mRS score, atherosclerotic etiology and hemorrhagic complications were independent predictor of poor clinical outcome.
Conclusion: Among BAO patient with NIHSS<10, the site of occlusion, the baseline pcASPECTS, the pre-event mRS and the etiology behind the event appear to be independent predictors of outcome after MT. Future, prospective studies are needed to confirm our observations.
Disclosure: Nothing to disclose.

Movement disorders 6

EPO-572 | NXRN1 syndrome: Presentation as myoclonic ataxia

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Background and Aims: The NRXN1 gene encodes a membrane protein belonging to the neurexin family, which is primarily expressed in the brain and plays a fundamental role in synaptic function. This syndrome is characterized by global developmental delay, severe intellectual disability, and the absence of expressive language. Other common features include muscular hypotonia, seizures, autistic behavior, and stereotyped movements.
Methods: A case of a 22-year-old woman with a history of autism spectrum disorder and developmental delay.
Results: We report the case of a female patient who presented at a movement disorder clinic with ataxia and distal myoclonus in the upper limbs. On examination, she exhibited generalized hyperreflexia and a wide-based gait with an inability to perform tandem walking. MRI findings were normal. Genetic testing revealed that she was a heterozygous carrier of a pathogenic deletion affecting at least intron 18 and exon 19 of the NRXN1 gene (NM_001135659.2). Family segregation studies are currently pending.
Conclusion: We continue to expand our understanding of the NRXN1 syndrome spectrum. Further knowledge about its clinical presentation and earlier diagnosis is crucial to improving the quality of life for these patients.
Disclosure: Nothing to disclose.

EPO-573 | Examination of the frequency and characteristics of impulse control disorders in Wilson's disease

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Background and Aims: Wilson's disease is a rare hereditary disorder that leads to copper accumulation, primarily in the liver and brain, due to impaired excretion. Impulse control disorder (ICD) is characterized by an inability to resist urges, resulting in repetitive behaviors, often associated with basal ganglia disorders. The aim of our study was to determine the frequency and characteristics of impulse control disorders and other psychiatric symptoms in Wilson's disease.
Methods: This observational study included consecutive patients on stable chelation therapy, examined at the Neurology Clinic, UKCS, Belgrade. Patients were assessed using the following scales and questionnaires: Impulsive-Compulsive Disorders Questionnaire, Beck Depression Inventory, Hamilton Anxiety Scale, Apathy Scale, Impulsivity Scale, and the Obsessive-Compulsive Symptoms Questionnaire. Demographic data were collected, and disease severity was assessed using the Unified Wilson's Disease Rating Scale. ICD diagnosis was based on established criteria.
Results: A total of 32 patients were examined, with an average age of 41.97 ± 10.8 years and disease duration of 16.7 ± 9.6 years. Nine patients (28%) had ICDs, including pathological gambling, binge-eating, and mixed impulse control disorder. No significant differences were found between groups with and without ICDs regarding disease severity, behavioral, and cognitive features. A logistic regression model for ICD diagnosis was significant ($p = 0.034$), correctly classifying 84% of patients, with higher apathy scores as a significant predictor (OR 0.730, 95% CI 0.548-0.971, $p = 0.031$).
Conclusion: ICDs affect 28% of Wilson's disease patients, with those exhibiting severe apathy at higher risk.
Disclosure: Keywords: Wilson's disease; impulse control disorder; impulsivity; apathy.

EPO-574 | The role of serotonergic mechanisms in the progression of Parkinson's disease in the population of Uzbekistan

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Background and Aims: This study explores the relationship between serotonin levels and both motor and non-motor symptoms in Parkinson's disease (PD), highlighting serotonergic dysfunction's role in disease progression.
Methods: A cohort of 150 PD patients and 150 matched healthy controls were assessed. Motor symptoms were evaluated using the Unified Parkinson's Disease Rating Scale (UPDRS), while non-motor symptoms, including depression, anxiety, sleep disturbances, and cognitive impairment, were analyzed. Plasma and cerebrospinal fluid (CSF) serotonin levels were measured using high-performance liquid chromatography (HPLC), and correlations with symptom severity were examined.
Results: Serotonin levels in both plasma and CSF were significantly lower in PD patients compared to controls ($p < 0.05$). Reduced serotonin was strongly linked to more severe non-motor symptoms, particularly depression and anxiety ($p < 0.01$), as well as cognitive impairment ($p < 0.05$). However, no significant association was found between serotonin levels and motor symptom severity.
Conclusion: Serotonergic dysfunction in PD is closely associated with non-motor symptoms, especially mood and cognitive impairments. These findings highlight the need for further research into serotonin-targeted therapies to improve the management of PD-related non-motor symptoms.
Disclosure: Nothing to disclose.

EPO-575 | Fecal microbiota transplantation for motor symptoms in Parkinson's disease: A systematic review and meta-analysis

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Background and Aims: Fecal Microbiota Transplantation (FMT) has emerged as a potential therapeutic intervention for managing motor symptoms in Parkinson's Disease (PD). This study aimed to synthesize evidence on the impact of FMT on motor symptom improvement in PD, specifically assessed by the MDS-UPDRS Part III.
Methods: This systematic review and meta-analysis included 3 studies investigating the efficacy of FMT for motor symptoms in PD. A comprehensive search was conducted across PubMed, Embase, Web of Science, Scopus, and Cochrane databases, adhering to PRISMA guidelines. Eligible studies evaluated FMT's impact on motor symptoms, measured by the MDS-UPDRS Part III score. The meta-analyses were performed using Review Manager 4.1. Risk of bias was assessed, and heterogeneity was explored.
Results: A total of 143 participants were included, 78 in the FMT group and 65 in the placebo group. FMT significantly improved motor symptoms compared to placebo (MD -2.75; 95% CI: -4.03, -1.47, $p < 0.0001$) in the MDS-UPDRS Part III score. Low heterogeneity was observed across studies ($I^2 = 5\%$, $p = 0.35$). Bruggeman et al. contributed the largest weight (85.5%) to the pooled estimate due to its robust sample size and lower variance. Risk of bias was moderate across included studies.

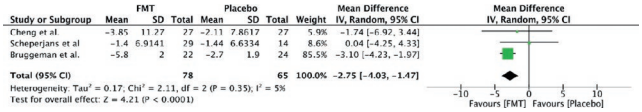

FIGURE 1 FMT in MDS-UPDRS Part III Scores

Conclusion: FMT shows promise in improving motor symptoms in patients with PD, as evidenced by a significant reduction in MDS-UPDRS Part III scores. These findings support the therapeutic potential of gut microbiota modulation in PD. However, further studies are needed to validate these results and explore long-term outcomes.
Disclosure: Nothing to disclose.

EPO-576 | Serum IGF-1 and IGF-2 as biomarkers in idiopathic Parkinson's disease: Correlation with disease stages

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Background and Aims: Idiopathic Parkinson's Disease (IPD) is a progressive neurodegenerative disorder characterized by tremor, rigidity, akinesia, and postural instability. Dysfunction in lysosomal autophagy, involving proteins like IGF-1(insulin like growth factor) and IGF-2, contributes to neuroinflammation and neuronal death. Reliable biomarkers for IPD diagnosis and monitoring remain elusive. This study investigates serum IGF-1 and IGF-2 levels to evaluate their biomarker potential.
Methods: Eighty-four individuals (43 IPD patients, 41 controls) aged 18–79 were included. Diagnoses followed UK Brain Bank Criteria; severity was assessed with Hoehn & Yahr (H&Y) and UPDRS (Unified Parkinson's Disease Rating Scale). Serum IGF-1 and IGF-2 levels were measured using ELISA. Statistical analyses included t-tests, Mann-Whitney U, Chi-square, and Spearman correlation, with $p < 0.05$ considered significant.
Results: Serum IGF-2 levels were significantly higher in patients compared to controls ($p = 0.006$), while IGF-1 levels showed no significant difference. Both IGF-1 and IGF-2 levels displayed negative correlated with disease duration ($p = 0.044$ and $p = 0.008$). Although IGF-1 and IGF-2 levels appeared elevated at H&Y stage 2, the differences were not statistically significant. No significant associations were observed between IGF levels and UPDRS scores or medication use.

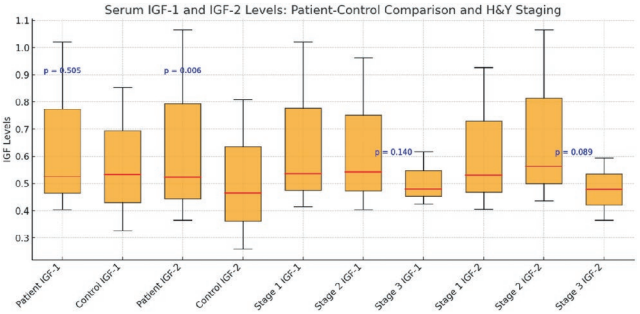

FIGURE 1 Serum igf- and igf2 levels patients and control comparison and staging.

Conclusion: Elevated serum IGF-2 levels indicate its potential as a biomarker for IPD. These findings contribute to a better understanding of the role of IGF-1 and IGF-2 in IPD pathophysiology, suggesting that further multicenter studies are needed to clarify their diagnostic and therapeutic potential.
Disclosure: Funding: This study was funded by the Scientific Research Projects Commission of Düzce University under project number 2020.04.03.1108. The funding body had no role in the study design, data collection, analysis, interpretation, or manuscript writing. Conflict of Interest: The authors declare no conflicts of interest regarding this research. There are no financial, personal, or professional relationships that could have influenced the findings of this study. Ethical Approval: This study was conducted in accordance with the principles of the Declaration of Helsinki and was approved by the Ethics Committee of Düzce University Faculty of Medicine (Approval Number: 2023/52). Informed Consent: Written informed consent was obtained from all participants before their inclusion in the study.

EPO-577 | Spectral domain and angiography optical coherence tomography in atypical parkinsonisms and Parkinson's disease

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Background and Aims: Research recently focused on identifying early and accurate biomarkers to differentiate Parkinson's disease (PD) from other degenerative parkinsonisms, as Progressive Supranuclear Palsy (PSP) and Multiple System Atrophy (MSA). We aimed to investigate changes in the retinal structure and choroidal vascular network (CVN) in PSP and MSA patients in comparison to PD and controls (Ctrl).
Methods: Spectral Domain-Optical Coherence Tomography (SD-OCT) was used to examine the ganglion cell complex (GCC), retinal nerve fiber layer (RNFL) and subfoveal choroidal thickness, and OCT Angiography (OCTA) for the vessel density (VD) of retinal and CVN assessment.
Results: We analyzed 22 eyes from 11 PSP, 14 from 7 MSA, 48 from 24 PD patients, and 50 from 25 Ctrl. In comparison to Ctrl, we observed decreased GCC thickness among PSP ($p = 0.001$) and PD patients ($p = 0.003$), and reduced RNFL thickness in all three groups of patients (PD $p = 0.043$; PSP $p < 0.001$; MSA $p < 0.001$). PD subjects showed lower values in VD of superficial capillary plexus (SCP, $p = 0.013$) and radial peripapillary capillary plexus (RPC, $p = 0.014$) in comparison to Ctrl, whereas MSA and PSP patients did not differ from them. Both groups presented significantly decreased RNFL thickness and higher VD of RPC plexus in comparison to PD group ($p < 0.001$).

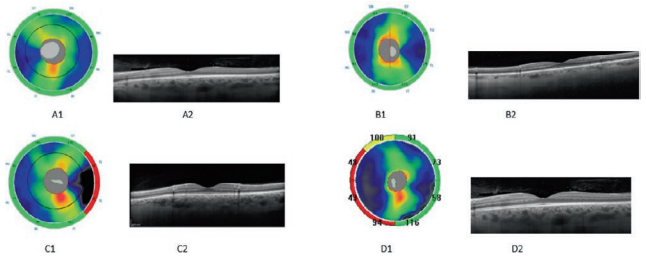

FIGURE 1 The figure shows normal RNFL thickness in Ctrl (A1), mild reduction in PD (B1), and severe reduction in PSP (C1) and MSA (D1) at SD-OCT. The subfoveal choroidal thickness was normal in Ctrl, PSP and MSA (A2, C2, D2), and slightly decreased in PD (B2).

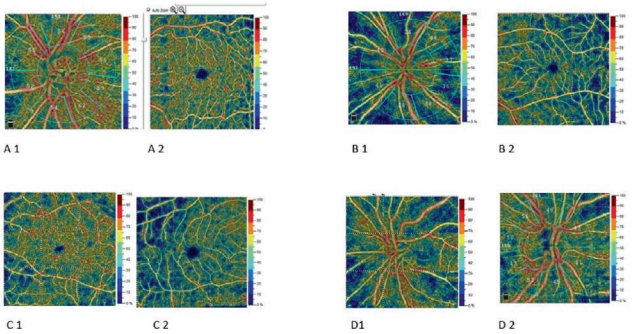

FIGURE 2 The figure shows preserved vessel density of RPC (A1) and SCP (A2) in a control subject and in PSP and MSA patients (C1, C2; D1, D2), and decreased vessel density of RPC and SCP in a PD patient (B1, B2), at the OCTA exam.

Conclusion: Compared to PD, the retina structural damage in PSP and MSA appears to be similar but more severe, whereas the CVN appears to be preserved. Our preliminary results should be confirmed in a larger series of patients to test whether OCTA can be used to differentiate degenerative parkinsonisms early.
Disclosure: Nothing to disclose.

EPO-578 | Opicapone in very elderly population: Safety overview of post-marketing data

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Background and Aims: Opicapone (OPC) is a catechol-O-methyltransferase inhibitor effective as adjunctive therapy to Levodopa for Parkinson's disease patients with motor fluctuations. There is limited clinical trial data in very elderly patients (85 years or older). This analysis primarily aims to evaluate the safety profile in this subgroup, considering data from 8 years of post-marketing experience.
Methods: OPC global safety database was searched for valid post-marketing reports (spontaneous reports, health authorities, literature reports, non-interventional studies) from launch (March 2016) to December 2024, in patients with age equal or superior to 85 years old. Expectedness was assessed based on the most recent European Summary of Product Characteristics for OPC.
Results: Cumulatively, 354 adverse events (AEs) were collected from 161 valid safety reports: 90 from female patients (55.9%) and 68 from male (42.2%) (unknown: 3). The 2 countries with most reports were Japan (93; 57.8%) and United States of America (37; 23.0%), with less than 10 reports in each of the remaining countries. The 3 most common Preferred Terms (PTs) were "dyskinesia" (22; 6.2%), "hallucination, visual" and "hallucination" (both 14; 4.0%); all 3 considered expected. 135 AEs led to drug withdrawn: "dyskinesia" (12; 8.9 %) and "hallucination, visual" and "nausea" (both 8; 5.9%) were the 3 most common. 250 AEs were non-serious (70.6%).
Conclusion: Most of the AEs were non-serious. The 3 most reported PTs were considered expected, in line with the known safety profile of OPC. OPC seems to maintain an adequate safety profile in patients with 85 years or older.
Disclosure: Supported by Bial-Portela & C[a], S.A.

EPO-579 | Sleep disorders in Parkinson's disease: Bridging nocturnal challenges and daytime impacts

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Background and Aims: Sleep disorders are a prevalent non-motor symptom in Parkinson's disease (PD) that significantly impair quality of life. This study aims to evaluate sleep quality and the prevalence of excessive daytime sleepiness (EDS) and nocturnal difficulties in PD patients.
Methods: We included PD patients diagnosed and followed in the neurology department of Monastir over one year. Disease stages were classified using the Hoehn & Yahr Scale (HYS), while severity was assessed with the Unified Parkinson's Disease Rating Scale (UPDRS). Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI), Parkinson's Disease Sleep Scale (PDSS), and Epworth Sleepiness Scale (ESS). Polysomnography (PSG) was conducted in 29 patients with significant sleep disturbances (ESS ≥10 and/or PSQI ≥7).
Results: Among 100 patients (62% men, 38% women; mean age: 66 ± 10 years), sleep disorders were identified in 69%. The most frequent were parasomnias (66.3%), snoring (62%), insomnia (56%), and hypersomnia (46%). Poor sleep quality was observed in 52% of patients, with a median PSQI of 7 [IQR: 3–10]. Hypersomnia correlated significantly with higher UPDRS motor scores ($p = 0.002$), while no association was found between insomnia and disease severity.

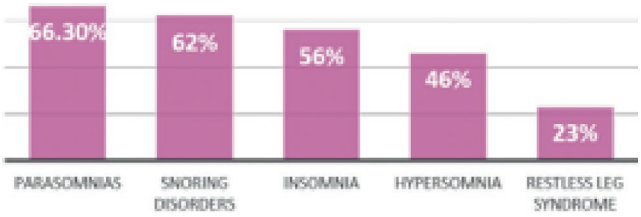

FIGURE 1 Prevalence and types of sleep disorders in PD patients

Conclusion: Sleep disorders are highly prevalent and impactful in PD, emphasizing the importance of systematic screening and targeted management. The correlation between hypersomnia and advanced motor impairment suggests a potential role of disease progression and treatment side effects. Addressing sleep issues in PD could improve patient quality of life and overall disease outcomes.
Disclosure: Nothing to disclosure.

EPO-580 | Causes of death in anti-IgLON5 disease: A novel case report and systematic literature review

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Background and Aims: Anti-IgLON5 disease is a neurological disorder characterized by both autoimmune and neurodegenerative pathomechanisms. Reported mortality rates vary between 19 and 59%, with the most common causes of death being sudden death, central hypoventilation, dysphagia, and aspiration. However, the high rate of largely unclear sudden deaths calls for further research in this area.
Methods: We performed a systematic literature search on causes of death in anti-IgLON5 disease following PRISMA guidelines. We also present a new case that was followed up in our clinic until death.
Results: Of 258 publications with anti-IgLON5 disease reported in the literature, 21 publications discussing 61 cases which reported causes of death were included in the analysis. The most common cause of death was death due to complications like pneumonia or falls (36.1 %), followed by sudden death (32.8%), either happening during sleep, wakefulness, or unknown times. Other causes include respiratory, cardiac, and unknown causes. The patient presented here as a novel case report was additionally diagnosed with cardiac amyloidosis and died from a cardiac cause of sudden death.
Conclusion: We found a strikingly high number of reports of sudden death among the specified causes of death. A progressive neurodegenerative process in the brain stem causing central hypoventilation is generally assumed as major causative factor. The case first reported here had concomitant cardiac amyloidosis which may raise the question whether unrecognised cardiac causes - which are not routinely screened for in this population - might represent another cause of sudden death, which would have important therapeutic implications.
Disclosure: Nothing to disclose.

EPO-581 | Parkinson's disease cardiovascular symptoms and the influence of DBS

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Background and Aims: The known impairments of the cardiovascular system in Parkinson's disease (PD) are orthostatic hypotension, chronotropic insufficiency, and reduced heart rate variability. Other dysfunctions, i.e. arrhythmias and heart morphology changes, are still the subject of research. Dopaminergic treatment does not influence these symptoms but less is known about the possible impact of deep brain stimulation (DBS).
Methods: Thirty PD patients without known cardiac comorbidities underwent bicycle ergometry, electrocardiogram Holter monitoring and CMR (cardiac MRI). Exercise and CMR parameters were compared with controls. The effect of DBS was evaluated, where available.
Results: PD patients had lower baseline systolic blood pressure (SBP) (117.8 vs. 128.3 mmHg, $p < 0.01$), peak SBP (155.8 vs. 170.8 mmHg, $p < 0.05$), and lower heart rate increase (49.7 vs. 64.3 beats per minute, $p < 0.01$) during exercise. PD patients had higher indexed left and right ventricular end-diastolic volumes (68.5 vs. 57.3, $p = 0.003$ and 73.5 vs. 61.0 mL/m^2, respectively) and also indexed left and right ventricular end-systolic volumes (44.1 vs. 39.0, $p = 0.013$ and 29.0 vs. 22.0 mL/m^2, $p = 0.013$). A high prevalence of atrial fibrillation (26.7%) was found. Our pilot data indicate that DBS might positively influence particularly the heart rate variability and the occurrence of arrythmias
Conclusion: Our study showed that PD is linked with weaker blood pressure and heart rate reaction during exercise, increased myocardial mass and heart volumes compared to controls, and a high prevalence of atrial fibrillation. DBS might improve some of the cardiac symptoms.
Disclosure: Nothing to disclose.

EPO-582 | Exploring the impact of diagnosis for people with Parkinson's disease and their caregivers in Tanzania

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Background and Aims: People with Parkinson's (PwP) and their caregivers in sub-Saharan Africa (SSA) are underrepresented in research investigating the lived experience of Parkinson's disease (PD). Previous research has highlighted the different challenges that PwP face in Tanzania, including stigmatising perceptions of symptoms and limited access to PD services and medicines. This research aims to understand the impact that a diagnosis has on PwP and their caregivers in Tanzania, to inform future policy and practice to better support people impacted by PD in Tanzania.
Methods: Qualitative data were collected using semi-structured interviews with PwP and caregivers in the Kilimanjaro region of northern Tanzania. Purposeful maximal variation sampling was used to recruit participants. Audio recordings were translated and transcribed and reflexive thematic analysis was applied.
Results: Twelve PwP and eight caregivers were interviewed. Data from interviews identified that a diagnosis shifted uncertainty from being driven by the unknown cause of symptoms and complex diagnostic journeys to the challenge of navigating a diagnosis of PD with limited information. Most participants reported acceptance and relief upon receiving a diagnosis. A diagnosis had varied impacts on hope for PwP and their caregivers, however consistent hope manifested through spirituality.
Conclusion: Receiving a diagnosis of PD is important to PwP and caregivers in Tanzania. It provides a sense of legitimacy and is a gateway to accessing medicines. Increasing awareness of PD and removing the financial barriers to healthcare would increase diagnoses. This should be accompanied by better availability of specialist neurological and informal services for PwP.
Disclosure: Research received funding from Transforming Parkinson's Care in Africa (TraPCAf), a National Institute for Health and Care Research (NIHR) funded project (Award ID NIHR133391).

EPO-583 | Friedreich's ataxia patient pathway in Europe

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Background and Aims: Friedreich's ataxia (FA) is a rare progressive and multi systemic neurodegenerative disorder characterized by loss of coordination, typically resulting in loss of ambulation. Cardiomyopathy, diabetes mellitus, and scoliosis are common and serious manifestations of the disease.
Methods: This project explores the FA patient pathways and compares their care experiences attending specialist ataxia centres (SAC) compared with care in non–specialist settings. We collected data in the UK, Germany and Italy using a patient survey, to gather information about the diagnosis and the management of the ataxias in specialist and non-specialist settings.
Results: Our population is patients with FA over 16 years old, living in UK ($N=27$), Germany ($N=14$) and Italy ($N=56$) with a confirmed diagnosis of FA. This cohort consists of three groups defining different pathways: currently attending SAC (UK $N=3$; Germany $N=13$; Italy $N=30$), never attended SAC (UK $N=12$; Germany $N=0$; Italy $N=5$), and used to attend SAC (UK $N=3$; Germany $N=1$; Italy $N=10$). We investigated the impact of SAC attendance on symptom management and care delivered to patients and found that some outcomes showed a favourable association with specialist care. All data on the patient pathway will be discussed.
Conclusion: This study shows the value of SAC specifically for the management of complex rare conditions like FA. We understand better FA patients' journey including the burden of the disease and their pathway in the care system. SAC are the best service to deliver new treatment that are FDA approved.
Disclosure: Nothing to disclose.

EPO-584 | Opsoclonus-myoclonus-ataxia syndrome in pregnancy with severe disease course and complete recovery: A case report

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Background and Aims: Opsoclonus-myoclonus-ataxia syndrome (OMAS) is a rare immune mediated neurological disorder characterized by opsoclonus (rapid, oscillatory eye movement), myoclonic jerks mostly in the face and limbs, cerebellar ataxia, tremors, and encephalopathy. OMAS is rare in adults and exceedingly rarer in pregnancy, as only a few cases in pregnancy have been reported. To the best of our knowledge, this is the fifth presented case of OMAS with a severe disease course and complete reversibility of neurological symptoms in a pregnant woman.
Methods: We report and discuss a challenging case of OMAS which presented at 36 weeks gestation in a 38 year old lady. Despite extensive infectious and malignancy evaluation, an underlying etiology was not readily apparent thus we treated presumptively for an idiopathic autoimmune OMAS with high dose intravenous steroids and intravenous immunoglobulin (IVIG).
Results: A significant clinical improvement was seen post-IVIG and upon childbirth through emergency C-section. The diagnostic workup showed a normal MRI neuroaxis, and positive CSF oligoclonal bands. At 6 months' follow up, there was evidence of further clinical improvement with a resolution of the movement disorder and opsoclonus.
Conclusion: The autoimmune response in OMAS is thought to occur by molecular mimicry with neuronal cell surface antigens from an infective agent. A preceding infection was absent in this case therefore we hypothesize that the immune trigger was the pregnancy.
Disclosure: Nothing to disclose.

EPO-585 | Using zebrafish model to investigate complex hereditary spastic paraplegia caused by variants in Kennedy pathway genes

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Background and Aims: Hereditary Spastic Paraplegia (HSP) is a wide and heterogeneous group of inherited degenerative and neurodevelopmental disorders. 19 genes of spastic paraplegia genes (SPG) are involved in membrane phospholipid metabolism. The Kennedy pathway is one of the major biosynthetic sources of PE. EPT1 gene encodes ethanolaminephosphotransferases converting CDP-ethanolamine to PE in PE branch of the pathway. The bi-allelic loss of function mutations in EPT1 have been described to cause a complex autosomal recessive HSP, SPG81.
Methods: CRISPR-Cas9 technique was used to create ept1 ex5 knock-out mutants and crispants. A series of phenotypic characterization, RNA sequencing and lipidomic profiling on these zebrafish models were conducted in the zebrafish model.

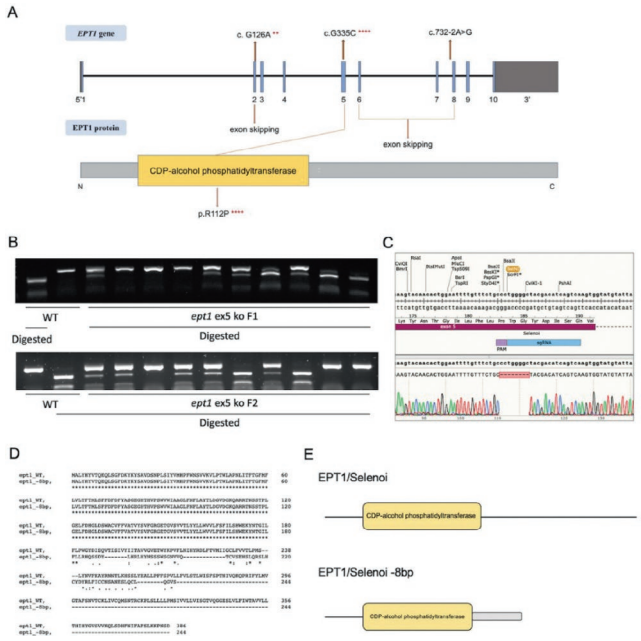

FIGURE 1 EPT1 gene and crispr guide design

Results: CRISPR-Cas9 technique was used to create ept1 ex5 knock-out mutants and crispants. A series of phenotypic characterization, RNA sequencing and lipidomic profiling on these zebrafish models were conducted in the zebrafish model.

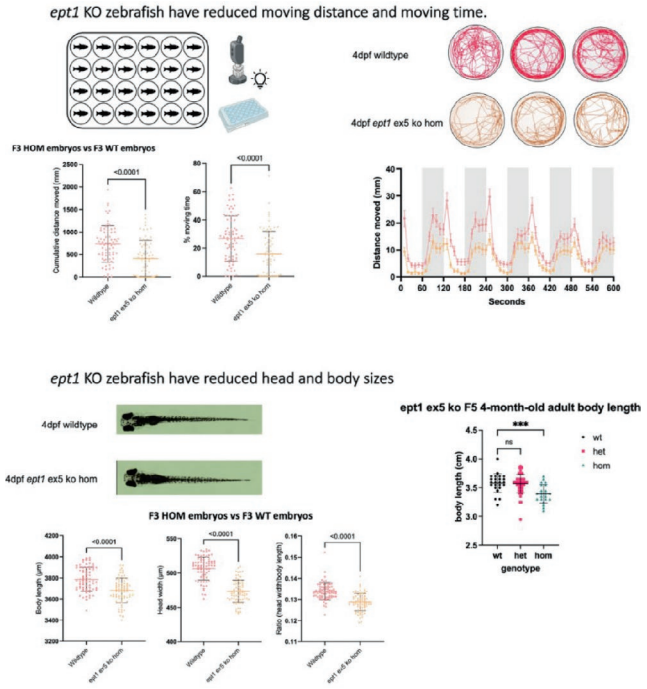

FIGURE 2 Movement and developmental changes in the knockouts

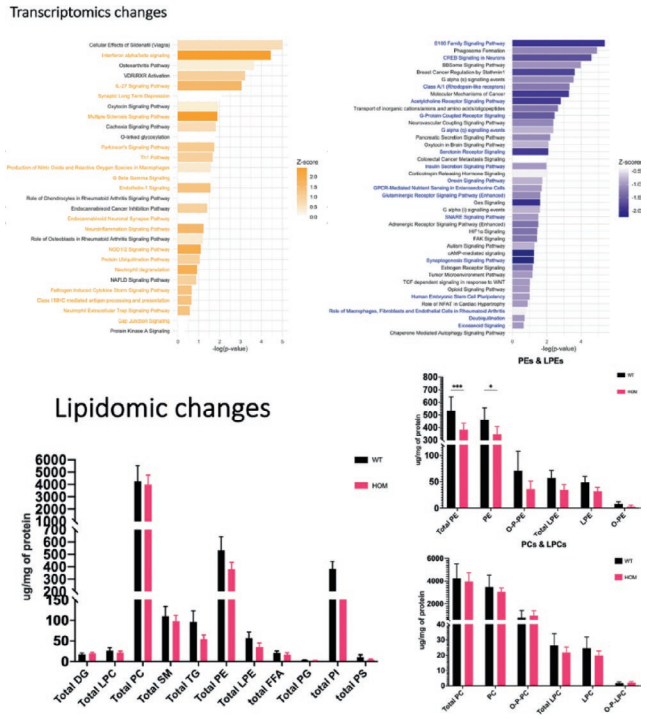

FIGURE 3 Transcriptomic and Lipidomic changes in the knockouts

Conclusion: CRISPR-Cas9 technique was used to create ept1 ex5 knock-out mutants and crispants. A series of phenotypic characterization, RNA sequencing and lipidomic profiling on these zebrafish models were conducted in the zebrafish model.
Disclosure: Nothing to disclose.

EPO-586 | A quantitative investigation of the handwriting kinematics in response to STN-DBS in Parkinson's disease patients

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Background and Aims: Micrographia is a disabling feature in Parkinson's disease (PD), yet its underlying mechanisms remain unclear. While STN-DBS is effective in improving motor symptoms, its impact on handwriting kinematics is not well established. We aimed to investigate handwriting changes, particularly micrographia, in PD patients with STN-DBS under different stimulation conditions.
Methods: We prospectively evaluated consecutive PD patients with STN-DBS who visited our movement disorders center between October and December 2023. Demographic and clinical parameters, along with MDS-UPDRS-III scores in stimulation "off" and "on" conditions, were recorded. Handwriting parameters—letter area, writing time, and pressure—were analyzed using a digital graphic tablet (Wacom Intuos Pro-Large) and an electronic pen. Micrographia-related metrics were assessed across four stimulation conditions: bilateral, left, right, and no stimulation.
Results: Twenty patients (mean age: 56.7 ±11.4 years, F/M = 7/13) were included. The median motor improvement rate with stimulation was 0.37. No significant differences in handwriting parameters were observed across stimulation conditions. However, longer writing duration (stim-off) correlated with higher HAM-A scores (CC = 0.662, $p = 0.007$) and HDRS scores (CC = 0.642, $p = 0.005$), suggesting an influence of anxiety and depression on handwriting performance.
Conclusion: STN-DBS did not induce significant changes in handwriting kinematics, suggesting that micrographia may result from non-dopaminergic dysfunctions resistant to DBS. These findings provide insights into the pathophysiology of micrographia and the differential effects of DBS on fine motor control.
Disclosure: Nothing to disclose.

Movement disorders 7

EPO-587 | Epidemiological and clinical profiles in Huntington's disease: Analysis from Pauls Stradiņš Clinical University Hospital

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Background and Aims: Huntington's disease (HD) is a genetically determined neurodegenerative disorder. While motor symptoms are hallmark features, non-motor manifestations—such as cognitive impairment, psychiatric disturbances, and behavioral changes—pose significant challenges in disease management.
Methods: Epidemiological data were collected from local HD patients. Functional independence was assessed using the Total Functional Capacity (TFC) scale, and non-motor symptoms, including psychiatric and cognitive impairments, were evaluated using the Non-Motor Symptoms Scale (MD-NMS).
Results: This study included 40 patients (47.5% male) observed between 2014 and 2024. Among them, five were asymptomatic, and ten died. The median age was 48 years (range: 23–76 years), and symptom onset occurred at a median age of 40 years (range: 29–47 years). Paternal inheritance was identified in 50% of cases, and maternal inheritance in 10%, 40% left unknown. Motor and psychiatric symptoms were the earliest and most disruptive. The median TFC score was 4 (IQR: 1–7), with 40.9% of patients classified in stage 3. Among 17 participants in the MD-NMS questionnaire, the mean total score was 156.29 (±42.90). Depression (mean: 23.59 ±10.57), cognition (mean: 21.94 ±11.42), and impulse control (mean: 19.94 ±9.85) were the most affected domains.
Conclusion: Motor and psychiatric symptoms significantly impair HD patients' functional independence. Non-motor symptoms further reduce quality of life, highlighting the need for comprehensive management strategies addressing both motor and non-motor manifestations.
Disclosure: ChatGPT was used to enhance readability.

EPO-588 | Essential tremor patient motivations and barriers for advanced treatment: From USA to Europe

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Background and Aims: Essential tremor (ET) impairs activities of daily living (ADL). Medications are ineffective in up to 50% of patients. Deep brain stimulation (DBS) and MR-guided focused ultrasound (MRgFUS) are included in advanced therapies guidelines. 6,000 MRgFUS procedures have been performed in Europe, over 22,000 worldwide, surpassing DBS for ET in the USA. To better understand living with tremor and motivations for advanced treatments, we explored patient-reported data from Insightec's USA-educator team.
Methods: Compliant with US-Regulations, the Insightec educator team provides information about tremor management, MRgFUS technology, and treatment eligibility to interested patients. From August 2015 to December 2024, patient-reported data were collected via questionnaires on tremor impact, medication satisfaction, clinical care, and motivations for advanced treatment.
Results: Out of 145,286 responders, 63,925 (44%) had an ET formal diagnosis. 98.76% of those interested in MRgFUS have tried medication, 80% being dissatisfied (Figure 1). 80% reported moderate-severe impact on ADLs. Tremor is mainly managed by general neurologists (46%) or primary care physicians (PCP) (43%), regardless of severity (Figure 2). Barriers to MRgFUS include low tremor severity and travel requirements. Respondents largely denied objection to MRgFUS-procedural considerations (Figure 3).

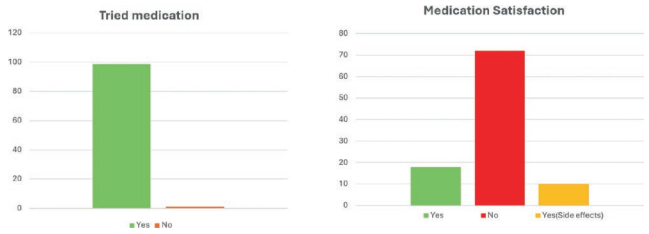

FIGURE 1 Representation of patients interested in MRgFUS who have tried medication, and their satisfaction with it.

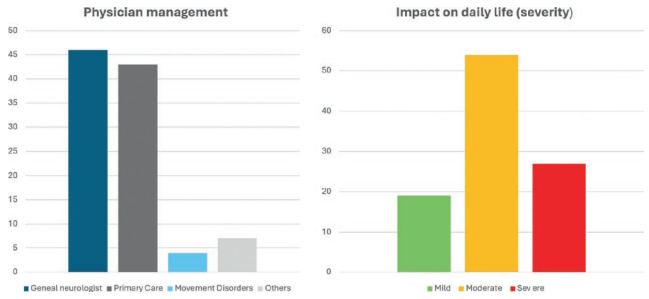

FIGURE 2 Representation of professionals in charge of patients' management, and impact on daily life.

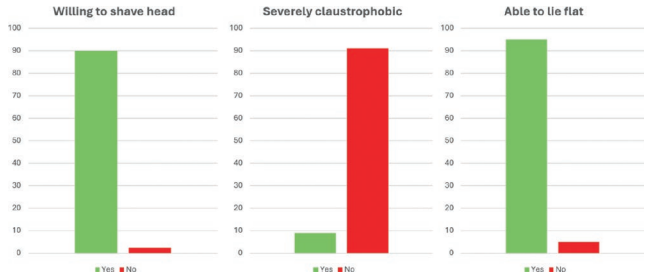

FIGURE 3 Each of the three categories listed (willing to shave head, being severely claustrophobic or having the ability to lay flat) are potential disqualification questions when considering MRgFUS.

Conclusion: This analysis demonstrates that among patients contacting our USA-educator team, more than 5000 per year are dissatisfied with pharmacotherapies and are interested in advanced treatments. These, in combination with high MRgFUS-procedural considerations acceptance may explain its growing adoption worldwide. Awareness and knowledge around ET's burden and advanced therapies' options are critical for neurologists and PCPs. Some barriers remain and further investigation is needed to understand if they translate to European Patients.
Disclosure: The authors are all Insightec employees.

EPO-589 | Long-term effectiveness of safinamide vs. rasagiline in Parkinson's disease: A real-world retrospective study

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Background and Aims: Parkinson's disease (PD) management involves levodopa and other treatments, including MAO-B inhibitors like safinamide and rasagiline. This study assesses their real-world use and effectiveness in Spanish PD patients.
Methods: Using IQVIA's Electronic Medical Records (EMR) database, this non-interventional, longitudinal retrospective study analysed adults treated with N04 - Anti Parkinson drugs between July 2022 and July 2023. 151,264 projected patients were grouped based on rasagiline or safinamide treatment, with a follow-up period of 24 months before and after their relevant index-prescription.
Results: Most patients were males aged > =76 years with comorbidities. Rasagiline did not demonstrate improvements in comorbid conditions. However, safinamide exhibited benefits after 24 months, especially in pain (reducing from 25% to 21%). Regarding concomitant medications, safinamide patients experienced reductions in the use of antipsychotics, hypnotics/sedatives, and analgesics by 2%, 6%, and 3%, respectively. Conversely, rasagiline patients increased the use of these medications by 2%, 1%, and 1%, respectively. After 24 months, 91% of safinamide patients remained persistent in their medication use, compared to 85% of rasagiline patients. Additionally, rasagiline patients increased their levodopa dose by 21% over 12 months. In contrast, safinamide patients maintained a steady dose throughout the same follow-up period, with their dosage varying only 2%. Also, rasagiline treatment led to a 4% increase in Dopamine Agonist Levodopa Equivalent Dose (LED-DA) while safinamide reduced it in 1%.
Conclusion: Safinamide may offer a better treatment option for PD patients, with higher persistence rates, better comorbidity management, stabilized levodopa dosage, and reduced use of additional medications compared to rasagiline.
Disclosure: The research conducted in this study received commercial and institutional support from Zambon.

EPO-590 | Imaging features and clinical outcomes in patients with ventriculomegaly and gait impairment

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Background and Aims: Ventriculomegaly, a key feature of idiopathic normal pressure hydrocephalus (iNPH), can also occur in neurodegenerative diseases like Alzheimer's disease (AD), Parkinson's disease (PD), dementia with Lewy bodies (DLB), and progressive supranuclear palsy (PSP). Imaging measures such as Evans's index (EI), Callosal angle (CA), and Disproportionately Enlarged Subarachnoid Space Hydrocephalus (DESH) are helpful, but differences in neurodegenerative contexts remain unclear
Methods: A retrospective study analyzed 55 patients with gait impairment and 40 matched controls (mean age 74.1 ± 5.4 years). Brain MRIs assessed ventriculomegaly using EI (>0.3) and CA (<90°), alongside DESH scoring. Patients were classified into neurodegeneration (PSP, AD, DLB, PD), iNPH, and controls based on diagnostic criteria, cognitive tests, CSF biomarkers, and ^{18}F-Dopa-PET, with ≥3 years of follow-up. Kruskal-Wallis and Bonferroni tests were applied for statistical analysis

Results: Of patients with ventriculomegaly, 44% met criteria for PSP, 14% for AD, 4% for DLB, 1 for PD, and 36% for iNPH. The CA was lower in neurodegeneration (ND) patients compared to iNPH and controls (79.9 ± 5.2 vs 87.5 ± 2.0 vs 129.7 ± 3.6, $p < 0.001$). EI was similar between ND and iNPH groups (Table 1). The DESH index was higher in ND patients compared to iNPH and controls (6.5 ± 1.3 vs 4.5 ± 0.9 vs 0.10 ± 0.3, $p < 0.001$).

Table 2. Distribution of patients with ventriculomegaly

PSP (F%)	24 (44%)
AD (F%)	8 (14%)
DLB (F%)	2 (4%)
PD (F%)	1 (2%)
iNPH (F%)	20 (36%)
Total	55 (100%)

Abbreviations: Frequency (F), Progressive supranuclear palsy (PSP), Alzheimer's disease (AD), dementia with Lewy bodies (DLB), Parkinson's disease (PD) and idiopathic normal pressure hydrocephalus (iNPH).

Table 1. Imaging, clinical and demographic characteristics of patients with neurodegeration, iNPH, and controls

	ND (n=35)	iNPH (n=20)	HC (n=40)	*p-value*
Age (years)[a]	73,8 ± 6,3	74,3 ± 5,09	74,3 ± 4,6	
Gender (F/M)[b]	15/20	7/13	17/23	
CA[a]	79,9 ± 5.2	87.5 ± 2.0	129.7 ± 3.6	ND vs iNPH ***p <0.001*** ND, iNPH vs HC ***p <0.001***
EI	0.344 ± 0.018	0.340 ± 0.028	0.265 ± 0.013	ND vs iNPH ***p 0,54*** ND, iNPH vs HC ***p <0,001***
DESH	6.5 ± 1.3	4.5 ± 0.9	0,10 ± 0.3	ND vs iNPH ***p <0,001*** ND, iNPH vs HC ***p <0,001***

Note: Values are given as means and standard deviation or absolute frequencies. Statistical significance is indicated by bold font. Abbreviations: ND, neurodegeneration; iNPH, idiopathic normal pressure hydrocephalus; HC, healthy control; F, female; M, male; **CA**, callosal angle; **EI**, Evans's Index; **DESH**, Disproportionately Enlarged Subarachnoid Space Hydrocephalus.
[a] Kruskal Wallis test analysis with adjustments for multiple comparisons using the Bonferroni test when appropriate.
[b] Chi-squared test.

Conclusion: Our findings indicate that patients with ventriculomegaly and neurodegeneration have a lower CA and higher DESH. These observations may help in assessing neurodegeneration but should be interpreted cautiously when considering shunting decisions
Disclosure: Nothing to disclose.

EPO-591 | The relation between upper limbs action tremor asymmetry, midline tremor and gait in essential tremor

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Department of Medical, Surgical Sciences and Advanced Technologies "G.F. Ingrassia", Section of Neurosciences, University of Catania, Catania, Italy

Background and Aims: Upper limbs action tremor represents the clinical hallmark of Essential Tremor (ET), which showed varying degrees of asymmetry. However, the possible role of the upper limbs action tremor asymmetry in the context of the broader ET motor phenotypical spectrum has never been addressed to date. The aim of the present study was to assess the possible relation between upper limbs action tremor asymmetry and other motor aspects which may characterize the ET syndrome.
Methods: Clinical tremor scores and instrumental kinematic gait parameters were assessed. An asymmetry index (AI) was computed based on clinical severity of each upper limbs action tremor component. Symmetric (S-ET, AI = 0) and Asymmetric (A-ET, AI≠0) patients were defined and compared based on the most asymmetric action tremor component.
Results: Thirty-seven tremor patients [8 pure ET (21.6%) and 29 ET-plus (78.4%)] were enrolled. Forward outstretched (FO) postural tremor represented the action tremor subtype showing the greater clinical asymmetry across the whole tremor population. No significant differences on action tremor AIs were reported between pure ET and ET-Plus. Based on FO tremor AI, two patients' subgroups were defined: A-ET ($N = 21$, 56.8%) and S-ET ($N = 16$, 43.2%), the latter showing higher midline tremor severity (i.e. head and voice) and worse instrumental gait parameters.
Conclusion: The study highlights the possible role of upper limbs action tremor asymmetry as an adjunctive feature to be considered in ET clinical phenotyping.
Disclosure: Nothing to disclose.

EPO-592 | Impact of beta glucocerebrosidase gene mutation on quality of life and activities of daily living in Parkinson's disease

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Background and Aims: The aim of this study was to investigate the impact of the beta glucocerebrosidase (GBA) gene mutation on quality of life (QoL) and activities of daily living (ADL) in patients with idiopathic Parkinson's disease (PD).
Methods: This cross-sectional study included patients with idiopathic PD. Patient data were obtained from the Movement Disorders Clinic at the University Hospital Centre Osijek. QoL and ADL were assessed using the Movement Disorder Society

– Unified Parkinson`s Disease Rating Scale (MDS-UPDRS) II and Parkison`s Disease Questionnairre-8 (PDQ-8) questionnaires through a telephone survey.
Results: The study included 51 patients with idiopathic PD (17 female, 34 male) that performed genetic testing for GBA mutation. Genetic testing identified 5 (9.8%) carriers of the heterozygous beta GBA mutation. There was no statistically significant correlation between age and measures of ADL and QoL in both patients with ($p=0.94$; $p=0.55$) and without GBA mutation ($p=0.13$; $p=0.89$). In patients without GBA mutation, a negative correlation was observed between age and sleep disturbances, sialorrhea and tremor ($p=0.01$, $p=0.005$, $p=0.04$). Episodes of "freezing of gait" were more frequent among carriers of GBA mutation ($p=0.05$). No significant differences in QoL or ADL were observed between GBA gene mutation carriers and non-carriers.
Conclusion: In this cohort, GBA mutation did not significantly influence QoL or ADL. However, further research with a larger sample size should be done to better evaluate the role of the beta GBA mutation on PD patients' lifestyles.
Disclosure: Nothing to disclose.

EPO-593 | Real-world and long-term safety of MR-guided focused ultrasound in movement disorders: A comprehensive review

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Background and Aims: Magnetic resonance–guided focused ultrasound (MRgFUS) is CE-approved for unilateral treatment of Parkinson's disease (PD) and both unilateral and staged-bilateral treatments of essential tremor (ET) and neuropathic pain (NP). To date, over 22,000 MRgFUS procedures have been performed globally, with over 6,000 conducted in Europe. This analysis provides a comprehensive review of safety outcomes reported since MRgFUS approval.
Methods: We reviewed long-term safety data from published literature, including clinical trials, manufacturer-reported safety data, and user surveys for MRgFUS treatments in ET and PD.
Results: In ET pivotal trials, adverse events (AEs) were predominantly mild (74% unilateral, 85% bilateral) with no severe AEs reported. Common AEs included paresthesias (38% unilateral, 33% bilateral) and gait disturbances (36% unilateral, 24% bilateral), often resolving within six months (48% and 52%, respectively). Dysarthria and taste disturbances were more frequent after bilateral MRgFUS (2% vs. 24% and 5% vs. 20%, respectively). Similarly, in unilateral PD treatments, AEs were mostly mild, with paresthesias (0–35%), gait disturbances (3–26%), and dysarthrias (3–19%) typically resolving within six months. Long-term follow-ups showed no worsening of AEs. Post-marketing surveillance of 19,850 procedures reported 193 AEs (1%), primarily paresthesias and gait disturbances.
Conclusion: Real-world data confirm the safety of unilateral and staged-bilateral MRgFUS, consistent with prior literature and without unexpected events. This analysis reinforces the favorable safety profile of MRgFUS and its role as an advanced therapy for movement disorders.
Disclosure: All authors are employees of Insightec.

EPO-594 | SL-START: A multicentre observational study of sublingual apomorphine titration and usage schemes in routine practice

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Background and Aims: People with Parkinson's disease (PD) experiencing motor fluctuations often suffer problems such as morning akinesia, delays in time-to-ON, and unpredictable OFF episodes with their levodopa regimen. Apomorphine sublingual film (SL-APO) is taken on demand for a quick and reliable transition from OFF to ON. SL-APO requires titration for optimal effect while balancing tolerability. The SL-START study aims to characterize how SL-APO is titrated and used in routine practice.
Methods: SL-START is a prospective, observational, 6-month study of SL-APO to be conducted at 12 sites across Germany. Patients (≥18y) with a PD diagnosis and experiencing intermittent OFF episodes not sufficiently controlled by oral antiparkinsonian medication are eligible if they have been prescribed SL-APO for the management of OFF episodes.
Results: Patients will be assessed at baseline, during titration, and after 3 and 6 months. The primary objective is to identify the different titration schemes, including number of days and OFF episodes needed to achieve the optimal SL-APO dose and the percentage of patients who achieve an optimal dose. Details of the SL-APO regimen, use of domperidone, and other PD medications will be documented. Clinician and Patient Global Impressions of Change and satisfaction with SL-APO will also be captured. Safety and tolerability will be assessed via adverse event reporting and the number of treatment discontinuations.
Conclusion: SL-START will inform on the factors of SL-APO titration that are important for patient retention and the titration strategies which work best in real-world practice.
Disclosure: Funded by BIAL.

EPO-595 | ROSSINI: Study in progress assessing long-term foslevodopa/foscarbidopa effectiveness and safety in Parkinson's disease

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[1]Parkinson-Klinik Ortenau, Wolfach, Germany; [2]Movement Disorder Clinic, University Hospital of Bispebjerg, Copenhagen, Denmark; [3]AbbVie Inc., North Chicago, Illinois, USA; [4]Department of Pharmacology, University of Gothenburg, Gothenburg, Sweden

Background and Aims: Clinical trials demonstrated the efficacy/safety of foslevodopa/foscarbidopa (LDp/CDp) in patients

with advanced Parkinson's disease (PD) and uncontrolled motor fluctuations. LDp/CDp has not been studied in real-world settings. The ROSSINI (Real-world Outcomes with continuouS Subcutaneous levodopa INfusIon) study is assessing the real-world effectiveness and safety/tolerability of LDp/CDp and evaluating whether outcomes are similar to those in clinical trials and sustained in the long-term.

Methods: ROSSINI is a prospective, observational, multicountry, dual-cohort, open-label study (NCT06107426) conducted in adults with levodopa-responsive PD. Patients received LDp/CDp per approved local label/reimbursement regulations. Enrolling patients are naive to LDp/CDp (cohort A) or transitioning from LDp/CDp open-label extension studies (cohort B; NCT04379050, NCT04750226). The primary endpoint is change from baseline to month 36 in "Off" time (measured by Movement Disorder Society-Unified PD Rating Scale Part IV item 4.3 [cohort A] and Hauser diaries [cohort B]). ROSSINI is also assessing quality of life, motor/nonmotor symptoms, and safety. Effectiveness outcomes are being evaluated during 7-10 study visits over 3 years. Analyses are being conducted separately for each cohort.

Results: ROSSINI will enrol ≈450 patients (cohort A, $n=300$; cohort B, $n=150$) across 77 sites in Europe, Australia, and North America. Baseline characteristics of the first 102 patients (all non-US [US enrolment had not yet started]) enrolled in cohort A were reflective of patients with advanced PD and uncontrolled motor fluctuations (Table).

Table. Baseline Characteristics in Cohort A

Characteristic	Cohort A – LDp/CDp-Naive (n = 102)
Age, years, mean (SD)	68.0 (9.4)
Age < 65 years, n (%)	32 (31.4)
Country, n (%)	
Germany	49 (48.0)
Denmark	17 (16.7)
Sweden	13 (12.7)
Israel	11 (10.8)
Spain	7 (6.9)
Romania	2 (2.0)
Austria	2 (2.0)
Canada	1 (1.0)
PD duration, years, mean (SD)	12.3 (5.7)[a]
< 10 years, n (%)	34 (35.1)[a]
>= 10 years, n (%)	63 (64.9)[a]
Time since onset of motor fluctuations, years, mean (SD)	6.6 (5.5)[b]
< 3 years, n (%)	27 (28.4)[b]
>= 3 years, n (%)	68 (71.6)[b]
Hoehn and Yahr stage, mean (SD)	2.9 (0.8)[c]
< 3, n (%)	27 (36.5)[c]
>= 3, n (%)	47 (63.5)[c]
MDS-UPDRS Part IV item 4.3 score (time spent in the "Off" state), mean (SD)	1.7 (0.8)[c]
MDS-UPDRS Part IV item 4.1 score (time spent with dyskinesias), mean (SD)	1.4 (1.1)[c]
MDS-UPDRS part II total score, mean (SD)	17.2 (10.2)[d]
PDQ-39 summary index score, mean (SD)	34.0 (15.1)[e]

LDp/CDp, foslevodopa/foscarbidopa; MDS-UPDRS, Movement Disorder Society-Unified Parkinson's Disease Rating Scale; PD, Parkinson's disease; PDQ-39, 39-item Parkinson's Disease Questionnaire.
[a]n = 97. [b]n = 95. [c]n = 74. [d]n = 51. [e]n = 57.

Conclusion: Final ROSSINI study results will extend findings from previous studies by providing up to 3 years of data on the real-world effectiveness and safety/tolerability of LDp/CDp in advanced PD.

Disclosure: WHJ serves as an advisor and speaker for AbbVie, Bial, Desitin, Stada, UCB, and Zambon. TH has served as a speaker for AbbVie, Britannia, Convatec, Nordic Infucare, and Lundbeck, and is a primary investigator for the M15-741 and M15-737 studies sponsored by AbbVie and the Elegance study sponsored by Brittania. She is also a board member of a data monitoring committee at a study sponsored by Lundbeck. LB, PK, RG, MS, JCP, and SC are full-time employees of AbbVie, and may hold AbbVie stock and/or stock options. FB has received financial compensation for lectures and advisory services as well as in-kind donations of PKG reports for clinical studies from GKC, and has received honoraria for lectures and advisory boards from AbbVie.

EPO-596 | COMT-inhibitors clinical experience in early motor fluctuations. Twelve months analysis of REONPARK study

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Background and Aims: In Parkinson's disease (PD), COMT inhibitor (iCOMT) usage extend the elimination half-life of levodopa and reduce peak-trough variations, contributing to optimize the dose of levodopa and stabilize plasma levels [1]. Available iCOMT include opicapone, entacapone and tolcapone. Although evidence indicates comparable iCOMT efficacy in reducing off-time and increasing on-time in both patients with recent and long-standing motor fluctuations, some studies suggest a benefit of earlier initiation of iCOMT [2-6]. The REONPARK study aims to evaluate iCOMT effectiveness and tolerability in alleviating motor complications associated with L-dopa treatment in PD patients with early motor fluctuations (EMF, signs of end-of-dose motor fluctuations within ≤2 years) in clinical practice.

Methods: REONPARK study is a Spanish iCOMT registry for PD patients treated with L-dopa/DDCI and EMF. Presenting here an interim analysis up to 12 months post iCOMT initiation.

Results: 89 evaluable patients (mean ± SD: 64.6 ±10.2 years old; 4.8 ±3.1 years PD duration; 463.8 ±191.7 mg/daily L-dopa; MDS-UPDRS III: 29 ±14.5; MDS-UPDRS IV: 4.5 ±1.9) initiated iCOMT (98.9% opicapone; 1.1% entacapone). After 3, 6 and 12 months the motor symptoms and motor complications (fluctuations and dyskinesias) were reduced (Table 1). Mean OFF time decreased from 3.8 ±2.6h at baseline to 1.9 ±2.2 h ($p<0.001$) after 12 months (Figure 1). Meanwhile, OFF severity seems to be reduced since the functional impact of the fluctuations was reduced, and patients experiencing no impact increased from 12.4% to 47.7% (Figure 2).

Variable	Mean change from baseline	p-Value
MDS-UPDRS part III*		
3 months	-4.44	<0.001
6 months	-5.98	<0.001
12 months	-5.17	<0.001
MDS-UPDRS part IV**		
3 months	-1.70	<0.001
6 months	-1.76	<0.001
12 months	-1.45	<0.001

SD, standard deviation; MDS-UPDRS, Movement Disorders Society-Unified Parkinson's Disease Rating Scale

* For MDS-UPDRS part III (N=81), 7 patients were excluded from this analysis due to missing scale data in some visits.

** For MDS-UPDRS part IV (N=74), 15 patients were excluded from this analysis due to missing scale data in some visits.

Table 1

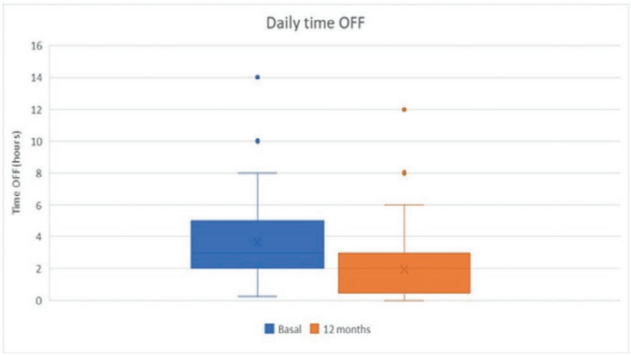

Figure 1

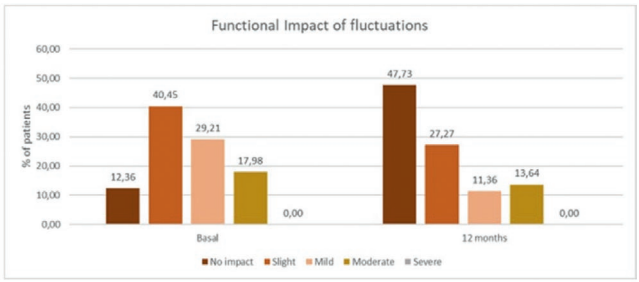

Figure 2

Conclusion: iCOMT (mainly opicapone) demonstrated a reduction on OFF time, improving the functional impact of fluctuations after up to 12 months treatment in real-world practice

Disclosure: Study supported by Laboratorios Bial S.A LLM received honoraria in the past 5 years from Abbott, AbbVie, Bial, Biogen, Esteve, Italfarmaco, Orion, STADA and Zambon. JGC received honoraria in the past 5 years from Bial, Zambon, Nutricia and Schwabe. DVR has received honoraria for educational presentations and consulting services in the past 5 years from Bial and Zambon. BSV has received honoraria for educational presentations and consulting services in the past 5 years from Bial and Zambon. MMA has received honoraria for educational presentations and consulting services in the past 5 years from Stada, Abbvie, Orion Pharma, Italfarmaco, Ever, Bial, Zambon, Esteve and Exeltis. JBA, ITA and MRM are employees of Bial.

EPO-597 | The non-motor characteristics of idiopathic Parkinson's disease in northern Tanzania, focusing on mood and cognition

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Background and Aims: This is an observational study set in the Hai district of Northern Tanzania. It aims to describe the non-motor symptom (NMS) profile of idiopathic Parkinson's disease (PD) in a rural setting in Sub-Saharan Africa, focusing on the domains of mood and cognition.
Methods: A door-to-door survey identified PD cases in the district. The following validated assessment tools were used to ascertain the participants' NMS burden: the Non-Motor Symptom Questionnaire (NMSQ), Movement Disorder Society Unified PD Rating Scale (MDS-UPDRS), Identification and Intervention for Dementia in Elderly Africans (IDEA) screening tool for cognitive impairment (CI), and Hospital Anxiety and Depression Scale (HADS). Statistical analysis was done to identify relationships within the dataset.
Results: 100% of the cohort ($n=29$) experienced NMS. The MDS-UPDRS cohort mean (+ SD) for total NMS score was 15.1 (+ 1.7) out of 52, and 15 people had CI. MDS-UPDRS data highlighted depressed ($n=12$), anxious ($n=13$), and apathetic ($n=11$) moods. The IDEA screen picked up 9 participants with signs of dementia. Participants experienced an average of 10 out of 30 symptoms within the NMSQ. 13 (48%) participants had borderline or abnormal results for both anxiety and depression in the HADS. There was a 100% treatment gap for mood and cognitive symptoms.
Conclusion: The study underscores a high prevalence of NMS in this cohort. PD patients in Tanzania are commonly affected by mood and cognitive symptoms, which are strongly associated with one another. Further research with a larger cohort will strengthen these conclusions and emphasise the need to develop accessible NMS therapies.
Disclosure: The research received funding from Transforming Parkinson's Care in Africa, a National Institute for Health and Care Research funded project (Award ID NIHR133391).

EPO-598 | Glymphatic dysfunction, cognitive and sleep disorders in patients with Parkinson's disease

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Background and Aims: Non-motor symptoms, including sleep and cognitive disturbances, are common in Parkinson's disease (PD). Sleep maintains brain homeostasis and promotes waste clearance via the glymphatic system (GS). Sleep fragmentation with reduced slow wave sleep (SWS) impairs cognition and promotes neurodegenerative changes. We investigated glymphatic dysfunction in relation to the brain bioelectrical

activity during sleep, cognitive abilities and MRI structural alteration in PD.

Methods: Participants included 26 non-demented PD patients aged 45-60 years and 30 age-matched controls. Polysomnography with quantitative EEG spectral power analysis was used for sleep assessment. Diffusion tensor image analysis with perivascular space (DTI-ALPS) index was calculated to investigate the GS. We also used MRI voxel-based morphometry and neuropsychological tests.

Results: Objective and subjective sleep disorders indicators were worse in the PDpatient. Additionally, they showed SWA reductions with greater decrease in frontal regions during NREM compared to controls (figure). A number of PDpatients showed mild cognitive impairment (MCI) and worse neuropsychological test scores. Along with the reduction in the brain structures volume related to the frontostriatal and posterior-cortical MCI subtype, PD patients had a reduced DTI-ALPS index compared to controls (table1). A relationship was found between DTI-ALPS index and frontal delta spectral power during N3, subjective sleep disturbances, as well as cognitive function in PD patients. Glymphatic influx correlates positively with decreased volume in the brain structures involved in executive function and memory formation (table2).

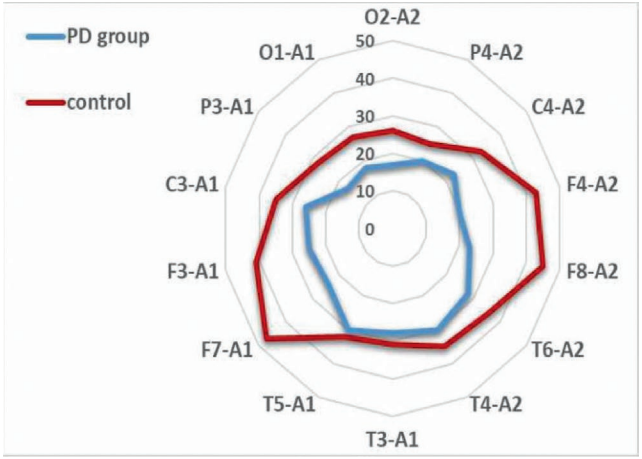

FIGURE 1 Distribution of relative delta-band power (SWA 1-4 Hz (%) between groups during slow wave sleep.

TABLE 1 Comparative assessment of the PD patients group and the controls.

Parameters	PD patients group n = 26	Control group n = 30
	Median (IQR)	
Age, years	55 (51 – 58)	53 (50 – 57)
H & Y stage	2,5 (2–3)	-
Disease duration (years)	7 (6 – 13)	-
UPDRS (part I)	17 (14 - 24)	-
UPDRS (part III)	34 (29 - 45)	-
Parkinson's disease sleep scale	22 (18 - 29)	-
Diffusion tensor magnetic resonance imaging		
DTI-ALPS index (left)	1,31 (1,22 – 1,39)	1,57 (1,41 – 1,68)*
DTI-ALPS index (right)	1,29 (1,27 – 1,42)	1,62 (1,43 – 1,67)*
Polysomnography		
Total sleep time (min)	324 (312- 357)	376 (341–422)*
Sleep onset latency (min)	39 (27 - 45)	15,3 (12,7–18,4)*
Duration of sleep stages (percentage of sleep time)		
N1 %	10,3 (8,4 – 13,1)	8,8 (7,1–10,5)
N2 %	53,9 (48,5 – 58,4)	52,5 (45,9–57,3)
N3 %	10,6 (9,3 – 12,9)	18,3 (15,0–22,7)*
REM%	22,8 (19,6 – 25,7)	19,5 (17,8–25,2)
Neuropsychological tests		
MMSE	28 (27 – 29)	29 (28 – 30)
MoCA	24 (22 – 28)	27 (26 – 29)
FAB	15 (14—17)	17 (15—18)*
Trails Making Test Part A (s)	58 (44 – 72)	43 (36 – 58) *
Trails Making Test Part B (s)	116 (95 – 163)	87 (76 – 120) *

MMSE - Mini-mental State Examination
MoCA - Montreal Cognitive Assessment
FAB - Frontal Assessment Battery
* - $p \leq 0,05$ - Significant differences between PD patients and control group (Mann-Whitney test)

TABLE 2 Statistical significance of the relationship between neuropsychological tests, sleep parameters, MRI voxel-based morphometry data and DTI-ALPS index according to Spearman correlation analysis.

Parameters	DTI-ALPS index	
	left	Right
Parkinson's disease sleep scale	P = 0,085	P = 0,078
Total sleep time (min)	P = 0,03	P = 0,03
SWA 1-4 Hz (%)	p<0,001	P = 0,005
MMSE	P=0,074	P = 0,06
MoCA	P=0,04	P=0,04
FAB	P=0,006	P=0,005
Trails Making Test Part A	P = 0,015	P = 0,02
Trails Making Test Part B	P = 0,003	P = 0,007
Medial orbitofrontal cortex	P=0,005	P = 0,017
Lateral orbitofrontal cortex	P = 0,03	P = 0,025
Dorsolateral prefrontal cortex	P = 0,025	P = 0,01
Hippocampus	P = 0,035	P = 0,03
Amygdala	P=0,043	P = 0,058
Cuneus	P=0,086	P = 0,06
Lingual gyrus	P=0,082	P = 0,073
Posterior cingulate gyrus	P=0,074	P = 0,076
Superior parietal lobe	P=0,04	P=0,055

Conclusion: The links between glymphatic clearance, sleep architecture and cognitive dysfunction are of interest and provide a basis for developing therapeutic strategies to prevent disease progression.
Disclosure: Nothing to disclose.

EPO-599 | Opicapone improves end-of-dose neuropsychiatric fluctuations in patients with Parkinson's disease

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Background and Aims: Non-motor fluctuations (NMF) represent one of the main complications that patients with Parkinson's disease (PD) may experience during long-term levodopa treatment. Opicapone (OPC), a COMT inhibitor indicated for end-of-dose motor fluctuations (MF), has not yet been extensively investigated for the management of NMF. We aim to evaluate the efficacy of OPC on end-of-dose neuropsychiatric fluctuations, the most frequent and severe NMF.
Methods: We assessed 15 PD patients (8 males/7 females; mean age ± SD: 69.5 ± 7.1 years; disease duration: 7.2 ± 1.7 years) with end-of-dose MF and NMF, confirmed by 19-item Wearing-Off Questionnaire (WOQ-19). For each patient, we identify the first end-of-dose deterioration period through MDS-UPDRS-III administered every 30 minutes over two consecutive days. On the third day, a comprehensive clinical and neuropsychological battery was administered during this designated period. Subsequently, OPC was prescribed. After 6 months, patients were re-evaluated using the same baseline assessments during the same end-of-dose period.
Results: At 6-month follow-up, PD patients showed a significant improvement in the following tests: WOQ-19 ($p < 0.001$), total MDS-UPDRS and each of its four parts ($p < 0.001$), NMSS scores ($p < 0.001$), neuropsychological tests assessing executive functions/attention (Weigl's, $p < 0.001$; FAS fluency, $p < 0.001$; STROOP, $p = 0.003$) and mood related symptoms (BDI-II, HAM-A; both $p < 0.001$). In contrast, there were no significant differences in the scores of Visual Search ($p = 0.033$), RAVLT-I ($p = 0.225$), and RAVLT-D ($p = 0.136$).
Conclusion: OPC improved end-of-dose fluctuations in anxiety, depression, and executive functions/attention, where dopamine plays a critical role, while less dopamine-dependent domains, such as memory and visuospatial abilities, showed no significant changes.
Disclosure: Nothing to disclose.

EPO-600 | Neurophysiological and clinical effect of botulinum toxin in essential blepharospasm

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University Hospital Santa Maria della Misericordia, Clinical Neurology department, Udine, Italy

Background and Aims: Botulinum toxin Type A might exert a central effect in distonias; however, the literature regarding its possible central effect in this setting is scarce. This study aims to investigate the central effect of this drug by the means of the amplitude ratio obtained with blink reflex recovery cycle before and after the treatment in patients affected by blepharospasm.
Methods: We treated 13 patients affected by essential blepharospasm. We performed a baseline (before botulinum toxin type A therapy) and a final evaluation 5 weeks after treatment. During the baseline and final evaluation, 3 clinical scales were administered (Blepharospasm Disability Scale, Jankovic Rating Scale, and Blepharospasm Severity Scale) and a R2 blink reflex recovery cycle was performed on both right and left side, using interstimulus intervals of 200, 300, 500 and 1.000 milliseconds. The amplitude ratios between the unconditioned R2 and conditioned R2 were calculated for each interval.
Results: The amplitude ratio of the blink reflex recovery cycle, when compared to the baseline, was significantly reduced after the treatment for every interstimulus interval applied. This data was confirmed considering both eyes and each eye individually. There was also a significant improvement in the scales used to quantify the therapeutic clinical outcome.

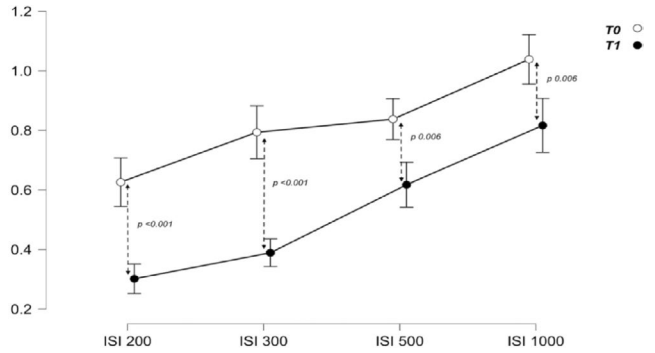

FIGURE 1 shows the plot line (with 95% confidence intervals) of the amplitude ratio at different paired pulses ISI (200 ms, 300 ms, 500 ms, and 1000 ms), considering both eyes. The RM ANOVA analysis confirmed a significant increase in the amplitude ratio with the inc.

Conclusion: The significant reduction of the amplitude ratios observed after the treatment with botulinum toxin type A could imply a central effect of this drug on reducing the hyperexcitability of the circuits underlying this form of dystonia.
Disclosure: Nothing to disclose.

Movement disorders 8

EPO-601 | Psychiatric comorbidity in patients with dystonia – Data from a retrospective analysis of adult patients in Bulgaria

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Background and Aims: Dystonia is the third most common movement disorder worldwide. The aim of our study was to analyze the non-motor psychiatric symptoms of an adult cohort of patients with dystonia in our hospital.
Methods: Data were retrospectively collected from all patients with dystonia hospitalized in University Hospital for Active Treatment in Neurology and Psychiatry, Sofia, Bulgaria in 2024. Psychiatric comorbidity, sex, age at onset, body distribution, disability, coexistence of tremor, duration of the disease and type of treatment were analyzed. Patients with dystonia with different etiologies were included – idiopathic, tardive, functional dystonia and dystonia in cerebral atrophy and cerebral small vessel disease.
Results: A total of 60 patients were hospitalized with dystonia in our hospital. Almost half of the patients - 25 (41.7%) were diagnosed with additional psychiatric disorder. The most common comorbidity was mixed anxiety-depressive disorder (7), followed by schizophrenia (2), bipolar (2), panic (2) and major depressive (2) disorder. One patient had a somatic symptom disorder. Nine of the patients were prescribed a psychiatric therapy from a specialist but either refused to show or didn't bring the official medical documentation. Ten (6%) of the patients had a tardive dystonia and five patients were diagnosed with functional dystonia.
Conclusion: Psychiatric disorders are highly prevalent in patients with dystonia. They appear to be under-recognized and undertreated. Complex approach with the participation of a neurologist and a psychiatrist is necessary.
Disclosure: Nothing to disclose.

EPO-602 | Impact of acupuncture on lowering accidental injury in patients with Parkinson's disease: A nationwide cohort study

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Background and Aims: Patients with Parkinson's disease (PD) face a heightened risk of accidental injuries due to motor and non-motor symptoms that impair mobility and balance. Acupuncture, known for improving balance and gait, has not been thoroughly studied for its role in injury prevention among PD patients. This study aimed to evaluate the impact of acupuncture on reducing accidental injury risk in this population.
Methods: A nationwide retrospective cohort study was conducted using Taiwan's National Health Insurance Research Database, including patients newly diagnosed with PD between 2001 and 2012. Propensity score matching was employed to balance demographics, comorbidities, and medication usage between patients who received acupuncture and those who did not. The incidence of accidental injuries was assessed, and adjusted hazard ratios (HRs) were calculated using Cox proportional hazards models.
Results: Among 24,467 PD patients, 32% underwent acupuncture. The acupuncture group experienced a lower incidence of accidental injuries (15.2%) compared to the non-acupuncture group (17.1%). Adjusted analyses indicated that acupuncture was associated with a 33% reduced risk of injury (adjusted HR: 0.67; 95% CI: 0.42–0.85). The protective effect was consistent across most subgroups, except for patients aged under 60, those in less urbanized areas, or those with high insurance coverage.

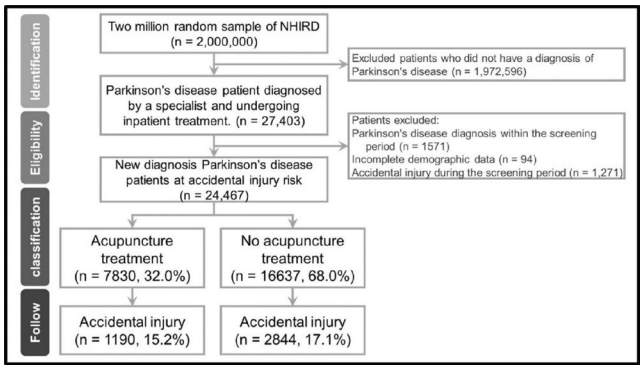

FIGURE 1 Flowchart depicting the selection of participants and assessment of accidental injuries in a study on Parkinson's disease patients.

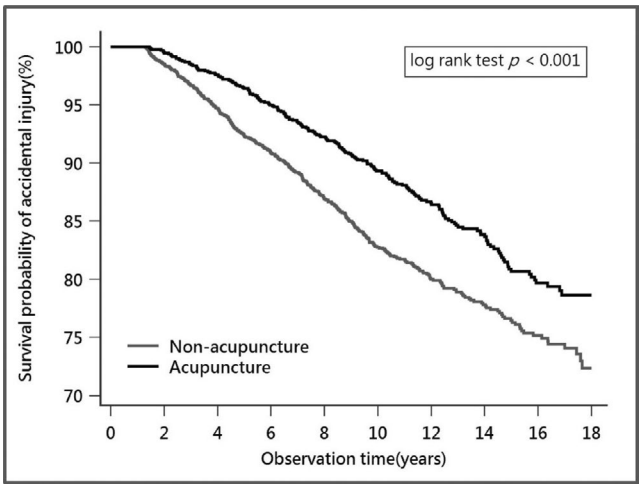

FIGURE 2 Kaplan-Meier analysis of Parkinson's disease patients based on acupuncture treatment.

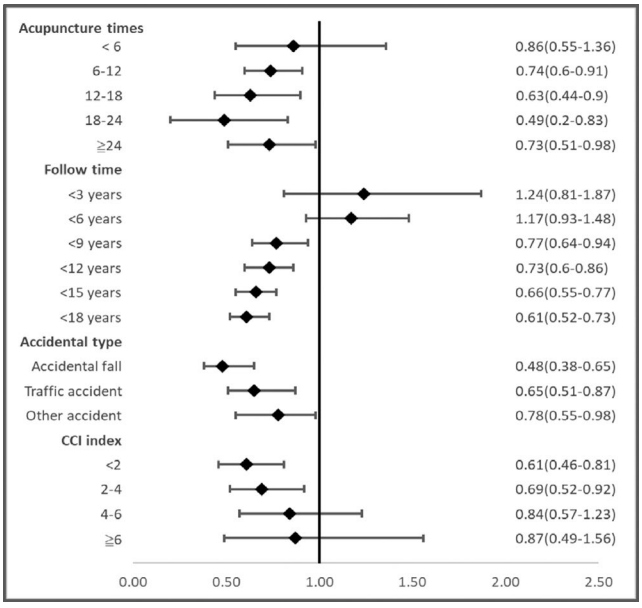

FIGURE 3 Adjusted hazard ratios for accidental injuries across different acupuncture frequencies, follow-up periods, and injury types; CCI index, Charlson Comorbidity Index.

Conclusion: Acupuncture significantly reduces the risk of accidental injuries in patients newly diagnosed with PD, suggesting its potential as a preventive strategy. Incorporating acupuncture into standard PD care may enhance safety and quality of life for these patients.
Disclosure: Nothing to disclose.

EPO-603 | Motor, nonmotor and cognitive predictors of early treatment-related motor fluctuations in Parkinson's disease patients

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Background and Aims: Treatment-related motor fluctuations may emerge within few years after levodopa initiation but may go unrecognized at office visits, particularly in patients with a shorter disease duration. We investigated motor, nonmotor and cognitive predictors associated with early development of motor fluctuations after 2 years of treatment.
Methods: The study sample was recruited from a longitudinal project enrolling drug-naïve PD. Patients underwent an extensive motor, nonmotor and cognitive assessments by means of validated scales at the time they were diagnosed with PD. After the baseline assessments, all patients were prescribed with dopaminergic treatment and yearly clinically assessed. At the 2-year follow-up, 73 patients have developed early signs of wearing-off, defined as having at least 1 h of daily OFF time for at least 4 weeks (PD early-fluctuators, PD-EF) and were automatically matched with 77 patients without motor fluctuations (PD non-fluctuators, PD-NF). Baseline motor, nonmotor and cognitive data were compared between the study groups. A multivariate regression model was used to explore clinical baseline predictors of treatment-related motor fluctuations at 2-year follow-up.
Results: At baseline, compared to PD-NF, PD-EF were presenting higher severity of pain, depression, autonomic dysfunction and worse performances in memory, executive and visuospatial cognitive domains.
Conclusion: Our findings demonstrated that specific nonmotor and cognitive features may characterize drug-naïve PD patients more prone to develop early treatment-related fluctuations. Identifying at-risk PD population prior to starting dopaminergic treatment may help clinical management and foster prevention strategies.
Disclosure: Nothing to disclose.

EPO-604 | Brain networks alterations based on EEG pattern assignment in at-risk of DLB subjects

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[1]Brain and Mind Research Program, CEITEC, Masaryk University, Brno, Czechia; [2]First Department of Neurology, Faculty of Medicine, Masaryk University and St. Anne's University Hospital, Brno, Czechia

Background and Aims: EEG microstates (EEG MS) provide spatial and temporal characteristics of large-scale brain networks. While EEG patterns described by Bonanni's group improve early diagnosis of dementia with Lewy bodies (DLB), EEG MS may enhance our understanding of early network changes.
Methods: Altogether 117 medication-naïve subjects at risk of DLB (mean age... ± ...) underwent a 5-minute recording of high-density resting state scalp EEG. Participants were sorted based on their EEG pattern assignment into three groups: pattern 1

(normal EEG), pattern 2 (early DLB) and pattern 5 (advanced DLB). We compared time coverage, mean duration and occurrence of individual EEG MS across EEG pattern groups.
Results: We identified altogether 5 EEG MS. We observed higher time coverage ($p=0.003$ and $p<0.001$) and higher occurrence ($p<0.001$ and $p<0.001$) of MS A (engaging mostly temporal cortices and representing sensory and arousal networks) in DLB EEG patterns 2 and 5 compared to pattern 1, respectively. Conversely, the same comparison revealed lower time coverage ($p=0.004$ and $p=0.004$) and lower mean duration ($p<0.001$ and $p=0.005$) of the EEG MS C (engaging anterior cingulate and insular cortices - representing salience network) in those with DLB EEG patterns.
Conclusion: We demonstrated that DLB-related EEG patterns were presented in almost half of at-risk of DLB/prodromal DLB subjects. Those with pathological EEG patterns as compared to those with normal EEG showed increased excitability of the sensory/arousal networks and decreased involvement of the salience network.
Disclosure: Nothing to disclose.

EPO-605 | Parkinson's disease and the metabolic syndrome: An integrated analysis of complex clinical and biochemical profiles

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Background and Aims: Parkinson's disease (PD) and metabolic syndrome are two complex and multidimensional diseases, the combination of which has a significant impact on the quality and life of patients. This study aims to link these two conditions to determine how their combination affects metabolic and neurodegenerative functions.
Methods: The study design was based on a retrospective analysis, in which data from patients in two different clinical groups were studied: 62 patients diagnosed with PD only and 32 patients diagnosed with PC and metabolic syndrome. Clinical data, neuropsychological test results, and biochemical parameters were collected and analyzed. Independent samples *t*-test, Mann-Whitney *U* test, and χ^2 test were used for data analysis.
Results: The clinical manifestations of PD were higher in the group with metabolic syndrome. In this group, the mean score on the MDS-UPDRS scale was 134.8 ± 6.1, and on the PD-CRS scale was 65.1 ± 2.1, both of which were considered significant at the $p<0.01$ level. The levels of glucose and urea in the blood were also significantly higher in the metabolic syndrome group (glucose 9.3 ± 0.55 mmol/L, $p<0.001$; urea 8.3 ± 0.54 mmol/L, $p<0.05$).
Conclusion: The results of this study demonstrate that the co-occurrence of metabolic syndrome and PCa produces complex clinical and biochemical profiles. Integrated management of these two conditions may lead to the development of new treatment strategies aimed at slowing disease progression and improving the overall health of patients.
Disclosure: Nothing to disclose.

EPO-606 | Genetic influences on Parkinson's disease clinical phenotype according to gene function and number of mutated variants

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Background and Aims: Parkinson's disease (PD) clinical phenotype may be influenced by genetic risk factors. We wanted to investigate the link between genetic characteristics and symptoms in a selected population of PD patients.
Methods: We collected clinical and genetic data of 143 PD patients with age at onset (AAO) $<=60$ years or with positive familial history for parkinsonism (FH+). We investigated if the distribution of clinical characteristics differed significantly between subjects with negative test (GT-) and positive test patients categorised according to the main function(s) of each mutated gene(s), and we evaluated the correlation between 12.5th percentiles and number of one-mutation and more-than-one-mutations carriers per percentile.
Results: We found no significant differences between positive and GT- patients when comparing AAO ($p=0.872$), FH+ ($p=0.764$) and each symptom. When considering patients divided in functional classes, we discovered in "lysosomal" class patients a higher prevalence of orthostatic hypotension ($p=0.038$) and, in "protein synthesis" class, a higher AAO ($p=0.012$) than in GT- subjects. We also detected a significant correlation between 12.5th percentiles' mean AAO and number of more-than-one-mutations carriers per percentile ($R = -0.796$; $p=0.018$).

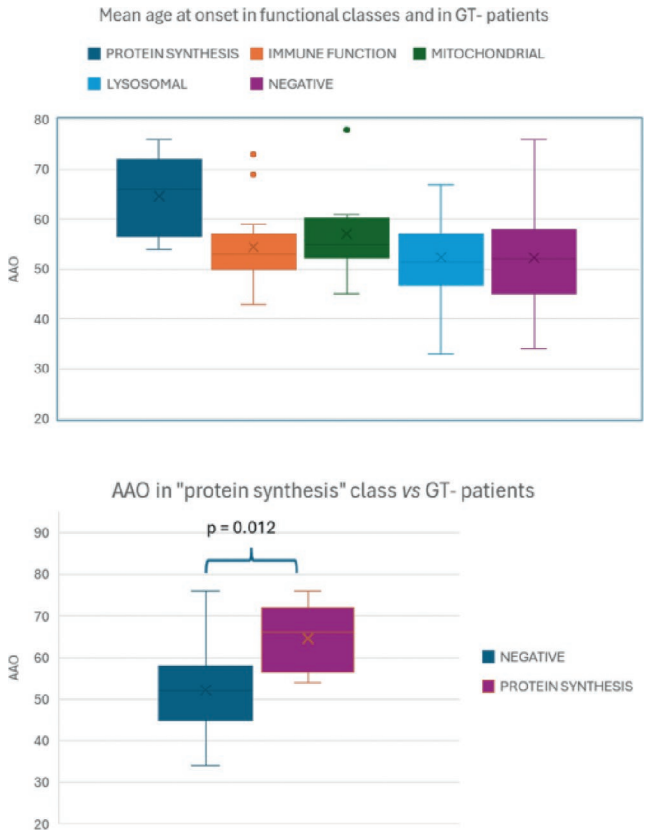

FIGURE 1 Top graph: mean AAO in functional classes and in GT- patients. Bottom graph: mean AAO between "protein synthesis" patients and GT- patients; the difference in AAO between these two categories proved to be significant ($p = 0.012$).

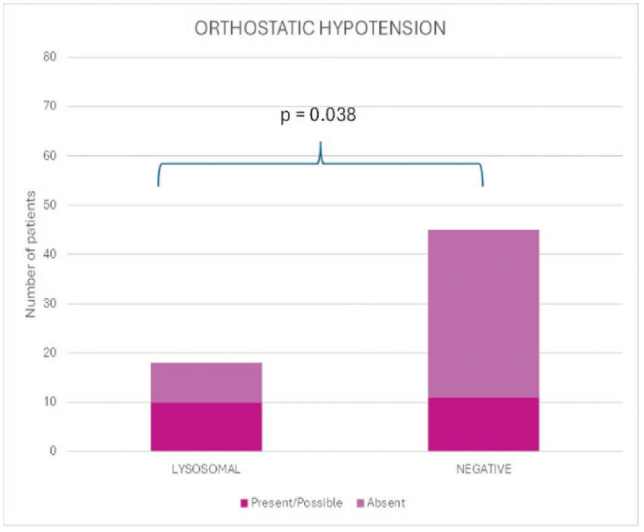

FIGURE 2 Distribution of orthostatic hypotension in patients with "lysosomal" mutation(s) in comparison with GT- patients, revealing a significant prevalence in mutated patients.

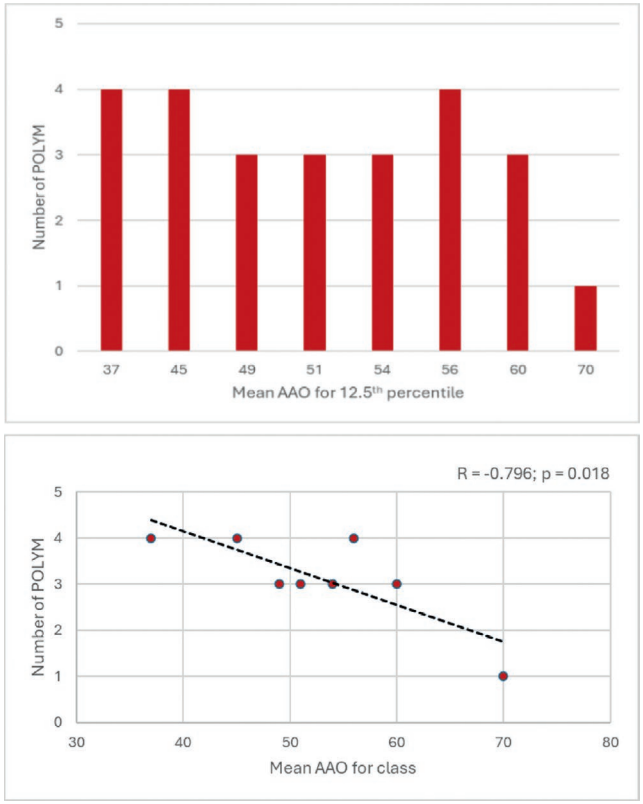

FIGURE 3 Distribution of more-than-one-mutations carriers (POLYM) and mean AAO for 12.5th percentile.

Conclusion: Based on our data, earlier AAO and FH+ seem not related to positive result at genetic test. We saw in "lysosomal" class mutations a higher prevalence of orthostatic hypotension and in "protein synthesis" subjects a higher AAO than in GT- subjects. We also observed an inverse association between AAO and chance of obtaining more than one mutation in positive genetic test results, possibly reflecting an additive role in favouring PD onset.
Disclosure: Nothing to disclose.

EPO-607 | Constipation and fecal biomarkers in a de novo Parkinson disease cohort

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Background and Aims: Parkinson's disease (PD) is the second growing neurodegenerative disorder characterized by motor and non-motor symptoms, including significant gastrointestinal (GI) dysfunction, particularly in early stages. This study aimed to explore blood, CSF and fecal biomarkers in a de novo PD cohort.
Methods: Clinical assessments included demographics, motor status by the Unified Parkinson's Disease Rating Scale, University of Pennsylvania Smell Identification Test, Montreal Cognitive Assessment, SCOPA-AUT. Calprotectin, zonulin and

interleukines and alfa syn levels total and aggregated in blood and CSF and stools were measured. Data were analyzed using R.
Results: 81 patients were included: 19 controls, 16 treated PD and 46 de novo PD. 42% women and mean age in all groups were 57 (+-2.9). Total UPDRS was higher in PD treated (57.6+-3) than in de novo PD and controls (table 1). Hiposmia and constipation was higher in de novo PD than healthy controls, and SCOPA-Aut was higher in PD treated than de novo PD. Serum calprotectine (intestinal permeability) was slightly higher in de novo PD than controls, Aggregated alfa syn was detected also in blood, CSF and stool of patients with PD (figure 1).

TABLE 1

Cohort	n_total	n_hombres	n_mujeres	Edad	UPDRS_total	UPDRS_III	SCOPA_AUT	Bristol	ROMA	UPSIT
Control	19	10	9	57.42 ± 3.08	3.89 ± 1.23	0.42 ± 0.19	6.74 ± 1.12	3.73 ± 0.28	0.53 ± 0.21	30.25 ± 1.05
PD	16	11	5	57.56 ± 2.9	68.6 ± 7	35.9 ± 2.96	15.4 ± 3.09	3.25 ± 0.31	1.5 ± 0.52	17.57 ± 1.99
PD de novo	46	26	20	59.85 ± 1.48	37.63 ± 2.26	25.67 ± 1.39	8.54 ± 0.85	3.14 ± 0.16	0.98 ± 0.24	20.38 ± 1.06

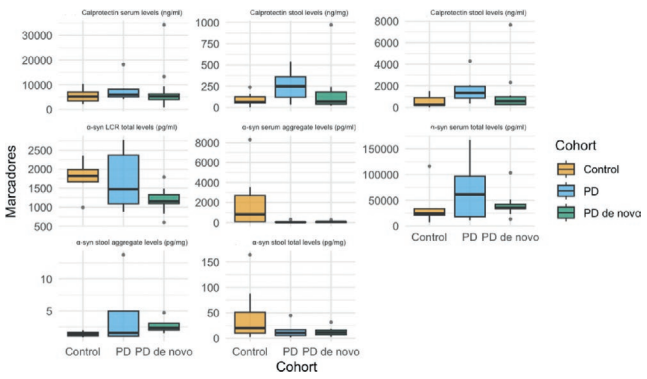

FIGURE 1

Conclusion: This study highlights the relevance of GI dysfunction in de novo PD. Innovative and less invasive biomarkers in stool could could aid in early diagnosis and classify clinical subgroups. Further longitudinal studies are needed to validate these findings and explore therapeutic implications.
Disclosure: Nothing to disclose.

EPO-608 | Longterm effect of EMG-guided botulinum toxin (BoNT) treatment of complex facial dystonia with initial progression involving oromandibular dystonia

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Background and Aims: Oromandibular dystonia (OMD) is a rare form of dystonia with involuntary movements of the jaw muscles, causing masticatory problems. In some patients, the OMD progresses, in-volving eyelid spasms (Meige syndrome). Symptoms may also progress to a more wide-spread dystonia. These case-presentations demonstrate distinct dystonic manifestations that illustrate a progression of a primary OMD to a wider head and neck involvement. The ob-jective is to illustrate the diagnostic and therapeutic benefits of employing EMG guidance for BoNT treatment, preceded by standardized evaluation.
Methods: Two patients with oromandibular dystonia initially progressing with involvement of head and neck area with amongst other OMD, were assessed with: • Clinical and orofacial examination • Muscle Strength (jaw opening force, hand grip strength) • Sensibility (oral stereognosis and two-point discrimination) • Burke-Fahn Marsden Dystonia rating scale, Pain Numeric rating Scale Treatment with needle-EMG-guided BoNT was based on the assessment. The patients were treated regularly, every three months.
Results: Case 1 symptoms onset in 2009. EMG guided treatment regime involved mm. digastricii, mm. thyerohyoideus and mm. obicularis oculi until 2013, when the treatment could be re-duced to aesthetic treatment with 47.5 U INCO-BoNT in mm. obicularis oculii bilat and plat-ysma. Case 2 had symptom onset in 2012. EMG guided treatment regime in. mm. orbicularis oris superior and inferior and dxt. M. pteryogoideus lateralis until 2019, henceforth estehtic treatment with 15 U INCO-BoNT in mm orbicularis oris inferior.
Conclusion: Conclusion: Standardized protocolled EMG-guided treatment of complex facial dystonia provides long-term benefit with stabilization of progression of symptoms.
Disclosure: Nothing to disclose.

EPO-609 | Association of urate with dopaminergic integrity and motor function in REM sleep behavior disorder: A multicenter study

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Background and Aims: Research on urate in idiopathic REM sleep behavior disorder (iRBD), a prodromal stage of synucleinopathies, is limited. This study examined the relationship between serum urate levels, presynaptic dopamine neuronal integrity, and motor deficits in iRBD.
Methods: We enrolled 18 patients with polysomnography (PSG)-confirmed iRBD who underwent positron emission tomography (PET) scans to assess dopamine transporter (DAT) availability in the posterior putamen. Relationships between serum urate levels, mean posterior putaminal DAT availability, and motor deficits were analyzed using Unified Parkinson's Disease Rating Scale Part III (UPDRS-III) scores and subthreshold parkinsonism status. For validation, 39 additional PSG-confirmed iRBD patients with serum urate measurements and dopamine transporter PET scans were recruited from another center.
Results: Serum urate levels were positively correlated with mean posterior putaminal DAT uptake ($n=18$; $\gamma=0.508$, $p=0.032$), a relationship that remained significant after adjusting for confounders such as age, sex, BMI, and alcohol use (β [SE] $=0.323$ [0.094], $p=0.005$). Although no significant association was found with UPDRS-III scores ($\gamma = -0.449$, $p=0.061$), iRBD patients without subthreshold parkinsonism had higher serum urate levels than those with subthreshold parkinsonism (median

[IQR], mg/dL = 5.2 [3.3] vs. 3.8 [1.7], $p = 0.040$). Validation confirmed the positive correlation between serum urate and posterior putaminal DAT uptake ($n = 39$; $\gamma = 0.488$, $p = 0.002$).
Conclusion: Elevated serum urate levels are associated with preserved posterior putaminal dopaminergic neurons and motor function in iRBD, suggesting a potential neuroprotective role of urate in early synucleinopathies.
Disclosure: Nothing to disclose.

EPO-610 | Motor phenotype as a factor in sleep disturbances in Parkinson's disease

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Background and Aims: In Parkinson's disease (PD), sleep disturbances such as insomnia or REM sleep behaviour disorder (RBD) are common. It is known that motor phenotypes exhibit heterogeneity in cognitive, psychiatric, and sleep symptoms.
Methods: A cross-sectional study was conducted from June 2022 to January 2025 in patients from a movement disorders clinic, using clinical surveys and the Movement Disorders Society Unified Parkinson's Disease Rating Scale (MDS-UPDRS). Patients were divided into three motor phenotype groups: postural instability and gait difficulty (PIGD), tremor-dominant (TD), and indeterminate (INDT). Parametric statistics were applied.
Results: A total of 138 patients were included: 64 PIGD (46.4%), of whom 51 (79.7%) presented sleep disturbances; 53 TD (38.4%), with 43 (81.1%) showing disturbances; and 21 INDT (15.2%), with 19 (90.5%) affected. Sleepiness was the most prevalent symptom across all three groups (41 (64.1%), 27 (50.9%), and 14 (66.7%), respectively). No significant differences ($p > 0.05$) were found in the presence of sleep disturbances RBD, insomnia, or sleepiness with respect to motor phenotype.

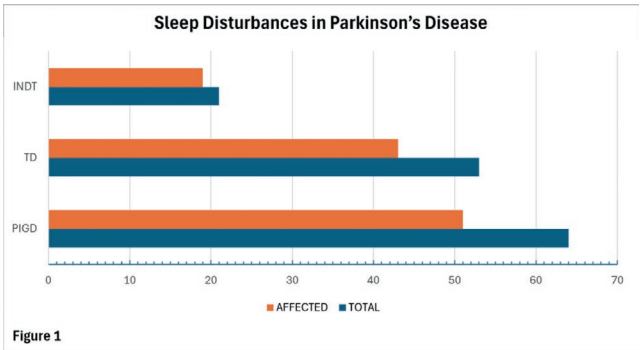

Figure 1

Symptomes	PIG		TD		INDT	
	n	%	*n*	%	*n*	%
Sleepiness	41	64.1	27	50.9	14	66.7
Insomnia	35	54.7	21	39.6	12	57.1
RBD	24	37.5	21	39.6	10	47.6

Table 1
Sleep Disturbances in Motor Phenotypes

Conclusion: Our results suggest that sleep disturbances are common symptoms in PD patients. Motor phenotype does not appear to be a determining factor in the presence of sleep disturbances. This highlights the need to individualise patient care, taking into account comorbidities and symptoms, with particular emphasis on assessing sleepiness.
Disclosure: Nothing to disclose.

EPO-611 | Double limb support as core feature of Parkinson's disease with mild motor fluctuations

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Background and Aims: Motor fluctuations are common in Parkinson's Disease (PD), and are associated with increased risk of falls and other complications. The aim of this study was to evaluate the presence of specific gait alternations during ON phases in patients with motor fluctuations (PD-F) using Mobile Health Technology (MHT), compared with patients without motor fluctuations (PD-NF) in groups of matched patients for motor and non-motor severity.
Methods: The study enrolled matched PD patients with and without motor fluctuations, who underwent extensive clinical assessment and supervised MHT evaluation in ON state at normal and fast paces and during dual-task performance.
Results: 60 subjects were included, 30 PD-F and 30 PD-NF. In the ON-phase gait analysis, PD-F exhibited a longer double limb support time compared to PD-NF patients during normal, fast, and dual-task walking conditions, with similar gait parameters were comparable.
Conclusion: Therefore, we conclude that the increased double limb support time may indicate greater postural instability in patients with motor fluctuations.
Disclosure: Nothing to disclose.

EPO-612 | Skin biopsy as a biomarker for parkinsonism: Differentiating synucleinopathies and tauopathies – A systematic review

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Background and Aims: The differentiation between synucleinopathies and tauopathies remains a significant challenge due to overlapping clinical presentations. Accurate biomarkers are needed to improve diagnostic precision. Skin biopsy has emerged as a minimally invasive method capable of detecting pathological seed aggregates. The aim of the study was to evaluate the

effectiveness of skin biopsy in differentiating synculeinopathies and tauopathies.

Methods: A systematic literature review was conducted using PubMed, Web of Science, and Scopus. The following combination of MeSH terms and Boolean operators was used: ((Parkinson*)AND(tauopathies)AND(synucleinopathies)) AND((skin)OR(cutaneous))AND((diagnosis)AND(specificity)). The search focused on articles published between 2014 and 2024. The main outcome was to assess the diagnostic accuracy and specificity of skin biopsy in distinguishing between synucleinopathies and tauopathies in patients exhibiting motor symptoms.

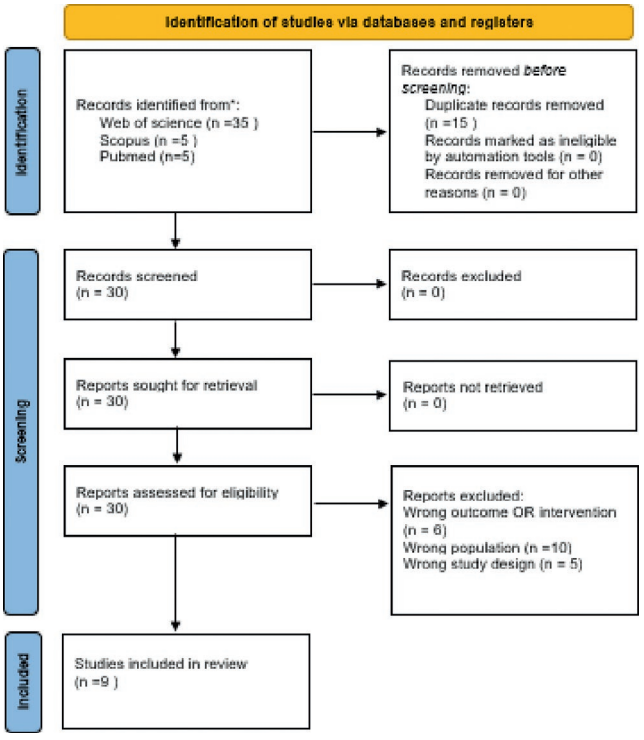

FIGURE 1 Prisma flow diagram

Results: From 35 studies identified, we selected 9 papers. The clinical features were dominated by parkinsonism. Of these studies, 4 used multiple biopsy sites targeting the lower leg, forearm, and cervical region. For synucleinopathies, skin biopsy demonstrated a high sensitivity and specificity in detecting seeds aggregates, with pathological tau also observed at lower levels. Tauopathies were diagnosed with a similar average of sensitivity and specificity. The Skin tau, using TauK18 and TauK19 as reaction substrates for 4R and 3R isoforms were used to differentiate both proteinopthies. Higher concentrations of synuclein seed aggregates were found in the cervical region, while tau aggregates were predominantly located in limbs

Conclusion: Our review highlights the potential of skin biopsy as a promising non-invasive diagnostic tool for synucleinopathies and tauopathies.

Disclosure: Nothing to disclose.

EPO-613 | Comparison of specialist ataxia centres with non-specialist services for ataxia care, resource use and costs in Italy

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Background and Aims: The ataxias are rare complex neurological disorders that represent a challenge for the clinicians to diagnose and manage. This study explored the patient pathways, costs associated and care satisfaction of individuals attending specialist ataxia centres (SAC) compared with non–specialist settings in Italy.

Methods: A patient survey was distributed to people with ataxia in Italy during May – September 2021 to gather information about the diagnosis and management of the ataxias in SAC and non-specialist settings including patients' satisfaction. We compared mean resource use for each contact type and health service costs per patient, stratifying patients by whether they were currently attending a SAC or had never attended a SAC.

Results: We had 174 participants in the survey; 44% of participants saw a neurologist within 6 months of seeking medical advice, and 56% went to a SAC as first referral. Traveling was a top reason why people stopped going to a SAC and why people never attend one. People attending SAC reported that such centres delivered better service in most aspects (coordinating referrals, offering opportunities to take part in research, communications with social care professionals).

Conclusion: There was a trend towards patients' appreciation for the delivery of service in SAC compared to non-SAC. However, we identified difficulties in attendance and adherence despite the higher number of SACs in Italy compared to other countries (UK and Germany). We believe that combination of face-to-face and telemedicine could improve the continuation of the patients attendance to SAC.

Disclosure: Nothing to disclose.

EPO-614 | Essential tremor patient journey, from caseload to advanced therapies: A neurology survey

A. Sanchez Fraga[1]; C. Tengelin[1]; K. Gant[2]; P. Crivelli[1]; C. Ferrer[1]; A. Grinspan[2]

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Background and Aims: Recent evidence on disease burden, tremor classification and treatment guidelines, including advanced therapies like magnetic resonance-guided focused ultrasound (MRgFUS), has changed the essential tremor (ET) landscape. We investigated neurologist perceptions on ET

caseload, tremor severity, advanced therapy and standard protocol use in Europe.

Methods: An anonymized web survey was conducted between 16-01-23 and 24-02-23, following relevant data privacy legislation and guidelines. General neurologists (GN) and movement disorder neurologists (MDN) were asked about ET patients' caseload, severity, prescription of advanced therapies and use of standardized protocols.

Results: The survey was completed by 68 MDN and 156 GN. Neurologists reported that 10.1 ±4.5% of their patients experienced ET; 62.5 ±6.7% of those presented a moderate to severe condition (Figure 1). Prescriptions for advanced therapies were deep brain stimulation (mild 3.3 ±1.3%; moderate 14.8 ±3.6%; severe 82.0 ±4.8%); MRgFUS (mild 7.7 ±2.2%; moderate 26.4 ±9.1%; severe 66.0 ±11.4%). Earlier prescription and higher variations, apart from severity, were observed between the MDN and GN groups for MRgFUS (Figure 2). Neurologists envisaged prescribing MRgFUS to 27.1 ±3.6% of their patients (Figure 3) with most neurologists (>70%) being satisfied. Only 37.5 ±16% of neurologists reported adhering to standardized pathways/protocols (Figure 3).

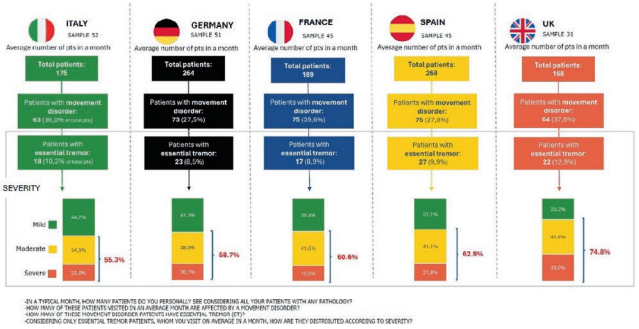

FIGURE 1 Origin and severity of essential tremor patients referred to general and movement disorder neurologists in Europe (Italy, Germany, France, Spain, and the UK). The sample number of neurologists per country is reported.

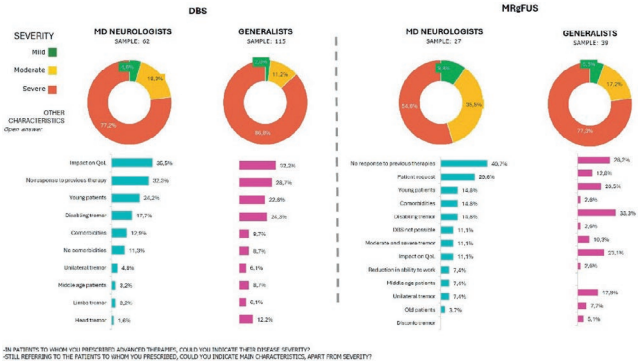

FIGURE 2 Severity and disease characteristics of patients who were prescribed advanced therapies for essential tremor. The sample number of neurologists is reported.

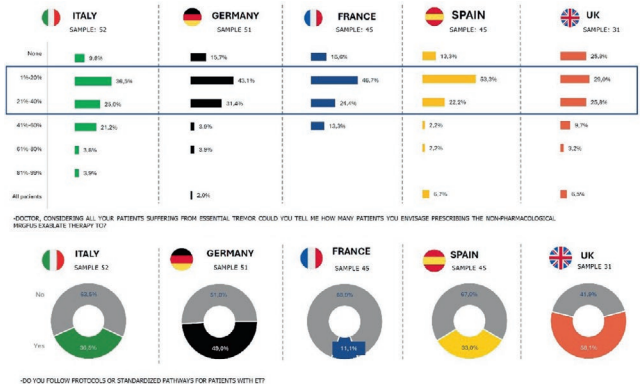

FIGURE 3 Proportion of patients with essential tremor (ET) likely to be prescribed MRgFUS by neurologists in Europe and the proportion of neurologists adhering to protocols/standardised pathways. The sample number of neurologists per country is reported.

Conclusion: In Europe, the ET caseload is high among neurologists, with most patients presenting moderate-to-severe symptoms. Nevertheless, access to advanced therapy remains low with a heterogenous patient profile. This may be related to the absence of standardized protocols. Further study is necessary to explain geographical differences and further work should focus on creating and disseminating protocols to enhance patient access to the appropriate therapies.

Disclosure: The authors are all Insightec employees. To carry out the survey, support was provided by Stethos Srl, Italy, Milan. Writing assistance was provided by Content Ed Net, Madrid, Spain. The survey responses were used for market research purposes.

MS and related disorders 4

EPO-615 | Treatment landscape and patient journey in MS: Experience from central military emergency hospital in Bucharest, Romania

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Background and Aims: Multiple sclerosis (MS) management requires timely access to diverse therapeutic options. We conducted a retrospective study spanning 2000–2021 to analyze treatment patterns, obstacles, and outcomes among 805 MS patients treated at Central Military Emergency Hospital "Dr. Carol Davila" (SUUMC) in Bucharest, Romania.

Methods: Data on therapy types, duration, changes, hospitalizations, and costs were extracted from medical records. Descriptive statistics and trend analysis were employed.

Results: Platform therapies were most commonly utilized (59%), followed by intermediary active drugs (24%), and highly active therapies (17%). 15.6% of patients changed treatment, primarily due to adverse reactions (54%) or lack of efficacy (39%). The most commonly changed drugs were platform therapies, first being recombinant human interferon beta-1b, followed

by recombinant human interferon beta-1a and glatiramer acetate, and were most frequently substituted with teriflunomide and natalizumab. The mean time until treatment change was 5.2 years. Moreover, 7.4% of patients transitioned to territorial centers, reflecting geographical dynamics. Day hospitalizations increased from 860 (2011) to 1518 (2021), mirroring evolving care needs. Treatment costs rose from 7.3 million lei (2011) to 15 million lei (2021), totaling approximately 119 million lei (approximately 24 million euros) over the study period.

Conclusion: The introduction of diverse therapies expanded treatment options for MS patients at SUUMC, allowing tailored management aligned with disease type and activity. Despite challenges such as delayed drug availability and treatment changes, our center witnessed improved patient access to appropriate therapies, reflected in increased hospitalizations and associated costs.

Disclosure: Nothing to disclose.

EPO-616 | Impact of single or multiple spinal regions pain on disability levels in multiple sclerosis: A meta-analysis study

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[2]*Department of Physiotherapy and Rehabilitation, Faculty of Health Sciences, Tokat Gaziosmanpaşa University, Tokat, Turkey*

Background and Aims: Pain is a common complaint in multiple sclerosis (MS), significantly impacts daily activities. Spinal pain (cervical, thoracic, or lumbal) can impair trunk stabilization and mobility. Clinicians may observe that pain in multiple spinal regions may increase disability, but does this pattern hold true from a broader perspective through meta-analysis? This study aimed to evaluate differences in disability between MS patients experiencing pain in a single spinal region (SSR) and those with pain in multiple spinal regions (MSR).

Methods: A systematic search was conducted in PubMed, Web of Science, and Scopus databases up to December 2024 (Figure-1). Studies were included if they assessed disability using the Expanded Disability Status Scale (EDSS) and reported spinal pain in MS patients. Subgroup analyses were conducted using the "meta" package in RStudio, applying both common-effect model (CEM) and random-effect models (REM). PROSPERO number is CRD42025632240.

Pubmed and Scopus:

(multiple sclerosis) AND (neck pain OR neck ache OR neckache OR cervical pain) AND (pain intensity OR pain severity OR disability OR quality of life)

(multiple sclerosis) AND (back pain OR back ache OR backache OR thoracic pain OR low back pain OR lumbal pain OR lumbar pain) AND (pain intensity OR pain severity OR disability OR quality of life)

Web of Science:

TS= ((multiple sclerosis) AND ((neck pain) OR (neck ache) OR (neckache) OR (cervical pain)) AND ((pain intensity) OR (pain severity) OR (disability) OR (quality of life)))

TS=((multiple sclerosis) AND ((back pain) OR (back ache) OR (backache) OR (thoracic pain) OR (low back pain) OR (lumbal pain) OR (lumbar pain)) AND ((pain intensity) OR (pain severity) OR (disability) OR (quality of life)))

FIGURE 1 Keyword searched in databases

Results: Seven studies met the inclusion criteria (Figure-2). The SSR group (336 patients) had a mean EDSS score of 3.70 (common-effect) and 3.90 (random-effect) with moderate heterogeneity ($I^2 = 82.2\%$). The MSR group (201 patients) scored 4.19 (common-effect) and 4.39 (random-effect) with high heterogeneity ($I^2 = 99\%$). A significant difference between groups was found in the CEM ($\chi^2 = 357.75$, $p < 0.0001$), but not in REM ($\chi^2 = 0.52$, $p = 0.4698$). CEM results showed a higher disability in MSR pain patients compared to SSR pain patients (Figure-3).

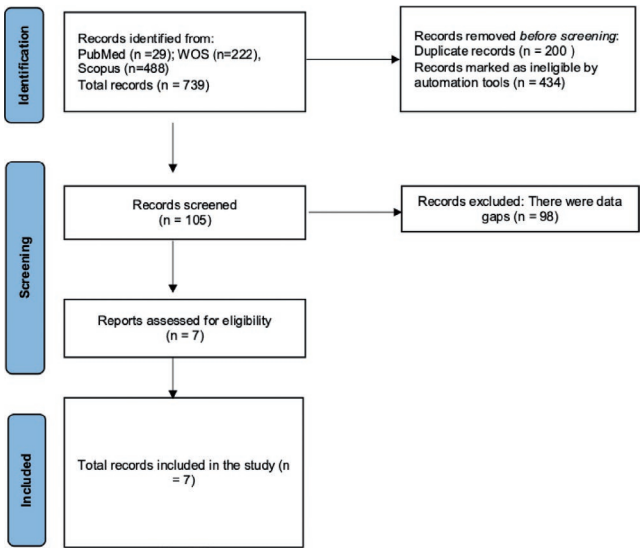

FIGURE 2 The PRISMA flowchart of the literature search

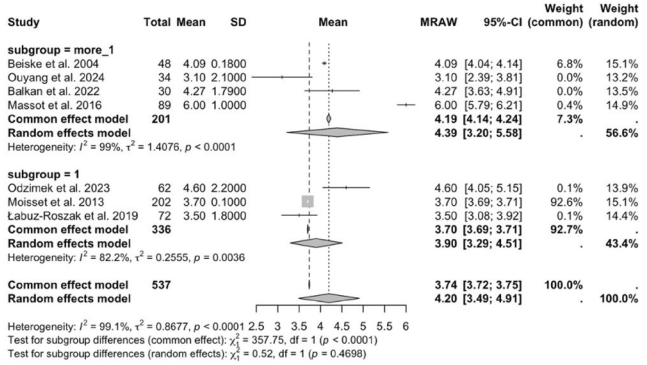

FIGURE 3 Forest Plot of MS disability and subgroups

Conclusion: Patients with MSR pain may have a higher disability. While CME demonstrated significant differences, REM did not confirm them, likely due to heterogeneity. Therefore, future studies should focus on heterogeneity sources and spinal pain management.

Disclosure: Nothing to disclose.

EPO-617 | Gut microbiome at the onset of multiple sclerosis: An Italian cohort study

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Background and Aims: Multiple Sclerosis (MS) etiopathogenesis is uncertain. Gut microbiota possibly affects brain activity, producing active metabolites. However, its composition in early disease stages remains undetermined. We aimed to explore differences in gut microbiota composition at disease onset compared with healthy donors (HD) and identify differences based on negative prognostic factors such as high lesion burden.
Methods: 53 MS patients (pMS) at the first clinical attack and 18 healthy controls (HC), matched on age, sex, diet, BMI, and lifestyle, were recruited in a multicenter case-control study. Stool, blood samples and radiological-clinical data were collected at baseline. DNA isolated from stools was subjected to shotgun metagenomic sequencing strategy; peripheral blood mononuclear cells were isolated and analyzed by flow cytometry to identify T helper (Th)17 and T regulatory cells. Taxonomic classification was performed using Kraken2. Results were processed using Bayesian re-estimation of abundance to provide accurate estimates.
Results: The overall gut microbiome structure of pMS did not differ from HC's, as indicated by α- and β-diversity between the two groups. However, several species in different taxa were found up- or down-regulated by comparing differential abundances between pMS and HC. Among clinical and radiological variables, glucocorticoid intake and MRI lesion burden were associated with microbiome diversity variations in pMS. Furthermore, some species correlated with increased pathogenic Th17 cells in the blood
Conclusion: Our results suggest that pMS displays a moderate gut microbial dysbiosis in the early stages, influencing not only the autoimmune peripheral response but also MS disease course.
Disclosure: Nothing to disclose.

EPO-618 | Functional evaluation of MS exacerbation treatment duration

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Background and Aims: Treatment of multiple sclerosis (MS) exacerbations has evolved, with pulse therapy of methylprednisolone for 3-5 consequent days as the standard approach, followed by plasma exchanges if needed. Still, longer pulse therapies regimens exist with no consensus or specific guidelines regarding the optimal duration of such treatments. This study aimed to evaluate the correlation between the Multiple Sclerosis Functional Composite (MSFC) dynamics and methylprednisolone therapy duration in patients with MS.
Methods: 27 MS patients (11 males, 16 females) aged 22–50 years (mean 33, SD ± 7.29) with baseline EDSS scores of 1.5–5.0 (mean 3.59, SD ± 1.08) were assessed. MSFC was measured at hospitalization and after pulse therapy with methylprednisolone (1 g/day for 3, 5, or 7 days). MSFC score formulas were used for calculations and Jamovi v. 2.3.28.0 Windows with χ^2 test and binomial logistic regression was used for statistical analysis.
Results: 14 participants showed MSFC improvement at discharge, while 13 deteriorated. Among the patients who underwent 7-day therapy, all deteriorated. Among improved patients, 10 received 5-day therapy, and 4 received 3-day therapy. The χ^2 test revealed a significant correlation between therapy duration and MSFC results ($\chi^2 = 7.3$, $p = 0.026$). Reducing the duration of therapy by 1 day increases the chances of improvement approximately 3 times (OR = 1/0.333 ≈ 3).
Conclusion: A 7-day pulse therapy in MS exacerbations does not show additional benefits compared to 3- or 5-day regimens. Shorter pulse therapies should be considered.
Disclosure: Nothing to disclose.

EPO-619 | Measuring frailty in multiple sclerosis: A systemic review of current frailty indices

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Background and Aims: Frailty in multiple sclerosis (MS) is an emerging concept linked to outcomes such as disability progression and disease activity, but standardized assessment methods are still lacking. This study evaluates existing evidence on frailty indices in MS.
Methods: A systematic review was conducted of studies published between 2014–2024 that reported original data or systematic reviews on frailty assessments in patients with MS (pwMS). Searches were performed in MEDLINE, EMBASE, and the Cochrane Library using the terms "multiple sclerosis" and "frailty." Quality of evidence was assessed by four raters using the GRADE approach.
Results: From 817 screened studies, 10 met inclusion criteria, encompassing 1,941 pwMS and three frailty indices: Fried Frailty (FF), Frailty Index (FI), and Tilburg Frailty Indicator (TFI). FI, analyzed in 8 studies (1,653 patients), showed correlations with higher relapse likelihood (adjusted OR = 0.69; $p < 0.01$, inverse), and greater disability (EDSS; $\beta = 0.47$, $R^2 = 0.26$, $p < 0.001$). Evidence quality was low due to bias and imprecision. FF and TFI were linked to higher disability (TFI: $\beta = 0.57$, $R^2 = 0.35$, $p < 0.001$), with TFI additionally associated with poorer quality of life ($p < 0.001$) and reduced autonomy ($p = 0.017$), though evidence quality was very low due to limited studies and high risk of bias.
Conclusion: This review highlights the potential of frailty indices in MS, yet reveals significant gaps in validation and applicability, with routine clinical use being premature. Further research is needed to develop and validate MS-specific frailty assessments.
Disclosure: Nothing to disclose.

EPO-620 | Measuring comorbidity in multiple sclerosis: A systemic review of current comorbidity scales

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Background and Aims: Comorbidity assessment in multiple sclerosis (MS) is crucial due to its impact disability progression and quality of life. However, comprehensive and systematic methods for assessing comorbidities in MS populations remain underexplored. This systematic review aimed to identify current comorbidity scales used in MS populations and assess their suitability for clinical implementation based on the quality of evidence.
Methods: Studies published between 2014–2024 that reported original data or systematic reviews on measures of comorbidity in patients with MS (pwMS) were included applying search terms "multiple sclerosis" and "comorbidity". Information sources included MEDLINE, EMBASE, and the Cochrane Library. Quality of evidence was assessed by four raters using the GRADE approach.
Results: From 3,178 screened studies, 31 met inclusion criteria, analyzing data from 234,089 MS patients. Four comorbidity scales were identified: Charlson Comorbidity Index (CCI), Elixhauser Comorbidity Index (ECI), Self-Administered Comorbidity Questionnaire (SCQ), and Self-Reported Comorbidity Questionnaire for MS (SRQ-MS). The CCI was most used and showed relevant associations with MS-specific outcomes (e.g. increased risk of reaching disability milestones from CCI ≥1 [HR 1.23–1.62, $p < 0.001$]) but had moderate to low evidence quality due to limited validation and reliance on retrospective study designs. Similarly, the ECI and SCQ lacked direct validation and demonstrated very low evidence quality. The SRQ-MS, validated for MS populations, showed moderate evidence quality but faced inconsistencies across studies.
Conclusion: Current comorbidity scales lack validation for routine use in MS populations. Further research is needed to develop and standardize MS-specific comorbidity assessment for clinical and research purposes.
Disclosure: Nothing to disclose.

EPO-621 | Relationship between OND and ONSD measured by TOS and clinical, radiological, electrophysiological parameters in MS

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Background and Aims: This study aimed to evaluate the reliability of optic nerve diameter (ONSD) and optic nerve sheath diameter (ONSD) measurements made with transorbital sonography (TOS) and MRI in patient groups that may progress with subclinical optic atrophy over time, such as MS.
Methods: A total of 102 patients (81 RRMS, 19 SPMS, 2 PPMS), and 34 healthy controls were included in the study. On the same day, each patient underwent TOS, orbital MRI, VEP, and OCT examinations for each eye.
Results: OND, ONSD, and OND/ONSD ratio measured by TOS were significantly lower in the MS patient group compared to the healthy controls ($p < 0.001$). Furthermore, in SPMS group, TOS measurements of OND and ONSD were significantly lower compared to the RRMS group ($p < 0.001$). In MS patients with an EDSS score >2, OND and ONSD measurements obtained by TOS were significantly lower ($p < 0.001$). A moderate positive correlation was found between the OND and ONSD measurements obtained by TOS and pRNFL thicknesses (G, T, TS, TI quadrants). No significant difference was found between the mean differences of OND and ONSD measurements obtained using TOS and MRI.
Conclusion: This study demonstrated the relationship and reliability of OND and ONSD measurements performed using TOS and MRI in patient groups that may exhibit subclinical optic atrophy over time, such as those with MS. These results indicate that OND and ONSD measurements obtained by TOS may be reliable methods for the early detection of disability and optic atrophy in SPMS patients, as well as those with RRMS.
Disclosure: Nothing to disclose.

EPO-622 | Longitudinal changes in sleep quality and their predictors in patients with multiple sclerosis

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Background and Aims: Sleep disturbances are common in patients with multiple sclerosis (PwMS) and significantly impact quality of life (QoL). However, the longitudinal courses and clinical factors influencing these disturbances remain unclear.
Methods: PwMS in remission were prospectively recruited from a single tertiary medical center. Sleep quality was measured using the Pittsburgh Sleep Quality Index (PSQI) at baseline and after 6–12 months. Poor sleep was defined as a PSQI score >5, with significant worsening characterized by a score increase of ≥3. QoL and MS symptoms were evaluated using the EQ-5D-5L index and Functional Systems (FS) score. Factors associated with baseline and future PSQI scores were analyzed. Predictors of future PSQI scores and significant sleep changes were also investigated.
Results: Of 116 participants (mean age: 46 years), 54% and 53% were classified as poor sleepers at baseline and follow-up, respectively. Poor sleep was independently associated with reduced QoL. Mean PSQI scores remained stable over follow-up, while 24 (20.7%) patients experienced significant worsening. Baseline cerebral and optic FS scores independently predicted both baseline and future PSQI scores.
Conclusion: Sleep disturbances are common and significantly impactful in PwMS over time. Cerebral and optic dysfunction

are key predictors, underscoring the need to prioritize targeted sleep care.
Disclosure: Nothing to disclose.

EPO-623 | Rituximab for the treatment of multiple sclerosis: A retrospective observational study of 50 cases from Morocco

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Background and Aims: Rituximab (RTX) showed to be effective and relatively safe in the treatment of relapsing-remitting and progressive forms of multiple sclerosis (MS), both in the phase II setting and in some observational studies.
Methods: We report a retrospective observational study to describe the effectiveness and safety of off-label rituximab in the treatment of a population of Moroccan MS patients including 50 relapsing-remitting (RRMS) and progressive multiple sclerosis (PMS) subjects.
Results: Our study showed that the RTX treatment was associated with the mean ARR decreasing by 0.72 at one year follow up. EDSS scores improved after 1 year of treatment with RTX by a score of 0.5-1.0 in 31 (62%) patients and remained stable in the second year of therapy. EDSS score remained same in 12 patients (24%), of which 9 had RRMS and 3 SPMS. EDSS worsened after 2years from RTX in 7 (14%) patients (5 SPMS, 2PPMS). Follow up MRI Brain with contrast at one year, show new T2 lesions in 6 patients (12%), with no enhancing lesions either old or new. Concerning safety issues in our patients, we observed a frequency of infusion associated reactions inferior to the data reported in other studies. Majority of patients (98%) tolerated RTX infusion well.
Conclusion: RTX could be an effective and safe treatment in RRMS. Some selected PMS patients could also benefit from this treatment.
Disclosure: Nothing to disclose.

EPO-624 | Primary histiocytic sarcoma of the central nervous system mimicking multiple sclerosis: A case report

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Background and Aims: Primary histiocytic sarcoma (HS) affecting the central nervous system (CNS) is an exceptionally rare lymphohematopoietic tumour with poor prognosis due to challenging diagnosis, aggressive clinical course and lack of standardised treatment guidelines.
Methods: Case description of a patient who developed primary HS of the CNS.
Results: A 50-year-old man presented in July 2022 progressive blurred vision. MRI in January 2023 showed three white matter lesions (WML) highly suggestive of an inflammatory demyelinating disease, located in the left medial and right superior cerebellar peduncles and the right temporal periventricular. Cerebrospinal fluid analysis showed no pleocytosis, negative microbiology findings and positive oligoclonal bands. A diagnosis of multiple sclerosis (MS) was made, he was treated with intravenous methylprednisolone and started Ofatumumab in April 2023. After 2 months of treatment, the patient presented a progressive clinical decline with gait instability, diplopia, dysmetria, vomiting, anorexia and weight loss. A follow-up MRI in June 2023 showed enlargement of the previously known lesions and new WML. Due to the atypical disease progression, a cerebral biopsy was made showing non-necrotizing granulomas, leading to empirical treatment against Nocardia, Actinomycosis and Tuberculosis. Despite antibiotics, the disease progressed both clinically and radiologically. A second biopsy was performed, in which the morphological and immunohistochemical profile confirmed HS with TP53 and PMS2 mutated. Chemotherapy with the MATRIX protocol achieved partial response; however, the patient died from urinary sepsis complications.

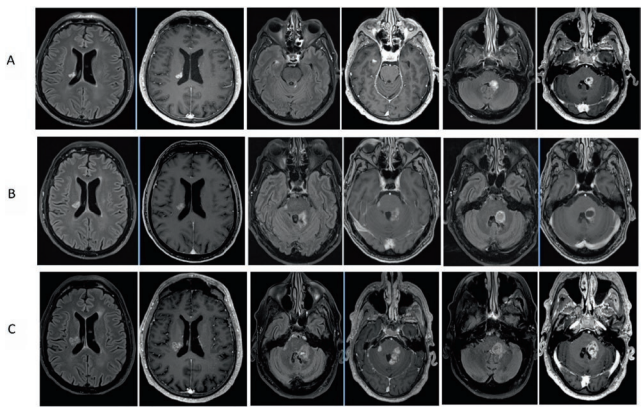

FIGURE 1 Progression within the months of the WML located in right temporal periventricular region and cerebellar peduncles. Contrast-enhanced T1 and T2-FLAIR acquired in (A) September 2023, (B) November 2023 and (C) January 2024.

Conclusion: Despite fulfilling MS diagnostic criteria, cases with atypical disease progression despite appropriate treatment, should prompt consideration of alternative etiologies, including rare malignancies like primary CNS HS.
Disclosure: Nothing to disclose.

EPO-625 | Long-term prognostic value of early NEDA-3 vs NEDA-4 status in relapsing-remitting multiple sclerosis

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[1]Neurosciences Unit, Department of Medicine and Surgery, University of Parma, Parma, Italy; [2]Neurology Unit, Emergency Department, Guglielmo da Saliceto Hospital, Piacenza, Italy; [3]Neurology Unit, Department of General and Specialized Medicine, Parma University Hospital, Parma, Italy

Background and Aims: Aim of the study was to evaluate the long-term prognostic value of maintaining NEDA-3 and NEDA-4 in the first two years of DMTs in people with recent diagnosis of RR multiple sclerosis.
Methods: All patients with early RRMS referred to Parma (IT) Centre between January 2015 and December 2018, taking DMT and with 5-year follow-up were included. Patients who stopped therapy within two years for reason other-than-efficacy were excluded. NEDA-3 was the absence of relapses, MRI activity and disability progression. NEDA-4 was NEDA-3 plus annualized brain volume loss (SIENA) inferior to 0.4%.

Tab.1 – Baseline population characteristics (n. 104 pts)

Sex (%F)	66.3
Age (years, mean ± SD)	39.5 ± 10.47
EDSS (median)	2.0
Follow-up (years, mean ± SD)	7.4 ± 1.2
DMT type (first line, %)	76.9

Results

Results: Included 104 patients (66.3% female, mean age 39.5y, median EDSS 2.0, mean follow-up 7.4y, first-line DMT in 76.9%). Patients with 2-year NEDA-3 (35.6%) and NEDA-4 (17.3%) had significantly less CDA events than non-NEDA patients (NEDA-3 24.3% and NEDA-4 11.1% vs 41.8% non-NEDA). CDA reduction was still more significant with 6md-NEDA (6md-NEDA-3 22.6% and 6md-NEDA4 10% vs 49% non-NEDA). Correlation between CDA and NEDA status was more evident between RAW and NEDA-3 (RAW 2.7% in NEDA-3 vs 23.9% non-NEDA) and between PIRA events and NEDA-4 and 6md-NEDA-4 (PIRA 10% in NEDA-4 vs 27.5 % non-NEDA). NEDA-4 outperformed NEDA-3 in terms of CDA and PIRA events.

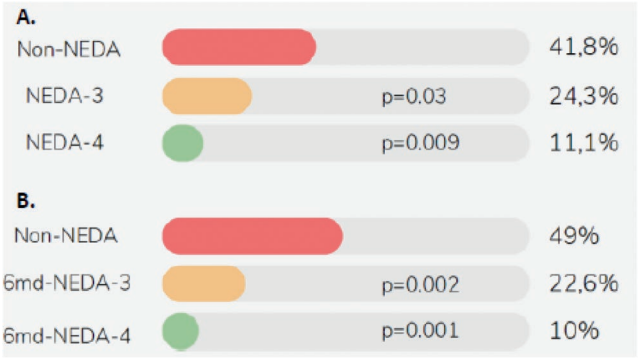

FIGURE 1 CDA events related to NEDA (A) and 6md-NEDA (B) status.

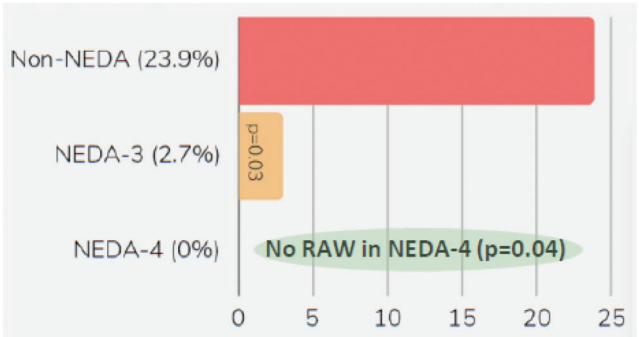

Fig.2 – RAW events related to NEDA status

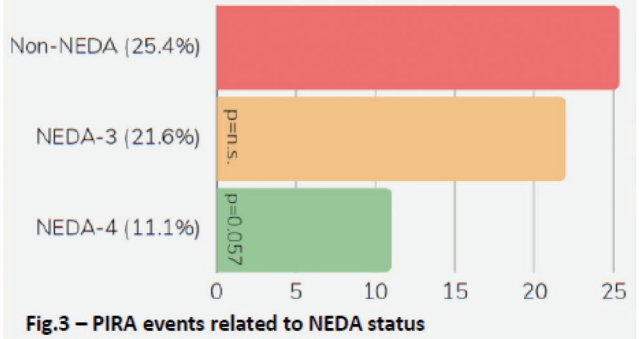

Fig.3 – PIRA events related to NEDA status

Conclusion: NEDA status has been proposed as long-term prognostic factor in MS. In our work NEDA-3 and NEDA-4 in the two first years of DMT showed a protective role against CDA in the long term, NEDA-4 exerting a stronger action, especially against PIRA. Our data underlined the importance of obtaining early NEDA-status, especially NEDA-4.
Disclosure: Nothing to disclose.

EPO-626 | Metabolomics of CSF and quantitative MRI data by AI based software Pixyl.Neuro.MS® in multiple sclerosis

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Background and Aims: Metabolomics is a method of analytical chemistry to detect/measure presence of small molecules

in investigated medium. Metabolomics of cerebrospinal fluid (CSF) may represent a new source of prognostic and/or diagnostic biomarkers of multiple sclerosis (MS). For example, histidine is significantly reduced in early stages of MS compared to controls. Aim of this study was to evaluate possible connection between amino/fatty acid concentrations in CSF and volume of MS specific brain lesions extracted by an AI based software.
Methods: We used clinical and paraclinical data of MS patients from our database as well as metabolomics results extracted from our previous study (1). We analysed brain MRI through AI software Pixyl.Neuro.MS® (1.8.X, Pixyl SAS, Grenoble, France) and extracted lesion volumes. We did correlation analyses among EDSS values, MRI lesion volumes and amino/fatty acid concentrations to judge their potential relationship.
Results: We have analysed metabolomic results, EDSS values and MRI data of 21 MS patients in early stages of their disease. We observed statistically significant correlation between lesion volumes and baseline EDSS ($r=0.65$; $p=0.001$) and EDSS after 1 year ($r=0.67$; $p=0.002$). We did not observe any significant correlation between concentrations of histidine, arginine, serine, choline, tyrosine, spermidine, glutamate, oleic, linoleic, palmitic acid and brain lesion volume.

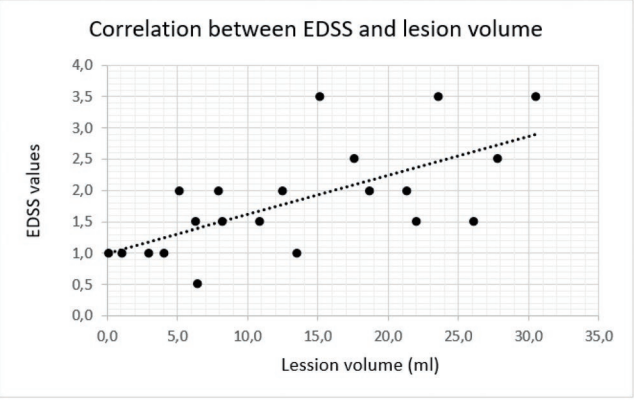

Figure 1 Correlation between EDSS values and brain lesion volume in early stages of MS

Conclusion: The volume of brain lesions in early stages of MS reflects the clinical state of patients in terms of EDSS values, but it did not show any significant connections with metabolomics results. However, it still needs further investigation.
Disclosure: Nothing to disclose.

EPO-627 | Intrathecal synthesis of Epstein-Barr virus antibodies 15 years before multiple sclerosis onset. A case report

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Background and Aims: Epstein-Barr virus (EBV) is considered the etiology of multiple sclerosis (MS). There is no consensus on the time between infection and clinical symptoms. A recent study has demonstrated that EBV infection previously was present in all cases of pediatric MS patients in the Netherlands, with b lood antibodies used as a screening and discriminating test.
Methods: A case-control study was conducted in paired serum and CSF samples from 76 MS patients and 75 control subjects. The study participants were recruited between January 2002 and April 2005 at the San Cecilio University Hospital in Granada, Spain, for an EBV DNA and antibody testing. The control group included patients scheduled for minor surgery under epidural anesthesia with no previous neurological symptoms. A comprehensive review of a ll clinical records of MS patients as well as control patients in this study has been conducted over the past year.
Results: In the course of the study review, one patient recruited from the surgical control group was identified with a high titer of intrathecal EBV antibodies in a lumbar puncture performed in 2003. In 2017 this patient (a 46- year-old female) consulted with paresthesias and Lhermitte·s sign as her first neurological symptoms. A brain MRI revealed demyelinating lesions disseminated in space with Gd enhancement. A CSF analysis revealed a leukocyte count 1 cell/ul. albumin 24.9 mg/dl, lgG 4 .43 mg/dl, and presence of oligoclonal bands.
Conclusion: When a diagnostic lumbar puncture is conducted for suspected demyelinating disease this test may be a valuable screening option.
Disclosure: Nothing to disclosure.

EPO-628 | Evaluation of treatment responses and prognosis in Marburg variant multiple sclerosis: A systematic review

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Background and Aims: Marburg variant multiple sclerosis (MS) represents an acute, fulminant form of MS, characterized by its aggressive nature, leading to significant disability or death. Due to its rarity, there is a scarcity of data regarding effective management strategies, highlighting the urgency for a comprehensive review of treatment outcomes.
Methods: A systematic literature review was conducted following PRISMA guidelines. Four databases (PubMed, Scopus, Embase, and Web of Science) were searched for case reports on Marburg variant MS up to September 2024. From an initial 1633 records, 18 studies were selected based on predefined inclusion and exclusion criteria. Data on demographics, clinical presentation, radiological findings, and therapeutic interventions were extracted and analyzed qualitatively.
Results: The review included 18 patients with Marburg variant MS, with a mean age of 34.9 years, predominantly female (88.9%). Lumbar puncture results showed lymphocytic pleocytosis in 71%, elevated protein in 64%, and positive oligoclonal bands in 50% of cases. MRI findings included hyperintense lesions on T2/FLAIR, most commonly in periventricular white matter. Treatment regimens involved high-dose intravenous steroids (100%), plasmapheresis (67%), and cyclophosphamide

(61%), followed by maintenance with monoclonal antibodies like ocrelizumab, rituximab, or alemtuzumab. Outcomes showed significant improvement in 78% of patients, complete remission in 11%, and a mortality rate of 11% within weeks of diagnosis.
Conclusion: This review underscores the potential for clinical and radiological improvement in Marburg variant MS with aggressive, multimodal treatment. However, the high early mortality rate emphasizes the critical need for swift and effective therapeutic interventions. Further research is needed to optimize treatment protocols.
Disclosure: Nothing to disclose.

EPO-629 | Gut microbiota alterations in young adults with relapsing-remitting multiple sclerosis onset

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Background and Aims: The gut microbiota functions as an independent organ influencing all body systems and contributing to various diseases. Its role in multiple sclerosis (MS) pathogenesis and the potential to modify the disease course via microbiota remain unclear. Objective: To evaluate gut microbiota composition in young individuals with relapsing-remitting multiple sclerosis (RRMS) onset and compare it to a control group.

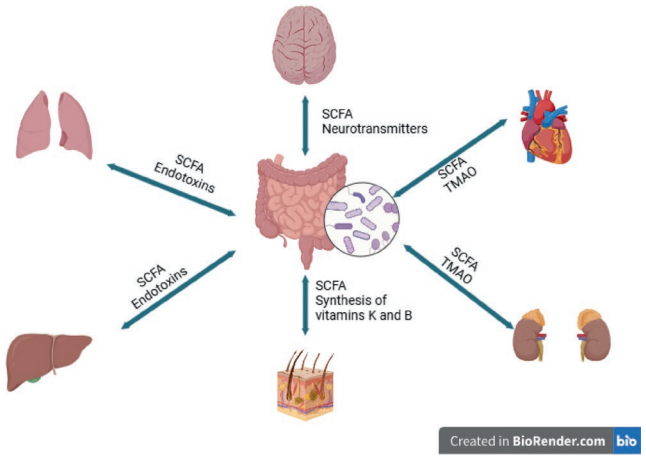

FIGURE 1 Bidirectional gut microbiota-organ relationships. SCFA – short-chain fatty acids, TMAO – trimethylamine-N-oxide. Illustrated using the app https://app.biorender.com/.

Methods: The study included 14 RRMS patients and 14 healthy volunteers. Fecal samples were analyzed using mass spectrometry (Osipov method) to measure microbial markers, including fungi and viruses. Statistical analysis was conducted using Statistica 12 and Microsoft Excel. Normality was assessed via Kolmogorov-Smirnov and Shapiro-Wilk tests, and group differences were evaluated with the Mann-Whitney *U*-test ($p \leq 0.05$).
Results: RRMS patients exhibited a significant predominance of Clostridium difficile and Propionibacterium spp. compared to healthy controls, with an absence of Kingella spp. and Pseudomonas aeruginosa. Fungal flora was quantitatively higher in RRMS patients, while the median Herpes spp. concentration was greater in healthy controls.

TABLE 1 Demographic data of the Study Group.

Characteristic	Control Group (n=14)	Comparison Group (RRMS Onset, n=14)
Age (years), Me [IQR]	31 [28;36]	33 [27;36]
Women, %	62	72
BMI, Me [IQR]	24 [24;25]	22 [21;24]

TABLE 2 Concentration of Microbial Markers in Fecal Analysis in the Control Group and Patients with RRMS at Onset (105 cells/gram).

Bacterial component (Phylotype)	Control Group	RRMS Onset Group
Clostridium difficile(Bacillota)	0 [0.0; 0.0]	0 [0.0; 889]
Propionibacterium spp. (Actinomycetota)	5414 [1437; 11152]	17313 [8876; 27545]
Kingella spp. (Pseudomonadota)	794.5 [0.0; 1200]	0 [0.0; 0.0]
Pseudomonas aeruginosa (Pseudomonadota)	70.5 [0.0; 105]	0 [0.0; 0.0]
Viral component		
Herpes spp.	663.5 [456; 1360]	137 [10; 890]

Results are presented as median and interquartile range [25th;75th percentiles]. For statistical significance, ps0.05 by Mann-Whitney U test was used.

Conclusion: Significant differences were found in the bacterial, fungal, and viral components of the gut microbiota between RRMS patients and healthy individuals. However, further studies are needed to identify the "key microbiota" associated with MS and its potential as a therapeutic target.
Disclosure: Nothing to disclose.

MS and related disorders 5

EPO-630 | Multiple sclerosis delayed diagnosis: Prevalence, causes and prognostic value

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Background and Aims: Over 83% of countries have barriers to early diagnosis of multiple sclerosis (MS), such as the lack of awareness of MS symptoms among patients, medical professionals and low availability of diagnostic tests. According to the Russian MS registry, only 36.2% patients were initially correctly diagnosed with MS.
Methods: We analyzed the prevalence and causes of diagnostic delay in 97 patients with MS, clinically isolated syndrome (CIS) and radiologically isolated syndrome (RIS) referred to the Research Center of Neurology from October 2023 to December 2024. We compared our data with the results the Russian MS registry, as well as studies conducted in Prague and in Egypt.
Results: The median time to diagnosis was 10 months, which is significantly longer than in Prague and Egypt. The rate of delayed diagnosis was 66%, which is 13% higher than in the Czechia study and 17% higher than in the Egypt. In the timely

diagnosis group the median EDSS score was 2 whereas in delayed diagnosis group the median EDSS score was 3.

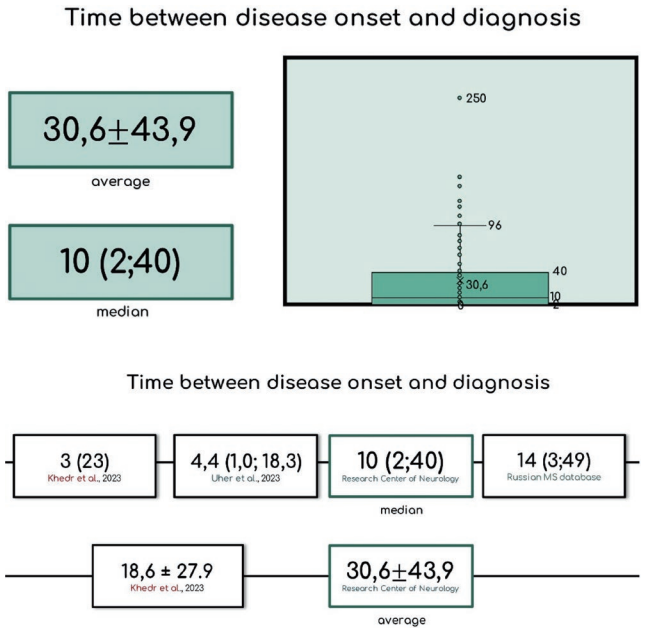

FIGURE 1 Time between disease onset and diagnosis: comparison with other studies

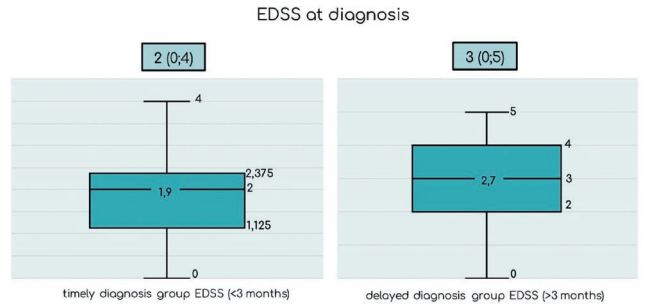

FIGURE 2 EDSS at diagnosis depending on diagnostic delay

Conclusion: Thus, the time to diagnosis in the Russian data was significantly longer than in foreign studies. It can be suggested that the 1-month achievable timeframe for MS diagnosis set by the consensus criteria is currently unrealistic. A diagnosis period of less than 3 months correlates with a lower degree of disability. The introduction of normative MS diagnosis timeframes into clinical guidelines could help reduce the frequency of delayed diagnosis and overcome one of the barriers to early DMT prescription.

Disclosure: Nothing to disclose.

EPO-631 | Tract density as additional marker of multiple sclerosis brain reorganization

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Background and Aims: The recent articles concerning tract-wise disconnection and tract-centered view in explaining multiple sclerosis (MS) disability are shown to be of great importance. Tract density (TD) is extensively studied as a potential MS marker. Statistical properties of TD distribution as a marker of brain reorganization for RRMS, PPMS, SPMS, active SPMS are analyzed.

Methods: MRI is performed with GE MR750w 3T as follows: resolution 2.0 mm (256x256), slice thickness 2.0 mm, 128 directions of b-value 4000 s/mm^2. Tractography is realized by DSI Studio with 4th Runge-Kutta method, 100 million tracts are calculated without sub-voxel interpolation. For each slice, the state of disorder is evaluated with Shannon entropy, entropy values over all slices are summarized.

Results: SPMS (dieses duration (DD) 15y) is shown to be characterized by the lowest TD entropy values (fig. 1), both sum and distribution in the space of brain (fig. 2): RRMS (DD 3y) is characterized by TD higher entropy, which sum exceeds on more than 50% the SPMS one; PPMS (DD 5y) is characterized by higher TD entropy, which sum exceeds on more than 20% the RRMS case; ASPMS (DD 14y) is shown to be characterized by the highest TD entropy, which sum exceeds on more than 20% the PPMS one (fig. 1,2).

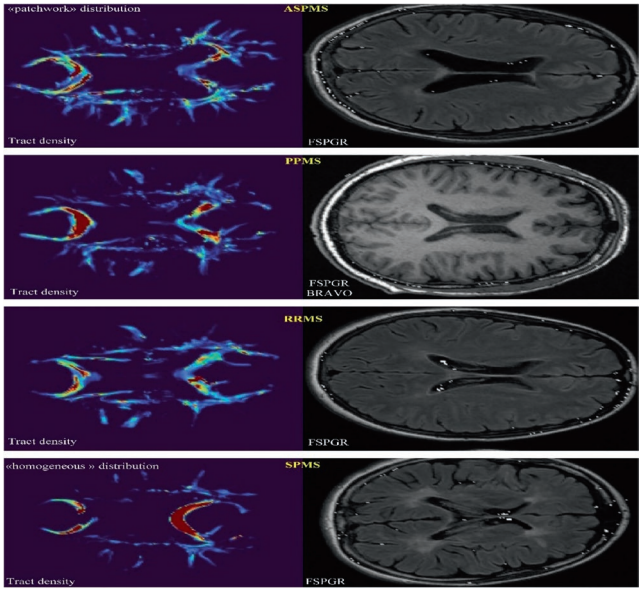

FIGURE 1 TD entropy values in different forms of MS

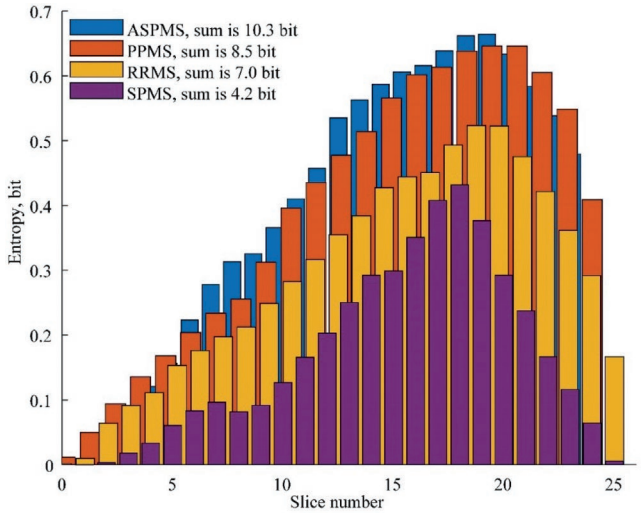

FIGURE 2 Sum and distribution TD entropy in the space of brain in different forms of MS

Conclusion: Low state of TD disorder in the case of SPMS indicates the lowest brain reorganization, intensity of brain reorganization increases in the following order: RRMS, PPMS, ASPMS, all of them are characterized by «patchwork» TD distribution. Further studies are required.
Disclosure: Nothing to disclose.

EPO-632 | Metacognition in multiple sclerosis: Assessing MCQ-30 reliability and its clinical implications

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Background and Aims: Metacognition, the ability to monitor and regulate thoughts, emotions and behaviors, plays a crucial role in psychological health. Its dysfunction is generally associated with higher levels of depression, anxiety and fatigue in the general population. This study aims to explore the relationship between Metacognition Questionnaire (MCQ-30) and its five subscales (PositiveBeliefsAboutWorry [POS], NegativeBeliefsAboutUncontrollabilityAndDanger [NES], CognitiveConfidence [CC], Need To Control Thoughts [NC], CognitiveSelfConsciousness [CSC]) with these symptoms in patients with Multiple Sclerosis (PwMS).
Methods: Sixty-five cognitively preserved PwMS underwent clinical (EDSS) and psychological evaluations (MCQ-30, Beck Depression Inventory [BDI], State-Trait-Anxiety-Inventory [STAI], Fatigue Severity Scale [FSS]). Spearman's correlations were calculated between the MCQ-30 total score (MCQ-30-ts), subscales and individual items. Gender differences and convergent validity with other psychological scales were also analyzed.
Results: Clinical and demographic data are shown in Tab.1. The internal consistency of MCQ-30 and its subscale was high, except for CSC (Tab.2). No gender differences were found in MCQ-30-ts or its subscales. Significant correlations were observed between the MCQ-30-ts and all items, except items 5 and 12 (rho: 0.26–0.71). All subscales correlated with all items: POS (rho > 0.55, $p < 0.05$), NES (rho > 0.55, $p < 0.05$), CC (rho > 0.79, $p < 0.05$), NC (rho > 0.49, $p < 0.05$) and CSC (rho > 0.41, $p < 0.05$). The MCQ-30-ts and all subscales showed significant intercorrelations (coefficient between 0.41–0.82). As shown in Tab.3, MCQ-30-ts, POS, NES, CC and NC correlated with STAI, BDI and FSS while MCQ-30-ts and CC also correlated with EDSS.

Age Median (IQR)	Female (%)	Education Median (IQR)	Disease Duration Median (IQR)	EDSS Median (IQR)
38 (22)	48 (71.6)	15 (5)	9.3 (15.3)	1 (1)

Abbreviations: EDSS Expanded Disability Status Scale, IQR Interquartile Range.

Tab 1 – Clinical and demographic characteristics of the sample

	Min	Max	Skewness	IQR	Alpha	Item
POS	6	22	0.768	10 (6)	0.867	1, 7, 10, 19, 23, 28
NES	6	24	0.549	13 (6)	0.828	2, 4, 9, 11, 15, 21
CC	6	24	0.551	11 (9)	0.907	8, 14, 17, 24, 26, 29
NC	6	22	0.463	12 (6)	0.768	6, 13, 20, 22, 25, 27
CSC	6	23	-0.661	17 (4)	0.567	3, 5, 12, 16, 18, 30
Tot	30	101	0.529	64 (19)	0.895	

Abbreviations: Alpha Cronbach's Alpha, CC Cognitive Confidence, CSC Cognitive Self-Consciousness, IQR Interquartile Range, Max Maximum, Min Minimum, NC Need to Control Thoughts, NES Negative Beliefs about Uncontrollability and Danger, POS Positive Beliefs about Worry, Tot Total.

Table 2 – Range of values, skewness and alpha of the scale and total score of MCQ-30

	EDSS	BDI	STAI	FSS
POS	0.351**	0.622**	0.550**	0.250
NES	0.163	0.547**	0.520**	0.479**
CC	0.403**	0.413**	0.292*	0.457**
NC	0.187	0.531**	0.378**	0.248
CSC	0.204	0.026	-0.054	-0.032
Tot	0.346**	0.658**	0.547**	0.430**

* 0.05
**0.01
Abbreviations: BDI Beck Depression Inventory, CC Cognitive Confidence, CSC Cognitive Self-Consciousness, EDSS Expanded Disability Status Scale, FSS Fatigue Severity Scale, NC Need to Control Thoughts, NES Negative Beliefs about Uncontrollability and Danger, STAI State-Trait Anxiety Inventory, POS Positive Beliefs about Worry, Tot Total.

Table 3 – Convergent validity between MCQ-30 total scale and subscales, EDSS and mood disorder scales.

Conclusion: The MCQ-30 is a reliable and valid tool for assessing metacognition in PwMS. Increased metacognitive dysfunction is associated with worsening symptoms of anxiety, depression and fatigue.
Disclosure: Quattropani, M. C., Lenzo, V., Mucciardi, M., and Toffle, M. E. (2014). Psychometric properties of the Italian version of the short form of the metacognitions questionnaire (MCQ-30). BPA Appl. Psychol. Bull. 62.

EPO-633 | The effect of dual-task on upper extremity functions in multiple sclerosis patients

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Background and Aims: Multiple Sclerosis is a neurodegenerative, chronic, autoimmune disorder of the central nervous

system and affects daily living activities. Daily living activities often require dual-task performance. Assessments that include dual tasks can show the impairments in PwMS' daily life. Although upper extremity dysfunctions are frequently seen in PwMS, research on the effect of dual-tasking on upper extremity functions and the dual-task interference is limited. This study aimed to investigate the effect of dual-tasking on upper extremity functions in PwMS and compare it with HC.

Methods: This case-control design study was conducted with 30 PwMS and 30 HC. Age and sex-matched controls were also randomly selected from the general population. The Edinburgh Handedness Questionnaire measured participants' hand preferences. Disability status is assessed using the EDSS, and cognitive status is assessed using the BICAMS. MMDT was used to evaluate the upper extremity function of the participants. The DTQ was used to evaluate the difficulties experienced during dual-task.

Results: There was no difference between single-task placement times, single-task turning times, dual-task turning times, and dual-task effects of PwMS and HC ($p > 0.05$). However, it was found that there was a statistically significant difference between the verbal fluency and turning errors made by PwMS and HC during dual-task performance and the dual-task questionnaire scores ($p < 0.05$).

Conclusion: The results of this study demonstrate that PwMS exhibits upper extremity performance similar to healthy controls under dual-task conditions. This finding provides reassurance about the potential for PwMS to lead everyday lives.

Disclosure: Nothing to disclose.

EPO-634 | Cortical excitability and cognitive impairment in individuals with multiple sclerosis

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Background and Aims: This study investigates cortical excitability and cognitive impairment in individuals with Multiple Sclerosis (MS) compared to matched healthy controls, aiming to explore their interrelationship and implications for disease pathology and management.

Methods: We assessed 44 individuals diagnosed with MS and a matched control group of 44 healthy participants. Cortical excitability was measured using transcranial magnetic stimulation (TMS), while cognitive performance was evaluated using standardized neuropsychological tests targeting memory, attention, and executive function. Demographic and clinical variables, including disease duration and disability scores, were analyzed to control for potential confounders.

Results: Participants with MS exhibited significantly altered cortical excitability parameters, including reduced motor threshold and increased intracortical facilitation, compared to healthy controls ($p < 0.05$). Cognitive assessments revealed deficits in attention, memory, and executive functioning among the MS group, with moderate to strong correlations observed between cortical excitability measures and cognitive performance ($r = 0.4–0.6$, $p < 0.01$). These relationships persisted after adjusting for age, education, and disease severity.

Conclusion: This study highlights the interplay between cortical excitability and cognitive impairment in individuals with MS, suggesting a potential neurophysiological basis for cognitive deficits in this population. These findings underscore the importance of integrating neurophysiological assessments into clinical evaluations and exploring interventions targeting cortical excitability to mitigate cognitive decline in MS.

Disclosure: Nothing to disclose.

EPO-635 | Discontinuation of disease-modifying therapies in patients with multiple sclerosis: A retrospective case-control study

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Background and Aims: Currently, there is no consensus on the strategies of discontinuation of disease-modifying therapy (DMT) in multiple sclerosis (MS) patients. This study evaluates confirmed disability progression (CDP) and evidence of disease activity-3 (EDA-3) after one year of DMT discontinuation compared with a control group.

Methods: Single-centre retrospective observational case-control study, including patients diagnosed with MS who had discontinued DMT and had a minimum follow-up of one year (June 2013-December 2024). Controls without DMT discontinuation were selected from a prospectively collected MS patients database by propensity score matching by age, sex, MS type and DMT. Controls exclusion criteria included less than one year follow-up and no clinical or radiological stability for at least 3 years. We classified patients according to VIAADISC scale. This scale predicts the risk of activity after DMT discontinuation according to age, and clinical and MRI data.

Results: After propensity score matching, 32 patients who discontinued DMT and 44 controls who did not discontinue DMT were included. No statistically significant differences were found between the two groups regarding age (median 54.2 vs 51.3 years), sex, MS phenotype, DMT, EDSS and VIAADISC score. After one year, there were no significant differences between the two groups in terms of CDP (OR 0.55, 0.07-2.85, p-value = 0.69) and EDA-3 (OR 1.05, 0.37-2.92, p-value = 0.6). There were no differences regarding new MRI lesions (p-value = 0.18), although slightly more relapses in the control group were observed (p-value = 0.04).

Conclusion: Discontinuation of DMT in selected MS patients showed no higher risk of disease activity and disability accumulation after one year.

Disclosure: Nothing to disclose.

EPO-636 | Myelin oligodendrocyte glycoprotein antibody-associated disease manifesting as idiopathic intracranial hypertension

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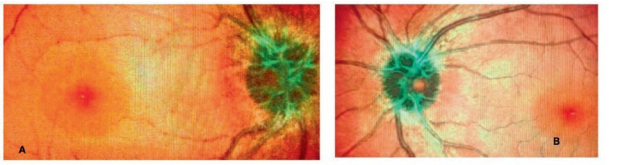
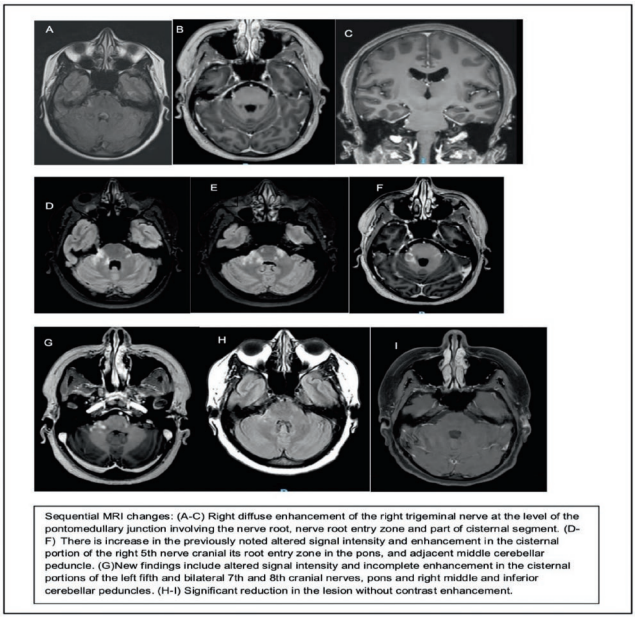
Background and Aims: This case report highlights the diagnostic challenges in a female presenting with mild visual disturbances and headache, initially diagnosed with idiopathic intracranial hypertension (IIH) but later identified as having Myelin Oligodendrocyte Glycoprotein Antibody-Associated Disease (MOGAD).
Methods: A 37-year-old woman with no significant medical history presented with a week-long history of visual disturbances, bifrontal headaches, and pain associated with eye movement Ophthalmological assessment revealed bilateral papilledema without focal neurological deficit. Her MRI and MRV of the brain were normal. Given the clinical suspicion IIH, the patient was recommended for a lumbar puncture, which she declined. Consequently, treatment with acetazolamide. During her follow-up, an acute exacerbation of her visual disturbances was observed Anti-MOG antibodies was positive, which was pivotal in confirming the diagnosis of MOGAD. The patient received intravenous methylprednisolone for five days, resulting in significant symptom relief for six months. However, she later developed right-sided facial numbness repeat MRI, which revealed enhancement of the right trigeminal nerve and a small enhancing lesion in the right pontine region, without evidence of associated mass effect.



(A-B) Bilateral disc swelling, Blurred edges, (A) Right cup could not be seen stage 3 Papilledema (B) Left Cup/disc ratio 0.2 Stage 2 Papilledema.

FIGURE 1 Fundus Pic



Sequential MRI changes: (A-C) Right diffuse enhancement of the right trigeminal nerve at the level of the pontomedullary junction involving the nerve root, nerve root entry zone and part of cisternal segment. (D-F) There is increase in the previously noted altered signal intensity and enhancement in the cisternal portion of the right 5th nerve cranial its root entry zone in the pons, and adjacent middle cerebellar peduncle. (G)New findings include altered signal intensity and incomplete enhancement in the cisternal portions of the left fifth and bilateral 7th and 8th cranial nerves, pons and right middle and inferior cerebellar peduncles. (H-I) Significant reduction in the lesion without contrast enhancement.

FIGURE 2 MRI Brain

Results: The combination of clinical findings, imaging results, and laboratory data led to the diagnosis of MOGAD. The patient received five additional doses of IVMP, and oral steroids complemented by the initiation of azathioprine as a disease-modifying therapy.
Conclusion: This case illustrates the necessity of a broad differential diagnosis in patients presenting with visual disturbances and papilledema. A comprehensive and multi-disciplinary approach is essential for the effective management of MOGAD, ensuring accurate diagnostics and improved patient outcomes.
Disclosure: Nothing to disclose.

EPO-637 | Efficacy of eculizumab and pharmacogenetic modulation by rs17611 in Chinese AQP4-IgG-positive relapsing neuromyelitis optica spectrum disorder: Implications for precision dosing

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Background and Aims: Complement-mediated pathogenesis underpins Neuromyelitis Optica Spectrum Disorders (NMOSD), with C5-driven membrane attack complex (MAC) formation being a therapeutic target. Eculizumab, a humanized anti-C5 monoclonal antibody, has been shown to significantly reduce relapse risk by blocking terminal complement activation. However, emerging evidence suggests that genetic polymorphisms modulating C5 cleavage dynamics—particularly rs17611, a risk allele enhancing neutrophil elastase (HNE)-mediated proteolysis into dysfunctional C5a/C5b variants—may critically alter MAC assembly efficiency. This study bridges a critical knowledge gap by evaluating eculizumab's clinical efficacy and its interplay with rs17611 pharmacogenetics in Chinese AQP4+ NMOSD patients, aiming to refine personalized therapeutic paradigms.

Methods: In this prospective observational study, five AQP4-IgG-seropositive NMOSD patients experiencing acute attacks received eculizumab at Xiangya Hospital, Central South University (August 2024–March 2025). Neurological recovery was longitudinally quantified using the Expanded Disability Status Scale (EDSS), while rs17611 genotyping was performed via whole-exome sequencing. Genotype-phenotype correlations were analyzed using non-parametric statistics (Mann-Whitney U test).

Results: rs17611 C>T variant carriers ($n = 2$) exhibited superior EDSS improvement (median reduction: 1.5 points, range: 1.0–2.0) versus wild-type patients ($n = 3$; median: 1.0 point, range: 1.0–1.5; $*p* = 0.042$). The rs17611 C>T variant group ($n = 2$) exhibited notable decreases in complement C3 (Δmedian = −32.5%), IgA (Δmedian = −23.9%), and IgM (Δmedian = −63.4%) following treatment, while wild-type controls ($n = 3$) demonstrated increases in complement C4 (Δmedian = +54.1%) and C3 (Δmedian = +20.0%). No treatment-related infections or mortality occurred, confirming short-term safety.

TABLE 1 Demographic, baseline characteristics and changes in EDSS scores.

Case	Sex	Age at onset	Age at onset of index attack	Clinical characteristics	Previous maintence therapy	Treatment for the index attack before ECU initiation	Days from the onset of index attack to ECU initiation	Baseline EDSS scores before the index attack	Worst EDSS scores during the index attack	EDSS scores at ECU initiation	EDSS scores after ECU treatment	Times of attack	ECU administration times	C5 mutation*	AQP4 titers
1	Male	38	48	Optic neuritis (bilateral) and Myelitis	NA	IVMP and PE	27	3.0	4.0	4.0	3.5	3	4	Mutation-free	1:3200
2	Female	55	58	Myelitis	Corticosteroids, Rituximab, Ofatumumab	IVMP and PE	19	1.0	8.5	8.5	7.5	5	5	rs17611 C>T	1:320
3	Female	57	58	Optic neuritis (bilateral) and Myelitis	Corticosteroids	IVMP and PE	24	2.0	8.0	8.0	7.5	3	4	rs17611 C>T	1:3200
4	Female	23	27	Optic neuritis (bilateral),Area postrema syndrome, Myelitis	Corticosteroids	IVIG and PE	20	0.0	8.0	8.0	7.5	3	11	Mutation-free	1:100
5	Female	41	45	Myelitis	MMF	IVMP and Efgartigimod	14	1.0	4.5	4.5	3.0	2	11	NA	1:100
6	Female	46	47	Optic neuritis (bilateral) and Myelitis	Corticosteroids, Rituximab	IVMP and Rituximab	142	2.0	3.5	3.5	3.5	3	8	NA	1:10
7	Female	47	55	Optic neuritis (bilateral) and Myelitis	Corticosteroids, MMF	Corticosteroids, MMF	NA	7.0	7.0	7.0	6.5	NA	3	NA	Negative
8	Male	46	47	Optic neuritis (bilateral)	Corticosteroids	IVMP and PE	14	3.0	4.0	4.0	3.0	2	6	NA	1:320
9	Female	35	35	Myelitis	NA	IVMP and PE	86	0.0	3.5	3.5	2.0	1	6	NA	1:100

EDSS: Expanded Disability Status Scale; ECU: eculizumab; IVMP: Intravenous methylprednisolone; PE: plasma exchange; IVIG:Intravenous Immunoglobulin, MMF:Mycophenolate Mofetil, NA:not applicable
*Mutation detection sites include rs17611, rs373599894, rs2274587, rs6504400
Patient#4, a pregnant woman, began treatment with eculizumab at 18 weeks and 5 days of gestation and had successfully delivered a live male baby via cesarean section on December 24.

Conclusion: We pioneer the discovery that rs17611—a putative risk allele in NMOSD pathogenesis—paradoxically predicts enhanced therapeutic response to eculizumab, likely through attenuated MAC formation via HNE-dominant C5 cleavage. This dual-context genetic effect challenges conventional pharmacogenetic frameworks and unveils a novel biomarker for precision dosing in NMOSD. Crucially, our findings advocate for genotype-guided escalation protocols in Asian populations, warranting validation in larger cohorts and mechanistic studies on C5 fragment bioactivity.

Disclosure: Approved by the Institutional Review Board of Xiangya Hospital. All participants provided written informed consent with anonymized data handling, adhering to the Declaration of Helsinki.

EPO-638 | The real-world effectiveness of natalizumab in relapsing-remitting multiple sclerosis in Algeria

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Background and Aims: Natalizumab therapy for MS patients has been demonstrated to be highly effective in several clinical trials. Data in Algerian population are needed on long-term effect of natalizumab (NTZ) in relapsing-remitting multiple sclerosis (RRMS).

Methods: We conducted a multicentre, observational and retrospective study at five department of neurology reported RRMS patients who initiated natalizumab ‡12 months prior to study conduction.

Results: 167 patients were included, with a mean age of 26.1 ± 7.6 years at diagnosis, and a mean age of 31.8 ± 9.4 years at NTZ initiation. The median number of infusions was 36. The Mean EDSS scores remained unchanged up to 3 years. It was 3.7 ± 1.6 (range, 0–5, median 4) at baseline and it was 3.4 ± 2.1 (range, 0–5, median 4) at the follow-up. The mean annualized relapse rate (ARR) previous, during and after NTZ was 2.3 ± 1.4, 0.4 ± 0.6 and 0.3 ± 0.5, respectively. 52.7% of patients remained relapse free and reached NEDA3 at 3 years. RIO 3 at 3 years was also achieved in 67% of cases. One case of progressive multifocal leucoencephalopathy was reported. Patients with an EDSS of 4 at the start of treatment had a better outcome, with a lower annual relapse rate, stabilisation of disability and no new T2 lesions on MRI.

Conclusion: Our data confirm natalizumab's overall safety profile and the low relapse rate and stabilised disability levels in Algerian RRMS patients treated with natalizumab in clinical practice.

Disclosure: Nothing to disclose.

EPO-639 | Assessment of multiple sclerosis awareness and knowledge among Saudi population

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Background and Aims: Although the Middle East region falls in the low-to-moderate multiple sclerosis (MS) prevalence zone, a lack of knowledge about MS symptoms may cause patients to miss the opportunity to reap the benefits of early interventions. This study examines the awareness and knowledge of MS in Saudi population to help better build targeted campaigns that aid in early interventions.

Methods: We did a convenience sample cross sectional study, assessing people's knowledge on MS from various regions of Saudi Arabia using a previously validated questionnaire.
Results: A total of 544 individuals have completed the survey. Majority (81.8 %) of participants ages fall between 18 and 45 years old, and females made up 45.2% of the sample. Also, over half of the participants are college students. According to our survey analysis, 72.6% had previously heard about the disease mainly through social media platforms (56.1%). Moreover, only 29% of participants knew someone with MS. Nevertheless, the majority (90.6%) believed that MS sufferers required support, and 53.3% were able to correctly answer questions on its symptoms. However, less than one third knew about the different treatment modalities. Also, majority (89.5%) believed that MS patients have a compromised professional life; and over half of the participants agreed that it is linked to depression.
Conclusion: The Saudi public's understanding of Multiple Sclerosis as a disease, its prevalence, and its treatment remains inadequate. However, they are slightly aware of certain elements in the condition's pathophysiology. Nevertheless, programs to raise public awareness should help increase MS knowledge in Saudi Arabia.
Disclosure: Nothing to disclose.

EPO-640 | Migraine and tension-type headache are associated with multiple sclerosis: A case-control study

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Background and Aims: Over the past decades there has been increased scientific interest in the prevalence of headache disorders among people with MS (pwMS). Although the latest data suggest an association between migraine and multiple sclerosis, studies have been providing inconsistent results largely due to methodological shortcomings. The aim of this study is to investigate the prevalence of primary headache disorders in pwMS and healthy controls (HCs) and examine the potential association between the two conditions.
Methods: Ninety-six pwMS from Eginition University Hospital, Athens, Greece and 96 matched HCs were recruited prospectively. Both groups were assessed for headache disorders using a semi-structured questionnaire and diagnosed according to the International Classification for Headache Disorders 3 (ICHD-3) criteria. A multivariable logistic regression model adjusted for age and sex, evaluated the association between MS and headache disorders.
Results: A higher prevalence of primary headache disorders in pwMS (71.9%) compared to HCs (43.8%) was observed. Specifically, 28.1% of pwMS had migraine, and 38.5% had tension-type headache (TTH). PwMS were significantly more likely to be diagnosed with any primary headache disorder (OR = 4.54; 95% CI: 2.28 to 9.04; $p = 1.7$), migraine (OR = 2.21 95% CI: 1.05 to 4.62; $p < 0.05$), and TTH (OR = 2.16 95% CI: 1.16 to 4; $p < 0.05$) compared to HCs.

Table 1. Participants demographics and clinical data.

Demographical & Clinical Data		
	MS	Controls
Gender		
Female - n (%)	69 (71.9)	66 (68.75%)
Male - n (%)	27 (28.1)	30 (31.25%)
Age (years) mean ± SD	42.15 (12.81)	37.16 (12.63)
Disease duration (years) mean ± SD	8.57 (8.52)	
EDSS mean ± SD	3.13 (1.88)	
Disease subtype		
RRMS - n (%)	77 (77.1)	
PPMS - n (%)	7 (7.3)	
SPMS - n (%)	15 (15.6)	

n:number of patients; SD: standard deviation; MS: multiple sclerosis; RRMS: relapsing remitting multiple sclerosis; SPMS: secondary progressive multiple sclerosis; PPMS: primary progressive multiple sclerosis; EDSS: Expanded Disability Status Scale

Table 2. Association between primary headache disorders and MS.

	Unadjusted		Adjusted	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Any headache	3.29 (1.80 to 5.99)	p < 0.05	4.54 (2.28 to 9.04)	p = 1.7
Migraine	2.18 (1.05 to 4.49)	p < 0.05	2.21 (1.05 to 4.63)	p < 0.05
TTH	1.82 (1.02 to 3.25)	p < 0.05	2.16 (1.16 to 4)	p < 0.05

MS: multiple sclerosis; TTH: tension-type headache

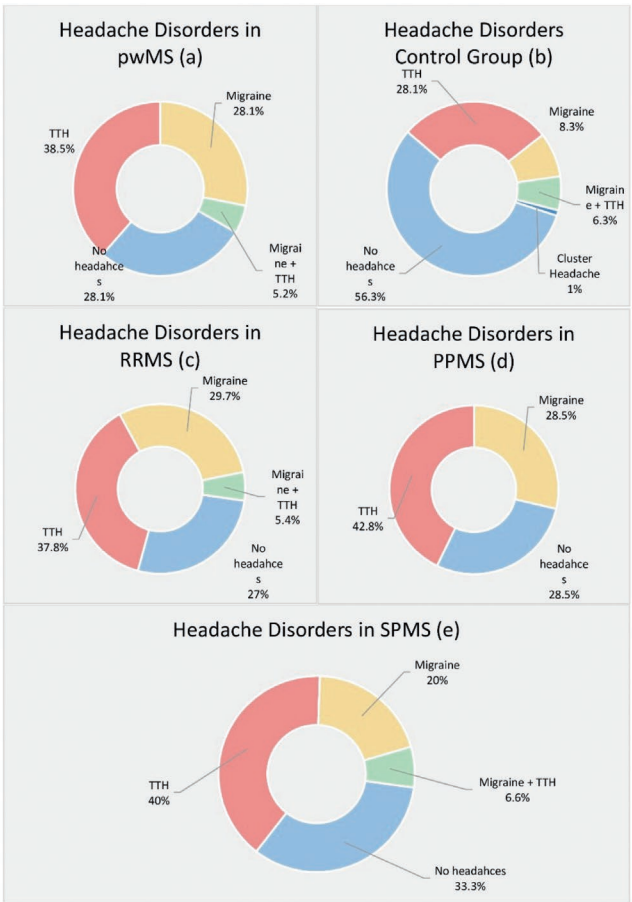

Figure 1. Prevalence of primary headache disorders across study groups. **(a)** People with MS (pwMS); **(b)** control group; **(c)** RRMS; **(d)** PPMS; **(e)** SPMS

Conclusion: Our study suggests a strong association of primary headache disorders and MS suggesting that MS-related changes may increase susceptibility to headache and highlights the need

for targeted headache management in pwMS. Prospective longitudinal studies are needed to draw more robust conclusions.
Disclosure: Nothing to disclose.

EPO-641 | Education on the rationale for BTK inhibitors significantly improves knowledge, confidence, and intention to learn more

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Background and Aims: Neurologists are unfamiliar with Bruton tyrosine kinase inhibitors (BTKis) and their relevance for future MS practice. We sought to improve knowledge of the rationale for BTKis in MS by providing expert-led education.
Methods: Neurologists participated in an online CME divided into 6 video + slide segments with synchronized slides.1 The education effects were assessed using a 3-question, repeated pairs, pre-assessment/post-assessment study design. One question assessed confidence. Differences pre- to post-assessment were evaluated using McNemar's test. $p \leq 05$ is significant. The activity launched in June 2024; data were collected over 8 weeks.
Results: 598 neurologists participated, with 78 completing all pre- and post-assessment questions. Significant overall improvements were seen, with a 43% correct response rate pre-assessment vs 63% post-assessment; $p < 0.001$, $N = 78$. Specifically, significant improvements were observed in knowledge that BTK inhibition within the CNS has a pharmacological effect on B cells and microglia; and that T1- and T2-weighted MRI can be used longitudinally to measure slowly expanding lesions, which may be driven by smoldering inflammation. After participating, 45% of neurologists had measurable improved confidence in describing the role of BTK inhibition within the CNS. 47% of neurologists said they intend to learn more about MS pathophysiology, and 19% said they would learn more about BTK inhibition in MS.
Conclusion: This study demonstrates the success of online, multi-component, multi-faculty, video-based CME in improving knowledge and intention to acquire more knowledge about a new class of therapy for MS. Improved knowledge on BTKis should result in increased confidence in their future implementation of these therapies.
Disclosure: Nothing to disclose for all authors except Veronica Popescu, MD, PhD, has the following relevant financial relationships: Consultant or advisor for: Almirall; Biogen; Medtronic, Inc.; Merck; Novartis; Roche; Sanofi-Genzyme; Teva Pharmaceutical Industries Ltd. Speaker or member of speakers bureau for: Biogen; Merck; Novartis; Roche; Sanofi-Genzyme.

EPO-642 | Cladribine impacts on clinical, radiological, cognitive and physical assessments of people with multiple sclerosis

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Background and Aims: This abstract comprehensively evaluates the efficacy and safety of cladribine treatment in MS, focusing on cognitive and physical outcomes besides clinical outcomes.
Methods: A cohort of participants diagnosed with MS underwent treatment with cladribine (n = 173), with cognitive and physical assessments (n = 32) included in the study. The physical and cognitive assessments were conducted at baseline (T0) and follow-up (first year = T1, second year = T2). Cognitive function was evaluated using the Brief International Cognitive Assessment for Multiple Sclerosis (BICAMS) battery, which included the California Verbal Learning Test (CVLT), Brief Visuospatial Memory Test-Revised (BVMTR), and Symbol Digit Modalities Test (SDMT) while physical function was assessed through the Timed 25-Foot Walk (T25FW) and Nine-Hole Peg Test (N-HPT). The Expanded Disability Status Scale (EDSS), disease duration, age, presence of new attacks and the new MRI findings of the participants were recorded.
Results: The mean age and disease duration were 36.75 ± 11.44 and 8.33 ± 6.85. Results revealed significant improvements in CVLT, BVMTR, and SDMT tests at the follow-up interval. However, no significant differences were observed in N-HPT. Fourteen participants had new attacks, while sixteen participants had new MRI findings.
Conclusion: These findings suggest that cladribine treatment is beneficial and safe for cognitive function in pwMS. However, further research is warranted to elucidate its impact on physical function. The significant efficacy demonstrated by cladribine treatment in treating MS is complemented by its favourable safety profile, as evidenced by the small number of new relapses and the emergence of new MRI findings.
Disclosure: Nothing to disclose.

EPO-643 | Maraviroc-responsive progressive multifocal leukoencephalopathy-associated immune reconstitution inflammatory syndrome

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Background and Aims: PML is an opportunistic infection of the brain caused by the human polyomavirus 2. Overall, PML is associated with severe disability and a relatively high mortality.
Methods: A 45-year-old male patient who had been receiving natalizumab therapy for MS for 3 years presented with complaints of apathy, disorientation, and weakness in the left arm and leg for 10 days.

Results: Brain MRI revealed lesions consistent with PML. The serum anti-JCV index was 3.93, CSF protein 37.5 mg/dl, and CSF JCV DNA 621 copies/ml. The patient was evaluated as consistent with a preliminary diagnosis of PML and underwent plasmapheresis. Following clinical and radiological progression, the patient was treated with 1 g/day of intravenous methylprednisolone under the preliminary diagnosis of IRIS. Based on the diagnosis of PML and PML-associated IRIS, peroral maraviroc at a dose of 2x300 mg was initiated. Radiological and clinical improvement were observed. At the 6th month of maraviroc treatment, the CSF JCV index decreased to 10 copies/ml, and no JCV DNA was detected in the CSF at 1 year.

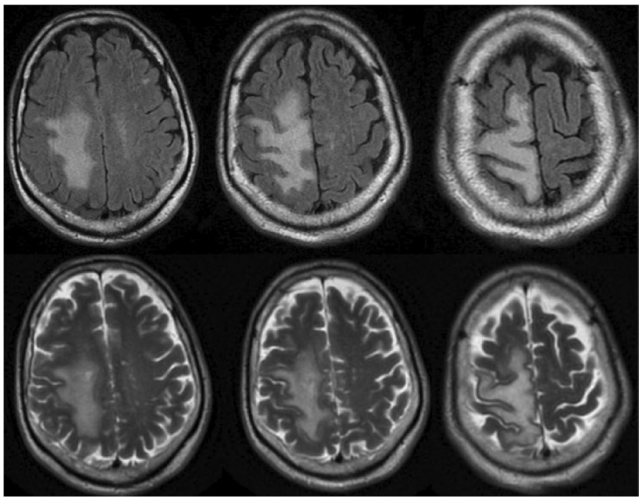

FIGURE 1 Axial FLAIR and T2-weighted MRI before maraviroc treatment.

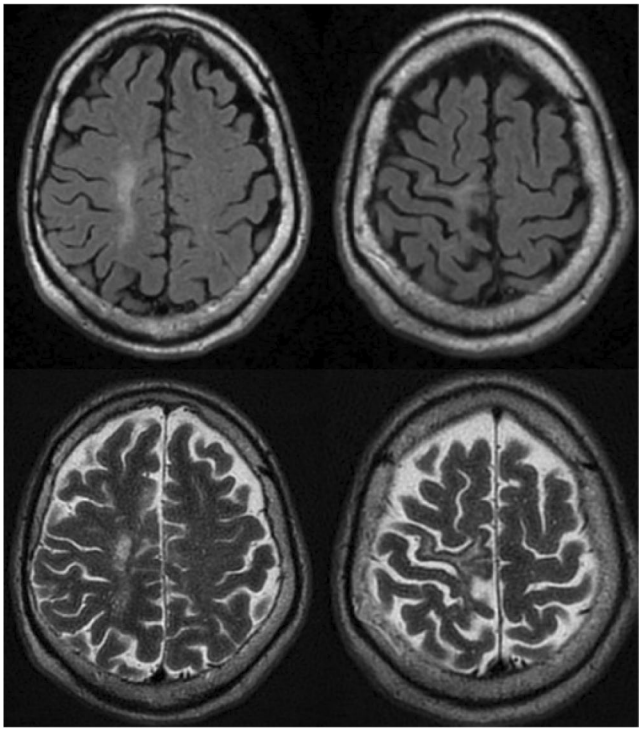

FIGURE 2 Axial FLAIR and T2-weighted MRI after maraviroc treatment.

Conclusion: In patients with natalizumab-associated PML, prognosis largely depends on the timing of diagnosis and the size of the lesions. Additionally, a condition known as PML-associated IRIS may also develop. Immune checkpoint inhibitors, T-cell therapies and and CCR5 agonists such as Maraviroc are among the treatment options. Distinguishing cases of PML-associated IRIS from MS relapses and administering appropriate treatments in a timely manner are crucial for reducing mortality and morbidity.
Disclosure: Nothing to disclose.

EPO-644 | Gender does not impact autonomic dysfunction among people with multiple sclerosis

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Background and Aims: During Multiple Sclerosis (MS), autonomic nervous system (ANS) dysfunction is described in 45 to 85% of cases. This study aims to assess the presence of ANS dysfunction among people with MS and to evaluate potential gender differences.
Methods: A cross-sectional study was conducted in the Department of Neurology of Razi Hospital (Tunisia) and included patients diagnosed with MS according to the 2017 McDonald criteria. Patients were divided into two groups according to gender. ANS was evaluated via the Composite Autonomic Symptom Score (COMPASS)-31. Six autonomic domains were evaluated: orthostatic intolerance, vasomotor, secretomotor, bowel, bladder and pupillomotor. Expanded Disability Status Scale (EDSS) score was used to assess the degree of disability. A p-value of <0.05 was considered statistically significant.
Results: A total of 82 patients with MS were enrolled with a female predominance ($n=64$, 78%). Mean age (33.7 years $\pm$9.7 vs 37.9 years $\pm$11.8; $p=0.1$), disease duration (7.8 years $\pm$5.7 vs 9.5 years $\pm$7.5; $p=0.2$), and EDSS score (2.2 $\pm$1.9 vs 3 $\pm$2.1; $p=0.1$) were comparable between females and males. ANS dysfunction was highly reported among females ($n=62$, 97%) and males ($n=16$, 89%) ($p=0.2$). COMPASS-31 scores were higher among females but did not reach a statistically significant difference (22.9 $\pm$14.4 vs 18.1 $\pm$13.7; $p=0.2$). Females exhibited higher scores in orthostatic intolerance, secretomotor, bowel, bladder and pupillomotor functions, but none of these differences reached statistical significance ($p>0.05$).
Conclusion: Autonomic dysfunction is highly prevalent among people with MS and appears to be independent from gender.
Disclosure: Nothing to disclose.

EPO-645 | Diagnostic delay and misdiagnosis of multiple sclerosis: Data from the iConquerMS patient registry

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Background and Aims: Recent data from research cohorts suggest that time to diagnosis of MS has diminished relative to revisions to MS diagnostic criteria, yet some studies have not replicated this finding more broadly. Several recent studies suggest that misdiagnosis of initial symptoms of MS are a frequent contributor to diagnostic delay.
Methods: A patient survey was available to participants of iConquerMS during from November 12, 2021, through December 22, 2021.
Results: There were 428 participants. Diagnostic delay was median of 2.0 months (mean of 22.8 months, range: 0–32.9 years). 173/428 (40.4%) reported misdiagnosis of symptoms that were later diagnosed as due to MS. Diagnostic delay evaluated by epoch proximal to revisions to MS diagnostic criteria decreased over time. Misdiagnosis was associated with a longer delay to MS diagnosis ($p < 0.001$). 208 reported earlier symptoms retrospectively recognized as referable to MS that were not clinically evaluated. Diagnostic delay from these symptoms was a median of 5.4 years and mean 8.9 years (range: 0–47.4 years).
Conclusion: Diagnostic delay was prevalent and associated with frequent misdiagnosis of initial symptoms of MS. Half the participants reported earlier symptoms that were not clinically evaluated and were later attributed to MS. Future studies tracing the diagnostic journey of patients with MS are needed to understand and prevent patient-specific and healthcare system-related causes of diagnostic delay.
Disclosure: AJS: has received research funding from Bristol Meyers Squibb; personal compensation for consulting, advisory boards, or non-promotional speaking from Bristol Meyers Squibb, EMD Serono, Horizon Therapeutics, Kiniksa Pharmaceuticals, Octave Bioscience, and TG Therapeutics; contract research with Sanofi, Actelion, Genetech/Roche, and Novartis. SMW: reports no disclosures. SMA: reports no disclosures. HS: reports no disclosures. RTS: personal compensation for consulting to Octave Bioscience and the American Medical Association. AS: has received personal fees for advisory board and non-promotional speaking for Almirall and Merck.

EPO-646 | Central vein sign in mitochondrial cytopathy, due to mutation in the NUBPL gene

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Background and Aims: Introduction: The central vein sign on MRI has been considered specific to multiple sclerosis and is part of the new diagnostic criteria (2024). The NUBPL mutation consists of the substitution of a T for a C at position 545 resulting in the replacement of a valine for an alanine at position 182. They have previously been associated with mitochondrial complex I deficiency, including ataxia, dysarthria, spasticity, and cognitive deterioration, usually early.
Methods: A 52-year-old accountant presented cognitive complaints evolving over a year, including disorganization and delays in completing professional and domestic tasks. She has a history of psoriatic arthritis, treated with adalimumab, and was referred to Neurology due to MRI-detected white matter changes, raising suspicion of demyelinating disease secondary to anti-TNF therapy. Family history revealed a sister with learning difficulties, behavioral changes, motor deficits, ataxia, cognitive decline, and epilepsy, who died at 43.
Results: Findings included cerebral MRI with supratentorial white matter hypersignal on T2/FLAIR, some ovoid and periventricular lesions, and multifocal subcortical frontal-parietotemporal expression. No cortical, posterior fossa, or corpus callosum involvement was noted. Lesions displayed T1-weighted hyposignal, and SWI sequences showed central linear hypointensities with a "central vein" sign. Genetic testing confirmed a deleterious NUBPL gene mutation, consistent with her sister's case. Neuropsychological assessment revealed attentional and executive difficulties. No oligoclonal bands.
Conclusion: The patient exhibits isolated cognitive impairments, atypical white matter lesions for MS, progressive supratentorial white matter hyperintensity, and a confirmed NUBPL gene mutation. Although the central vein sign strongly suggests MS, it can also occur in other conditions.
Disclosure: Nothing to disclose.

EPO-647 | Diagnostic and therapeutic challenges in LGI1 autoimmune encephalitis with paraneoplastic features

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Background and Aims: Autoimmune encephalitis associated with LGI1 antibodies is a rare and potentially severe condition, often linked to paraneoplastic syndromes. Its nonspecific symptoms, including behavioral disturbances, cognitive decline and seizures, complicate timely diagnosis. Prompt recognition is essential, as its paraneoplastic nature may reflect an underlying malignancy requiring targeted management.

Methods: We report the case of a 56-year-old woman with a history of anxiety and depression treated with sertraline since 2020. In March 2024, she presented with diarrhea and hyponatremia, initially attributed to SIADH, prompting sertraline discontinuation. Over the following months, her family observed worsening mood, confusion and memory deficits, resulting in multiple emergency visits. By June, she exhibited erratic behavior, anxiety, visual hallucinations, and worsening memory, prompting admission to Neurology. Examination revealed temporal disorientation, impaired short-term memory, bradypsychia, confabulations, a persistent glabellar reflex, and myoclonic intrusions.
Results: Diagnostic workup showed a normal MRI and CSF (including tau/beta-amyloid ratio and absence of 14-3-3 protein). EEG confirmed epileptiform activity, which resolved after dual treatment with brivaracetam and valproic acid. PET-FDG was compatible with encephalitis, while serum LGI1 antibodies were positive. Immunoglobulins and corticosteroids achieved significant clinical stabilization, with marked improvement in memory (MoCA 30/30) and functional independence at six months. Further CSF analysis revealed oligoclonal bands with an IgG lambda monoclonal component. Flow cytometry identified a B-cell lymphoproliferative syndrome (CD5+), consistent with marginal zone lymphoma. Hematology favored monitoring and potential Rituximab therapy if needed.
Conclusion: This case highlights the diagnostic challenges of LGI1 encephalitis and its paraneoplastic implications, emphasizing the need for individualized, interdisciplinary care.
Disclosure: Nothing to disclose.

EPO-648 | Clinical spectrum of anti-Gq1b antibody syndrome

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Background and Aims: Antibody based studies revealed Miller Fisher Syndrome and Bickerstaff Brainstem Encephalitis were commonly linked to Anti-Gq1b antibody, although with certain additional clinical features which were not a part of the core features of Miller Fisher or Bickerstaff Encephalitis. Our study aims to study the spectrum of Anti-Gq1b related disease.
Methods: Twenty one newly diagnosed Anti-GQ1b antibody positive patients between 2019 and 2024 were included in the study.
Results: 63% patients had an antecedent illness; 6/18 (28%) had diarrhea and 7/18 (33%) had URTI. 17/18 patients had ophthalmoplegia (85%), 13/18 (72%) had ataxia, 12/18 (66%) had areflexia while 1/18 (5%) had hyperreflexia. 13/18 (63%) had ocular motor nerve involvement, 10/18 (55%) had lower cranial nerves involvement and 6/18 (33%) had bifacial involvement. 7/18 (39%) patients had motor weakness. CSF routine microscopy was abnormal in 5/18 (28%) patients. NCV studies were abnormal in 6/18 (33%).
Conclusion: Antecedent illness is not uncommon in Anti-Gq1b (60-70%); URTI is most common followed by gastroenteritis. Partial Gq1b syndromes and Overlap Gq1b antibody syndrome commoner than Classic MFS/Bickerstaff Encephalitis. Ophthalmoplegia is the most common presenting and sign, followed by ataxia and areflexia. Limb weakness is seen in upto 40% as a part of Anti-Gq1b Antibody Related Disease/Overlap syndrome. Bulbar palsy can occur in 40-70% of patients, although not a part of the classic triad. CSF albumin-cytological dissociation can be present in 27-40% patients. CSF leucocytosis is rare. NCV was abnormal in 28% cases but can be abnormal in upto 80% patients. Intravenous Immunoglobulin is the treatment of choice and 80-95% patients show good recovery.
Disclosure: Nothing to disclose.

EPO-649 | Resolution of myelin oligodendrocyte glycoprotein-IgG-associated disorders after treatment with efgartigimod

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Background and Aims: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a distinct central nervous system inflammatory disease. Documented studies or reports on the use of efgartigimod for the treatment of MOGAD are currently lacking.
Methods: The patient was admitted to the hospital for fever and headache, altered consciousness, and unsteady walking with weakness in the limbs. Magnetic resonance imaging revealed abnormal signals within the brain tissue and intracranial enhancement of several leptomeninges. Cerebrospinal fluid examination revealed a slight increase in the protein concentration (0.681 g/L). The anti-MOG antibody titer in the CSF was 1:100. It was serologically negative with IgG-oligoclonal bands categorized as type II, suggesting intrathecal IgG synthesis in the central nervous system. Treatment with intravenous methylprednisolone 1000 mg once a day failed to completely control the symptoms of the patient. Thus, 10 mg/kg of efgartigimod was administered intravenously once a week for 3 weeks. The serum anti-MOG antibody and IgG concentrations decreased, and the clinical symptoms improved.
Results: A case of MOGAD accompanied by encephalitis, with the anti-MOG antibody titer in the CSF was 1:100, where the patient was administered efgartigimod and subsequently exhibited favorable therapeutic outcomes. To our knowledge, this treatment for MOGAD is the first attempt currently.

Table 1 Changes in cerebrospinal fluid parameters during the patient's hospitalization

CSF parameters	Date		
	2024/8/21	2024/8/27	2024/9/10
Pressure (mmH_2O)	210	160	165
Total protein(g/L)	0.681	0.347(normal)	0.396(normal)
White blood cell (cells/μL)	147	48	25
Neutrophils (%)	53	1	0
Infectious pathogens(mNGs)		negative	
Autoimmune encephalitis antibodies (12-autoantibody panel, including antibodies for NMDA, AMPA1, AMPA2, LGI1, GABAB, CASPR2, IgLON5, DPPX, GlyR1, DRD2, GAD65, and mGluR5 receptors)		negative	

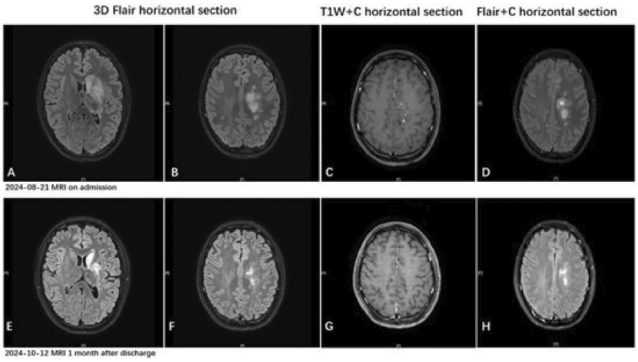

FIGURE 1 The MRI at admission, the review MRI during hospital stay, and the review MRI at one month post-discharge.

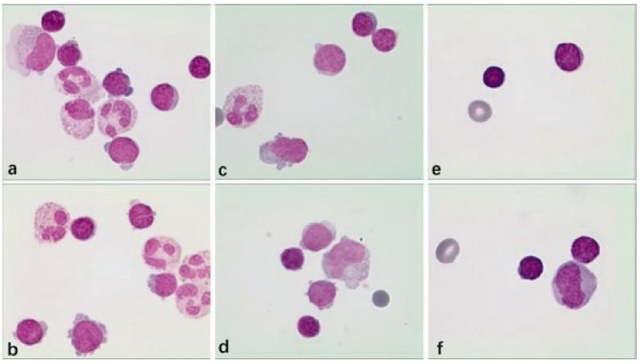

FIGURE 2 The CSF at admission, the review during hospital stay, and on discharge.

Conclusion: The combination of efgartigimod with methylprednisolone yielded positive outcomes and is a promising therapeutic strategy for MOGAD.
Disclosure: Nothing to disclose.

EPO-650 | Safety and efficacy of cladribine in patients discontinuing fingolimod due to elevated liver enzymes: FinClad study

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Background and Aims: Fingolimod is an effective disease-modifying therapy (DMT) for relapsing-remitting multiple sclerosis (RRMS), but elevated liver enzyme levels often necessitate treatment discontinuation. Cladribine, an oral DMT with comparable efficacy, has a more favorable hepatic safety profile. However, data on the safety and short-term efficacy of switching from fingolimod to cladribine in patients with liver enzyme elevation remain limited.
Methods: This retrospective, multicenter study included 45 RRMS patients (aged 18–65) who transitioned from fingolimod to cladribine due to elevated liver enzymes (AST and ALT > 3× ULN). Clinical and demographic data, liver function tests (LFTs), and disease activity parameters were collected at six time points: before fingolimod initiation, at fingolimod discontinuation, immediately before cladribine initiation, and at 1, 2, and 3 months post-treatment. Disease activity was assessed based on relapses and MRI findings (new/enlarging T2 or gadolinium-enhancing lesions). Statistical analyses included repeated-measures ANOVA and logistic regression.

Results: AST and ALT levels significantly declined after cladribine initiation ($p < 0.001$). No serious liver-related adverse events were reported. Disease activity remained controlled in 86.7% of patients; five had relapses, and one showed radiological activity. Longer washout duration (>9 weeks) was associated with increased disease activity ($p = 0.011$). Younger age was a potential risk factor. EDSS scores remained stable.
Conclusion: Cladribine is a safe and effective option for RRMS patients discontinuing fingolimod due to elevated liver enzymes. Short washout periods and close monitoring are essential to minimize disease reactivation.
Disclosure: Nothing to disclose.

EPO-651 | Physician- and patient-reported outcomes by disease severity in a United States real-world Myasthenia Gravis population

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Background and Aims: Myasthenia gravis (MG) is a rare neuromuscular condition causing muscle weakness and fatigue. This study describes physician- and patient-reported outcomes in patients with MG stratified by MG Foundation of America (MGFA) severity classification.
Methods: Physicians provided patient-level data via the Adelphi MG II Disease Specific Programme™ (DSP) from February–August 2024; a different cohort of patients (PAT) self-reported data in October 2024. Information on patient demographics, MGFA classification, clinical outcomes, and MG-Activities of Daily Living (MG-ADL) was collected.
Results: Fifty-two physicians reported on 390 DSP patients; 243 PAT patients self-reported. DSP patients had a mean (SD) age of 55.1 (13.7) years, a mean (SD) time since diagnosis of 3.8 (5.6) years, and 46.9% were female. PAT patients had a mean (SD) age of 49.1 (14.6) years, self-reported experiencing symptoms for a mean (SD) of 13.0 (2.2) years, and 87.7% were female. The proportions of MGFA class I, class II, and class III/IV/V patients in the DSP population were 20.5%, 63.3% and 16.2%, respectively; corresponding proportions in the PAT cohort were 6.6%, 30.0%, and 63.4%, respectively. Clinical and MG-ADL outcomes by MGFA classification are in Table 1. MG-related hospitalizations in the year prior to the survey occurred in 7.1%, 16.3% and 18.3% of MGFA class I, II, and III/IV/V DSP patients, respectively; corresponding proportions in the PAT cohort were12.5%, 23.3% and 48.7%.

TABLE 1 MG-ADL total scores derived from physician- and patient-reporting by MGFA classification at time of survey.

	MGFA classification at time of survey			
	Overall	Class I	Class II	Class III/IV/V
Physician-reported (DSP sample), n	**390**	**80**	**247**	**63**
MG-ADL total score, mean (SD)	4.4 (3.3)	1.9 (1.5)	4.3 (2.9)	7.9 (3.7)
Per patient, in the year prior to survey;				
...Myasthenic crises, mean (SD)	0.0 (0.3)	0.0 (0.1)	0.0 (0.3)	0.1 (0.3)
...Exacerbations of symptoms, mean (SD)	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)	0.1 (0.5)
...Hospitalisations, mean (SD)	0.2 (0.6)	0.1 (0.2)	0.2 (0.5)	0.3 (0.9)
Patient-reported (PAT sample), n	**243**	**16**	**73**	**154**
MG-ADL total score, mean (SD)	8.3 (3.6)	4.6 (3.1)	6.5 (3.2)	9.5 (3.2)
Per patient, in the year prior to survey;				
...Myasthenic crises, mean (SD)	0.3 (1.3)	0.0 (0.0)	0.3 (1.8)	0.4 (1.2)
...Exacerbations of symptoms, mean (SD)	5.1 (10.5)	1.2 (1.6)	2.3 (4.9)	6.9 (12.4)
...Hospitalisations, mean (SD)	0.9 (1.7)	0.2 (0.5)	0.5 (1.2)	1.1 (1.9)

MG-ADL, Myasthenia Gravis Activities of Daily Living; MGFA, Myasthenia Gravis Foundation of America.

Conclusion: Increased activity impairment and worse clinical outcomes were observed with higher MGFA classification in both cohorts. Treatments delivering greater improvements for patients with moderate-to-severe MG are needed.
Disclosure: LAMW, LL and YE are employees of Immunovant, Inc., JC, SLB, HC and GG are employees of Adelphi Real World.

EPO-652 | Two cases of progressive multifocal leukoencephalopathy linked to siponimod in multiple sclerosis

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Background and Aims: Sphingosine-1-phosphate (SP1) modulators, used in multiple sclerosis (MS), have been linked to progressive multifocal leukoencephalopathy (PML), predominantly with fingolimod and only one reported case with Siponimod.
Methods: We report one confirmed and another probable case of PML associated with Siponimod in MS patients treated at a tertiary hospital in 2024.
Results: Case 1: A 65-year-old male with secondary progressive MS (SPMS), previously treated with interferon beta-1a (INF-B), natalizumab (discontinued in 2012) and fingolimod, initiated Siponimod in March 2023. In July 2024, he developed severe left hemiparesis. Magnetic resonance imaging (MRI) revealed a fronto-parietal juxta-subcortical white matter lesion, highly suggestive of PML, which was later confirmed by biopsy. Treatment with pembrolizumab stabilized his clinical condition, with partial neurological recovery and lesion reduction on follow-up MRI. Case2: A 48-year-old male with SPMS, previously treated with INF-B and dimethylfumarate, began Siponimod in 2023. One year after he reported headaches and visual disturbances

initially diagnosed as migraine. In July 2024, MRI revealed a new occipital juxtacortical lesion, highly suggestive of PML. JC virus in cerebrospinal fluid was negative twice and biopsy was deferred due to clinical stability. Siponimod was discontinued, but the patient developed myelitis shortly after. Teriflunomide was initiated, with stability of the occipital lesion but persistence of progressive MS-related disability.

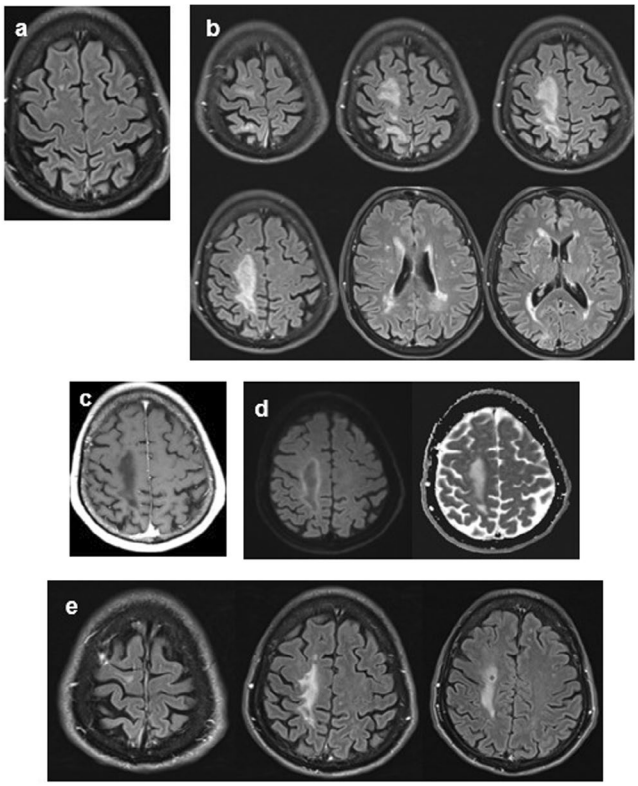

FIGURE 1 Case 1. Baseline brain MRI (a). Right fronto-parietal juxta-subcortical white matter lesion hyperintense on FLAIR (b), with no contrast enhancement (c) and mild peripheral diffusion restriction on DWI (d). Reduction in size in follow-up MRI (d).

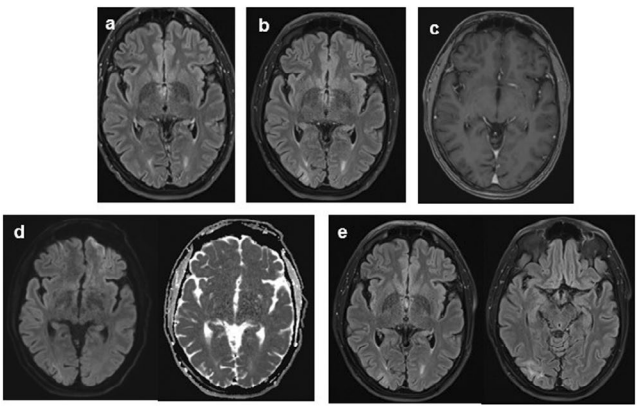

FIGURE 2 Case 2. Baseline brain MRI (a). Hyperintense right occipital juxtacortical lesion (b), with no contrast enhancement (c) and mild peripheral diffusion restriction on DWI (d). Stability on follow-up MRI (e).

Conclusion: Newer S1P modulators, such as Siponimod, now have long follow-up data in real-world settings, with safety remaining a critical concern. Our cases highlight the importance of MRI in detecting rare but severe complications, such as PML. Continued vigilance is essential to mitigate risks.
Disclosure: Nothing to disclose.

EPO-653 | Incidence of COVID-19 in the phase 3 Myasthenia Gravis inebilizumab trial randomized controlled period

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Background and Aims: B-cell-depleting therapies have the potential to lessen humoral responses. It is unclear whether this leads to a higher risk of Coronavirus Disease 2019 (COVID-19) incidence. This post-hoc analysis of the Myasthenia Gravis Inebilizumab Trial (MINT) examined whether inebilizumab treatment is associated with an increased risk of COVID-19 infection in participants with generalized Myasthenia Gravis (gMG).
Methods: MINT (NCT04524273) was a phase 3 study which evaluated the efficacy and safety of inebilizumab in adult patients with gMG. First participant was enrolled August 30, 2020, after COVID-19 was initially reported (December 2019) and before the first vaccine received approval (December 2020). Participants were given 300mg of intravenous inebilizumab or placebo on RCP Day-1, Day-15, and Day-183 (AChR+ only). Descriptive statistics/analysis completed.
Results: A total of 238 participants were randomized (placebo 119, inebilizumab 119). Considering the timeline of trial enrollment and vaccine availability, 4 (3.4%) placebo-treated participants and 9 (7.6%) inebilizumab-treated participants received a COVID-19 vaccine on/after the 1st dose. COVID-19 infection was reported in 19 (16.0%) placebo-treated and in 21 (17.7%) inebilizumab-treated participants during the RCP. Most infections were in participants <65 years of age (100% placebo, 90.5% inebilizumab). Most of the reported infections were Grade 1 [placebo: 8/19 (42.1%); inebilizumab: 10/21 (47.6%)] or Grade 2 [placebo: 8/19 (42.1%); inebilizumab: 8/21 (38.1%)]. COVID-19 related hospitalizations occurred in 4 placebo-treated participants and 4 inebilizumab-treated participants with a mean ± SD hospitalization length of 10.8 ± 8.8 days and 22.8 ± 25.9 days, respectively.

TABLE 1 COVID-19 in MINT clinical trial (randomized control period).

	Placebo (N = 119)	Inebilizumab (N = 119)	Overall (N = 238)
COVID-19 vaccine, n (%)			
Yes			
Before 1st dose	0 (0.0)	0 (0.0)	0 (0.0)
On/After 1st dose	4 (3.4)	9 (7.6)	13 (5.5)
Date not reported	0 (0.0)	0 (0.0)	0 (0.0)
Not reported	115 (96.6)	110 (92.4)	225 (94.5)
COVID-19 infections,[a] n (%)			
<65 years	19 (16.0)	19 (16.0)	38 (16.0)
≥65 years	0 (0.0)	2 (1.7)	2 (0.8)
Severity[b]			
Grade 1	8 (6.7)	10 (8.4)	18 (7.6)
Grade 2	8 (6.7)	8 (6.7)	16 (6.7)
Grade 3	3 (2.5)	3 (2.5)	6 (2.5)
Grade 4	0 (0.0)	0 (0.0)	0 (0.0)
Grade 5	0 (0.0)	0 (0.0)	0 (0.0)
COVID-19 related hospitalization,[b] n (%)	4 (3.4)	4 (3.4)	8 (3.4)
Length of stay (days), mean ± SD	10.8 ± 8.8	22.8 ± 25.9	16.8 ± 19.0

N = number of subjects in the analysis set. n = number of subjects with observed data.
[a]The AE terms included for the Covid-19 infection are: Asymptomatic COVID-19, COVID-19, COVID-19 pneumonia, SARS-CoV-2 test positive.
[b]If a subject has multiple occurrences; the worst grade will be used.

Conclusion: Inebilizumab treatment did not increase the incidence of COVID-19 in participants with gMG.

Disclosure: RJN research support from NIH, Genentech, Alexion, argenx, Annexon Biosciences, UCB S.A., the MGFA Inc., Janssen, Immunovant, Grifols & Amgen Inc. Consultant/advisor to Alexion, argenx, Cabaletta Bio., Cour, UCB S.A., Immunovant, Janssen & Amgen Inc. KU consultant to UCB, argenx, Janssen, Amgen Inc., Chugai, Hanall BioPharma, Merck & Mitsubishi Tanabe. Honoraria from Argenx, Alexion, UCB & the Japan Blood Products Organization. MB research support from Immunovant & Alexion. Consultant to Alexion, Cartesian, Amgen Inc., Immunovant, Sanofi, Takeda, & UCB. EC advisor/consultant to Alexion, argenx, Biogen, Amicus, Pfizer, Italfarmaco, Sarepta, Janssen, NS Pharma & Roche. MIL funded by NHS & University of Oxford. Grants from Myaware, Muscular Dystrophy UK & the University of Oxford. Honoraria/travel from Biogen, Novartis, UCB & the Guthy-Jackson Charitable Foundation. Advisory boards for UCB, argenx & Amgen Inc. JV advisory boards for Regeneron, UCB, argenx, Alexion, Amgen Inc., Dianthus Therapeutics, Janssen & Roche. FT, CN, SC are employees/stockholders of Amgen Inc. JFH funding from Ad Scientiam, Alexion, argenx, Cartesian, CDC, Prevention, MGFA, MDA, NIH, PCORI & UCB; honoraria/consulting from Academic CME, Alexion AstraZeneca RD, argenx, Biohaven, Biologix, CheckRare CME, Curie.bio, F. Hoffmann-LaRoche, Amgen Inc., Medscape CME, Merck EMB Serono, NMD Pharma, Novartis, PeerView CME, Physicians' Education Resource CME, PlatformQ CME, Regeneron, Sanofi, UCB, & Zai Labs.

EPO-654 | Movement disorders and limbic encephalitis: An uncommon presentation of autoimmune GFAP astrocytophaty

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Background and Aims: Antibodies targeting glial fibrillary acidic protein (GFAP), an intermediate filament protein in adult astrocytes, have recently been identified as a cause of autoimmune meningoencephalomyelitis. This condition demonstrates significant clinical heterogeneity, with impaired consciousness, confusion and headache being the most commonly described symptoms. We describe a distinctive presentation of autoimmune GFAP astrocytopathy.

Methods: A 63-year-old male with no significant medical history presented with a progressive 3-month history of tremor, myoclonus, gait disturbances, and cognitive decline.

Results: On examination, he exhibited somnolence, disorientation, limited speech, generalized bradykinesia, myoclonus, positional tremor in both arms, left-sided rigidity, left-sided pyramidal signs, bilateral clonus, and frontal release signs. Brain MRI revealed T2-FLAIR cortical and juxtacortical hyperintensities in the temporal lobes and bilateral temporomesial regions. CSF analysis demonstrated mononuclear-predominant pleocytosis (30 cells, 90% mononuclear) and elevated protein levels (102 mg/dL) with negative microbiological and cytological studies. These findings were consistent with autoimmune limbic encephalitis. Given the suspicion, treatment with high-dose methylprednisolone (1 g/day, 5 days) and IV immunoglobulins (2 g/kg, 5 days) were followed by corticosteroid tapering, achieving improvement. Rituximab (1 g, twice, 2 weeks apart) was added to sustain the response. Autoimmune GFAP astrocytopathy was confirmed by anti-GFAP antibodies detected via cell-based assay at a reference laboratory. Systemic evaluation for neoplasia is negative, and the patient remains clinically stable 2 months post-treatment.

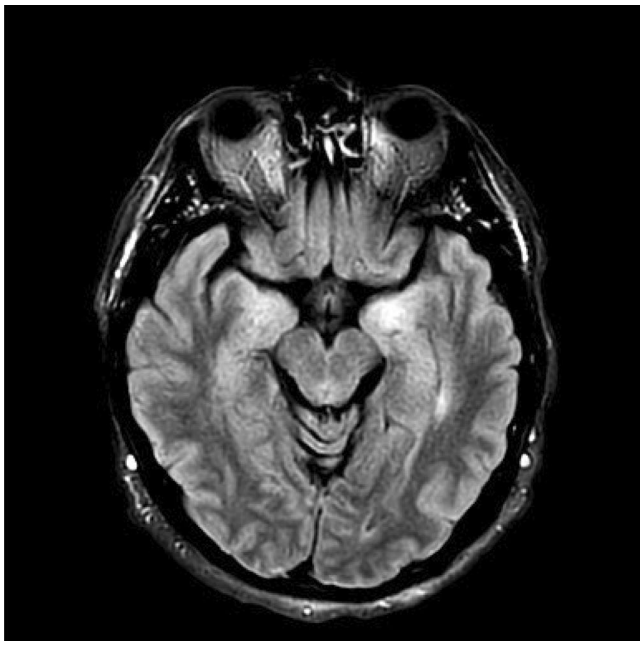

FIGURE 1 Brain RM T2-FLAIR revealing hyperintensities in bilateral temporomesial regions.

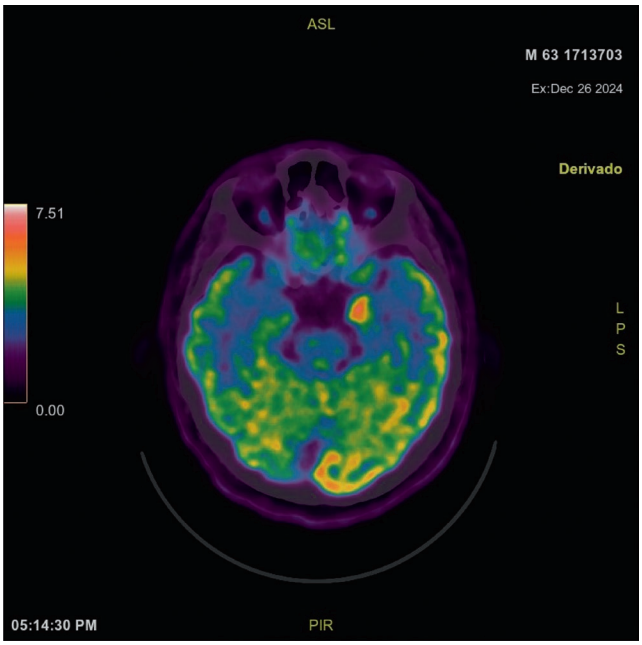

FIGURE 2 Brain PET/CT scan revealing enhancement in the medial area of the left temporal lobe.

Conclusion: This case highlights the need to consider autoimmune GFAP astrocytopathy in patients with movement disorders or limbic encephalitis. Increased awareness of its clinical and radiological features may facilitate earlier diagnosis and treatment.
Disclosure: Nothing to disclose.

EPO-656 | Function and inflammation of the blood-brain barrier after a primary exposure to SARS-CoV-2

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Background and Aims: SARS-CoV-2 can damage the blood-brain barrier (BBB) and lead to several central nervous system (CNS) disorders, however, its involvement remains poorly understood.
Methods: We analysed serum and cerebrospinal fluid (CSF) samples from 39 adults admitted to a neurological emergency in Northeastern Brazil with acute neurological complaints. Patients had no clinical signs of COVID-19 and were classified into three groups: CNS syndrome and SARS-CoV-2 exposure ($n=16$), exposed without a CNS syndrome ($n=17$), and unexposed to SARS-CoV-2 ($n=7$). Inflammatory cytokines (interleukins-IL 6/8) and chemokines (CCL 2, CXCL 5/8/9/10) were measured using flow cytometry, as well as protein profile via gel electrophoresis. BBB function was assessed using CSF:serum coefficients of albumin (QAlb), gamaglobulin (QGgb), while intrathecal inflammation was evaluated through cytokine CSF:serum coefficients.
Results: CSF:serum coefficients of IL-6, IL-8, and CXCL8 were higher in both exposed groups when compared with the unexposed group. Higher coefficients of CXCL5 and CXCL10 were observed in CNS syndromes patients exposed to SARS-CoV-2, compared to the other two groups. No significant differences were observed in QAlb, QGgb, and QGgb:QAlb indices.
Conclusion: These findings suggest no evidence of BBB breakdown or intrathecal immunoglobulin production following subclinical SARS-CoV-2 exposure. However, a systemic profile of inflammation plus intrathecal production of chemokines involved in the modulation of immune cells were evident in CNS manifestations after primary exposure to SARS-CoV-2, even in the absence of COVID-19 symptoms.
Disclosure: Nothing to disclose.

EPO-657 | Dysautonomia preceding the diagnosis of LGI1 encephalitis requiring cardioneuroablation

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Background and Aims: Encephalitis associated with antibodies against Leucine-rich glioma inactivated 1 protein (LGI1) commonly manifests with cognitive impairment, psychiatric symptoms, and epileptic seizures, including the pathognomonic faciobrachial dystonic seizures (FBDS). However, rarely, patients may initially present with dysautonomic symptoms. We report a patient who presented initially with bradyarrhythmia requiring close cardiac monitoring with subsequent cardioneuroablation prior to the diagnosis of LGI1 encephalitis.
Methods: Case Report.
Results: A 39-year-old previously healthy man presented with an 8-day history of recurrent loss of consciousness. He was referred to emergency cardiology service and was diagnosed with recurrent asystole due to vagotonia. A cardioneuroablation was performed and was successful in treating the patient's syncopes. Two weeks after the procedure, the patient developed short-term memory impairment and episodes of confusion with migrating paraesthesias with impaired consciousness, implying the possibility of focal unaware seizures. Electroencephalogram (EEG) demonstrated focal slowing in the fronto-temporal region bilaterally with episodes of lateralised periodic discharges. Magnetic resonance imaging (MRI) findings included enlargement of the left hippocampus and parahippocampal gyrus, consistent with signs of unilateral limbic encephalitis. Cerebrospinal fluid (CSF) analysis showed lymphocytic predominant pleocytosis, no infectious agents, and ultimately the serum was positive for antibodies against LGI1. The patient initially did not respond well to methylprednisolone. Then, five cycles of immunoadsorption therapy were administered, resulting in clinical improvement.
Conclusion: We present to our knowledge the first case of a patient with LGI1 encephalitis whose severe dysautonomia (prolonged asystole with loss of consciousness) required cardioneuroablation, which successfully treated his syncopes.

Disclosure: KYS (medical student) has nothing in relation to this manuscript to disclose. KD has nothing in relation to this manuscript to disclose. JP has nothing in relation to this manuscript to disclose. EM and MH disclose participation in Roche trial recruiting patients with LGI1 encephalitis.

Neuroepidemiology and ethics in neurology

EPO-658 | Prevalence estimation of tremor syndromes in Hungary based on the National Health Insurance Fund database

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Background and Aims: Essential tremor is one of the most common movement disorders, and its differential diagnosis is often challenging. The published prevalence of essential tremor is variable worldwide and lacking in Central Europe. We aimed to estimate its prevalence in Hungary and to explore the use of the available therapeutic approaches recommended by the international guidelines.
Methods: We collected data from the National Health Insurance Fund database and the pharmacy database of medication refills from all pharmacies throughout the country registered between 2010 and 2020. By matching the specified codes of the International Classification of Diseases and the individually tailored combination of interventions, we attempted to exclude Parkinson's disease and other tremor-evoking conditions.
Results: We estimated the prevalence of essential tremor age-standardized to the European Standard Population to be 378–388/100,000. After excluding patients with possible Parkinsonian syndromes, we found that 36.4% of the patients with tremor did not take any medication during the study period. Most of the rest used alprazolam, followed by propranolol for the longest period; the alprazolam-propranolol combination was the most preferred. Deep brain stimulation and ablative surgery were chosen for less than 0.5% of the patients.
Conclusion: Our strict methods underestimate the prevalence of essential tremor in Hungary; however, the results do not differ considerably from the international results. Given the limitations of the medication therapy, expanding and improving neurosurgical interventions may help to provide a better quality of life to patients with essential tremor.
Disclosure: Nothing to disclose.

EPO-659 | Ethical challenges in neurology: Navigating clinical and technological dilemmas

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Background and Aims: Neurology presents unique ethical challenges due to the complex nature of neurological disorders and advancements in neuro technologies. Key concerns include informed consent, patient autonomy, and the ethical use of emerging treatments. This study explores ethical dilemmas in clinical practice and research within neurology, focusing on neurodegenerative diseases, neuro ethics, and novel neuro technologies.
Methods: A systematic review was conducted of literature from journals such as Neurology, Brain, The Lancet Neurology, Neuroethics, Journal of Medical Ethics, Frontiers in Neurology, American Journal of Bioethics, Journal of Alzheimer's Disease, and Journal of Clinical Neuroscience. Articles were selected based on their relevance to ethical issues, including informed consent in cognitively impaired patients, the ethical implications of neuro technologies like deep brain stimulation and neuro prosthetics, decision-making in end-of-life care, and ethical concerns in neurological research. Data were analysed thematically to identify recurring ethical challenges in clinical and research contexts.
Results: The review identified key ethical issues: (1) Informed consent and decision-making in cognitively impaired patients, (2) Ethical concerns with neuro technologies, (3) End-of-life decisions in neurological diseases, and (4) Research ethics regarding vulnerable populations. Additionally, the potential ethical dilemmas surrounding neuroenhancement and brain-computer interfaces were discussed.
Conclusion: Ethical challenges in neurology require adaptive frameworks that balance scientific progress with patient autonomy and dignity. As neuro technologies evolve, ongoing interdisciplinary discussions are necessary to develop comprehensive ethical guidelines for clinical practice and research.
Disclosure: Nothing to disclose.

EPO-660 | Maternal prenatal nut and seafood consumption and child neuropsychological function from 4 to 15 years of age

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Background and Aims: Understanding the role of maternal diet in early brain development is critical, as pregnancy represents a period of significant vulnerability and growth for the developing brain. The aim of this study was to assess the long-term association of maternal nuts and seafood consumption during pregnancy with neuropsychological function in the offspring up to 15 years of age considering the potential mediation of omega-3 fatty acids.
Methods: Conducted as part of the population-based birth cohort study of the Spanish Childhood and Environment (INMA) Project, it followed 1737 mother-child pairs from pregnancy until the children reached 15 years of age. Maternal dietary intake was evaluated using a semi-quantitative food frequency questionnaire, and children's neuropsychological function was measured through standardized computer-based tests. Linear mixed-effects regression models were used to assess

the association of nuts and seafood with all neuropsychological outcomes, while generalized structural equation modelling was used for mediation analyses.

Results: Results showed that higher maternal nut consumption was significantly linked to improved attention (HRT-SE β = −0.05 milliseconds (ms), 95% CI = −0.09; −0.00, *p* for trend = 0.041) and working memory (d2' β = 0.05, 95% CI = 0.00; 0.09, *p* for trend = 0.043, and d3' β = 0.06, 95%CI = 0.02; 0.11, *p* for trend = 0.007) in offspring. Similarly, greater consumption of large fatty fish was associated with better attention (HRT-SE β = −0.06 ms, 95% CI = −0.10; −0.02, *p* for trend = 0.004; and HRT β = −0.04 ms, 95% CI = −0.08; −0.00, *p* for trend = 0.032, respectively) and fluid intelligence (β = 0.08, 95% CI = 0.02; 0.13, *p* for trend = 0.006). Omega-3 fatty acids mediated 8-14% of these effects on attention.

Conclusion: Findings highlight the crucial role of maternal diet and omega-3 intake in supporting long-term cognitive development in children and adolescents.

Disclosure: Nothing to disclose.

EPO-661 | Multiple sclerosis from onset to secondary progression: A 30-years Italian register study

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Background and Aims: Three decades have passed since the initial approval of disease modifying therapies (DMTs). Ongoing discussion is focused on fundamental aspects of the disease, highlighting a growing division between successes in managing relapsing Multiple Sclerosis (MS) and the persistent challenges posed by disease progression.

Methods: A cohort study on prospectively acquired data from the Italian MS register. The primary outcome was to describe the MS disease course from onset to secondary progression (SP) defined according to a data driven algorithm over 30-years follow up and according to five different eras of disease onset.

Results: A total cohort of 9,958 patients was analyzed; 1,364 converted to SP after a mean of 8·5 (SD 5·5) years. A higher rate of patients converting to SP had never been exposed to DMTs (135, 9.9% vs 424, 5.2%) than non-converting ones. The treatment coverage was also lower in patients converting to SP than non-converting ones 58·4 (SD 31.5) vs 73·6 (SD 27.6). The 10-years SP incidence rate was 1·26 (1.19–1.32) overall. The rates showed a downward trend among the different era: from 1st era 1·98 (1.73–2.27) to 5th era 1·15 (0.97–1.35). In the multivariable Cox model 10% increase of treatment coverage was associated to 19% lower risk to convert to SP (10% HR = 0.89, 95% CI = 0.87–0.90).

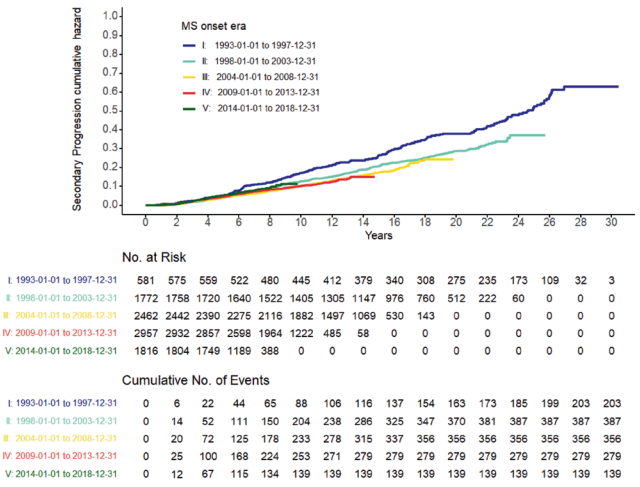

FIGURE 1 Kaplan-Meier curves for time to SPMS conversion according to disease onset era

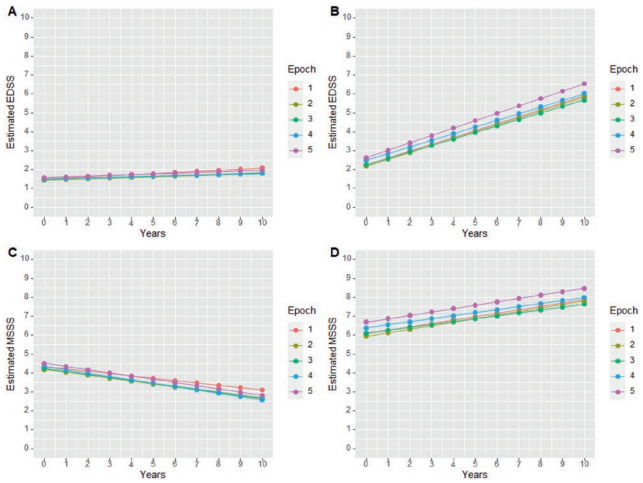

FIGURE 2 Ten years longitudinal trajectories of EDSS and MSSS for converting to SP vs non converting patients (A) EDSS in non-converting patients (B) EDSS in converting to SP patients (C) MSSS in non-converting patients (D) MSSS in converting to SP patients E.

Conclusion: Further research is needed to explore the roles of inflammation and neurodegeneration in MS progression. These findings could inform clinical practice and health policy, emphasizing the need for continued therapeutic advancements.

Disclosure: Nothing to disclose.

EPO-663 | Exploring migration patterns and experiences of EAN RRFS members

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Background and Aims: Trainees and young professionals are essential to advancing neurology and neuroscience, with migration significantly impacting their careers, and health systems. The EAN Residents and Research Fellows Section (RRFS) Migration Survey examined migration trends among its members, focusing on motivations, challenges, and personal and professional outcomes.
Methods: An anonymous online questionnaire was distributed to RRFS members from June to September 2024, collecting quantitative and qualitative data on demographics, migration history, and perceived impacts. Statistical and thematic analyses were conducted.
Results: The survey included 273 participants, with a median age of 31 years (IQR 5); 63.37% identified as female. Most were residents (59.23%), followed by young neurologists (20.77%) and PhD students (7.69%). 78.4% were from Europe, 16.14% from Asia, and 4.06% from Africa. 24.42% had already migrated, 27.91% were considering it, and 34.8% had considered but decided against it. Most migration occurred within Europe (52.38%), followed by Asia to Europe (14.29%) and Africa to Europe (6.35%). The primary motivations for migration were better working conditions and expanded education in emerging neurological fields (73.47%). Main challenges were language barriers and differences in teaching methods (52.35%). 30.64% would not return, but 83.87% would migrate again, and 56.45% would return if conditions improved. Respondents recommended expanding training, mentorship, and addressing workforce shortages to retain young professionals.
Conclusion: This survey underscores the significant role migration plays in shaping the careers of RRFS members, with implications for professional development and possibly for health professional shortage. Addressing integration challenges and improving conditions could support these professionals and mitigate long-term workforce shortages.
Disclosure: Nothing to disclose.

EPO-664 | Abstract withdrawn

EPO-665 | Trends in ischemic stroke mortality among adults with atrial fibrillation in the US from 1999 to 2020

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Background and Aims: Ischemic stroke (IS), a sequela of Atrial Fibrillation (AF), continues to be the world's second leading cause of death. Our study aims to identify demographic and regional disparities in mortality from IS amongst adult US population with AF.
Methods: Data from the National Vital Statistics System (1999–2020) was analyzed using CDC WONDER. IS deaths with AF as a contributing factor were identified, with results reported as age-adjusted mortality rates (AAMR) per 100,000. Joinpoint regression analyzed trends and annual percentage changes (APCs).
Results: There were 130,937 IS deaths (AAMR=2.7, 95% CI: 2.7–2.8). Females had higher AAMR (2.87) than males (2.45). Non-Hispanic Whites (NHW) had the highest AAMR (2.8), followed by Non-Hispanic Blacks (NHB) (2.06), Non-Hispanic Asian/Pacific Islanders (NH-API) (2.05), and Hispanics (1.8). Non-Hispanic American Indian/Alaska Natives (NH-AIAN) had the lowest (1.4). The West had the highest regional AAMR (3.3), with rural areas showing higher rates (3.1) than urban areas (2.6). Overall AAMR declined from 1999 to 2020 (APC: -0.4). NHW and NH-API showed declines, while NHB and Hispanics had rising rates.

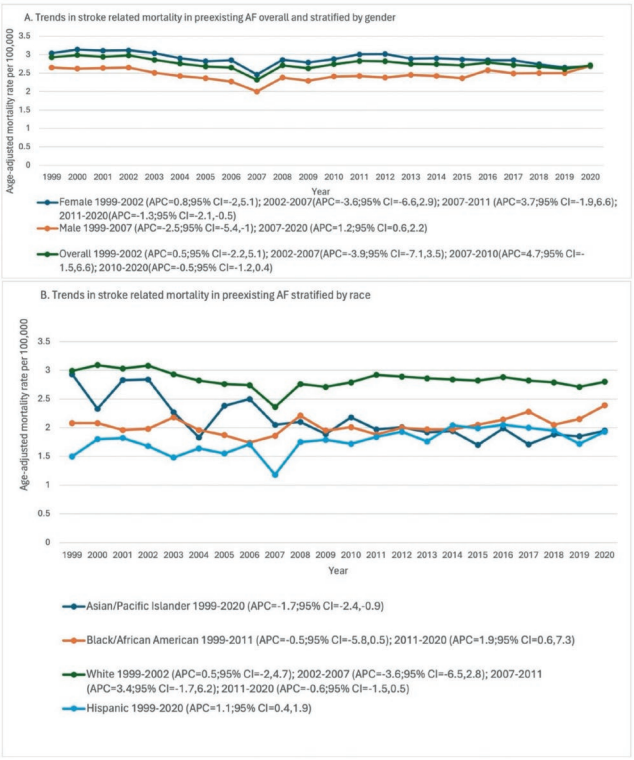

FIGURE 1 Trends in mortality from ischemic stroke in adult US patients with atrial fibrillation from 1999 to 2020. (Panel A) Age-adjusted mortality rates stratified by overall population and sex, (Panel B) Age-adjusted mortality rates stratified by race

Conclusion: Our study reveals significant disparities in IS-related mortality with females, NHW, and residents in the West as well as rural areas exhibiting higher mortality rates. These findings highlight the need of focused interventions and thoughtful healthcare resources allocation to enhance outcomes for the vulnerable populations.
Disclosure: NA.

EPO-666 | No increased risk of amyotrophic lateral sclerosis after traumatic head injury

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Background and Aims: Studies have identified an association between traumatic head injury and amyotrophic lateral sclerosis (ALS), but the causal relation remains uncertain. We aimed to determine whether hospital–diagnosed traumatic head injury is an ALS risk factor.
Methods: In this population-based case-control study, we used Danish nationwide health registers from 1980 to 2021 to identify hospital–diagnosed ALS patients. Each patient was matched 1:10 with individuals from the general population by age, sex, and calendar year. We used conditional logistic regression to examine the odds ratio (OR) of ALS associated with having prior hospital-diagnosed traumatic head injury.
Results: Traumatic head injury was observed in 4.7% of 5,943 ALS cases vs 3.7% of 59,426 controls, with an OR of 1.3 (95% CI, 1.1–1.4). However, this association was caused by head injuries sustained shortly before the ALS diagnosis was made. Thus, the OR was 4.5 (95% CI, 2.8–7.3) within the 6 months prior to ALS diagnosis, and declined to 2.4 (95% CI, 1.4–4.0) 6 to 12 months prior to ALS diagnosis. Going further back in time, more than 3 years prior to ALS diagnosis, we found no association between traumatic head injury and ALS (OR,1.1 (95% CI, 1.0–1.3).

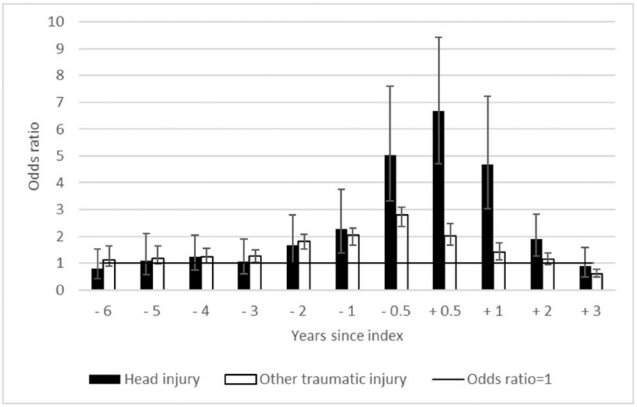

FIGURE 1 Amyotrophic lateral sclerosis risk according to timing of traumatic head injury and other traumatic injuries.

Conclusion: There was a strong association of ALS with head injury experienced ≤1 year before ALS diagnosis, however our results suggest that this is due to reverse causation. Consequently, we do not consider hospital-diagnosed traumatic head injury an ALS risk factor.
Disclosure: Nothing to disclose.

EPO-667 | Missing medical data in neurological emergency care compromise patient safety and healthcare resources

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Background and Aims: We observed complications in the acute care of patients in the neurological emergency department (ED) when patients arrived without proper medical information in our clinical practice. The aim of this study was to assess systematically the frequency and consequences of incomplete medical data upon ED admission.
Methods: We assessed the availability and accuracy of medical data of all patients upon arrival to our neurological ED. Complications in emergency treatment due to missing medical information were recorded. Furthermore, we investigated

whether initially missing data affect the inpatient stay of patients admitted via the ED.

Results: Our data show that medical data of 27% of the 272 included patients were incomplete upon admission. In this group, phone calls to gather information caused relevant delays, as they were necessary in 57% of those cases (vs. 22% in patients with complete data, $p < 0.0001$). Furthermore, unnecessary diagnostic procedures were performed in 5% of these patients, thus compromising patient safety. We show that even the inpatient stay was affected by initially missing data. Retrospectively, 5% of hospitalizations could have been avoided if all medical information had been available upon ED admission.

Conclusion: The acute care and the inpatient care of neurological patients is complicated by missing medical information. Our data show that this can compromise patient safety and lead to a waste of medical resources. We postulate that the implementation of a digital data management system in Germany could help to improve patient safety and facilitate efficient patient care in the ED and beyond.

Disclosure: Nothing to disclose.

EPO-668 | Equality in neuromuscular research: Analysis of 20 years of clinical trials

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Background and Aims: Equitable access to clinical research is a critical imperative, yet underrepresentation of non-white and non-male individuals remains a widespread issue, constituting a widespread lack of diversity in clinical trials.

Methods: In this study, we conducted a systematic analysis of clinical trials on neuromuscular diseases registered on ClinicalTtrials.gov over the last 20 years to assess the representation of sex, race and ethnicity.

Results: Two thousand fifty-four studies were screened for eligibility and 469 studies were included in the analysis. Race was reported in standard terminology in 223 studies, encompassing 17860 patients. Thirtynine (0.2%) patients were American Indian or Alaska Native, 8.4% were Asian, 2.2% were Black, 0.2% were Native Hawaian or other pacific islander, 83.5% were White; 0.6% patients were listed as more than one race and 4.8% as unknown. Race and ethnicity distributions per diseases are shown in Fig.1. We observed a significant increase in study reporting race over time ($p < 0.001$). However, year did not significantly influence the racial composition nor the ethnicity in the clinical studies over time ($p = 1$) (Fig. 2). All the studies reported sex amongst two categories (i.e.: male, female), while one observational study reported gender without sex. Most patients, both in observational and in interventional studies were male (60.1% and 60.4%, respectively) (Fig. 3).

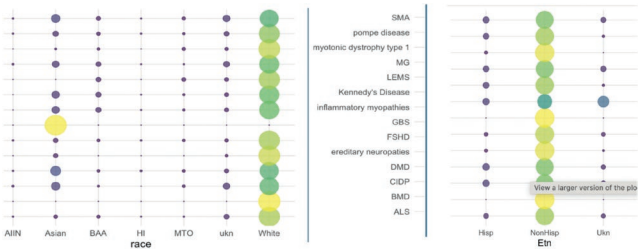

FIGURE 1 Race and ethnicity distribution across neuromuscular diseases. The majority of people are non hispanic white.

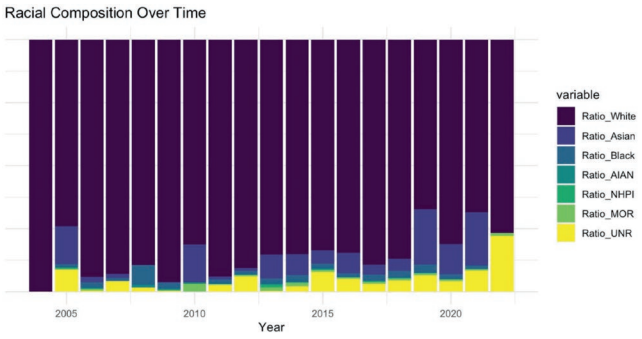

FIGURE 2 Race composition over time. We did not find any significant difference of racial composition over time.

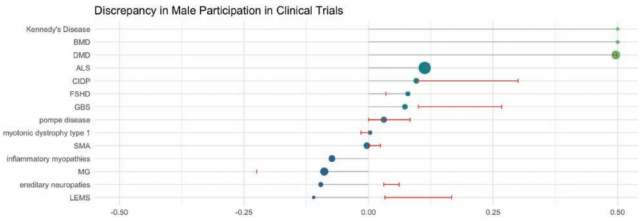

FIGURE 3 Sex distribution across neuromuscular diseases. Zero means equal number of male and female. Disease male/female ratio is represented by red lines.

Conclusion: This study quantify sex, race and ethnicity disproportion in neuromuscular diseases trials. Over time, race reporting increases, while majority of patients continue to be non hispanic white. While the majority of people are male, the distribution varies across diseases.

Disclosure: Nothing to disclose.

EPO-669 | Epidemiology of functional neurological disorders: A systematic review

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Background and Aims: Fnctional neurological disorders (FND) are characterized by motor, sensory, and/or cognitive

symptoms that relate to functional rather than structural abnormalities. Although these disorders are common in neurology, their epidemiology is not well-documented.
Methods: Following the Preferred Reporting Items for Systematic Reviews and Meta-analyses guidelines, we searched PubMed and Embase for articles reporting on the incidence or prevalence of FND in adults, published in French or English between 1972 and 2022. We used The Joanna Briggs Institute Prevalence Critical Appraisal Tool to assess the quality of the studies. This study was registered under the ID CRD42023434331 in the PROSPERO database.
Results: Out of 4,260 screened articles, 27 were included, primarily from India, the US, and Europe. The prevalence estimates for hysteria, conversion disorders or FND ranged from 37.2 to 6,900 per 100,000, with an incidence ranging from 10.7 to 186 per 100,000. Functional dissociative seizures had a prevalence of 23.8 to 890 per 100,000 and an of 0.91 to 4.9 per 100,000. Functional motor disorders had an incidence of 3.9 to 5.0 per 100,000. Most cases involved young women. Only 8 studies were rated as high quality. Overall, the rapidly changing nosology and diagnostic criteria complicate the interpretations of existing data.
Conclusion: Our findings highlight the urgent need for large-scale, rigorous studies targeting the multiple forms of FND to obtain reliable epidemiological data that are essential to develop an adequate health policy for FND.
Disclosure: Nothing to disclose.

EPO-670 | The age at onset of LRRK2-related Parkinson's disease across ancestries and countries of origin

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Background and Aims: The LRRK2 p.G2019S pathogenic variant has reduced penetrance and presents with a wide range of age at onset (AAO) in patients with Parkinson's disease (PD). Herein, we investigate cumulative incidence differences of LRRK2-PD across ancestries and countries.
Methods: We included $N=922$ unrelated LRRK2 p.G2019S variant carriers (affected: $N=762$, unaffected: $N=160$) from the Global Parkinson's Genetics Program (GP2) in addition to cohorts from the Israeli Ashkenazi Jewish and Tunisian Arab-Berber population. The sex-adjusted Cox proportional-hazards model and Kaplan-Meier analysis were applied to examine differences in cumulative incidence between ancestries derived from genetic data and countries.
Results: We observed ancestry-specific differences, as there was a median five-year younger AAO of LRRK2-PD in the North African (HR = 1.48, $p=7.0e-4$) compared to the European ancestry group. In contrast, the median AAO was five years older in the Ashkenazi Jewish ancestry group (HR = 0.61, $p=4.0e-6$). Secondly, the country also showed differences. Patients from Israel (HR = 1.59, $p=4.0e-6$) and Tunisia (HR = 2.57, $p<2.0e-16$) had a median 5-year and 10-year younger AAO compared to patients from the USA, respectively. Thirdly, when focusing only on individuals with Ashkenazi Jewish ancestry, persons from Israel still had a younger AAO than those from the USA (HR = 1.82, $p=1.5e-8$). Analogously, assessing only persons from the USA, the Ashkenazi Jewish ancestry group still had an older AAO than the European (HR = 0.51, $p=1.3e-6$).
Conclusion: Our results provide evidence that a person's ancestry and country of origin are associated with the AAO of LRRK2-PD. This highlights the impact of both genetic and environmental factors on LRRK2-PD AAO.
Disclosure: This project was supported by the DFG RU ProtectMove (DFG FOR2488) and by a DFG Heisenberg Grant to JT. Data used in the preparation of this abstract were obtained from Global Parkinson's Genetics Program (GP2). GP2 is funded by the Aligning Science Across Parkinson's (ASAP) initiative and implemented by The Michael J. Fox Foundation for Parkinson's Research (https://gp2.org). For a complete list of GP2 members see https://gp2.org.

EPO-671 | Impact of hospital teaching status, insurance status, race, & income on mortality in subarachnoid hemorrhage (2019–2021)

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Background and Aims: Subarachnoid Hemorrhage (SAH) is a stroke caused by artery rupture, leading to bleeding in the brain. SAH can have profound neurologic effects, including severe disability and death if not promptly diagnosed and treated. This study examines mortality differences based on hospital teaching status, payer status, income, and race in the United States (US).
Methods: Data was sourced from 2019 to 2021 National Inpatient Sample (NIS), representing a 20% stratified sample of US community hospitals. Mortality rates were compared across rural, urban non-teaching, and urban-teaching hospitals. Statistical analyses were performed using Chi Square and Logistic regression in StataNow18.
Results: Of 137,537 SAH admissions, 88.6% were treated at urban-teaching hospitals, 9.1% at urban non-teaching hospitals, and 2.3% at rural hospitals. The overall mortality rate was 23.5%, highest at rural (26.8%, OR = 1.21) and urban non-teaching hospitals (25.7%, OR = 1.15), and lowest at urban-teaching hospitals (23.2%) ($p<0.05$). Self-pay patients had the highest mortality rate (30.0%, OR = 1.33), followed by Medicare (24.4%) and Medicaid (23.7%), while private insurance had the lowest (19.8%,

OR = 0.77). Native Americans had the highest mortality rate (30.6%, OR = 1.49), followed by Asian/Pacific Islanders (27.1%, OR = 1.25), compared to Whites (22.9%) ($p < 0.05$). Mortality decreased with increasing income, from 24.8% in the lowest income quartile to 22.5% in the highest ($p < 0.05$).

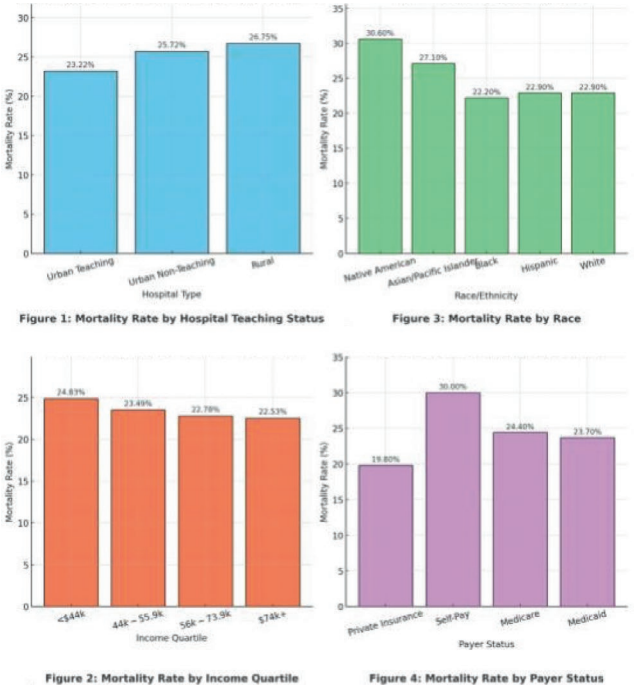

FIGURE 1 Mortality Rates by Hospital Teaching Status, Race, Income, and Payer Status: Hospital death rates were highest among Native American patients, uninsured individuals, and those treated in non-teaching hospitals.

Conclusion: This study reveals disparities in mortality among patients with SAH across hospital teaching status, socioeconomic status, and race. Notably, mortality rates were highest in non-teaching hospitals, which likely reflects the substantial impact of limited resources and access to specialized care in these settings.

Disclosure: Nothing to disclose.

Motor neurone diseases & spinal cord and root disorders

EPO-672 | Spontaneous intracranial hypotension: A tertiary centre experience

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Background and Aims: Spontaneous intracranial hypotension (SIH) requires a systematic and early therapeutic approach to prevent complications. The aim of this study is to describe patients with SIH followed up in a tertiary hospital.

Methods: Retrospective observational study including adults with HIE in a tertiary centre (2017–2024). We describe demographic parameters, clinical presentation, complementary diagnostic methods, treatments and outcomes.

Results: Fourteen of the 22 patients were female (64%), with a mean age of 42 (23-57) years. In thirteen patients, a trigger was identified (Valsalva manoeuvre or minor trauma). All of them presented with orthostatic headache, associated with nausea/vomiting (82%) and neck pain (73%). Six patients had neurological examination alterations and eleven (50%) had complications – unilateral ($n = 1$) and bilateral ($n = 9$) subdural haematoma, cerebral venous thrombosis ($n = 2$) and high convexity subarachnoid haemorrhage ($n = 1$). All underwent brain computed tomography/magnetic resonance (MRI), thirteen proceed with myelo-MRI. No aetiology was identified in twelve patients, with dural defect being the most common cause ($n = 9$). All were treated conservatively according to internal protocol, with complete resolution in four patients. Eighteen patients required a non-targeted blood patch, with 11 requiring more than one. Three patients underwent a blood patch directed at the point of fistula. Two patients required neurosurgical intervention. After discharge, two patients were left with residual headaches.

Conclusion: Half of the patients had pre-treatment complications and the majority did not respond to conservative treatment. The authors advocate an interdisciplinary, protocol-based approach that allows early symptomatic relief and minimises complications.

Disclosure: Nothing to disclose.

EPO-673 | Relative leukopenia in C9ALS

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Background and Aims: Hexanucleotide repeat expansions in C9ORF72 are the most frequent genetic cause of familial and sporadic amyotrophic lateral sclerosis (ALS). Among the functions attributed to C9ORF72 there's a role in inflammation and immunity. Knock-out of C9ORF72 in preclinical models resulted in autoimmune and neuroinflammatory phenotypes without clear signs of neurodegeneration. Considering the established role of C9ORF72 in immunity, we searched for alterations in the blood cells count (BCC) in C9ALS patients.
Methods: We retrospectively collected the BCC and the main clinical parameters from 92 C9ALS patients and 184 sex, age and diagnostic delay-matched sporadic ALS controls as close as possible to diagnosis, carefully avoiding samples drawn in cases of concomitant infections and other acute conditions that could temporarily modify the BCC.
Results: We found a significant reduction for C9ALS in the global leukocyte count and in all the subpopulations (neutrophils, lymphocytes, monocytes, basophils, eosinophils), as well as a significant increase in neutrophils to eosinophils ratio, lymphocytes to eosinophils ratio and monocyte to eosinophils ratio. Despite the time from diagnosis to sampling was shorter in C9ALS patients compared to sporadic patients, no correlation with the sampling delay was found. No significant correlation with the main clinical parameters and with overall survival was found.
Conclusion: Our work shows that C9ALS is characterized by a relative leukopenia that involves both the myeloid and in the lymphoid lines, which only partially overlap with what is known from previous studies on animals and humans, suggesting that immune dysregulation in C9ALS could differ from that of sporadic ALS patients.
Disclosure: Nothing to disclose.

EPO-674 | A nationwide survey of prevalence and symptom burden of pseudobulbar affect in amyotrophic lateral sclerosis

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Background and Aims: Our aim was to determine diagnostic prevalence of pseudobulbar affect (PBA) and symptom burden in patients with amyotrophic lateral sclerosis (ALS) in Denmark.
Methods: In this nationwide cross-sectional survey, we included citizens diagnosed with ALS who had a hospital contact in Denmark between January 2010 and July 2024 according to the Danish National Patient Register. Patients were invited between August and November 2024 to complete an online survey. The survey contained questions including known PBA diagnosis, treatment and quantification of symptoms through the CNS-Lability Scale (CNS-LS). A CNS-LS score of 13 or higher served as a threshold for possible symptoms of PBA.
Results: As shown in Figure 1, 679 patients were invited, of whom 157 patients with ALS completed the survey. 12.1% reported known PBA and the entire study population had a mean CNS-LS score of 11.3 $\pm$4.8. Patients with known PBA had a higher mean CNS-LS score (17.2 $\pm$4.7) compared to those not diagnosed with PBA (10.5 $\pm$4.3, $p < 0.001$). Patients with known PBA were more likely to receive antidepressant medication (47.4% compared to 15.2%, $p = 0.002$). In treated PBA, patients were predominantly treated with citalopram (78%). In the entire study population, 30.6% scored 13 or higher in the CNS-LS. Of those not known with PBA, 23.2% scored 13 or higher.

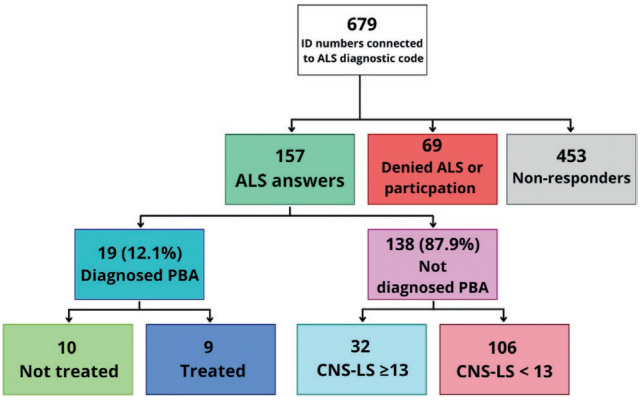

FIGURE 1 Flowchart of recruitment and highlighted survey response findings. ALS: amyotrophic lateral sclerosis, PBA: Pseudobulbar Affect, CNS-LS: CNS-Lability Scale.

Conclusion: While the proportion of known PBA among the ALS population was relatively low, the proportion of patients with symptoms of possible PBA was markedly higher. These findings may indicate under- or misdiagnosis of PBA among ALS patients, leading to lack of recommended symptomatic treatment.
Disclosure: Nothing to disclose.

EPO-675 | iRNA nanoparticles in ALS mouse model treatment

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Background and Aims: Amyotrophic lateral sclerosis (ALS) is caused by the progressive death of nerve cells in the spinal cord and brain. This rare disease causes weakness, loss of muscle mass, and eventually paralysis. There is currently no treatment for ALS, and existing therapies can only slightly slow the progression of the disease
Methods: The therapeutic agent in this study was a small interfering RNA (siRNA) molecule designed to suppress the expression of the tau protein, which is believed to play a key role in neurodegenerative changes. The base material for the nanoparticles was a polymer consisting of chains of lactic and glycolic acid. It has been previously discovered that mesenchymal stromal cells, stem cells that can turn into bone, muscle, fat, and other tissues, can also replace dead motor neurons in spinal cord of ALS patients. siRNA nanoparticles significantly enhance the therapeutic effect of mesenchymal stromal cells. We studied surface properties of the nanoparticles to maximize their penetration across the intact BBB in transgenic SOD1 mutant mice, analysed locomotor activity of tyese mice before and after electrophoresis with siRNA nanoparticles, also IL2, and IL6 cytokines, recombinant proteins of adhesion molecules were evaluated.
Results: iRNA nanoparticles causes better locomotion activity, normalization of IL2, and IL6 cytokines, recombinant proteins of adhesion molecules SOD1 mutant mice serum.

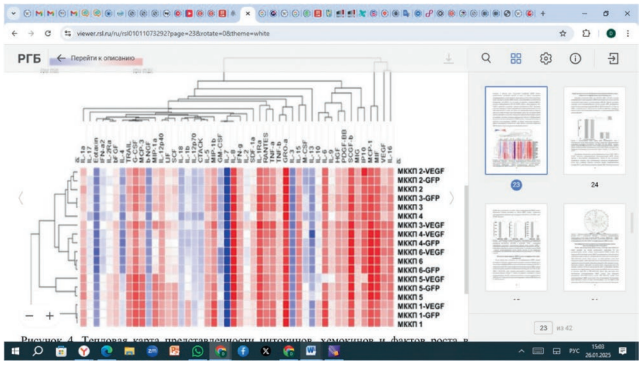

FIGURE 1 Cytokines in SOD1 mice

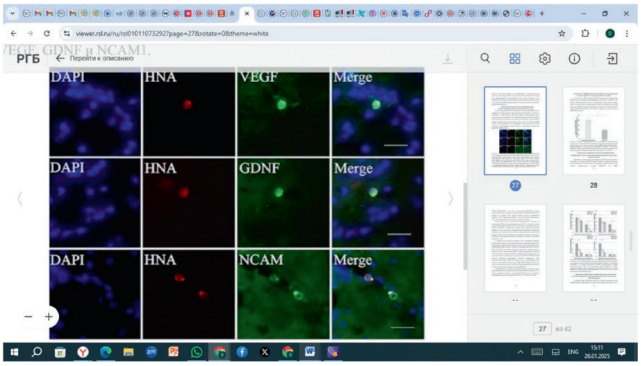

FIGURE 2 Recombinant proteins in SOD 1mice

Conclusion: This led to the identification of a unique nanoparticle design that increased the transport of encapsulated siRNA across the intact BBB and significantly improved the uptake of the drug by brain cells.
Disclosure: Nothing to disclose.

EPO-676 | Sphingosine-1-phosphate as a predictor of neurological deterioration in spinal bulbar muscular atrophy

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Background and Aims: Spinal and bulbar muscular atrophy (SBMA) is a genetic motor neuron disease that show slowly progressive muscular weakness and atrophy, caused by increased CAG repeats in the exon 1 of the androgen receptor gene. There are clinical markers that are used to predict neurological deterioration but the lack of quantitative biomarkers limits the sensitive evaluation. This study aimed to identify potential biomarkers associated with SBMA progression.
Methods: Plasma samples from 21 SBMA patients were collected at baseline and 3-4 years post-diagnosis, were employed to untargeted and targeted metabolomics using liquid chromatography-mass spectrometry. The levels of identified metabolites were further analyzed in relation to the rate of disease progression, which was defined by changes in ALSFRS-R scores during the follow-up period.
Results: Plasma S1P concentrations emerged as a promising marker for diagnosing and monitoring SBMA progression, as identified through targeted and untargeted metabolomics. Plasma S1P levels showed a significant decrease over the follow-up period in the fast progression group, defined by ALSFRS-R changes greater than -3 points. Additionally, follow-up S1P concentrations showed positive correlations with ALSFRS-R that showed negative correlation with serum creatine kinase levels.
Conclusion: Plasma S1P showed a promising diagnostic marker for SBMA. Despite the inherent variability in S1P levels requiring careful interpretation, it might be a novel marker reflecting neurological progression. More studies are needed to understand the underlying patho-mechanism of S1P and its regulation in SBMA, to strengthen the validity of these findings.
Disclosure: Nothing to disclose.

EPO-677 | Spontaneous spinal cord infarction: A rare disease with less frequent aetiologies

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Background and Aims: Spinal cord infarction is a rare condition, most often seen as a surgical complication. Spontaneous causes closely resemble those of ischaemic stroke. This case highlights the challenges in finding the etiology of spinal cord infarction.
Methods: N/A.
Results: A 60-year-old woman with a history of hypertension presented with sudden onset of severe abdominal pain, followed by bilateral sensory loss up to the umbilicus and reduced muscle strength in the lower limbs. Surgical acute abdomen and trauma were excluded. Neurological examination revealed flaccid hyperreflexic grade 2 paraparesis and anaesthesia with a sensory level at D7, raising suspicion of spinal cord involvement. Thoracic-abdominal-pelvic CT angiography excluded aortic dissection but identified pulmonary thromboembolism (PTE). The patient was outside the therapeutic window for thrombolysis, and anticoagulation was initiated for PTE. During inpatient care, MRI confirmed infarction of the anterior spinal artery spanning levels D8 to D12. Transcranial Doppler ultrasound, performed to detect microembolic signals, identified a right-to-left shunt, and transoesophageal echocardiography confirmed the presence of patent foramen ovale (PFO). Anticoagulation was complicated by lower bowel bleeding, prompting a colonoscopy that revealed a colonic adenocarcinoma, subsequently resected. At discharge, following rehabilitation, the patient had not yet achieved autonomous gait.
Conclusion: Two less common potential causes of spinal cord infarction: paradoxical embolism through a PFO in the context of PTE, and a prothrombotic state induced by neoplasia, implicated in the occurrence of PTE and spinal cord ischemia. Management in such cases should consider PFO closure and the maintenance of long-term anticoagulation.
Disclosure: Nothing to disclose.

EPO-678 | Subacute myelopathy due to nitrous oxide inhalation: An emerging etiology among young adults. A case series

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Background and Aims: Inhaling nitrous oxide (N_2O) can result in functional deficiency of vitamin B12, which may cause neurological toxicity, including myelopathy. The objective is to describe two cases of subacute myelopathy caused by N_2O inhalation.
Methods: We report two patients diagnosed with subacute myelopathy due to N_2O inhalation admitted to our center.
Results: A 33-year-old male with a 4-week-progressive-ascending hypoesthesia following a stocking-and-glove pattern associated with areflexia and dysautonomia. Slightly decreased B12 levels (291 pg/mL). Brain and spinal cord MRI showed a longitudinally extensive spinal cord lesion from C1 to T10, mainly involving dorsal columns, mimicking Neuromielitis optica spectrum disorder lesions. A 20-year-old male with a 3-month-progressive-ascending hypoesthesia with a sensory level in T10–T12 associated with areflexia and sensory ataxia. Decreased B12 levels (153 pg/mL). Despite a normal MRI, the neurophysiological study revealed severe involvement of dorsal columns and pyramidal tract in the lower limbs, alongside axonal sensorimotor polyneuropathy. Both patients disclosed prior use of inhaled nitrous oxide (N_2O) in a binge pattern before the onset of symptoms and other potential etiologies were excluded. The 1st case was treated with 1g of intravenous methylprednisolone once daily for 5 days and B12 supplementation, while the 2nd only received B12 supplementation. In the subsequent days, both patients experienced remarkable clinical improvement, presenting only mild symptoms by the time of discharge.
Conclusion: N_2O is a rare cause of subacute myelopathy in young individuals and should be taken into account in the differential diagnosis due to its reversibility when treated promptly.
Disclosure: Nothing to disclose.

EPO-679 | Neutrophil percentage-to-albumin ratio as a possible biomarker for disease progression in amyotrophic lateral sclerosis

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Background and Aims: recent studies highlight the role of serum inflammatory markers in Amyotrophic Lateral Sclerosis (ALS) and the neutrophil-to-lymphocyte ratio (NLR) has proposed as a reliable marker. Recently, the neutrophil percentage-to-albumin ratio (NPAR) has proposed as a marker of inflammation, demonstrating prognostic utility in ischemic stroke, intracerebral haemorrhage, and cognitive decline. This study investigates its role in ALS.
Methods: we retrospectively analyzed 3,263 ALS patients with NPAR values recorded within ±90 days of recruitment from PRO-ACT. The median age was 57 years (IQR: 49–75); 62.7% were male and 37.3% female. During follow-up, 28.7% of patients died or underwent tracheostomy. NPAR values were stratified into tertiles. Statistical comparisons between groups were conducted with Chi-square and Kruskal-Wallis test as appropriate. Logistic regression was employed to evaluate associations between tertiles and clinical outcomes. Patient survival was assessed via Cox regression.
Results: NPAR showed significant differences across tertiles in age at symptom onset, ALSFRS-R score, disease progression rate (DPR) at recruitment, and follow-up days ($p < 0.001$). Higher NPAR values were associated with later diagnoses, lower ALSFRS-R scores, faster DPR, and shorter follow-up. Logistic

regression revealed significant associations with clinical outcomes ($p < 0.001$). Cox regression showed reduced survival in group with higher NPAR (OR: 1.32; CI: 1.12–1.54), even after adjusting for age, gender, ethnicity, and site of symptom onset. The work was done using a public database (PRO-ACT).
Conclusion: in a large cohort of ALS patients, NPAR appears to be a potential accessible blood biomarker for predicting clinical outcomes, supporting the role of neuroinflammation in ALS.
Disclosure: Nothing to disclose.

EPO-680 | West Yorkshire miniseries cases studies of split-hand feature in appendicular and bulbar onset MND and MND mimics

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Background and Aims: Split-hand phenomenon is reportedly seen in 70% of ALS in early stages of MND. A neurophysiological tool to support a clinical diagnosis of a MND appeared as split hand index (CMAP APB X FDI/CMAP ADM) = <5.2 and two CMAP ratios of thenar/hypothenar muscles (APB/ADM = <0.6, FDI/ADM = <0.9, ADM/APB >1.7). We assessed the utility of this in our cases.
Methods: Data were collected from the records of patients diagnosed as possible MND in our neurophysiology clinics from (8/2020 to 11/2024).
Results: Twelve appendicular onset (AO) MND patients and eight bulbar onset (BO) cases were included. There were four cases of Hirayama. None of the bulbar onset MND cases and Hirayama's cases revealed the split hand phenomenon. All AO cases did. AO cases were seen six months to a year from symptoms onset. BO cases were seen within a year. Dysarthria, dysphagia, dysphonia and respiratory failure were seen in BO cases and four of them died in two months to two years later. One patient never developed appendicular symptoms. The others developed appendicular weakness in three months. AO cases started as weakness and cramps in one limb and spread to involve all four limbs. Three patients developed bulbar symptoms and one died. Four are still surviving. Split hand index were negative for all bulbar and Hirayama cases.
Conclusion: Any test to support the clinical diagnosis of MND is valuable. We found those ratios and index helpful in appendicular onset MND. They were negative in our series for bulbar onset MND and MND mimics cases.
Disclosure: Nothing to disclose.

EPO-681 | Subacute combined degeneration in relation to nitrous oxide abuse: An emerging disorder

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Background and Aims: Neurological symptoms resulting from recreational use of nitrous oxide (N2O), also known as laughing gas, are an emerging social problem in Europe. This drug is easily available at nightclubs and online shops, producing an epidemic that affects young adults. We report six patients with neurological impairment after excessive N_2O consumption.
Methods: We identified all patients with final diagnosis of neurological disorder due to N_2O abuse, presenting to a tertiary hospital in Spain, in the year 2023–2024.
Results: Total of six cases: Young men (19–30 years old) with a history of both chronic and high-dose N_2O inhalation. The predominant feature in all of them was ascending paresthesias in the lower limbs and associated gait ataxia. Altered MRI signal as myelopathy was observed in four out of six patients. Demyelinating features in the motor nerves were found in four of the six cases. One patient developed visual impairment in the form of retinitis. Additional tests ruled out other etiologies. Vitamin B12 treatment was initiated in five patients. Three patients discontinued N_2O use with partial clinical improvement, persisting mild sensitive symptoms.
Conclusion: Neurological disorders due to N_2O have been linked to vitamin B12 deficiency through interference with its metabolism, leading to demyelination. Empirical treatment consists of hydroxocobalamin injections, with uncertain functional prognosis. It is imperative to raise awareness among clinicians about the risks associated with this practice, including visual loss (not reported in existing literature) and the importance of considering N2O abuse in the differential diagnosis of central and/or peripheral demyelinating diseases in young patients.
Disclosure: Nothing to disclose.

EPO-683 | Cramp-fasciculation syndrome and anti-N-methyl-D-aspartate receptor positivity: A case report

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Background and Aims: Anti-NMDAR antibodies, traditionally associated with anti-NMDAR encephalitis, have also been identified in cases of optic neuritis and myelitis, leading to the broader classification of NMDAR spectrum disorder. Here, we present a case of confirmed anti-NMDAR positivity in both cerebrospinal fluid and serum, manifesting as cramp-fasciculation syndrome (CFS) with atypical radiological features, including myelitis and leptomeningeal enhancement.
Methods: A 63-year-old male patient presenting with painful cramps, spontaneous fasciculations and back pain was admitted and evaluated with a full neurological examination, nerve conduction studies (NCS) and electromyography (EMG), brain and spinal cord MRI, lumbar puncture, and serum/cerebrospinal fluid (CSF) analysis for infectious and autoimmune diseases.

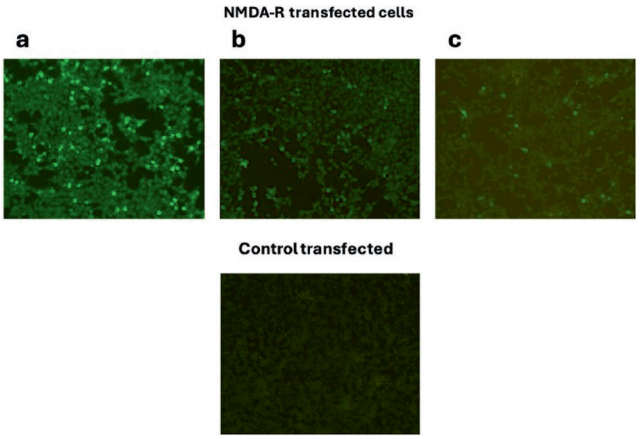

FIGURE 1 Indirect Immunofluorescence Assay of transfected EU90 cells expressing NMDAR and control transfected cells. a, b: Serum 1:10 and 1:320; c: CSF, undiluted, followed by incubation with anti-human IgG fluorescent antibody.

Results: Neurological examination was remarkable for increased deep-tendon reflexes and clonus in both lower limbs but there was no muscle weakness. Despite normal NCS, EMG revealed acute-subacute and chronic denervation in upper and lower limbs (especially tibialis anterior). MRI indicated a short-segment myelitis lesion at T6 level, with leptomeningeal enhancement. Serum and CSF analysis excluded infectious causes. Type IV oligoclonal bands were detected. An extensive autoantibody screening with cell- and tissue-based assays revealed anti-NMDAR positivity in serum and CSF. Despite relapses, there was clinical and radiological response to immunotherapy (intravenous corticosteroids and plasmapheresis).

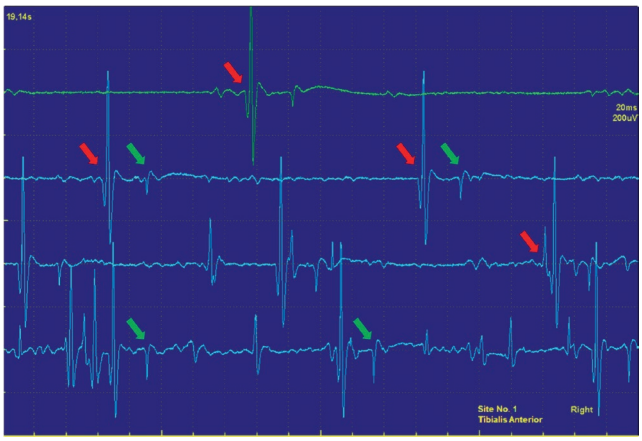

FIGURE 2 Electromyography with abnormal spontaneous activity. Positive sharp waves (green arrows) and fibrillation potentials (red arrows)

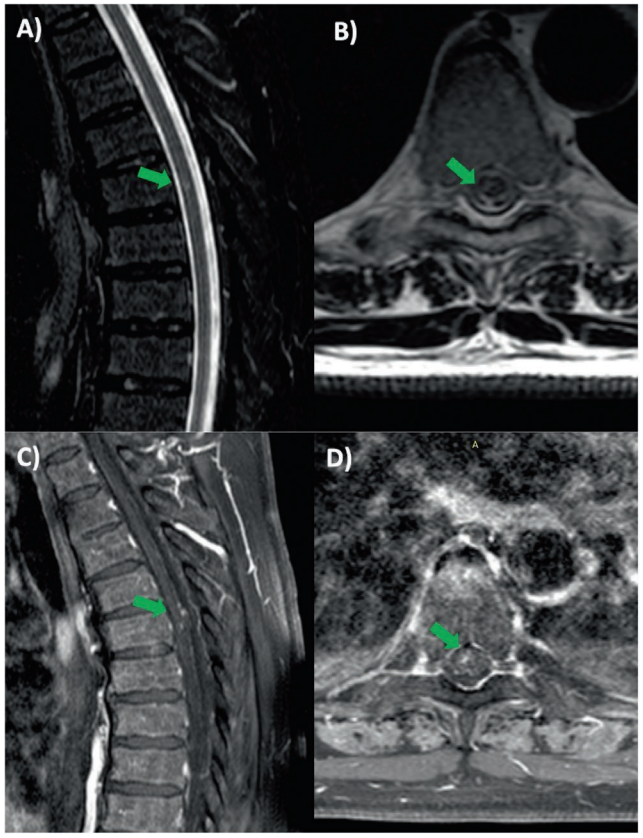

FIGURE 3 Lesion at T6 level on thoracic spinal cord MRI at first admission A. STIR, B. T2WI, C and D. T1WI with fat suppression after intravenous administration of contrast agent

Conclusion: Our anti-NMDAR case presents atypical clinical and imaging features. Although the exact mechanism remains unclear, cramp-fasciculation-like phenotype and leptomeningeal enhancement suggest spinal nerve root involvement. We support the need for increased awareness of the syndrome's diverse phenotypes.

Disclosure: Nothing to disclose.

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ABSTRACT

ePosters Virtual

EPV-001 | Lewy body dementia mimic: A shocking diagnosis

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EPV-002 | Can yerba mate reduce the risk of cognitive impairment? A pilot study

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EPV-003 | Unraveling disparities in Alzheimer's disease-related mortality trends in United States: 1999-2022

A. Ali; M. Imaz Bhatti; M. Usman Ahmed
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EPV-004 | Characteristics of clinical symptoms of vascular dementia

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EPV-005 | Staging Alzheimer's disease with instrumental activities of daily living: a crosswalk with mini mental state examination

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EPV-006 | Biomarkers of neurodegenerative diseases

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EPV-007 | Thyroid hormones and association with Alzheimer's disease: A systematic review and meta-analysis

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EPV-008 | The cerebellum in frontotemporal dementia: A promising neuromodulatory target

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EPV-009 | Usefulness and profile of safinamide in lewy body dementia

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EPV-010 | The diagnostic challenge of biomarkers in rapidly progressive dementia: sCJD vs. vCJD

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EPV-011 | Unraveling gut microbiota's role in Alzheimer's disease: Pathophysiology and emerging therapeutic strategies

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EPV-012 | Particulate matter (PM2.5) and Alzheimer's disease: Exploring environmental risk factors and pathophysiology

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EPV-013 | Glymphatic system dysfunction in Alzheimer's disease: Exploring AQP4 as a therapeutic target

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EPV-014 | Relationships between CSF biomarkers, neuroimaging, and cognitive outcomes in patients with Alzheimer's disease

C. Manco[1]; D. Righi[1]; F. Galasso[2]; B. Pucci[1]; L. Lucchetti[3]; M. Battaglini[3]; A. Cerase[2]; N. De Stefano[1]; D. Plantone[1]
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EPV-015 | Correlates of functional impairment in the behavioral variant of frontotemporal dementia (bvFTD)

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EPV-016 | A new variant of the TBK1 gene in a case of familial fronto-temporal dementia

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EPV-017 | The calcium channel blocker Cav2.1 combined with amyloid beta monoclonal antibodies may reduce the occurrence of ARIA-E

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EPV-018 | Cognitive dysfunction and duration of education: Diving into cognitive domains

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EPV-019 | The relationship between APOE genotype and mild behavioral impairment: A systematic review

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EPV-020 | Exploring the impact of cognitive function on balance control in older people with comorbidities: The SMARTBEAR project

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EPV-021 | Resilience among informal caregivers for patients with mild cognitive impairment

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EPV-022 | Cognitive deficits in a Turkish migrant population: observations from a memory clinic in Germany

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EPV-023 | Semantic variant primary progressive aphasia in a patient with right temporal atrophy: A case study

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EPV-024 | The pilot Geneva Brain Health Services program: patients' feedback and baseline data of the first patients enrolled

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EPV-025 | Cross-cultural dementia screening: Comparing mini-mental state examination and rowland universal dementia scale

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EPV-026 | Association between CSF Tau/Amyloid biomarkers and cerebral microbleeds in patients with and without Alzheimer's disease

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EPV-027 | Predicting conversion in cognitively normal and MCI subjects with machine learning. Is the CSF status still relevant?

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EPV-028 | Thyroid dysfunction and cognitive impairment; Relationship with MMSE subscores

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EPV-029 | EEG biomarkers in Alzheimer's disease

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EPV-030 | NAD metabolite alteration within neurodegeneration in Alzheimer's and Parkinson´s disease

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EPV-031 | Exploring ipidacrine's potential to improve cognitive function and quality of life in mild cognitive impairment

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EPV-032 | Addressing challenges in remote care: Telemedicine for dementia and Parkinson's disease in the Aegean islands

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EPV-033 | Currents in diagnosing Alzheimer's disease in northern Serbia: A single center experience

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EPV-034 | Cognitive functioning in healthy females with different APOE4 carrier status

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EPV-035 | Acoustic speech analysis and machine learning in the diagnosis and monitoring of neurodegenerative disorders

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EPV-036 | Patient and public involvement and engagement in research of neurodegeneration using speech and artificial intelligence

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EPV-037 | Assessment of the burden experienced by caregivers of patients with Alzheimer's disease and its associated factors

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EPV-038 | Development of a comprehensive protocol for specialized assessment of patients with cognitive disorders via telemedicine

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EPV-039 | Early detection of cognitive disorders and dementia in hypertensive patients

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EPV-040 | Handwriting analysis as a diagnostic tool in dementia evaluation

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EPV-041 | Pro-inflammatory S100A9 protein in amyloid self-assembly and its inhibition in Alzheimer's disease

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EPV-042 | Whispers of the mind: A deep learning framework for dementia prediction through EEG patterns in drowsy drivers

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EPV-043 | Evaluation of serious games platform for cognitive stimulation and dementia prevention in patients with MCI

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EPV-044 | White matter hyperintensities and Alzheimer's disease - considerations on a clinical case

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EPV-045 | Cathepsin-A-related arteriopathy with stroke and leukoencephalopathy (CARASAL): Case report and literature review

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EPV-046 | Posterior cortical atrophy: A case of progressive loss of reading and writing abilities

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EPV-047 | Role of multivesicular bodies in tau protein aggregation

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EPV-048 | Cellular communication of gut amyloids

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EPV-049 | Revolutionizing neurological care: The impact of ai in advancing early diagnosis of Alzheimer's Disease

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EPV-050 | Demographic and neuropsychological correlates of cognitive reserve in healthy females

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EPV-051 | Staging dementia with instrumental activities of daily living: A crosswalk with the Saint Louis University Mental Status

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EPV-052 | Gastrointestinal adverse events of Antidementia medications: A pharmacovigilance study

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EPV-053 | Overcoming challenges in clinical trial development in Europe: Alzheimer's disease as a case study for innovation

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EPV-054 | **Adapting the Spanish healthcare system for disease-modifying treatments for early symptomatic Alzheimer's disease (eAD)**

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EPV-055 | **Knowledge and attitudes toward Alzheimer's disease and dementia among medical students in Sudan**

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EPV-056 | **Thriving in later life: Exploring happiness, frailty, and perceived health**

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EPV-057 | **Promoting cognitive and emotional health in the aging brain: the effects of rTMS**

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EPV-058 | **Isolated dementia syndrome in a patient with LRRK2 mutation**

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EPV-059 | **Challenges in distinguishing nonconvulsive status epilepticus and creutzfeldt jakob disease based on EEG findings**

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EPV-060 | **Does subclinical seizure activity contribute to the development of dementia in cerebral small vessel disease (CSVD)?**

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EPV-061 | **Neuronavigated low energy shockwaves ameliorate cognitive deficits and depressive symptoms in Alzheimer's disease**

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EPV-062 | **Watercolor and McCollough Effects: visual illusions that fade in early Alzheimer's disease**

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EPV-063 | **Transcranial pulse stimulation (TPS) as a suitable add-on treatment of patients with Alzheimer's disease?**

V. Rößner-Ruff; M. Ziegenbein; C. Penkov; K. Friedrich; J. Krieger; J. Michaelsen
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EPV-064 | Deep brain stimulation for Alzheimer's: How close are we to a breakthrough?

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EPV-065 | Survival in cerebral amyloid angiopathy: Identifying key factors

Y. Krichene; A. Gharbi; A. Souissi; A. Atrous; Y. Abida; A. Gargouri; I. Kacem; R. Gouider
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EPV-066 | Autonomous enteric neuropathy in young adults: Two case reports

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EPV-067 | Anti-TNF medications and autonomic nervous system dysfunction: Insights from the FAERS database

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EPV-068 | Centrally driven Pathological Function of the Autonomous Nervous System Determines the Heart Arrhythmia Trigger State

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EPV-069 | Late window (>6 h) vs early window

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EPV-070 | Post-stroke epilepsy in patients taking direct oral anticoagulants for atrial fibrillation

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EPV-071 | The integration of neurosonology in the acute phase of ischemic stroke improves diagnostic and therapeutical accuracy

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EPV-072 | A disease of multiple faces: 5-year prospective observational study of cerebral venous thrombosis

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EPV-073 | The role of obesity in the development of ischemic stroke

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EPV-074 | CADASIL Manifested during pregnancy and the postpartum period: A case report

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EPV-075 | Abusive consumption of oxymetazoline (sympathomimetic) as a trigger for hypertensive intracerebral Hemorrhage

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EPV-076 | Association of CHA2DS2-VASc score with clinical and technical outcomes in thrombectomy patients

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EPV-077 | Perimesenecphalic subarachnoid hemmorrhage—Is it always a benign condition?

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EPV-078 | In-hospital stroke mortality at a comprehensive stroke center in Armenia

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EPV-079 | The beneficial effect of Angong Niuhuang Pill on ischemic stroke via regulating brain-gut axis

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EPV-080 | PFO closure for stroke prevention in older patients: recurrence and AF risk

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EPV-081 | Carotid web: An uncommon cause of stroke

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EPV-082 | Muscle ultrasonography in the diagnosis of sarcopenia in stroke patients

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EPV-083 | Neurovascular manifestations of celiac disease

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EPV-084 | Cerebral venous thrombosis in Behçet's disease: Clinical insights and therapeutic challenges

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EPV-085 | Septic embolism and stroke: An unusual case of aspergillus-associated thrombosis

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EPV-086 | COL4A1 as a cause of small vessel disease: A case series

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EPV-087 | Primary Moyamoya disease in an elderly patient: Diagnostic and therapeutic challenges

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EPV-088 | Ischemic stroke in atrial fibrillation patients despite anticoagulation: Challenging mechanisms and management

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EPV-089 | Complex postpartum presentation of cerebral arteriovenous malformation: A multidisciplinary challenge

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EPV-090 | Ischemic stroke in young adults: A cohort study on prognosis

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EPV-091 | Paradoxical embolism and stroke in the young: A rare presentation of pulmonary arteriovenous malformations

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EPV-092 | Multiple cerebral ischemic events as the presentation of paroxysmal nocturnal hemoglobinuria

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EPV-093 | Forewarned is forearmed

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EPV-094 | Ischemic stroke with negative diffusion: A report of 3 cases

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EPV-095 | Ischemic stroke following immunoglobulin administration: A rare but notable complication

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EPV-096 | Thrombolysis and orolingual angioedema: An overview of an uncommon complication

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EPV-097 | Area postrema syndrome due to lateral medulla oblongata infarction

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EPV-098 | Dural arteriovenous fistula of the spinal cord: A case of longitudinally extensive myelopathy with subtle manifestations

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EPV-099 | Amyloid does not always come alone: Inflammation related to cerebral amyloid angiopathy (CAA-RI)

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EPV-100 | Collision of emergencies: Thalamic infarction in the context of pituitary apoplexy

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EPV-101 | Bilingual aphasia as an atypical stroke presentation: case report and literature review

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EPV-102 | CADASIL disease; case series

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EPV-103 | Case series, different clinical signs and causes of stroke in perinatal period in Neurovascular Service in Albania

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EPV-104 | The role of ESR as a prognostic factor in ICH: An Albanian patients study

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EPV-105 | Burden of stroke and its impact on the quality of life of family caregivers in Senegal

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EPV-106 | Middle meningeal artery embolization in the management of nonacute subdural hematoma (NASDH)

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EPV-107 | Claude's syndrome: A rare presentation of midbrain strokes

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EPV-108 | Forecasting neurological emergency cases using synoptic weather patterns: Insights from a budapest hospital ER

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EPV-109 | Impaired emotional processing and reduced system segregation in insular stroke

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EPV-110 | Venous clot, arterial catastrophe: The mystery of a hidden shunt

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EPV-111 | Comparative role of S100 protein and NSE in predicting hemorrhagic transformation in ischemic stroke patients

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EPV-112 | Association of high glycated albumin with early neurological deterioration in patients with acute ischemic stroke

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EPV-113 | Prevalence of thrombophilia in strokes among young adults

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EPV-114 | Essential thrombocythemia possible cause of ischemic cerebrovascular disease: A case of study

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EPV-115 | Myasthenia Gravis as a 'stroke mimic'

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EPV-116 | Post stroke aphasia: A hospital-based case series

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EPV-117 | Bilateral vertebral artery dissection presenting with opalski syndrome: A case report

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EPV-118 | Cerebral Microbleeds Prevalence in Ischemic Stroke Patients: MRI Analysis of 110 Patients

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EPV-119 | Free-floating thrombus within the Aorta and Supra-aortic arteries: A Tunisian experience

O. Ayadi; E. Jarrar; S. Bouzidi; A. Rekik; H. Slimen; A. Hassine; S. Naijja; S. Ben Amor
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EPV-120 | Stroke secondary to giant cell arteritis in a Moroccan population-based cohort of 40 patients

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EPV-121 | A case of aphasia in the emergency department

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EPV-122 | Percheron artery infarction as a presentation of cryoglobulinemic vasculitis

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EPV-123 | Endothelial and circulating progenitor cells as prognostic biomarkers of stroke: A systematic review and meta-analysis

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EPV-124 | Impact of the cerebrovascular disease care network: A systematic review

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EPV-125 | Comparative analysis of stroke risk in endovascular coiling vs surgical clipping for intracranial aneurysm management

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EPV-126 | Carotid Web: case series and review of the literature

J. Villamor Rodríguez; D. Barbero Jiménez; M. González Gómez; F. Sánchez García; E. Gismera Fontes; M. Andrés del Barrio
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EPV-127 | Direct carotid artery puncture for mechanical thrombectomy in acute ischemic stroke with tandem occlusion: A case report

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EPV-128 | Clinical, radiological and prognostic Features of cervical artery dissection in North Africa: A bicentric study

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EPV-129 | Cerebral Venous Thrombosis Associated with Homozygous C677T Mutation in the MTHFR Gene: Case Report

M. Messelmani[1]; K. Chekili[1]; Y. Missaoui[1]; A. Hajmabrouk[1]; N. Fekih Mrissa[2]; I. Bedoui[1]; H. Derbali[1]; M. Mansour[1]; J. Zaouali[1]
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EPV-130 | Coagulation test indicators and severity of ischemic stroke in women

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EPV-131 | The influence of place of residence on laboratory parameters and genetic polymorphisms in women with ischemic stroke

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EPV-132 | Cannabis and antidepressants as the cause of reversible cerebral vasoconstriction syndrome

L. Gil Martinez; A. Sánchez Asensio; J. Cortina García; J. Romero Ferro; N. Mena García; G. Cabañas Engenios; M. Campos Jimenez; R. Pastor Gonzalez; A. de Felipe Mimbrera; M. Matute Lozano; S. García Madrona; A. Cruz Culebras; J. Masjuán Vallejo; R. Vera Lechuga
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EPV-133 | Iron status or WBC with relative ratio: which is the best predictor in ischemic patient treated with rTPA?

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EPV-134 | Basilar artery occlusion: Improvement with mechanical thrombectomy and conservative treatment

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EPV-135 | Advanced diagnostic approach in embolic stroke of undetermined source (ESUS): Our center's experience

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EPV-136 | Impacts of cerebrovascular diseases on long-term cognition: a systematic review

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EPV-137 | Cerebral venous thrombosis as a manifestation of essential thrombocythemia: The role of Janus Kinase 2 enzyme mutation

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EPV-138 | Specificity of hemorrhagic stroke in patients with Covid-19

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EPV-139 | "Uncommon presentation of reversible cerebral vasoconstriction syndrome: A diagnostic challenge"

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EPV-140 | Acute cerebrovascular infarction due to traumatic intracranial vertebral artery dissection - Case report

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EPV-141 | Arterial dissection and polycythemia: A case report and literature review

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EPV-142 | Myotonic dystrophy type 1 complicated with stroke: A case report

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EPV-143 | Clinical and neurological characteristics of sleep disorders in stroke

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EPV-144 | Antiphospholipid syndrome (APS) and stroke: A diagnostic and therapeutic challenge

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EPV-145 | Graft-versus-host disease: Cause or coincidence?

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EPV-146 | Ischemic stroke despite oral anticoagulation—What next?

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EPV-147 | How to assess and manage resistance to clopidogrel in the population of patients undergoing endovascular treatment

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EPV-148 | Premature ventricular complexes and ischemic stroke risk: A systematic review and meta-analysis

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EPV-149 | Ischemic strokes in young adults: Etiological profile in a Tunisian population

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EPV-150 | Characterization of a portuguese cohort of cadasil patients: Genotypic and phenotypic insights

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EPV-151 | Measurement properties of functional tests for post-stroke patients: A systematic review

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EPV-152 | Liver–brain axis: Hepatic encephalopathy presenting as stroke in decompensated cirrhosis

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EPV-153 | Cerebral venous thrombosis in diffuse scleroderma: A case report of a rare association

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EPV-154 | Symptomatic hemorrhagic transformations in ischemic stroke: comparative study of Multicenter Stroke Survey and GRASPS

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EPV-155 | Claude syndrome caused by young-onset ischemic stroke: A case report

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EPV-156 | Safety and efficacy of reduced-dose intravenous RTPA in Asian stroke populations: evidence from a Malaysian cohort

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EPV-157 | Diagnosis of Obstructive Sleep Apnea in Stroke Patients by Portable Watchpat Test

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EPV-158 | Efficacy and safety of dabigatran compared with dose-adjusted warfarin in the treatment of CSVT

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EPV-159 | Thrombolysis in acute ischemic stroke—Is it always safe?

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EPV-160 | Relationship between Sleep Disorders and Dementia Severity in Post-stroke dementia

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EPV-161 | Diagnosis and treatment principles improvement of chronic cerebral ischemia and somatovegetative syndromes

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EPV-162 | Acquired stuttering as the presenting manifestation of acute stroke

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EPV-163 | Acute ischemic stroke after beach chair position surgery

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EPV-164 | Association of selected cytokine levels with ischemic stroke severity: A preliminary study

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EPV-165 | Comparative efficacy and safety of cilostazol and clopidogrel in secondary stroke prevention: A meta-analysis

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EPV-166 | Atrial fibrillation detected after stroke: A unique entity or just another face of known atrial fibrillation?

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EPV-167 | Comparative study of predictive signs of hematoma expansion in intracerebral hemorrhage

R. Berbegal; M. Paz; E. Cañada; S. Lozano; P. Iriarte; J. Alonso; C. Ramos; E. Capilla; A. Barbosa; C. Alonso; J. Vega; S. Trillo
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EPV-168 | Utility of a biomarker profile in the stroke code: an exploratory study

R. Berbegal; C. Sanabria; V. Escribano; B. Colino; E. Salgado; M. Sobrado; J. Alonso; C. Ramos; S. Lozano; E. Cañada; E. Valiente; A. González-Martínez; G. Reig; S. Trillo
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EPV-169 | CAA-RI: Early diagnosis is key to effective treatment

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EPV-170 | Prevalence in the population of the aral sea region of the republic of karakalpakstan

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EPV-171 | Management of post-stroke dysphagia in ischemic stroke patients aged ≥80 years treated with reperfusion therapies

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EPV-172 | Correlation of variation in weather conditions and non-traumatic intracerebral hemorrhage (NTICH)

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EPV-173 | T.E.D.R.A.S. Ii - Transoesophageal echocardiography as dysphagia risk in acute stroke - Protocol for a controlled trial

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EPV-174 | Comparison of muiphase CT angiography and collateral map for predicting functional outcomes in acute ischemic stroke

S. Lee[1]; H. Roh[2]; J. Park[3]; T. Lee[1]; Y. Jeon[4]; H. Ki[5]; J. Choi[2]; J. Kwak[6]; J. Lee[7]; H. Kim[8]
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EPV-175 | Left or right? Uncovering the effect of lateralization on insular stroke clinical outcomes

S. Tartaglia[1]; F. Kuris[1]; R. Sperotto[1]; L. Ceccarelli[1]; D. Bagatto[2]; G. Merlino[1]; S. Lorenzut[3]; L. Verriello[3]; M. Valente[1]; G. Pauletto[3]
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EPV-176 | Evaluation of the effectiveness of treatment of neurological insufficiency in recurrent ischemic strokes

S. Kuranbaeva; S. Hakimov; R. Makhmudov; S. Rustambekova; S. Kalandarova; G. Rakhimbaeva
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EPV-177 | Possibilities of CT scan of the brain in the acute period of ischemic stroke to predict the outcome of the disease

S. Kuranbaeva; S. Hakimov; R. Makhmudov; S. Rustambekova; S. Kalandarova
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EPV-178 | The impact of hemorrhagic stroke on quality of life in the context of different comorbidities

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EPV-179 | Chronic kidney disease as a risk factor for developing silent brain infarction

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EPV-180 | Features of cerebrovascular disease in young patients with hypercoagulation syndrome and angiodysplasias

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EPV-181 | Reassessing the use of repeat brain imaging before anticoagulation in stroke

S. Marinho Pinto; D. de Araújo; J. Menezes Barbosa; A. Aldomiro; G. V. Bonifácio
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EPV-182 | A not so obvious etiology for a complex case of recurrent ischemic strokes

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EPV-183 | Relationship between early neurological deterioration and transcranial doppler parameters in mechanical thrombectomy

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EPV-184 | Acute onset hemiparesis in a young man with Crohn's disease: don't miss extraintestinal manifestations!

V. Iacobelli[1]; S. Tagliabue[1]; B. Modello[2]; D. Velardo[3]; E. Abati[1]; F. Triulzi[2]; G. Comi[3]; S. Corti[4]; D. Gagliardi[3]; M. Parisi[3]
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EPV-185 | Traumatic vertebral artery dissection associated with cervical neck traction devices

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EPV-186 | Artificial Intelligence in Predicting Asymptomatic Carotid Artery Stenosis: A systematic review

Y. Alajlouni; L. Alnatour; A. Tarazi; A. Musleh
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EPV-187 | Regulation of gut microbiota in acute ischemic stroke patients

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EPV-188 | Posterior reversible encephalopathy syndrome: Insights from a series of 15 cases

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EPV-189 | Tuberous sclerosis complex: Clinical and radiological study of a tunisian pediatric cohort

A. Kalfat; Z. Miladi; A. Zioudi; M. Jamoussi; T. Ben Younes; H. Ben Rhouma; I. Ben Youssef Turki; H. Klaa; I. Kraoua
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EPV-190 | Transcranial magnetic stimulation in children with tic disorders: Neurophysiological features and clinical effectiveness

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EPV-191 | Neurophysiological effects of binaural beats on EEG patterns and ADHD symptoms

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EPV-192 | Electroencephalographic findings and posterior reversible encephalopathy syndrome in Mexican pediatric patients

D. Narváez González; G. Segura Polina; B. Chávez Luévanos; A. Cantú Salinas; A. Carrión García; S. Vázquez Fuentes; O. De la Garza Pineda
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EPV-193 | Beware of thyroid hormones: Rare cause of children's hypotonia

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EPV-194 | The role of transcranial magnetic stimulation (TMS) in modulating brain plasticity in children with cerebral palsy

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EPV-195 | Prognostic factors for the development of epilepsy in children with febrile seizures

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EPV-196 | Dyslexia: A word game to develop phonological awareness

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EPV-197 | Polyneuritis cranialis: A rare guillain–barré syndrome variant in a 10-year-old girl

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EPV-198 | Canavan disease: Systematic literature review on genetic insights and prognostic perspectives

M. Saint-Felix[1]; D. Almánzar[1]; A. Reyes[1]; K. Rodríguez-Manso[1]; A. Tejada[1]; K. Yorro[1]; C. Lizardo[1]; M. Rodríguez[2]
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EPV-199 | Safety and efficacy cerliponase alfa in neuronal ceroid lipofuscinosis type 2: A systematic review and meta-analysis

M. Saddique[1]; J. Oliveira[4]; M. Qadri[2]; F. Shahid[1]; N. Saleem[3]; A. de Jesus[5]; S. Shamoon[6]
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EPV-200 | Social & psychological factors among the autism spectrum disorder child bearing families and their coping strategies

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EPV-201 | Epileptic spasms—Clinical characteristics, etiology, treatment and prognosis

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EPV-202 | Assessment of the effect of DMT on the health status of newborns

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EPV-203 | Novel cell counting whole slide imaging (WSI) algorithm for slide images

A. Mahapatra; V. Giunchiglia; S. Gentleman; R. Nicholas
Department of Brain Science, Faculty of Life Sciences, Imperial College London, UK

EPV-204 | Agent-guided AI-powered interpretation and reporting of Nerve conduction studies and EMG (INSPIRE)

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EPV-205 | Video-oculography: A diagnostic tool for functional neurological disorder?

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EPV-206 | Dynamic changes in key coagulation parameters in ischemic stroke patients undergoing intravenous alteplase therapy

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EPV-207 | Effect of acute transcutaneous auricular vagus nerve stimulation on EEG frequency bands and connectivity

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EPV-208 | Analysis of the nervous system and movement disorders in organic acidemias: An electrophysiological study

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EPV-209 | "Red flag": When motor potentials are "small" without an apparent cause

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EPV-210 | The efficacy of transcranial direct current stimulation in essential tremor: An open-label study

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EPV-211 | Hyperreligiosity as a clinical manifestation of charles bonnet syndrome: A case report

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EPV-212 | Morphological defects and cognitive impairments after ischemic stroke: Long-term impact of chornobyl liquidation

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EPV-213 | The social media/smartphone world: Effect on attention and memory

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EPV-214 | The relationship between cognitive decline, surgical interventions and general anesthesia: A pilot retrospective study

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EPV-215 | The interrelation between cerebrovascular risk factors and cognitive impairment in general population

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EPV-216 | Behavioral disturbances in primary progressive aphasia: A longitudinal comparative pilot study

E. Bergamin; V. Nicoletti; S. Cintoli; S. Corsi; G. Siciliano; G. Tognoni
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EPV-217 | Clinical and biomarker diagnoses of Alzheimer's disease: Insights from a serbian cohort of patients with memory disorder

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EPV-218 | Error patterns in the assessment of Limb Apraxia in neurodegenerative disorders: Insights from a pilot study

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EPV-219 | Safety and efficacy of paliperidone palmitate 1-month formulation in schizophrenia: A systematic review & meta-analysis

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EPV-220 | Abstract withdrawn

EPV-221 | Prosopometamorphopsia as a manifestation of epileptic seizures in a face-selective network stroke: A case report

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EPV-222 | Transient global amnesia and hippocampal lesions with restricted diffusion: A truly benign condition?

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EPV-223 | **Cognitive impairment as a predictor of prognosis in heart failure: A systemic review and meta-analysis**

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EPV-224 | **Neurobiological extreme stress and its impact on offspring: A three-generation study of Holocaust survivors**

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EPV-225 | Cognitive impairment in hypertensive patients with multiple drug intolerance syndrome—Preliminary results.

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EPV-226 | **Psychosocial stressors and PTSD risk in medical personnel in Ukraine**

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EPV-227 | **Biomarkers of neurodegeneration: Comparison between iNPH, LOVA, and other neurodegenerative diseases**

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EPV-228 | **Virtual vs. in-person administration of the kaufman brief intelligence test in prader–willi syndrome: An agreement study**

L. Nunes Campos; C. Rocío Ruidíaz; M. del Pilar Jaime; A. Gerk; Mendiola; J. Stegmann
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EPV-229 | **Characterizing language aspects in people with prader–willi syndrome: A cross-sectional study**

L. Nunes Campos; F. Candela Rocha; A. Maria Fariña; C. Rocío Ruidíaz; D. Mendiola; J. Stegmann
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EPV-230 | **Isolated social cognition impairment: A novel cognitive phenotype in multiple sclerosis?**

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EPV-231 | **Associations between chronic coronary syndromes and risk of cognitive decline and depression**

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EPV-232 | Effects of Neonatal 3D Orbital Shaking on Stress-Induced Neurodegeneration in Rats

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EPV-233 | Cardiovascular factors and clinical response to CSF drainage in normal pressure hydrocephalus

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EPV-234 | Smartphone addiction and its impact on cognitive function and fatigue levels among medical students in Sudan

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EPV-235 | Fatty acid patterns and cognitive functions in an adolescent population: A cross-sectional and multicohort study

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EPV-236 | Vitamin D receptor polymorphisms as tool for early screening of senile dementia in the elderly women

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EPV-237 | Does functional cognitive disorder overlap with functional neurological disorder?

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EPV-238 | Evaluation of CCAS (Schmahmann's Syndrome) in patients with acquired non-genetic cerebellar lesions

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EPV-239 | Developing a language-dependent diagnostic tool for cognitive assessment: A methodological approach

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EPV-240 | Metacognitive intervention in youth with oncological disease - The mio study

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EPV-241 | **Abstract withdrawn**

EPV-242 | **Validation of a new discourse assessment tool for early detection of neurodegenerative diseases: A pilot study**

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EPV-243 | **Predicting the efficacy of bilateral DLPFC rTMS application in Alzheimer's disease using the RCI: A preliminary study**

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EPV-244 | **Hidden in plain sight: Heidenhain variant of Creutzfeldt–Jakob Disease**

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EPV-245 | **Characteristics of neuropsychological disorders in men with androgen deficiency syndrome**

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EPV-246 | **The effects of retatrutide used in streptozotocin-induced diabetic rats on learning and memory**

U. Keskin[1]; E. Altin[2]; B. Tekin[2]; M. Kara[2]; K. Cakircoban[2]; F. Ozatik[1]; N. Ari[3]; A. Kocak Sezgin[4]; E. Gungor[5]
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EPV-247 | **Cognitive functioning in healthy females with different levels of cognitive reserve**

U. Lazic[1]; P. Aleksic[1]; M. Sarcevic[1]; I. Dzodic[2]; A. Vrljes[2]; A. Lesic[2]; B. Salak Djokic[1]; V. Ilic[1]; G. Mandic Stojmenovic[3]; E. Stefanova[3]; T. Stojkovic[3]
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EPV-248 | **Changes in cognitive functions after carotid endarterectomy and carotid stenting**

X. Alidjanov; S. Karimov; A. Yulbarisov; B. Nosirjonov
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EPV-249 | **Transient global amnesia: Reliability of diagnosis and examination algorithm**

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EPV-250 | **Comparison of information processing speed in relapse and non-relapse phases of patients with MS using the ICA test**

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EPV-251 | The efficacy of biofeedback in enhancing neurological adaptation in martial arts athletes

Z. Akbarkhodjaeva
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EPV-252 | Neuropsychological adaptation and resilience in martial arts athletes: cognitive and emotional impacts

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EPV-253 | Role of hyperbaric oxygen therapy in gas geyser-related stroke and hypoxic brain injury

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EPV-254 | TMS-evoked potentials track neural disconnection and recovery following severe TBI

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EPV-255 | Use of mesenchymal stem cells in diffuse brain Lesions

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EPV-256 | A longitudinal retrospective study on determinants of survival of chronic patients with Disorders of Consciousness

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EPV-257 | Dynamic 31P-MRI of the anterior tibialis muscle in patients with post-COVID-19 myopathy

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EPV-258 | Severe neurological manifestations associated with Sars-Cov-2 in children

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EPV-259 | Autoantibodies to gaba receptors are associated with pathological fatigue in patients with post-COVID-19 syndrome

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EPV-260 | Neurological symptoms 3.5 Years after COVID-19: A cross-sectional study

G. Zorgör[1]; N. Bülbül[1]; E. Erdoğan[2]; B. Selbest[3]; M. Al Hasan[4]; U. Şimşek[1]; M. Ateş[5]; F. Eren[6]; Z. Kocakaya[7]; F. Erdoğan[4]
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EPV-261 | Telemedicine beyond Covid-19: The 4-year experience of a tertiary cognitive and movement disorders clinic in the Aegean

I. Stamelos; E. Angelopoulou; E. Smaragdaki; K. Vourou; E. Stanitsa; D. Kontaxopoulou; J. Papatriantafyllou; S. Papageorgiou
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EPV-262 | **Natural neurotropic autoantibodies in the blood serum of patients with COVID-19-associated ischemic strokes**

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EPV-263 | **Evaluation of psychiatric history and symptom discordance in Neuro-PASC patients: A cross-sectional study**

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EPV-264 | **Clinicoradiological and prognostic features of COVID-19-associated acute disseminated encephalomyelitis**

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EPV-265 | **Longitudinal electrophysiological follow-up in hospitalized coronavirus disease 2019 patients**

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EPV-266 | **Healthcare system around the world and COVID-19 outbreak: A ecological study**

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EPV-267 | **Late-onset anti-aquaporin 4 neuromyelitis optica triggered by COVID-19 infection**

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EPV-268 | **Cognitive complaint and post-traumatic stress disorder in a large long-covid cohort up to 23 months post-infection**

S. Indart; A. Boutelier; C. Paquet
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EPV-269 | Neurological impairment and brain fog in long-COVID: A systematic review of adult and pediatric populations

S. Chodnekar
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EPV-270 | Patients' perspective on neurological trials; gaps and opportunities toward more meaningful and inclusive research

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EPV-271 | Integration of artificial intelligence technologies into the educational process of training neurologists

J. Abdullaev
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EPV-272 | Immersive mixed reality interventions for brain anatomy education: Impact on emotions and knowledge acquisition

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EPV-273 | Triggers precipitating seizure in adult libyan patients with primary epilepsy in 2025

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EPV-274 | A rare adverse effect of intravenous levetiracetam administration: Maculopapular skin rash

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EPV-275 | Exploring the epilepsy-depression relationship with machine learning on real-world Data in Germany, France, Italy, Spain

A. Ruggieri[1]; J. Leach[1]; E. Alvarez-Baron[1]; E. Salvatori[1]; V. Di Franco[1]; A. Comandini[1]; T. Constandse[2]; M. Pili[3]; J. Gallinaro[3]; P. Farhadi Ghalati[4]; F. Bayard[5]; A. Sattar Raslan[3]; A. O'Loughlin[3]; B. Vamosi[6]; A. Cattaneo[1]
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EPV-276 | Hippocampal sclerosis as a marker of predisposition to secondary affective disorders in patients with epilepsy

A. Bolshakova; N. Shova; V. Mikhailov
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EPV-277 | Hippocampal Atrophy in Temporal Lobe Epilepsy: Associations with Clinical, Demographic, and Neuroimaging Features

A. Abbes; R. Ben Dhia; N. Gouta; M. Mhiri; M. Frih Ayed
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EPV-278 | Mapping epilepsy awareness and attitudes: Perspectives from Egypt's future healthcare providers

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EPV-279 | Clinical and encephalographic profile of febrile convulsions in Abidjan

A. Abbe[1]; Essoin-De Souza[1]; C. Agbo-Panzo[2]; N. Broh[1]; A. Beuseize[1]; N. Yeo[1]; I. Diakite[1]; K. Kouassi[1]; M. Doumbia[1]
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EPV-280 | Ketogenic diet in adults with refractory and super-refractory status epilepticus

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EPV-281 | At a loss for words: Clinical and electrographic insights from three cases of aphasic status epilepticus

A. Chotoura; V. Poulidou; A. Frontistis; D. Striki; E. Pityrigkas; Z. Kallia; E. Chatzikyriakou; M. Spilioti; V. Kimiskidis
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EPV-282 | The impact of epilepsy on child development, cognition, and behavior: A meta-analysis

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EPV-283 | Epilepsy in the context of remittent recurrent multiple sclerosis (RR-MS)

A. Garcia Maruenda; L. Quirós Illán; I. Martín Sobrino; N. Pilar; P. Gómez Ramirez; M. El Harmochi Daoud; A. Sánchez Gómez; A. Herrera Ortega; A. Hernandez Gonzalez
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EPV-284 | ABCB1 polymorphisms and Antiseizure medication resistance: Study power, effect size, and sample size considerations

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EPV-285 | Exploring the efficacy and safety of antidepressants in pediatric epilepsy: Addressing the gap in current research

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EPV-286 | Anti-GAD encephalitis revealed by an isolated epileptic seizure

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EPV-287 | Phase 1 multiple ascending dose studies demonstrate favorable safety and tolerability of BHV-7000, a Novel Kv7 Activator

B. Awsare; J. Lerner; E. Ashbrenner; H. Sevinsky; M. Bozik; S. Dworetzky; C. Jensen; R. Killingsworth; A. Ivans; I. Qureshi; V. Coric
Biohaven Pharmaceuticals

EPV-288 | Seizure characteristics of temporal lobe epilepsy with encephaloceles

C. Aykut Bingol
Berrin Aktekin

EPV-289 | Heliotropism and epilepsy. A case report of sunflower syndrome

C. Brenlla Lorenzo[1]; E. Conde[2]; A. Donaire[2]; M. Carreño[2]; M. Centeno[2]
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EPV-290 | Cenobamate and the effect on plasmatic concentration of concomitant anti-seizure medications

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EPV-291 | Impact of sleep disturbances on cognitive impairment in patients with epilepsy

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EPV-292 | Electrophysiological features in patients with a history of seizure of ruptured arterial aneurysms

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EPV-293 | Lance-Adams Syndrome: Systematic Literature review of case report analysis on EEG and treatment findings

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EPV-294 | The effects of anticonvulsants on vitamin D levels and bone metabolism in women with epilepsy

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EPV-295 | Bone mineral density assessment of women with epilepsy on long-term antiepileptic therapy

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EPV-296 | Evaluating the impact of vagus nerve stimulation on seizure frequency, intensity, quality of life and mood

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EPV-297 | Dementia is an Underacknowledged Cause of Late-onset Unexplained Epilepsy

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EPV-298 | Clinical and neuroimmunological correlations in post-stroke epilepsy

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EPV-299 | KCNK4 variant: Refractory epilepsy with facial dysmorphism, hypertrichosis, and gingival overgrowth

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EPV-300 | Cognitive profile and family dynamics of patients with psychogenic non-epileptic, epileptic, and coexisting seizure

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EPV-301 | Myoclonic status epilecticus without coma: A case series of 19 patients

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EPV-302 | First epileptic seizure in adult as a predictor of diagnosis Dyke–Davidoff–Masson syndrome: Case report

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EPV-303 | Functional gastrointestinal disorders in patients with Epilepsy: Relationship with epilepsy type, depression and anxiety

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EPV-304 | Levetiracetam-induced pancytopenia: A Systematic Review of case reports

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EPV-305 | Pregnancy outcome of mothers with epilepsy on antiseizure medicaments treatment

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EPV-306 | Cerebral cavernous malformations: Behind a quid pro quo of lesion and epileptogenic networks

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EPV-307 | Remote parenchymal hemorrhages observed following epilepsy surgery

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EPV-308 | Effect of the duration of anticonvulsant treatment on bone mineral density

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EPV-309 | Exploring atypical lafora disease: A case of genetic and clinical challenges in a mexican tertiary hospital

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EPV-310 | Beliefs, misconceptions, and practices regarding epilepsy in sudan 2024: A cross-sectional study

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EPV-311 | Seizure types in mild and moderate mental impaired patients with epilepsy

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EPV-312 | Relationship between quality of life and depression of omani patients living with epilepsy

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EPV-313 | Generalized rhythmic alpha activity in non-convulsive status epilepticus. A case report

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EPV-314 | Stigma and epilepsy: Impact of social barriers on quality of life and coping strategies

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EPV-315 | Refractory and super-refractory status epilepticus in a secondary hospital. Descriptive analysis

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EPV-316 | Alternating hemiplegia of childhood - A single center Study

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EPV-317 | Comparison of the use of cannabidiol in pediatric patients with drug-resistant epilepsy

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EPV-318 | Systematic literature review hemiconvulsion-hemiplegia-epilepsy syndrome: Unraveling a new perspective

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EPV-319 | Untargeted metabolomics reveal key metabolic changes in pediatric epilepsy: Tryptophan and gut-brain axis insights

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EPV-320 | Does co-medication with methylphenidate and lisdexamfetamine influence seizure control in focal epilepsy? A case study.

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EPV-321 | Adjunctive Cenobamate in refractory focal epilepsy: A retrospective study in real-world clinical practice

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EPV-322 | Epidemiological trends of epilepsy in Brazil: Mortality over the last 20 years

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EPV-323 | Perspectives and challenges in managing uncontrolled Epilepsy in Spain

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EPV-324 | Frequency of structural epilepsy in patients with Cerebrovascular disease at the salvador B. Gautier Hospital (HSBG)

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EPV-325 | Focal Status Epilepticus Secondary to Intracranial Dural Arteriovenous Fistula

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EPV-326 | Negative ictal symptoms mimicking stroke: A case series of six patients

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EPV-327 | EEG characteristics in patients with epilepsy and dissociative disorders

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EPV-328 | Video-game induced orofacial reflex myoclonus

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EPV-329 | Echoes of epilepsy: A youtube documentary playing in the mind—Auditory hallucinations in temporal lobe seizures

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EPV-330 | The impact of valproate discontinuation on seizure control and patient safety in idiopathic/genetic epilepsy

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EPV-331 | Epileptic palinopsia following a prolonged latent period after remote brain hemorrhage

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EPV-332 | Exploring the roles of nesfatin-1 and ghrelin as potential biomarkers in human epilepsy

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EPV-333 | Efficacy and safety of cenobamate in Spanish adults with uncontrolled focal seizures: A Phase-3 retrospective study

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EPV-334 | Defining seizure freedom in epilepsy: A pragmatic literature review

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EPV-335 | Cenobamate in generalized epilepsies and combined focal and generalized epilepsies in adult patients: A case series

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EPV-336 | Beyond seizure reduction: Evaluating the impact of multifocal cTBS on quality of life in generalized epilepsy

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EPV-337 | Temporal lobe epilepsy with amygdala enlargement - cause or consequence?

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EPV-338 | Are treatment outcomes and quality of life worse in women with juvenile myoclonic epilepsy?

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EPV-339 | Description of electrocorticographic manifestations in focal cortical dysplasia

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EPV-340 | Comparative analysis between drug-resistant and controlled patients with mesial temporal lobe epilepsy

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EPV-341 | Epilepsy beyond seizures: Exploring psychosocial determinants of treatment adherence in patients with epilepsy

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EPV-342 | MCP-1 cytokine levels in epilepsy patients following COVID-19: Insights from Uzbekistan

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EPV-343 | Impact of post-COVID-19 inflammation on epilepsy patients in Uzbekistan: An analysis of MCP-1 cytokine levels

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EPV-344 | Exploring acute intermittent porphyria: Focal status epilepticus and PRES in focus

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EPV-345 | Caught in the jerk: Navigating lance-adams syndrome and epilepsia partialis continua

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EPV-346 | Hippocampal sclerosis as a neuroimaging marker of suicidal tendencies in patients with epilepsy

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EPV-347 | Epilepsy literacy in turkish society: A pre-study

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EPV-348 | Clock drawing Test: a screening tool for cognitive impairment in people with epilepsy (PWE)

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EPV-349 | To study the knowledge, attitude and practices of Indian psychiatrists on Sudden death in epilepsy

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EPV-350 | Morphological findings in patients with drug-resistant temporal lobe epilepsy with a history of status epilepticus

S. Kravtsova; Y. Zabrodskaya; N. Paramonova; V. Nezdorovina; D. Sitovskaya; A. Vasilenko; E. Skiteva; G. Odintsova; A. Gerasimow; A. Ulitin
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EPV-351 | Epidemiological features of status epilepticus in women with epilepsy

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EPV-352 | ATP1A3-related status epilepticus: the potential benefit of early treatment with ketogenic diet

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EPV-353 | Retinal nerve fiber layer attenuation in epilepsy: A meta-analysis

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EPV-354 | Tocilizumab treatment for new onset refractory status epilepticus. Case report

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EPV-355 | Novel PCHD19 gene variant in male patients with nonsyndromic focal epilepsy

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EPV-356 | Understanding seizure potential of antidepressant medications

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EPV-357 | Anti-seizure drugs and cutaneous hypersensitivity syndromes: DRESS, SJS, and TEN

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EPV-358 | Evaluating the implementation of the finnish epilepsy care pathway: Neurologists' and pediatric neurologists' survey

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EPV-359 | Transgender health in multiple sclerosis: clinical case of a woman assigned male at birth

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EPV-360 | Patients' and doctors' googling, self-medication and self-diagnosis in Russia

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EPV-361 | Preliminary results of the first Russian study of discrimination against doctors

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EPV-362 | A Conservative estimate of the annual carbon cost of in-person major international neurological conferences

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EPV-363 | Suicide in Huntington disease: A reality we cannot ignore

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EPV-364 | Screen time as a potential trigger for migraines in young adults: A cross-sectional perspective

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EPV-365 | SUNCT: A rare type of headache related to COVID-19

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EPV-366 | Real-world evidence: Eptinezumab in patients after multiple preventive therapy failures

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EPV-367 | Fremanezumab is effective in patients with comorbid central sensitization syndromes (SSC) and migraine

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EPV-368 | Sexual dysfunction in migraine patients receiving anti-cgrp monoclonal antibodies: Evaluation with two screening test

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EPV-369 | A case of headache in outpatient practice

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EPV-370 | Behavioral and emotional burden in episodic and chronic cluster headache

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EPV-371 | Is an altered control of intracranial pressure involved in the pathogenesis of migraine?

A. Miele; C. Russo; S. Braca; G. Cretella; A. Stornaiuolo; R. De Simone
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EPV-372 | Exploring gender disparities in the effects of long-term botulinum toxin a treatment for chronic migraine

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EPV-373 | Anti-CGRP monoclonal antibodies in refractory headache associated with behçet disease

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EPV-374 | The prevalence of headaches among undergraduate medical students

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EPV-375 | Does galcanezumab improve depression and sexual dysfunction in migrainous women?

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EPV-376 | The role of high homocysteine levels in migraine with aura

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EPV-377 | Determining the gender level of men with cluster headache using the Bem's sex-role inventory

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EPV-378 | Lacosamide in acute exacerbations of trigeminal neuralgia in emergency department. A retrospective analysis

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EPV-379 | Neuroimaging utilization in telemedicine visits for migraine and headache

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EPV-380 | White matter hyperintensities in patients with vestibular migraine

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EPV-381 | A head-to-head cohort study on the efficacy and safety of Indomethacin and Ibuprofen for the acute treatment of migraine

C. Giannini; S. Braca; G. Cretella; A. Stornaiuolo; A. Miele; C. Russo; R. De Simone
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EPV-382 | Impact of specific migraine prophylactics on the occurrence of aura in episodic migraine patients

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EPV-383 | Predictors of acute headache at stroke onset: A prospective study; clinical and radiological evaluation

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EPV-384 | Minoxidil use and severe migraine attacks: A clinical observation

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EPV-385 | Dose-failure end (DFE) in subcutaneous anti-CGRP monoclonal antibody treatment: A challenge in migraine management

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EPV-386 | Cervical meningioma underlying facial episodic paresthesia, tinnitus, and vertigo: A case report

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EPV-387 | Relationship between inflammatory markers of cerebrospinal fluid and post-dural puncture headache

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EPV-388 | Comparing personality profiles of episodic and chronic cluster headache using the MMPI-3

G. Zmork Martinez; A. Higuera Ruiz de la Hermosa; L. Portocarrero Sánchez; J. Díaz de Terán
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EPV-389 | Evaluation of personality profiles in cluster headache patients via the minnesota multiphasic personality inventory-3

G. Zmork Martinez; A. Higuera Ruiz de la Hermosa; L. Portocarrero Sánchez; J. Díaz de Terán
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EPV-390 | A rare case of cluster-like headache following intracranial endovascular procedures

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EPV-391 | Effectiveness and predictors of response to high-flow oxygen in patients with cluster headache – A service evaluation

P. Amarasena; L. Alves; M. Njohjam; W. Sulaiman; M. Villar-Martinez; N. Karsan; P. Goadsby
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EPV-392 | Botulinumtoxin a for post-traumatic headache: A systematic review of case reports and case series

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EPV-393 | Navigating intracranial hypotension syndrome: A silent challenge in modern neurology

I. Nitu; A. Ribigan; A. Resiga; M. Moldovan; C. Andrei-Cristian; S. Stefan; S. Socolov; F. Antochi
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EPV-394 | Greater occipital nerve block in episodic cluster headache: An ambispective cohort study

I. Ros González; Á. Sierra Mencía; R. Navarro González; E. Varas Martíb; M. Peñas García; A. Recio García; Á. Guerrero Peral
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EPV-395 | Tolosa–hunt syndrome, a challenge for neurology

J. Pérez Ceballos
Renata Petruta Dodu

EPV-396 | Reversible cerebral vasoconstriction syndrome: Not just a "reversible" condition. Case series and literature review

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EPV-397 | Magnetic resonance imaging in migraine: Predictors of white matter lesions

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EPV-398 | Vascular insights into stroke and migraine association in a clinical cohort of over 700 patients

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EPV-399 | Investigating the burden of medication overuse in episodic and chronic migraine: A comparative analysis

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EPV-400 | Occipital nerve stimulation in patients with refractory chronic cluster headache: Long-term follow-up

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EPV-401 | Effectiveness and safety of eptinezumab in patients with refractory chronic migraine in a headache unit

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EPV-402 | Impact of multiple sclerosis and trigeminal neuralgia on quality of life: A retrospective observational study

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EPV-403 | Clinical characteristics of idiopathic intracranial hypertension at a Tertiary University Hospital

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EPV-404 | Spontaneous intracranial hypotension: A case report

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EPV-405 | Identifying risk markers for triptan-failure among first-time users. A real-world retrospective cohort study

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EPV-406 | Triptans treatment patterns among first-time users. A real-world retrospective cohort study

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EPV-407 | Headache associated with cardiac angiographic intervention: Case series

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EPV-408 | Spontaneous intracranial hypotension after coughing bout, in a patient with idiopathic intracranial hypertension

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EPV-409 | Burden of migraine: An Egyptian study of prevalence, disability, and Insomnia

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EPV-410 | Prevalence of screen-related headache & migraine among children & adolescents: A systematic review and meta-analysis

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EPV-411 | Venous circulation disorders and non-specific headache syndromes: A prospective study

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EPV-412 | Experience in implementing anti-CGRP mAbs in clinical practice under financial constraints in war-affected patients

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EPV-413 | Predictors of cranial autonomic symptom frequency in cluster headache

N. Karsan; P. Amarasena; L. Bastos Salves; M. Villar Martinez; D. Moreno Ajona; P. Goadsby
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EPV-414 | Evaluation of crystal-clear days in migraine patients receiving CGRP monoclonal antibodies

N. Liguori; M. Silvestro; I. Orologio; L. Tartaglione; V. Dortucci; M. Marziani; F. Chianese; A. Tessitore; A. Russo
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EPV-415 | Clinical features of patients with migraine depending on vitamin D level introduction

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EPV-416 | Hyperprolactinaemia and associated factors among treatment-seeking patients with migraine (PwM) in Tanzania

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EPV-417 | Sex hormones as a key factor in medication-overuse headache: Insights and perspectives

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EPV-418 | Migraine research with smartwatch application (MIRA) - A prospective migraine study with wearables

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EPV-419 | Efficacy of Eptinezumab in migraine patients with prior CGRP antibody treatment: Insights from a tertiary care hospital

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EPV-420 | Hormonal influence on migraine: Efficacy of anti-CGRP antibodies during the perimenstrual phase of the female cycle

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EPV-421 | Short-term psychodynamic psychotherapy: Profiling responders and predictive factors

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EPV-422 | Migraine and structural brain changes: A systematic review

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EPV-423 | Chronic migraine and anti-CGRP monoclonal antibodies: 3-year treatment persistence in real-world practice

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EPV-424 | Preventive treatment for chronic migraine: Patient experiences and perspectives

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EPV-425 | Immunomodulatory therapy effect on the nervous system: A focus on migraine headaches

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EPV-426 | Poor lifestyle and Life's Essential 8 are linked to a higher risk of new-onset migraine

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EPV-427 | Migraine triggers and severity among libyan medical students during ramadan fasting

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EPV-428 | Exploring the mechanisms behind the therapeutic effects of vagus nerve stimulation

S. Tukaiev[1]; J. Alves Ferreira[2]; N. Vysokov[3]; Y. Gachshenko[3]; D. Toleukhanov[3]; I. Brak[4]; G. Datkhabayeva[5]; O. Korbush[1]; S. Danylov[6]; V. Komarenko[6]; M. Makarchuk[1]
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EPV-429 | EEG frequency patterns as indicators of emotional burnout during the anxiety-Tension phase

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EPV-430 | Hippocampal lesions on diffusion-weighted imaging and memory outcomes in transient global amnesia: Spanish cohort study

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EPV-431 | Transient global amnesia: Pathophysiology and prognosis

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EPV-432 | Posterior cortical atrophy phenotype due to a GRN gene mutation

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EPV-433 | Drug-Induced yawning: Mechanisms, patterns, and clinical applications

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EPV-434 | Differential Diagnosis for Sudden Visual Deficits: A Case Series and Literature Review on Anton-Babinski Syndrome

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EPV-435 | Abstract withdrawn

EPV-436 | Endoplasmic reticulum dysfunction as a frontier in the pathogenesis of ALS- a historical perspective

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EPV-437 | Historical milestones in neurology for promotion of global brain health

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EPV-438 | Fronto-temporal dementia and lysosomal lipid storage: the pick cousins and their contributions to neurology

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EPV-439 | Trends in mortality from bacterial meningitis in the United States: A CDC WONDER analysis (2018-2023)

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EPV-440 | Neurological manifestations associated with a novel diagnosed HIV infection

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EPV-441 | West Nile Virus neuroinvasive disease: analysis of hospitalized cases in a tertiary care center from Southern Europe

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EPV-442 | Two very rare causes of meningitis: Listeria monocytogenes and Klebsiella pneumoniae

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EPV-443 | Cryptococcal meningitis and HIV: The correct diagnosis of a young patient referred with a diagnosis of ischemic stroke

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EPV-444 | Rhombencephalitis and myelitis due to Listeria infection in an immunocompetent patient

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EPV-445 | Study of varicella-zoster reactivation in the central nervous system in the guadalajara population

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EPV-446 | Aseptic meningitis induced by metronidazole: A case report

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EPV-447 | Sporadic fatal insomnia: A systematic review of pathogenesis, biomarkers, and therapeutic avenues

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EPV-448 | Acute necrotizing encephalomyelitis caused by listeria monocytogenes: A case report

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EPV-449 | When neurosyphilis surprises: Meningoencephalitis with ictal-onset as an unusual presentation

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EPV-450 | Is Rickettsia conorii an overlooked cause of Bilateral Facial Palsy? A case series

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EPV-451 | Cerebral vasculopathy leading to brainstem stroke and encephalitis after ophthalmic VZV reactivation: Shared etiology?

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EPV-452 | Personal medical history—friend of foe? A case report

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EPV-453 | Lungs to spinal cord: Mycoplasma pneumoniae unveiled as a rare cause for longitudinally extensive transverse myelitis

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EPV-454 | Filoviral infection from a neurological perspective

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EPV-455 | An unusual case of overlap of neuro-AIDS and CMV encephaloradiculitis in a patient treated with biological therapy

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EPV-456 | Autoimmune antibody panel negative autoimmune encephalitis case

T. Kaya; M. Erkan; M. Tutuncu; Z. Gul; V. Kabeloglu; A. Soysal
Bakirkoy Prof Dr Mazhar Osman Training and Research Hospital, Neurology Department, Istanbul, Turkey

EPV-457 | Nerve Root Enhancement and albuminocytologic dissociation in four SOD1-Linked Amyotrophic Lateral Sclerosis Patients

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EPV-458 | Risdiplam in adult patients with spinal muscular amyotrophy: Effectiveness after one year of follow-up

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EPV-459 | Neutrophil-to-lymphocyte ratio as a possible tool to monitor disease progression in amyotrophic lateral sclerosis

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EPV-460 | Apathy and its relation with motor severity in undemented amyotrophic lateral sclerosis

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EPV-461 | Decremental response in patients with amyotrophic lateral sclerosis

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EPV-462 | A Case of ALS with an SQSTM1 mutation: implications for individualized therapeutic strategies

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EPV-463 | Study of body composition in ALS patients

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EPV-464 | Thrombomodulin-positive neurons in thoracic intermediolateral nucleus in amyotrophic lateral sclerosis

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EPV-465 | Co-existence of amyotrophic lateral sclerosis and myasthenia gravis with clustered AchR antibodies: A case report

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EPV-466 | Progressive generalized muscular weakness presenting as severe post-traumatic foot drop

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EPV-467 | Late-onset tay–sachs disease: A four-decade diagnostic journey

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EPV-468 | Glucose and lipid metabolism disorders in adults with spinal muscular atrophy type 3

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EPV-469 | Fecal microbiota transplantation for Parkinson's disease: A systematic review

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EPV-470 | A rare case of tofersen-associated myelitis: Challenges in Als treatment

P. Hernández Vitorique; C. Ortega Hiraldo; M. Carbonell Corvillo; F. Pinel Rios; M. Mañez Sierra
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EPV-471 | Syphilitic amyotrophy (SA): A forgotten entity in the neurological differential diagnosis

P. Gómez Ramírez; M. Nieto Palomares; A. García Maruenda; M. El Harmochi Daoud; A. Sánchez Gómez; A. Herrera Ortega; I. Martín Sobrino; A. Hernández González
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EPV-472 | Motor neuron disorder in the context of sjögren's syndrome: A case report

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EPV-473 | Neuroimmune dysregulation in ALS: Meta-analysis of CSF cytokine and chemokines

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EPV-474 | Safety of repeated intravenous or intrathecal transplantation of Wharton's jelly derived mesenchymal stem cells in ALS

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EPV-475 | Action-language processing in motor neuron diseases

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EPV-476 | Strategies for choosing therapy in adult patients with SMA in clinical practice in Russia

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EPV-477 | Impulse control disorders in idiopathic Parkinson's disease

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EPV-478 | Aspiration Pneumonia Mortality in Parkinson's Disease: Trends & disparities in the U.S. (1999-2023)

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EPV-479 | Two sides of the spectrum: Exploring the coexistence of Fhar's disease and Parkinson disease

A. Lagüela[1]; V. Anciones[1]; A. Rebollo[1]; V. Fernández[1]; L. Fernández[1]; C. Valido[1]; M. Martínez[1]; Á. López[1]; M. Callejo[1]; N. Marcos[1]; G. Bilbao[2]; M. Ruíz[2]; A. Rodríguez-Antigüedad[1]; T. Fernández[3]; B. Tijero[3]; M. Ruíz[3]
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EPV-480 | From bench to bedside: A meta-analysis of translational research in duchenne muscular dystrophy

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EPV-481 | Progressive supranuclear palsy, a multifaceted pathology

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EPV-482 | Treatment of head tremor with botulinum toxin: a descriptive analysis of injection patterns and outcomes

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EPV-483 | MRgFUS thalamotomy in patients over 80 years with essential tremor: Is age a contraindication?

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EPV-484 | Pathogenic variant in the POLR3A gene in a patient with predominantly vermian ataxia and head tremor

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EPV-485 | Impacts of dysarthria on quality of life in Parkinson‘s disease

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EPV-486 | Use of inhaled levodopa in morning akinesia: has it an impact on other fluctuations in Parkinson´s disease? Case report

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EPV-487 | Social stigma predicts discontinuation of Levodopa-Carbi-Dopa intestinal gel infusion therapy in parkinson disease

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EPV-488 | Phase-amplitude coupling in the STN and its clinical correlates in Parkinson's disease

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EPV-489 | Subthalamic deep brain stimulation and impulse control disorders in PD patients: own results and unresolved issues

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EPV-490 | Smell comparison among patients with Bipolar Disorder and parkinsonian symptoms, Parkinson's Disease and controls

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EPV-491 | Multifaceted impulse control disorders in early-onset Parkinson's disease: A comprehensive case analysis

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EPV-492 | Flask-based levodopa therapy among Tunisian patients with advanced Parkinson's disease: The old but gold technique

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EPV-493 | Vitamin B12 levels among Parkinson's disease patients and its motor clinical correlates

A. Rekik; A. Mili; K. Jemai; H. Slimene; E. Jarrar; S. Naija; A. Hassine; S. Ben Amor
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EPV-494 | Abstract withdrawn

EPV-495 | Analysis of interleukin-6 levels in patients with Parkinson's disease by disease

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EPV-496 | Hemichorea–hemiballism: A manifestation of hyperglycemia without ketosis even with normal blood glucose

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EPV-497 | Switching from LCIG infusion to LECIG infusion—data from the ELEGANCE interim analysis

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EPV-498 | Register for functional motor disorders in vienna: An integrative treatment approach (FMD-VITA)

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EPV-499 | Intensive aerobic exercise in Parkinson's disease: preliminary results from the multicentric PD 2.0 study

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EPV-500 | The role of cognitive reserve in coping with subjective cognitive complaints: an exploratory study on people with PD

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EPV-501 | Can art therapy improve emotion recognition in Parkinson's disease? A pilot study

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EPV-502 | Long-term dopaminergic treatment effect in de novo Parkinson's disease: the DNA-PD digital longitudinal study

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EPV-503 | Enhancing patient outcomes through lived insights in Parkinson's Disease care

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EPV-504 | Levodopa effects in swedd: Clinical and kinematic insights from a case report

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EPV-505 | Device-aided therapies (DATs) in Parkinson's disease (PD). The DATs-PD GETM Spanish registry

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EPV-506 | Changes in serum MCP-1 concentration in Parkinson's disease and its association with neuroinflammatory processes

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EPV-507 | Parkinson's disease is characterized by an increased concentration of trace elements in the blood serum and vitamin D

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EPV-508 | Serotonin levels in patients with different forms of Parkinson's disease in the population of Uzbekistan

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EPV-509 | Non-motor symptoms in patients with Parkinson's disease in the Kyrgyz Republic

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EPV-510 | Isoniazid-related bithalamic toxicity and parkinsonism: a case report

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EPV-511 | Paroxysmal events secondary to cryptogenic brainstem and diencephalic lesions

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EPV-512 | A phase 2 RCT to investigate oral semaglutide tablets for Parkinson disease

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EPV-513 | Abstract withdrawn

EPV-514 | The path to diagnosis of early-onset Parkinson's disease – a slow and bumpy ride

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EPV-515 | Clinical outcome of botulinum toxin injections in patients with post facial palsy synkinesis

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EPV-516 | Considering Parkinson's disease quality of life: Patients linked to illness time frame and non-motor symptoms

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EPV-517 | A survey on the onset of non-motor symptoms in multiple system atrophy

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EPV-518 | Absolute beta power predicts fatigue scores in Parkinson's disease

A. Hurtado-Martínez[1]; M. Martín Buro García de Dionisio[2]; Y. González-Zamorano[3]; M. Moreno-Verdú[4]; F. Sánchez-Cuesta[1]; I. Muro[1]; J. Romero[1]
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EPV-519 | A qualitative study exploring the perception of pain in people with Parkinson's disease

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EPV-520 | Impact of escitalopram on Parkinson's tremor and role of dopamine agonists in symptom management

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EPV-521 | When gait tells a genetic tale: a case study of SCA8

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EPV-522 | Movement disorders in emergencies: A single-center cohort study

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EPV-523 | MASCOT: A randomized, placebo-controlled phase 3 trial of amlenetug in patients with multiple system atrophy

L. Kjærsgaard; M. Nørbæk Jørgensen; S. Zanigni; J. Wiedemann; J. Luthman
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EPV-524 | Glioma in Parkinson's disease patients treated with the deep brain stimulation of the subthalamic nucleus-Case series

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EPV-525 | Stones in the neural path: Fahr syndrome as a manifestation of familial hypoparathyroidism

M. Vargas Cobos; M. Capra; A. De Luca; C. Gómez López de San Román; L. Caballero Sánchez; D. Cerdán Santacruz; A. Mendoza Rodriguez; A. Castrillo Sanz
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EPV-526 | Functional neurologic disorders in Republic of Moldova – A case series

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EPV-527 | Patient perspectives on the therapeutic effects of botulinum neurotoxin in cervical dystonia

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EPV-528 | Motor state, park-pain and noradrenergic subtype of Parkinson's disease

Y. González-Zamorano[1]; M. Chiriac[2]; C. Georgiou[3]; V. Leta[4]; P. Svennigsson[5]; K. Bannister[6]; K. Poplawska-Domaszewicz[4]; K. Chaudhuri[4]
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EPV-529 | The Burden of Friedreich Ataxia—a Global Patient and Caregiver Study Design

L. Corben[1]; P. Giunti[14]; F. Saccà[2]; M. França Júnior[3]; M. Grobe-Einsler[4]; M. Kauffman[5]; C. Marelli[6]; A. Darling[7]; H. Shinawi[8]; B. Kearney[9]; J. Greenfield[10]; M. Rai[11]; J. Schmier[12]; J. Tsai[12]; S. Jayade[12]; A. Drenth[13]; A. Harrington[13]; M. Gianinazzi[13]
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EPV-530 | In the shadows of innovation: Unveiling awareness gaps in parkinson's device-assisted therapies—A survey study

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EPV-531 | Clinical, structural, and network-based radiological analysis of functional motor disorders: A case-control study

M. Demirel[1]; M. Karataş[2]; İ. Yıldız[7]; A. Fil-Balkan[8]; T. Demirsöz[7]; E. Gümeler[3]; K. Karlı-Oğuz[4]; B. Elibol[6]; G. Yalçın-Çakmaklı[1]
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EPV-532 | Neural repair reagent ALEETO™ can efficiently treat amyotrophic lateral sclerosis (ALS), from bench to clinic

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EPV-533 | The intersection of nutritional interventions and DMD management: A systematic review of dietary impacts

M. Abouelseoud[2]; O. Hafez[2]; A. mohamed[2]; A. Abouzeid[2]; M. Walaa[2]; N. Abdelmalek[2]; A. Elsayed[1]; M. Elsayed[1]
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EPV-534 | Psychosocial impacts of duchenne muscular dystrophy: A meta-analysis of quality of life studies

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EPV-535 | Evaluation of the cognitive impairments and depressive symptoms in patients with Parkinson's disease

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EPV-536 | Hemichorea in context of fluctuating glycemic control

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EPV-537 | Combining deep brain stimulation and foslevodopa/foscarbidopa pump in advanced Parkinson's disease: A case report

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EPV-538 | The lived experiences of antero-medial globus pallidus internus deep brain stimulation in Tourette syndrome

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EPV-539 | The impact of conventional and adaptive deep brain stimulation on systemic oxy-inflammation in Parkinson's disease

N. Maiorana[1]; S. Marceglia[1]; S. Mrakic-Sposta[2]; A. Vezzoli[2]; M. Guidetti[1]; T. Bocci[1]; S. Oliveri[1]; R. Ferrucci[1]; A. Priori[1]
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EPV-540 | Lipidic changes and neuroprotective effects of tDCS in Parkinson's Disease: preliminary data and insights

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EPV-541 | Sarcopenia in Parkinson' s disease: Assessing with a new method, temporal muscle thickness

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EPV-542 | GAD 1 antibody induced ataxia in a Type 2 diabetic Patient

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EPV-543 | Unusual presentation of POLR3A-associated leukodystrophy—two cases reported

N. Mazalica; M. Sarcevic; A. Milovanovic; A. Tomic; V. Markovic; M. Brankovic; A. Marjanovic; N. Dragasevic Miskovic
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EPV-544 | Social cognition in different types of neurodegenerative cerebellar ataxias

O. Tamaš[1]; M. Kostić[2]; B. Salak Đokić[1]; E. Stefanova[1]; A. Milovanović[1]; M. Kovačević[1]; N. Veljančić[1]; N. Dragašević-Mišković[1]
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EPV-545 | Unilateral MRgFUS thalamotomy in essential tremor: Reporting calvarial bone infarction as a potential complication

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EPV-546 | Real-world data on the use of safinamide in a Parkinson's disease unit in Madrid, Spain

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EPV-547 | Parkinson's disease and legal capacity

P. Voskou
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EPV-548 | The Role of MAO-B inhibitors in fatigue in Parkinson's disease

P. Pacilio; S. Galli; E. Bianchini; M. Alborghetti; L. De Carolis; P. Lombardo; F. Garramone; M. Salvetti; D. Rinaldi
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EPV-549 | Innovative approaches to DMD: A systematic review of emerging therapies and their mechanisms of action

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EPV-550 | Neurophysiological and clinical effect of botulinum toxin in essential blepharospasm

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EPV-551 | Difficulty in teeing off on the golf course is a red flag for Orthostatic Tremor

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EPV-552 | Clinical and genetic characterization of woodhouse-sakati syndrome in Iranian patients: Insights from five cases

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EPV-553 | GPER1 attenuates antipsychotic-induced neurological damage in vitro and in vivo models

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EPV-554 | Asymptomatic nigrostriatal dysfunction in a CANVAS patient with a biallelic repeat expansion in RFC1

S. Casanova[1]; I. Barbosa[2]; F. Costa[2]; A. Martins Campos[3]; J. Parente Freixo[4]; J. Oliveira[4]; P. Barros[1]; M. Malaquias[1]
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EPV-555 | A case of very late onset SCA27B

S. Kalampokini[1]; P. Bargiotas[2]; S. Labrianides[3]; C. Votsi[4]; A. Georghiou[4]; K. Christodoulou[4]; G. Hadjigeorgiou[2]
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EPV-556 | Breast carcinoma and progressive supranuclear palsy – Etiological relation or simple coincidence?

S. Moreira; A. Costa; A. Câmara; S. Lopes; J. Araújo; S. Varanda
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EPV-557 | Intractable postoperative delirium following deep brain stimulation surgery for Parkinson's disease: A case report

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EPV-558 | When the pocket does not hide an infection

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EPV-559 | Genetic and clinical data in familial Parkinson's disease: Evaluation of motor, non-motor, demographic data

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EPV-560 | Familial GBA1 mutation in Parkinson's disease: A comparative study with genetically negative patients

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EPV-561 | Genetic mutations and clinical progression in familial Parkinson's disease: A retrospective analysis over three years

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EPV-562 | Archimedes spiral in patients with essential tremor treated with deep brain stimulations

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EPV-563 | Acute hemichorea in a 76-year-old patient: A diagnostic challenge

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EPV-564 | Essential tremor and essential tremor-plus: A comparative analysis

V. Mendes Ferreira; M. Magriço; D. Krupka; M. Serôdio; R. Ventura; A. Sobral-Pinho; B. Meira; P. Bugalho
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EPV-565 | Efficacy of fecal microbiota transplantation in Parkinson's disease: A systematic review and meta-analysis

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EPV-566 | Patient-centric approaches in DMD research: A Systematic review of quality of life outcomes

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EPV-567 | A novel usage of alphasynuclein as a biomarker for screening parkison's disease

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EPV-568 | Efficacy of levodopa/carbidopa intestinal gel infusion on neuropsychiatric fluctuations in parkinson's disease

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EPV-569 | Neurotoxin injections in the treatment of essential tremors – A systematic review

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EPV-570 | Efficacy and safety of evobrutinib in relapsing multiple sclerosis: A meta-Analysis of randomized trials

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EPV-571 | On Siponimod's path: Tracking mobility, mind, and MS progression

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EPV-572 | Multiple sclerosis & systemic lupus erythematosus: Is a common treatment possible?

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EPV-573 | Efficacy and safety of ocrelizumab in routine clinical practice

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EPV-574 | Natalizumab versus Fingolimod—clinical and demographic analysis of MS patients -5 year observational study

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EPV-575 | Expression of immune-checkpoint in multiple sclerosis regarding the presence of infections and disease progression

A. Garcia Leal; G. Torres Iglesias; M. Lopez Molina; L. Vidal Guerrero; M. Fernandez Fournier; B. Chamorro Hernández; I. Puertas Muñoz; E. Diez-Tejedor; M. Gutierrez-Fernandez; L. Otero-Ortega
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EPV-576 | Effect of fampridine on functional brain networks in multiple sclerosis patients: A resting state EEG study

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EPV-577 | Probiotics for oxidative stress in multiple sclerosis: secondary analysis of an RCT

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EPV-578 | BRILL -EU study– (Briumvi® - Real World Experience Study): non-interventional study to evaluate the use of ublituximab

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EPV-579 | Efficacy and tolerability of THC and CBD formulations in patients with multiple sclerosis suffering from spasticity

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EPV-580 | Navigating the dual burden: Understanding the relationship between neurofibromatosis Type 1 and multiple sclerosis

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EPV-581 | Effect of air pollution on Prevalence and Age at Diagnosis of Multiple Sclerosis

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EPV-582 | **Cladribine in older people with Multiple Sclerosis: the experience of a tertiary centre**

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EPV-583 | **Expression of miR-30b-5p in plasma-derived extracellular vesicles as diagnostic marker in central demyelinating diseases**

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EPV-584 | **Hypogammaglobulinemia in multiple sclerosis patients receiving ocrelizumab therapy: Who is at risk for infections?**

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EPV-585 | **Ocrelizumab in real clinical practice at a Moscow Hospital. Case of anti-CD20-induced inflammatory bowel disease (IBD)**

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EPV-586 | **Interconnection of fatigue, affective, cognitive disorders with functional status, brain volumes in multiple sclerosis**

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EPV-587 | **Use of high-efficacy therapies of early- and late-onset multiple sclerosis compared to adult-onset multiple sclerosis**

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EPV-588 | **A rare presentation of stiff-person syndrome (SPS) and myelin oligodendrocytes glycoprotein antibody Disease (MOGAD)**

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EPV-589 | **Schizophrenia as the sole clinical presentation of pediatric-onset MS: A case report and systematic review**

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EPV-590 | **Expanded monitoring of patients with MS: Insights from the Vienna MS-nurse pilot project in clinical practice**

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EPV-591 | Cladribine treatment beyond year 4: Experience of our center

F. Peral Dorado; A. Paz Tamayo; A. Romero Villarrubia
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EPV-592 | Cognitive and motor trajectories in multiple sclerosis phenotypes

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EPV-593 | Risk of progression independent of relapse activity among different regimes of DMTs in people with multiple sclerosis

G. Schirò[1]; P. Ragonese[2]; S. Iacono[1]; G. Callari[1]; G. Vitello[1]; B. Palmeri[1]; F. Ruscica[1]; G. Sorbello[2]; M. Andolina[2]; A. Calì[2]; G. Salemi[2]; L. Grimaldi[1]
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EPV-594 | Comparison of the efficacy of fingolimod and ocrelizumab treatments in relapsing remitting multiple sclerosis patients

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EPV-595 | Impact of natalizumab exposure duration on clinical progression in multiple sclerosis: A retrospective study

H. Boussaid
Narjes Gouta

EPV-596 | Influence of clinical and biological factors on second-line MS treatment response in Tunisia: A retrospective study

H. Boussaid
Mariem Mhiri

EPV-597 | Multiple sclerosis (MS) epidemiology in our area: Relevance of MS in old age

I. Martín Sobrino; M. Cervantes Navarro; L. Quirós Illán; M. El Harmochi Daoud; P. Nieto Palomares; A. García Maruenda; P. Gómez Ramírez; A. Sánchez Gómez; A. Herrera Ortega; A. Hernández González
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EPV-598 | Vaccine-induced cellular and humoral response to SARS-Cov-2 in multiple sclerosis patients on ocrelizumab

J. Drulovic[1]; O. Tamas[1]; D. Miljkovic[2]; N. Momcilovic[1]; V. Radisic[1]; M. Andabaka[1]; N. Djedovic[2]; N. Veselinovic[1]; M. Budimkic[1]; S. Mesaros[1]; T. Pekmezovic[3]
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EPV-599 | A Randomized study (CHARGE) to evaluate peginterferon beta-1a in participants aged 10-18 with relapsing-remitting MS

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EPV-600 | Neuromyelitis optica spectrum Disorder and Sjögren's syndrome: A challenging case of longitudinally extensive myelitis

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EPV-601 | Isolated cognitive relapses: A possible phenotype of multiple sclerosis relapse

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EPV-602 | The impact of stem cell transplantation in multiple sclerosis: A systematic literature review

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EPV-603 | A systematic framework for assessing and monitoring disability accumulation in ms for integration into clinical practice

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EPV-604 | Can neurofilament light chain (NFL) differentiate peripheral from central demyelination?

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EPV-605 | Epidemiology and clinical management of non-Relapsing secondary progressive multiple sclerosis in the benelux region

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EPV-606 | Alterations in the expression of regulatory molecules in B Cells: Implications for disability progression in MS

M. López Molina; L. Vidal Guerrero; G. Torres Iglesias; A. García Leal; B. Chamorro; I. Puertas; E. Díez-Tejedor; M. Gutiérrez-Fernández; L. Otero-Ortega
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EPV-607 | Identification of high-efficacy treatment candidates in MS through immunophenotypic characterization of immune system

L. Vidal Guerrero; M. López Molina; G. Torres Iglesias; A. García Leal; B. Chamorro; I. Puertas; E. Díez-Tejedor; M. Gutiérrez-Fernández; L. Otero-Ortega
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EPV-608 | Expression of immune checkpoint molecules as biomarkers of treatment response in multiple sclerosis patients

M. López Molina; L. Vidal Guerrero; A. García Leal; G. Torres Iglesias; B. Chamorro; I. Puertas; E. Díez-Tejedor; M. Gutiérrez-Fernández; L. Otero-Ortega
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EPV-609 | CADASIL and multiple sclerosis: Diagnostic challenges in differentiating white matter lesions

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EPV-610 | Real clinical experience with second-generation S1P receptor modulators in multiple sclerosis patients

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EPV-611 | Evolution of patients diagnosed with Multiple Sclerosis (MS) without disease-modifying treatments (DMTs)

M. Nieto Palomares; A. García Maruenda; P. Gómez Ramírez; M. El Harmochi Daoud; A. Sánchez Gómez; A. Herrera Ortega; A. Hernández González; M. Corrales Arroyo; M. Del Real Francia; M. Gudín Rodrigez Magariños; I. Martín Sobrino
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EPV-612 | Nystagmus as a predictor of exacerbation of multiple sclerosis in pregnant women

M. Kolmykova; Y. Strelchenko; D. Labunskiy; S. Kiryukhina; T. Sakharova
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EPV-613 | Variations of the cortical excitability in patients with RRMS and comorbid primary headache

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EPV-614 | Benefits of 12-week melatonin supplementation on lipid profile and body composition in multiple sclerosis patients

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EPV-615 | Eculizumab for Severe acute relapse in anti AQP4-Ab+ neuromyelitis optica spectrum disorders (NMOSD): A case report

M. Rotolo; R. Capuano; C. Giordano; A. Rienzo; U. De Marca; A. D'amico; F. Di Filippo; S. Scannapieco; P. Barone; M. Di Gregorio
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EPV-616 | Prognostic factors in adult and pediatric onset multiple sclerosis: a systematic literature review

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EPV-617 | A real-world survey assessing the extent and clinical impact of misdiagnosis for patients with AQP4-Ab+ NMOSD in Europe

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EPV-618 | Evaluation of cognitive impairments in multiple sclerosis: A comparative analysis of RCFT and SDMT

M. Koseoglu[1]; M. Demir[1]; A. Yaman Kula[2]; E. Temiz Adıgüzel[1]; G. Yaman[1]; A. Güngördü[1]; T. Yazar[1]; S. Ozben[3]
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EPV-619 | Neuromyelitis optica with a positive AQP4 Antibody in a patient defying the classical demographics b

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EPV-620 | The assessment of BMI, lipid and carbohydrate metabolism parameters in patients with RRMS

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EPV-621 | The role of selected serum peptide hormones in patients with RRMS treated with II-line drugs

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EPV-622 | Evaluation of selected serum adipocytokines levels in patients with RRMS treated with second-line therapies

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EPV-623 | Interaction between hidden symptoms and disability level in multiple sclerosis patients

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EPV-624 | The Arrhythmogenic profile of disease-modifying therapies in multiple sclerosis

O. Hamdan; R. Abu Zayed; Y. Alajlouni; Y. Zayed
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EPV-625 | Neuromyelitis optica spectrum disorders: Comparative study of seropositive versus seronegative forms in a tunisian cohort

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EPV-626 | Baseline characteristics in the tolebrutinib Phase 3 primary progressive multiple sclerosis PERSEUS clinical trial

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EPV-627 | Recurrent late-onset neutropenia induced by ocrelizumab

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EPV-628 | Efficacy and safety of intravenous natalizumab in multiple sclerosis patients Older than 50 Years Old

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EPV-629 | Impact of stigma on patients with Parkinson's disease. Psychological, occupational, and social dimensions

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EPV-630 | Pediatric multiple sclerosis: Experience of the Marrakech University Hospital

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EPV-631 | Predictors of disability progression in multiple sclerosis patients: A retrospective analysis

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EPV-632 | Evolutionary profile of pediatric-onset multiple sclerosis

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EPV-633 | The torturous quest to diagnosing a primary CNS demyelinating disorder

S. Palma; A. Cordeiro; A. Rachão
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EPV-634 | Dysbiosis in patients with multiple sclerosis onset

S. Talapbek Kyzy
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EPV-635 | Severe and atypical multiple sclerosis: A diagnostic challenge in Marburg's variant

S. Daoudi[1]; Y. Yousfi[2]; R. Adjmi[1]; S. Bouaouina[1]; G. Imache[1]; A. Mazari[1]; N. Bahmani[1]; H. Siahmed[1]
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EPV-636 | Experience of cladribine treatment in multiple sclerosis patients at Bilkent City Hospital

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EPV-637 | Varicella–zoster virus vasculitis in the context of natalizumab treatment in a patient with multiple sclerosis

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EPV-638 | Features of the clinical course of multiple sclerosis in elderly patients

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EPV-639 | Multiple sclerosis and amyotrophic lateral sclerosis overlap: A case report

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EPV-640 | Neutral lipid storage disease with myopathy in two siblings

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EPV-641 | Investigation of the relationship between single-fiber EMG and myasthenia gravis

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EPV-642 | "Very" late-onset Pompe disease—case presentation

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EPV-643 | Myotubular myopathy in an adult

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EPV-644 | Development and validation of the myotonia symptom checker

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EPV-645 | Pupil dynamics as physiological biomarker in Duchenne muscular dystrophy

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EPV-646 | Myopathy, axonal sensory neuropathy and myelopathy in MADD: A case-report

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EPV-647 | Difficulties in diagnosing a very rare disease: Mitchell Syndrome, A heterozygous mutation in Acox1 gene

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EPV-648 | Seronegative myasthenia gravis: Clinical and neurophysiological characteristics from a neuromuscular center in Brazil

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EPV-649 | Role of muscle biopsy in mitochondrial myopathy: genotype-phenotype correlation

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EPV-650 | Assessment of quality of life in myasthenia gravis patients in central Kazakhstan: A case series with MGQOL15

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EPV-651 | Efgartigimod alfa in myasthenia gravis: Searching for patient profiles

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EPV-652 | Subjective assessment of sleep quality in adult patients with dystrophinopathy: A preliminary single center experience

E. Olivieri[1]; L. Ferullo[1]; L. Poli[2]; B. Risi[3]; V. Bozzoni[2]; B. Labella[1]; A. Padovani[1]; M. Filosto[1]
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EPV-653 | Vascular variant of late-onset pompe disease: A case study

F. Peral Dorado; I. Pérez Ortega; A. Carvajal Hernández
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EPV-654 | Real-world experience with ravulizumab in myasthenia gravis: Efficacy, challenges, and need for combination therapy

J. Fuwa; G. Watanabe; K. Tsukita; T. Miyamoto; N. Tokashiki; Y. Suzuki
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EPV-655 | CANVAS: "This story sounds familiar to me". A series of cases

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EPV-656 | Case series of primary skeletal muscle peripheral T-cell lymphoma

H. Sato[1]; S. Harigae[1]; A. Tamagake[1]; G. Watanabe[1]; K. Tsukita[1]; E. Furukawa[2]; N. Oka[3]; T. Nakagawa[4]; Y. Suzuki[1]
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EPV-657 | A real-world study on the treatment and economic burden of generalized myasthenia gravis acute exacerbation in China

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EPV-658 | Peculiar pattern of muscle weakness in Oculopharyngeal muscular dystrophy: A case report and literature review

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EPV-659 | Quantitative assessment of coenzyme Q10 and respiratory chain in muscle of patients with limb-girdle muscular dystrophy

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EPV-660 | Key differences based on diagnosis categories in Macedonian patients with neuromuscular diseases

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EPV-661 | Retrospective analysis of demographics and comorbidities affecting prognosis in Myasthenia Gravis patients in Albania

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EPV-662 | Prognostic value of repetitive stimulation and single-fiber electromyography in a Portuguese myasthenia gravis cohort

J. Moura[1]; M. Pereira[1]; D. Costa[1]; D. Pereira[1]; A. Sousa[2]; T. Coelho[2]; M. Cardoso[2]; E. Santos[1]
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EPV-663 | Late-onset Tropomyosin 3-related myopathy presenting with scapuloperoneal weakness in two unrelated patients

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EPV-664 | Leigh syndrome due to the compound heterozygous variants c.1162A>C/c.1138G>C in NDUFV1

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EPV-665 | Evaluating ravulizumab in generalized myasthenia gravis: Patient satisfaction and real-world evidence from Germany

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EPV-666 | The full cost of living with facio scapulo humeral muscular dystrophy

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EPV-667 | Predictors of composite response in MG—Based on patient and clinician-reported assessments—In vivacity-MG3 Phase 3 trial

E. Cortés-Vicente[1]; I. Turkoz[2]; M. Ait-Tihyaty[3]; K. Gandhi[3]; Z. Choudhry[4]; B. Sattin[5]; W. Noel[6]; C. Gary[7]; M. Dimachkie[8]
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EPV-668 | Difficulties of diagnosis in immune-mediated necrotizing myopathy associated with statins in an elderly person case

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EPV-669 | Health-related quality of life in generalized myasthenia gravis (gMG) patients without self-reported AChR antibodies

M. Orlovic[1]; J. Guptill[2]; S. Chiroli[3]; C. Qi[2]; F. De Ruyck[1]; R. Mantegazza[4]; H. Murai[5]; N. Tollenaar[6]; S. Dewilde[6]
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EPV-670 | Treatment patterns and glucocorticoid use in ocular myasthenia gravis

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EPV-671 | The effect of daily/constant diplopia and ptosis on HRQoL in patients with persistent ocular MG

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EPV-672 | Serotonin reuptake inhibitors improve muscle stem cell function and muscle regeneration in male mice

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EPV-673 | Slowly progressing form of anti-SRP associated myopathy: A single center experience

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EPV-674 | Prenatal and postnatal diagnostics of spinal muscular atrophy: a case report and overview of therapeutic possibilities

P. Ruminski; A. Lemska; M. Pietruszka; K. Dzwilewski; M. Mazurkiewicz-Bełdzinska
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EPV-675 | Parsonage-turner syndrome: Bilateral presentation

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EPV-676 | Is it really myositis? Think about differential diagnosis

F. Hakim[1]; S. Sakka[1]; M. Snoussi[2]; I. Belhassen[1]; K. Moalla[1]; T. Boudawara[3]; S. Marzouk[2]; M. Damak[1]
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EPV-677 | Phase 3 study of gefurulimab in paediatric patients with generalised myasthenia gravis: trial in progress

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EPV-678 | FcRn blocker efgartigimod: Unique Fc fragment allowing IgG reduction without reducing albumin or increasing cholesterol

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EPV-679 | Case Series: Eculizumab for patients with highly active myasthenia gravis complicated by severe infections

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EPV-680 | Double trouble: A case of oculopharyngeal muscular dystrophy and myasthenia gravis

Z. Kallia; V. Poulidou; E. Pityrigkas; S. Kalampokini; A. Kiryttopoulos; A. Chotoura; M. Moschou; M. Arnaoutoglou; V. Kimiskidis
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EPV-681 | Clinical prognostic factors of mortality due to aneurysmal subarachnoid hemorrhage

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EPV-682 | Development of a prognostic score for clinical outcome prediction in neurological inpatients: A single-center study

B. Gumina; E. Olivieri; M. Trevisan; F. Berinato; T. Merati; A. Morotti; A. Pilotto; S. Gipponi; M. Filosto; A. Padovani
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EPV-683 | The role of endothelial dysfunction in pneumonia development after ischemic stroke

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EPV-684 | Acute respiratory compromise in a patient with recurrent anti-GQ1b positive miller fisher syndrome: A triple rarity

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EPV-685 | EEG patterns in the "indeterminate" outcome patients after cardiac arrest

M. Vasilieva[1]; I. Plesca[2]; R. Racila[1]; D. Efremova[1]; A. Vataman[1]; I. Vasilieva[3]; S. Groppa[2]
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EPV-686 | Symptomatic vasospasm in traumatic brain injury, a case report

M. Capra; M. Vargas Cobos; C. Gómez López de San Román; L. Caballero Sánchez; I. Bermejo Casado; D. Cerdán Santacruz; A. Castrillo Sanz; A. Mendoza Rodríguez; C. Tabernero García
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EPV-687 | Symptomatic vasospasm in traumatic brain injury, a case report

M. Capra; M. Vargas Cobos; C. Gómez López de San Román; L. Caballero Sánchez; I. Bermejo Casado; D. Cerdán Santacruz; A. Castrillo Sanz; A. Mendoza Rodríguez; C. Tabernero García
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EPV-688 | Prognostic value of scalp EEG findings in comatose patients receiving amantadine

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EPV-689 | Network meta-analysis of thrombectomy devices in acute ischemic stroke: Insights from 201 studies

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EPV-690 | Mortality-related predictive factors in patients with acute ischemic stroke from Myanmar

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EPV-691 | Mortality trends in spinal muscular atrophy : A demographic and geographic analysis from 1999 to 2020

B. Alrabadi; M. Marouf; A. Aldalati; N. Bandak; Y. Refai
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EPV-692 | **The rising mortality of Alzheimer's disease in insulin-independent diabetes: A retrospective study**

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EPV-693 | **The burden of stroke: Costs and mortality in the brazilian health system**

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EPV-694 | **Impact of socioeconomic disparities on the incidence of Alzheimer's disease in Brazil**

C. Rosa Gabriel Fernandes; C. Keiti Rech; C. Frederico de Almeida Rodrigues
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EPV-695 | **Vaccination coverage and mortality from bacterial meningitis in Brazil: Evidence from a historical series (2012–2023)**

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EPV-696 | **Comparative Study on the underreporting of dementia in recife versus in Amsterdam in 2022**

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EPV-697 | **Visual Pareidolia in non-demented patients of a stroke unit**

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EPV-698 | **Alzheimer's, epidemiological study of Brazil**

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EPV-699 | **Clinical and epidemiological characteristics of cerebral stroke in Uzbekistan**

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EPV-700 | **The frequency of neurological disease in orthopedic hospital in Hokkaido, Japan**

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EPV-701 | **Epidemiological study of Parkinson's disease in an underdeveloped country of continental size**

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EPV-702 | **Ischemic stroke in the North of Tenerife in the last 6 years**

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EPV-703 | **Comparative Analysis of Multiple Sclerosis in the Northern and Southern Regions of Azerbaijan**

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EPV-704 | Recurrent acute necrotizing encephalopathy associated with RANBP2 gene variant, a case report and brief review

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EPV-705 | Migraine and primary open-angle glaucoma: investigating the association through two-sample Mendelian randomization

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EPV-706 | Clinical correlation of preliminary diagnosis of Parkinson's disease based on genetic panel results

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EPV-707 | Neurometabolic diseases: When a novel Variant of Unknown Significance is enough to justify treatment

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EPV-708 | Drug-refractory epilepsy as the principal manifestation of a genetic syndrome

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EPV-709 | Systematic literature review on adrenoleukodystrophy: Outcomes after treating the untreatable

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EPV-710 | Neurological involvement in fabry disease: A clinical and radiological study

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EPV-711 | Epilepsy and leukoencephalopathy involving extreme capsules: case report and literature review of COL4A1/A2 duplications

C. Santos Martín; C. Amarante Cuadrado; M. González Arbizu; J. Alcalá Torres
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EPV-712 | When genetic diseases combine: An atypical presentation of adrenoleukodystrophy

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EPV-713 | Hereditary Transthyretin Amyloidosis in Northeast Brazil: Ile127Val mutation and a proposal for a new intermediate phase

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EPV-714 | The role of clinical exome sequencing in diagnosing hereditary ataxias

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EPV-715 | From dynamic mutation of FMR1 gene to variable phenotypes: A case series from a tunisian family and a literature review

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EPV-716 | The genetic landscape of ALS in Greece: identification of known and novel causative variants in a 353-patient cohort

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EPV-717 | Genetic study of copy number variants in Greek patients with early-onset Parkinson's disease

N. Ragazos[1]; C. Kartanou[1]; Z. Kontogeorgiou[1]; N. Papagiannakis[2]; C. Koros[2]; A. Simitsi[2]; I. Alefanti[2]; M. Maniati[3]; G. Xiromerisiou[4]; I. Boura[5]; C. Spanaki[5]; L. Stefanis[2]; G. Koutsis[1]; G. Karadima[1]
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EPV-718 | A case of CLCN2-related leukoencephalopathy and normal pressure hydrocephalus

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EPV-719 | Allgrove syndrome: A case report

M. González Gómez; M. Hernández Ramírez; J. Villamor Rodríguez; F. Sánchez García; E. Gismera Fontes; A. Andrés Bartolomé
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EPV-720 | Who wants to undergo genetic testing and why?

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EPV-721 | Very-late-onset huntington disease: Case report

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EPV-722 | White matter damage and cortical atrophy in adult patients with myotonic dystrophy type 1

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EPV-723 | Cognitive impairment and emotional disorders in adult patients with myotonic dystrophy type 1

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EPV-724 | LAMA2 mutation in a Tunisian sibling pair with congenital muscular dystrophy

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EPV-725 | A case of CAMK2A-associated neurodevelopmental disorder: Diagnostic insights through whole exome sequencing

M. Krygier; M. Pietruszka; K. Dzwilewski; P. Rumiński; M. Zawadzka; M. Mazurkiewicz-Bełdzińska
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EPV-726 | Phenotypical characterization in a cohort of adult patients with tuberous sclerosis complex

M. Borioni; A. Morano; E. Cerulli Irelli; L. Giordano; F. Giaculli; P. Moro; A. Giallonardo; C. Di Bonaventura
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EPV-727 | The role of C-174G polymorphism in the IL6 gene in patients with cavernous sinus thrombosis associated with COVID-19

M. Yakubova; G. Rakhmatullaeva; S. Said-Akhmedova; C. Rustamova
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EPV-728 | Association of AQP-4 polymorphisms with phenotypic characteristics of patients with NMOSD

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EPV-729 | POLR3A related hereditary spastic paraplegia associated with diabetes mellitus type 1—a case report

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EPV-730 | Exploring the genetic landscape of DMD: A meta-analysis of genetic variants & their clinical implications

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EPV-731 | Insights into developmental epileptic encephalopathy: A novel SULT4A1 variant and genetic challenges

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EPV-732 | Genotype-phenotype correlations in myoclonus-dystonia (Dyt11): Study of 27 patients with sgce mutations

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EPV-733 | The correlation between serum creatinine as a biomarker in spinal amyotrophy

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EPV-734 | Comparative effectiveness of gene editing techniques in DMD: A systematic review and meta-analysis

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EPV-735 | A Novel SYNE1 gene mutation in several members of a Turkish family

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EPV-736 | Genetic variations in TREM2: A case of Nasu–Hakola disease

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EPV-737 | When to consider genetic origin. A case of suspected inflammatory leukoencephalomyelopathy

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EPV-738 | Describing the first case of dystonic hand tremor in horizontal gaze palsy with progressive scoliosis

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EPV-739 | Huntington's disease: Diagnostic challenges and genetic insights of mimicking disorders

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EPV-740 | Intronic pathogenic variants in epilepsy: A case study and literature review

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EPV-741 | Patient with CADASIL and hot cross bun sign associated with a missense variant in EXON 6 of the NOTCH3 gene

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EPV-742 | Advances in gene therapy in Phelan–McDermid syndrome: An integrative review

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EPV-743 | Autosomal dominant inheritance of SCN4A gene (Val1589Met) associated with paramyotonia congenita: A turkish family

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EPV-744 | SPG 79 A, the first ItaliaN case described: A novel UCHL1 mutation expands our understanding

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EPV-745 | A rare case of a patient with ethylmalonic encephalopathy with a homozygous genetic mutation

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EPV-746 | The -244G/A (rs673) TNFα polymorphism Is Not associated with Alzheimer's disease in a tunisian population

Y. Missaoui; S. Fray; A. Achouri Rasssas; M. Adouania; M. Ben Mahmoud; H. Jamoussi; N. Ben Ali; M. Fradj
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EPV-747 | Watershed venous infarcts: A rare image

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EPV-748 | Reinforcing neuroimaging with stereotactic biopsy for cerebral lesions in chronic lymphocytic leukemia - A case report

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EPV-749 | Impact of massive trauma on brain structures: MRI volumetric analysis post-february 6 earthquake

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EPV-750 | Adult onset neuronal intranuclear inclusion disease presented with atypical parkinsonism

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EPV-751 | Cerebral hemodynamics in acute stroke: 4D flow MRI post-thrombectomy

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EPV-752 | Description of the familial case of horizontal gaze palsy with progressive scoliosis

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EPV-753 | Foix–Chavany–Marie Syndrome as result of bilateral opercular strokes

M. González Gómez; J. Villamor Rodríguez; M. Hernández Ramírez; F. Sánchez García; E. Gismera Fontes
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EPV-754 | Crossed cerebellar diaschisis in anti-NMDAR-E: Functional imaging insights into cerebello-cortical network disruptions

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EPV-755 | Pre-episode hyperperfusion and EEG patterns in HaNDL syndrome: Unveiling diagnostic insights of HaNDL syndrome

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EPV-756 | Brainstem encephalitis in neuroborreliosis

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EPV-757 | Polyphenol-based self-assembled carrier-free nanoparticles for imaging and treatment of acute ischemic stroke

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EPV-758 | Examination of the relationship between hand function and cortical changes in patients with brain tumors

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EPV-759 | Multi-modal investigation of the role of brain gyrification in early Alzheimer's disease

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EPV-760 | Reproducibility of manual segmentations of the red nucleus in healthy humans

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EPV-761 | MR predictors of invasiveness and density of pituitary adenoma: access choice, impact on the totality of removal

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EPV-762 | Clinical cases of transsphenoidal endoscopic removal of collisional tumors: the complexity of neuroimaging

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EPV-763 | Inflammatory Amyloid Angiopathy, the next Trending Topic?

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EPV-764 | Conversion of clinically isolated syndrome to primary progression multiple sclerosis: A retrospective study of 32 cases

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EPV-765 | Assessing Blood-Brain barrier Impairments in non-enhancing multiple sclerosis lesions with perfusion MRI

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EPV-766 | Cortical changes reveal the neural basis of motor and neuropsychological disorders, suggesting potential ALS biomarkers

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EPV-767 | Utility of NCCT imaging markers for early prediction of hematoma expansion in spontaneous intracerebral hemorrhage

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EPV-768 | Hot cross bun sign: Not always multiple system atrophy? A unicentric experience and literature review

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EPV-769 | Reproducibility of brain volume measurements in patients with secondary progressive multiple sclerosis with black holes

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EPV-770 | Case report: Non-ischemic cerebral lesions following endovascular treatment of infraophthalmic aneurysm

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EPV-771 | Diffusion MRI-based analysis of functional alterations of the glymphatic system in children with non-lesional epilepsy

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EPV-772 | fMRI study on the rich-club organization of brain networks in children with growth hormone deficiency

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EPV-773 | Perivascular space network function in children with sensorineural hearing loss

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EPV-774 | Spinal cord lesions and SPMS conversion: A study of 66 cases

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EPV-775 | Research on diffusion magnetic resonance imaging in insomnia patients based on free water correction

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EPV-776 | Brain network localization of high-frequency heart rate variability

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EPV-777 | An insight into anti-GAD autoimmune encephalitis: A less explored cause of late-onset seizures

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EPV-778 | Retrospective analysis of the clinical, radiological characteristics, and therapeutic approach of neuro-Behçet

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EPV-779 | Encephalitis NMDA+ as an immune-mediated adverse effect of immune checkpoint inhibitors: A clinical case report

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EPV-780 | Comparison of laboratory methods and correlation with clinical phenotype: ANTI-NF155, CNTN1, CASPR1 autoantibodies

A. Lechiara[1]; E. Mobilia[1]; F. Bozzano[1]; E. Baroncelli[2]; M. Bellucci[2]; C. Castellano[2]; G. Capodivento[3]; A. Uccelli[3]; L. Benedetti[3]; G. Pesce[1]
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EPV-781 | Hyperacute rapidly progressive cerebellar syndrome: Case-report

A. Parejo Olivera; N. Valverde Mata; M. Mesa Hernández; S. Jiménez Arenas; P. Blanco Ramírez; I. Córdoba Bueno; M. García Falcón; D. Ceberino Muñoz
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EPV-782 | PET imaging of skull inflammation in patients with isolated REM-sleep behavior disorder

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EPV-783 | Corticosteroid allergy and tolosa-hunt syndrome – What is next?

A. Chesnoiu-Dobrota; S. Stefan; I. Nitu; S. Socolov; M. Moldovan; F. Antochi; A. Ribigan; A. Resiga
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EPV-784 | Neuropathic pain as an initial presentation of Isaac's disease in a patient with Myasthenia gravis

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EPV-785 | Seasonal variability and increased incidence in the onset of Susac's syndrome in Israel

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EPV-786 | Effective treatment of rituximab followed within one half-life of efgartigimod in anti-Caspr1 autoimmune nodopathy

B. Sun; F. Li; L. Zou; J. Li; H. Yang; S. Chen
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EPV-787 | Cerebellar syndrome as an atypical and rare presentation of Anti-NMDA receptor encephalitis

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EPV-788 | The paraneoplastic mirage: A case of anti-hu encephalitis with an elusive underlying cause

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EPV-789 | Double trouble: The concurrence of multiple sclerosis and incidental vascular pathology – A short case series

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EPV-790 | Mechanisms and interventions for cognitive and psychiatric complications in NMOSD: Evidence-based insights

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EPV-791 | A rare encounter: The catastrophic face of antiphospholipid syndrome in systemic lupus erythematosus

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EPV-792 | Neurological disorders with GAD antibodies: Clinical characteristics and short-term outcomes in a Russian cohort

E. Chekanova; E. Nuzhnyi; E. Fedotova; E. Shalimanova; E. Golovneva; A. Shabalina; M. Zakharova
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EPV-793 | Refractory myasthenia gravis—Clinical course and predictive factors in a large cohort of patients

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EPV-794 | Clinical features and outcome of 64 Patients with Glial Fibrillary Acidic Protein Antibodies

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EPV-795 | Abstract withdrawn

EPV-796 | Phenotypical analysis of innate immune system in neuropathy by antibodies anti-myelin associated glycoprotein

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EPV-797 | Circulating extracellular vesicle microRNAs as molecular biomarkers of treatment response in multiple sclerosis

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EPV-798 | Treatment of multiple sclerosis with ocrelizumab and rituximab: Long-term immunological monitoring

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EPV-799 | Immune mediated movement disorder in young

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EPV-800 | Diagnostic challenge: Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) manifesting as Papilledema

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EPV-801 | Rare association of tolosa–hunt syndrome with Sjogren's syndrome

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EPV-802 | Disease progression in a mouse model of neuromyelitis optica spectrum disorders with aquaporin-4 autoimmunity

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EPV-803 | Autoimmune encephalitis due to GABA(B) antibodies as paraneoplastic presentation of neuroendocrine urothelial carcinoma

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EPV-804 | Bickerstaff brainstem encephalitis: A clinical case report

I. Ghorbel; K. Moalla; H. Hadj Kacem; N. Bouattour; S. Daoud; M. Damak
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EPV-805 | **Aquaporin 4 – A biomarker in pediatric status epilepticus**

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EPV-806 | **Efficacy of cladribine in RRMS patients in a Singapore tertiary neurological center—Year 3 and beyond**

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EPV-807 | **Case report: A myasthenia gravis patient complicated with renal failure was effectively treated with efgartigimod**

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EPV-808 | **Extended interval dosing of natalizumab in multiple sclerosis**

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EPV-809 | Immune-mediated neurological syndromes following COVID-19 vaccination. Role of the lymphocyte transformation test.

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EPV-810 | **Case report: Effective treatment of anti-NMDAR encephalitis using Eculizumab**

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EPV-811 | **The central vein sign and paramagnetic rim lesions in differentiating MOGAD from multiple sclerosis**

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EPV-812 | Paraneoplastic stiff leg syndrome or focal dystonia? A report of 2 cases.

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EPV-813 | **Painful paroxysmal tonic spasms in the context of neuromyelitis optica: a case report**

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EPV-814 | **Diagnostic puzzle: Separating the pieces of multiple sclerosis from toxoplasmosis**

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EPV-815 | **Changing the prognosis of rheumatoid meningitis: from early suspicion to treatment challenges**

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EPV-816 | Clinical meaning of PROMs in a large cohort of myasthenia gravis patients

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EPV-817 | Acute necrotizing encephalopathy in adults: therapeutic and prognostic challenges in a rare condition

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EPV-818 | Unveiling autoimmune pathogenesis in post malaria delayed cerebellar ataxia: Case report and literature review

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EPV-819 | Over-testing in autoimmune encephalitis: Clinical rationale or diagnostic overreach?

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EPV-820 | Rapid symptom relief and imaging improvement in AQP4 antibody-positive NMOSD patients treated with eculizumab

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EPV-821 | MOGAD: Clinical and radiological characteristics of patients in Serbia – A single-centre experience

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EPV-822 | Susac syndrome with underlying rheumatoid arthritis: A case of dual autoimmune pathology

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EPV-823 | Demographic, clinical, and radiological characteristics of CASPR2 positive autoimmune encephalitis patients

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EPV-824 | Management and outcomes of pediatric optic neuritis in a tertiary hospital in Riyadh, Saudi Arabia

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EPV-825 | NORSE and autoimmune encephalitis- loss of Purkinje cells. Do we really have connections?

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EPV-826 | Unveiling GFAP astrocytopathy: Insights from case studies and a comprehensive review of literature

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EPV-827 | An unusual clinical manifestation of leucine-rich glioma inactivated antibody encephalitis

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EPV-828 | CLIPPERS: When to stick with the diagnosis and when to question it

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EPV-829 | Natalizumab for immune checkpoint inhibitor-induced anti-Hu paraneoplastic neurological syndrome: A case report

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EPV-830 | A case of brachial plexus neuritis following upper respiratory tract infection

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EPV-831 | Myelin oligodendrocyte glycoprotein antibody associated disease: A tertiary hospital cohort study

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EPV-832 | The prognostic value of oligoclonal bands to predict the clinical course at diagnosis of multiple sclerosis

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EPV-833 | Painful tonic spasms revealing cervical myelitis in neuromyelitis optica spectrum disorder

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EPV-834 | A case report of anti-MOG antibody associated myelitis in combination with Hodgkin's lymphoma

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EPV-835 | CAR- T cells therapy: A new hope in Myasthenia Gravis

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EPV-836 | Temporal variation of acute encephalitis etiologies in a portuguese tertiary center introduction

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EPV-837 | Efficacy and safety of therapy of anti-NMDAR-associated autoimmune encephalitis with Efgartigimod: three cases report

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EPV-838 | Neurological Complications of Immunosuppressant Therapy: Insights into PRES and PML

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EPV-839 | Multiple sclerosis-associated HLA demarcates EBV-specific CD8+ T cells with an exhausted and brain residency phenotype

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EPV-840 | Overexpressed of ferrous iron triggers Neutrophil extracellular trap formation and contributes to multiple sclerosis

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EPV-841 | Case report: An effective treatment of Chinese relapse NMOSD using eculizumab during pregnancy

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EPV-842 | Treatment of NMOSD and multiple rheumatologic comorbidities with anti-IL23 Therapies: a case report

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EPV-843 | Therapeutic effect of efgartigimod in Guillain–Barré syndrome: a case series

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EPV-844 | The enigma of MOGAD: Unraveling a rare case of acute encephalomyelitis in a young adult

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EPV-845 | Studying neurogenesis of olfactory chemoreceptor neurons by differential analysis of their gene expression data

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EPV-846 | Hypertrophic pachymeningitis associated with MPO-ANCA+: A rare cause of secondary headache

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EPV-847 | Recurrent transient global amnesia and epilepsy in a patient with antiphospholipid antibodies: A diagnostic challenge

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EPV-848 | Mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS): A case report

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EPV-849 | Overlapping syndrome: A case of systemic lupus erythematosus and Sjögren's syndrome with extended longitudinal myelitis

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EPV-850 | Acute neurotoxicity following intravenous amiodarone treatment: A rare clinical condition mimicking brainstem stroke

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EPV-851 | One year observation: Neurological manifestations in nephrology service

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EPV-852 | Uncommon initial manifestations of Sjögren's syndrome: Renal tubular acidosis and central pontine myelinolysis

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EPV-853 | Therapeutic Adherence in Wilson's Disease

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EPV-854 | Hypereosinophilia as a potential cause of central nervous system demyelination

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EPV-855 | Developing an evidence-based follow-up plan for neurological manifestations in Bardet–Biedl Syndrome

L. Nunes Campos; G. Pintos; R. Benítez Yazbek; I. Dávila Rivera; I. Valentin Rudzinski; S. Curto; S. Miguel Maximowicz; A. Gerk; F. Fernandez Zelcer; C. Stegmann; C. Francisca Argüelles; J. Stegmann
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EPV-856 | Lymphocytic hypophysitis and secondary headache as atypical debut of IgG4-related disease

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EPV-857 | Neurological complications of giant cell arteritis: A study of 15 cases

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EPV-858 | Multiple dural implants of bronchial neuroendocrine tumor mimicking multiple meningiomatosis

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EPV-859 | Neurologic impairment prediction in systemic lupus erythematosus

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EPV-860 | Triheptanoin VS placebo in Glut1 deficiency syndrome: Systematic review

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EPV-861 | Parkinsonism associated with extrapontine myelinosis of the Basal ganglia: Case report

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EPV-862 | The impact of art on well-being: Insights from the NeuroART competition

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EPV-863 | Well-being and headache among spanish dance professional and semi-professional dancers: An exploratory study

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EPV-864 | Adult cerebral palsy treated with tanfarid cranioplasty and duraplasty: A case study

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EPV-865 | Prefrontal cortex dynamics and shifting of cognitive demands during musical activity

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EPV-866 | Cognitive skills assessment in deaf & hard of hearing school children

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EPV-867 | "You are not you" and "blackbird": Motor neuron disease in cinema: Raising social and moral issues

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EPV-868 | A case of multiple brain and spine metastasis with an unknown primary breast carcinoma

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EPV-869 | Neurolymphomatosis in diffuse large B-Cell Lymphoma: A rare and challenging neurological complication – Case report

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EPV-870 | Stroke mimic: primary CNS lymphoma in patient with bone marrow aplasia

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EPV-871 | Multifocal cranial neuropathy as a rare central nervous system relapse of mantle cell lymphoma: A case report

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EPV-872 | Stroke Mimic-like Glioblastoma

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EPV-873 | Clinical characteristics of brain tumors from a tertiary neurology clinic from Republic of Moldova

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EPV-874 | Recurrence and management of an incompletely resected cavernous sinus meningioma: A Case Report

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EPV-875 | Presence of headaches due to brain tumors

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EPV-876 | Rapidly progressive tetraparesis – An atypical presentation of a glial series tumor

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EPV-877 | In silico heat dissipation study for magneto hyperthermia on glioblastoma-on-a-chip vascular network models

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EPV-878 | Anti-NMDAR receptor encephalitis secondary to bladder urothelial carcinoma presenting as subacute aphasia

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EPV-879 | Reversible Cerebral Vasoconstriction Syndrome and sorafenib: first case reported in literature

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EPV-880 | Carcinomatous meningitis: Two case reports

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EPV-881 | Liquid biopsy for detection of H3K27M mutation in pediatric diffuse midline glioma: An updated systematic review

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EPV-882 | Lhermitte–Duclos disease: An unexpected diagnosis

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EPV-883 | Atypical presentation of Glioma mimicking inflammatory demyelinating Lesions

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EPV-884 | Bilateral mental hypoesthesia syndrome as an unusual presentation of mantle cell lymphoma

P. Garrido Jiménez; S. López Anguita; J. Rodríguez Quinchanegua; A. Lorenzo Montilla; A. Rodríguez Herrera; J. Aparcero Suero; B. Gutiérrez Ruano; F. Valenzuela Rojas; M. Olmedilla González
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EPV-885 | Understanding different methods of meningioma diagnosis and its improvements

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EPV-886 | Unexpected end stage manifestation of signet ring cell gastric carcinoma

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EPV-887 | Neurological immune-related adverse events in patients treated with anti-PD-1 agent, Pembrolizumab: A case series

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EPV-888 | Paraneoplastic neurological syndromes: A single institution 5-year case series

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EPV-889 | Endolymphatic sac tumor: A case report

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EPV-890 | Clinical aspects of headache in brain gliomas

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EPV-891 | Retinal status and oculomotor responses in patients with chronic headaches

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EPV-892 | Rare complication of ophthalmic herpes zoster

A. Gómez González; P. Hernández Vitorique; C. Ortega Hiraldo; A. Campos Villegas; A. Guzmán Téllez; P. Carbonell Corvillo
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EPV-893 | Relationship between vestibular dysfunction and Parkinson's disease clinical symptoms and morphometric changes on MRI

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EPV-894 | Comprehensive review of visual snow syndrome: Clinical features, risk factors, and prognostic outcomes

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EPV-895 | The effect of cochleovestibular disorders on the quality of life of patients with Meniere's disease

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EPV-896 | Role of Vestibular evoked myogenic potentials in the diagnosis of Meniere's disease

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EPV-897 | Fluctuating abducens nerve palsy

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EPV-898 | A unique intersection: Vertical one-and-a-half syndrome and contralesional pseudo-abducens palsy

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EPV-899 | Dehabituation phenomena in patients with visual snow syndrome. Can we see the snow?

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EPV-900 | Erythrocyte transketolase activity in the diagnosis of a case of multiple ocular cranial neuropathy

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EPV-901 | Optic neuropathy in giant cell arteritis: A case report highlighting diagnostic and therapeutic challenges

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EPV-902 | Acute third nerve palsy as the presenting feature of a posterior communicating artery aneurysm: A case report

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EPV-903 | Cognitive-functional correlation and retinal findings by OCT in Parkinson's disease patients treated with DBS

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EPV-904 | Unrecognized leber hereditary optic neuropathy and differential diagnosis of suspected pediatric multiple sclerosis

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EPV-905 | Cognitive impairment and quality of life in sensorineural deafness

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EPV-906 | Optic neuropathy as a manifestation of syphilis-HIV co-infection: A report of three cases

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EPV-907 | Adie's tonic pupil in migrainous patient: A case report

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EPV-908 | Herpes zoster ophthalmicus as a cause of cranial neuropathy: A case report and literature review

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EPV-909 | Optic nerve metastasis in lung mucinous adenocarcinoma: A rare case report

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EPV-910 | Video head impulse test in Wernicke's encephalopathy

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EPV-911 | Optic neuritis in children: A study of a tunisian cohort

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EPV-912 | Influence of pain on quality of life, anxiety and depression in patients with AIDP

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EPV-913 | CIDP with prominent craniobulbar features

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EPV-914 | CANVAS - an unusual cause for a progressive sensory neuropathy

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EPV-915 | Are there any sex differenes in carpal tunnel syndrome? - Short prospective observational study from split, Croatia

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EPV-916 | Parkinson anxiety scale in persons with Parkinson's disease ketevan toloraia

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EPV-917 | Neurophysiological aspects of chronic polyradiculoneuritis in a Tunisian population

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EPV-918 | lack of animal model in chronic traumatic encephalopathy

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EPV-919 | A systematic review on the differential diagnosis between peripheral neuropathy and myopathies

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EPV-920 | Polyneuropathy associated with IgM monoclonal gammopathy: Unraveling treatment-resistant tremor in Parkinson's Disease

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EPV-921 | Combined congenital and deficiency neuropathy: A case report

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EPV-922 | Post PDdisease depression prevalence study depression questionnaires in Uzbek people with ischaemic stroke and migraine

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EPV-923 | Placental growth factor as a biomarker for neurological diseases: A systematic review of emerging evidence

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EPV-924 | Nerve ultrasonographic description of patients with IgLon5 disease

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EPV-925 | A holistic spinal cord stimulation approach to treat painful diabetic peripheral neuropathy: The INSPIRE study

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EPV-926 | Virtual reality for cognitive rehabilitation of severe brain injury: Preliminary data of a randomized controlled trial

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EPV-927 | Gender and functional status in individuals with multiple sclerosis: A cross-sectional study

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EPV-928 | Biological movement recognition in multiple sclerosis. A case-control study

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EPV-929 | Primary results of the initial validation of the SMD Decision Tree – I-REFER

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EPV-930 | Barriers to Post-Stroke Rehabilitation: A Single-Center Study of Stroke Survivors in Rural Albania

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EPV-931 | Investigation of the effects of long-term binaural beats application on tinnitus patients

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EPV-932 | The effects of movement-based interventions in supporting stroke recovery

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EPV-933 | **Cognitive training compared to relaxation one using virtual reality in patients with subjective cognitive impairments**

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EPV-934 | **Getting the right care: Physiotherapy for patients with dystonia in the UK**

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EPV-935 | **Sensory afferent electrostimulation: Effects on motor rehabilitation & cerebral mechanisms in children with hemiparesis**

K. Lory[1]; A. Gschaidmeier[1]; M. Von Gunten[2]; K. Möri[3]; R. Wiest[4]; K. Seidel[5]; T. Nef[3]; C. Simon-Martinez[6]; R. Everts[1]; S. Grunt[1]
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EPV-936 | **Use of technology-driven haptic illusions in the rehabilitation of neurological disorders: A systematic review**

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EPV-937 | Swallowing disorders in Ischemic Stroke: an analysis of dysphagia severity based on hemisphere damage and age**.**

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EPV-938 | **Combined robotic verticalization and mobilization in severe acquired brain injury: Preliminary data of an RCT**

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EPV-939 | **Electroencephalogram in the acute phase of ischemic stroke: A prognostic biomarker for functional recovery**

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EPV-940 | **Pharmacophysiotherapy rehabilitation of patients with stroke**

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EPV-941 | Regression of postpartum sexual dysfunction by interstitial electrical neurostimulation of the pudendal nerve

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EPV-942 | Efficiency of low-level laser therapy in improving fine motor skills of the hand after carpal decompression surgery

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EPV-943 | Efficiency of Trigger Point Injections in the treatment of residual pain syndrome after lumbar decompression surgery

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EPV-944 | Perception about upper limb functional recovery, barriers & use of training devices among stroke survivors

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EPV-945 | Motor learning of the paretic upper extremity in chronic stroke survivors: DO we have to consider interference?

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EPV-946 | Validity of an Android device for assessing mobility in people with visual impairment: a cross-sectional study

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EPV-947 | Barriers to the use of information and communication technologies in people with chronic stroke: preliminary findings

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EPV-948 | Efficiency of brain-computer interfaces in the treatment of post-stroke cognitive impairment

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EPV-949 | The relationship between balance performance and fear of falling in patients with stroke

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EPV-950 | Physical activity and related factors in patients with chronic stroke

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EPV-951 | Clinical study of autologous adipose-derived stromal vascular fraction (SVF) in the treatment of multiple system atrophy

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EPV-952 | Treatment of obstructive sleep apnoea as a prevention strategy for recurrent stroke: A review

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EPV-953 | When mycophenolate strikes: Unveiling the neurotoxic danger of immunosuppressive therapy

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EPV-954 | Neuropsychological disorders in patients with severe intoxication with carbon monoxide

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EPV-955 | Functional vitamin B12 deficiency in a patient with mercury exposure, a case report and literature review

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EPV-956 | Lithium intoxication in elderly patients treated for bipolar disorder

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EPV-957 | Discovery of gallic acid-based mitochondriotropic antioxidant attenuates LPS-induced neuroinflammation

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EPV-958 | Toxic optic neuropathy and encephalopathy after closantel intoxication in human

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EPV-959 | Autonomic nervous system dysfunction in military personnel with blast injuries

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EPV-960 | Case of subacute posttraumatic ascending myelopathy with paraparesis and dysfunction of the pelvic organs

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EPV-961 | The long-term impact and ongoing risks of the lack of a national strategy on pain medicine in Armenia

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EPV-962 | Gender differences in long-term botulinum toxin type A treatment of trigeminal neuralgia

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EPV-963 | Design of a trial on the prognostic value of biomarkers and the effect of tolperisone in acute low back pain

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EPV-964 | Multimodal treatment approaches for facial pain

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EPV-965 | Association between low ferritin levels and chronic tension - type headache

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EPV-966 | Chronic functional pain and irritable bowel syndrome: the place of histamine producing gut bacteria

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EPV-967 | Self-administration of painkillers medications among students of medicine in bosnia and herzegovina

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EPV-968 | Chronic neurological manifestations in acute porphyria

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EPV-969 | Neural and molecular pathways in FOP: Mechanisms and therapies for chronic pain and motor dysfunction

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EPV-970 | Low back pain at the neurology emergency department - short retrospective study from split, croatia

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EPV-971 | Transcranial magnetic stimulation of the insula and the motor area in migraine prophylaxis: Superiority clinical trial

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EPV-972 | Features of intestinal microbiota in patients with different subtypes of post-stroke pain

N. Usava; I. Stoma; A. Kovalev; O. Osipkina; A. Zyat'kov; A. Shaforost
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EPV-973 | Clinical and phenotypic features of nonspecific connective tissue dysplasia in dorsopathies

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EPV-974 | Indicators of chronic anterior knee pain syndrome after arthroscopy

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EPV-975 | Sleep quality profile of patients with chronic non-specific low back pain

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EPV-976 | Treatment of phantom pain syndrome with botulinum neurotoxin

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EPV-977 | Breaking the Brain's defense: A Systematic Review of Immune-Evasion Mechanisms in Glioblastoma and CNS Metastasis

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EPV-978 | Palliative need and dying in stroke-can we do better?

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EPV-979 | Insulin-immunoreactive myenteric neurons and their gut region-dependent alterations in a type 1 diabetic rat model

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EPV-980 | Clinical, neurophysiological, and radiological characteristics of peripheral neuropathy in rheumatoid arthritis

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EPV-981 | Prognostic evaluation of antiganglioside antibodies in Guillain-Barré Syndrome

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EPV-982 | Expanding the phenotypic spectrum of CANVAS

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EPV-983 | Comparability of pharmacokinetics between HyQvia and TAK-881 in CIDP: a phase 3 study design

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EPV-984 | Anti-MAG neuropathy with monoclonal gammopathy leading to Chronic Lymphocytic Leukemia diagnosis: A case study

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EPV-985 | Patient reported outcomes from the inspire study in patients with sorbitol dehydrogenase Deficiency

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EPV-986 | Hereditary transthyretin amyloidosis: Clinical profiles in a Colombian cohort

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EPV-987 | Determinants of therapeutic inertia in chronic inflammatory demyelinating polyneuropathy: A retrospective study

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EPV-988 | Multifocal neuropathy as a presentation of primary neurolymphomatosis: case report and systematic review of literature

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EPV-989 | Tracking polyneuropathy in patients with early Parkinson's disease

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EPV-990 | NF155-positive peripheral neuropathy and Type 1 hyperoxaluria: A case of ambiguous genetic-autoimmune link

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EPV-991 | POEMS - A case of plasma cell dyscrasia disguised as CIDP

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EPV-992 | Compound muscle action potential amplitude ratio to distinguish CMT1A from CIDP: a single-center experience

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EPV-993 | Pharyngeal-cervical-brachial variant of Guillain-Barré syndrome: a neurophysiologic and immunologic continuum

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EPV-994 | Therapy monitoring for patients with chronic inflammatory demyelinating polyradiculoneuropathy

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EPV-995 | Retransplantation after acquired amyloidosis post-domino liver transplantation: outcomes and challenges

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EPV-996 | The help of divine action in the form of anastomosis in patients with common entrapment neuropathy

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EPV-997 | Peripheral nervous system involvement in bortezomib treatment: Is abnormal findings related to double etiology?

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EPV-998 | Peripheral nervous system complications in vasculitis and autoimmune connective tissue diseases

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EPV-999 | Bell's palsy treated with doxycycline

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EPV-1000 | Foot Drop: beyond peroneal nerve entrapment

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EPV-1001 | The impact of arteriovenous fistula on carpal tunnel syndrome signs and peripheral neuropathy in haemodialysis patients

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EPV-1002 | Sequential administration of efgartigimod shortened the course of Guillain-Barré syndrome: A case series

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EPV-1003 | Social and quality of life impacts of brachial plexus injuries and surgical interventions

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EPV-1004 | Can the clinical course of guillain-barré syndrome be predicted? Prognostic clues

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EPV-1005 | Clinical Characterisation and skin biopsy findings in a series of patients with small fiber neuropathy

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EPV-1006 | Efficacy of efgartigimod in the treatment of MFS/GBS overlap syndrome: Two case reports

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EPV-1007 | Asymmetric muscle atrophy in critical illness neuropathy: A case report highlighting COVID-19 complications

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EPV-1008 | The REM connection: Hallucinations, morning inertia, and naps in hypersomnolence disorders

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EPV-1009 | Myocardial infarction and circadian rhythm disruption: A systematic review

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EPV-1010 | Polysomnography for sleep characteristics and dysautonomia in 6 probable Sporadic Creutzfeldt-Jakob disease patients

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EPV-1011 | Association between cognitive decline and dysautonomia in REM sleep behavior disorder

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EPV-1012 | Insights on the therapeutic potential of cannabidiol for managing sleep disorders

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EPV-1013 | Anxiolytique activity of *Mentha pulegium* L

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EPV-1014 | Evaluation of sedative and hypnotic activity of polyphenols from Mentha using Rota rod test and open field test

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EPV-1015 | Multiple sclerosis and narcolepsy: A case report

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EPV-1016 | RLS and other sleep disorders among young people of Georgia

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EPV-1017 | Obstructive sleep apnea and Parkinson's disease: characteristics and associated factors of a cohort study

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EPV-1018 | The efficacy of exogenous Melatonin in Patients with Parkinson's disease with sleep disturbance

L. Alqassass; A. Abdelfatah; M. Gadelrab; A. Genidy; M. Ghazal; Y. Galab; R. Ghazal; K. Gadallah; B. Touhami; I. Omar
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EPV-1019 | Levels of daytime sleepiness and loneliness among foreign undergraduate students: a cross-sectional study

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EPV-1020 | Focal seizures, non-epileptic paroxysmal episodes or "sleep attack"? A case report

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EPV-1021 | Regional and Demographic Trends in Mortality from Sleep Apnea in United States from 1999-2019: A Retrospective Analysis

S. Cheema[1]; Prateek[2]; F. Shahid[1]; L. Sarfraz[1]; M. Hassan[1]; H. Ijaz[1]; A. Sanan[3]
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EPV-1022 | Screening for REM sleep behavior disorder: a retrospective analysis of 6 years of single sleep center data

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EPV-1023 | Efficacy and safety of histamine H3 receptor inverse agonists in narcolepsy: a systematic review and meta-analysis

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EPV-1024 | Assessment of sleep disorders in patients with Type 1 diabetes mellitus: A questionnaire-based survey

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EPV-1025 | Spinal cord ischemia in TEVAR: A case report

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EPV-1026 | The aftermath of subarachnoid hemorrhage: arachnoiditis and its impact

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EPV-1027 | Myelopathies associated with chemotherapeutic agents: review and case studies

J. Luisi de Moura; A. Sauter Dalbem; V. Rebelo Procacci; N. Hamershlak; R. Franco Morgulis
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EPV-1028 | Laughter isn't always the best medicine: a disguised myelopathy

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EPV-1029 | Spinal cord ischemia – Thrombolytic treatment alone or in combination with surgery – A good treatment alternative

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EPV-1030 | cervical spinal epidural abscess in the very elderly: A case report and literature review

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EPV-1031 | Benign monomelic amyotrophy due to focal involvement of the anterior horn

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EPV-1032 | **Bi-brachial amyotrophy presentation of intracranial hypotension – A treatable motor neuron disease mimic**

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EPV-1033 | **Congenital dermal sinus condition: A case study of spinal dysraphism in a adult**

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EPV-1034 | **A rare cause of myelopathy: Copper deficiency due to gastrointestinal surgery**

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EPV-1035 | **Elsberg syndrome as a presentation of primary HSV-2 Infection**

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EPV-1036 | **An uncommon stroke in a common autoimmune disorder**

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ABSTRACT

Late Breaking News

Monday, June 23 2025

LBN_01 | Achieving higher standards in real-world migraine care with anti-CGRP monoclonal antibodies

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Background and Aims: The International Headache Society has proposed new treatment goals for migraine prevention in real world, as a way to set higher standards of care. This study provides the first assessment of the proportion of individuals achieving them after 6 months of migraine-specific treatment with anti-CGRP monoclonal antibodies (MAbs).

Methods: European multicenter, prospective, real-world study, including adults with migraine treated with anti-CGRP MAbs (EUREkA cohort). We assessed the proportions of individuals in each treatment goal category – migraine freedom (0 monthly migraine days – MMD); optimal control (≤4 MMD), modest control (4–6 MMD); insufficient control (>6 MMD) – after 6 months of treatment. We also assessed the proportions of individuals with ≥50% reduction in monthly headache days – MHD in the insufficient control group.

Results: 4963 had 6 months data: 82.3% (4086/4963) were female and median age was 48.0 [40.0–55.0] years. At baseline, the median MHD, MMD were 20.0 [13.3–28.0] days/months and 15.0 [10.0–20.0] days/months, respectively. All the cohort at baseline was classified as having insufficient control. At month 6, 6.9% (342/4963) had migraine freedom, 32.0% (1589/4,963) optimal control, 15.5% (771/4963) modest control and 45.6% (2261/4963) insufficient control. In the insufficient control group, 27.1% (613/2261) of individuals were ≥50% responders.

Conclusion: High standards of care, defined as optimal disease control or even migraine freedom, are achieved in real-world settings with anti-CGRP MAbs in approximately 40% of individuals with a high migraine burden. These findings highlight the need to expand global access to these treatments.

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LBN_02 | Shared neural signatures of photophobia in migraine and post-traumatic headache: A task-based fMRI study

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Background and Aims: Persistent post-traumatic headache (PPTH) and migraine frequently present with photic hypersensitivity that exacerbates headache symptoms. We sought to determine whether PPTH is associated with altered brain responses to visual stimuli and to explore shared neural mechanisms of photophobia with migraine.
Methods: This cross-sectional functional magnetic resonance imaging (fMRI) study included 80 adults with PPTH, 261 with migraine, and 143 healthy controls (HCs). All participants underwent visual stimulation using a flickering checkerboard during a 3T fMRI session. Blood oxygen level-dependent (BOLD) responses were examined using whole-brain and region-of-interest (ROI) analyses. All analyses were adjusted for age and sex.
Results: Whole-brain analysis revealed no significant BOLD differences across the full PPTH, migraine, and HC groups. However, participants with PPTH who experienced photophobia ($n=41$) showed greater activation in the anterior and mid-cingulate cortex compared with HCs (PFWE = 0.010). No differences were observed between photophobic participants with PPTH and those with migraine who reported an attack during the fMRI session. ROI analyses identified greater activation in the anterior cingulate, mid-cingulate, and insular cortices in both photophobic participants with PPTH and ictal participants with migraine, relative to HCs (all $p<0.05$). No significant differences were found between photophobic participants with PPTH and ictal participants with migraine.
Conclusion: Photophobia in persistent PPTH is associated with greater activation in cortical regions implicated in pain processing. These patterns parallel those observed during migraine attacks, indicating shared neural mechanisms between the two headache disorders.
Disclosure: This work received support by research grants from the Lundbeck Foundation (R403-2022-1352 and R310-2018-3711).

LBN_03 | Increased serum neurofilament light chain levels in Parkinson's disease patients carrying the p.A53T SNCA mutation

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Background and Aims: Neurofilament light chain (NfLs) is an intermediate filament neuronal-specific cytoskeletal axonal protein, whose blood and CSF levels are increased in various neurodegenerative diseases, reflecting neuro-axonal degeneration; in uncomplicated Parkinson's Disease (PD) however, such levels are within normal limits. A53T-PD, due to the p.A53T mutation in the SNCA gene, is a severe and rapidly progressive genetic synucleinopathy. We report here serum NfL measurements in this rare condition.
Methods: Serum NfL and demographic data were acquired from Parkinson's Progression Markers Initiative (PPMI) database. A propensity score matching based technique was used to match PD patients without genetic causes (iPD) and healthy controls, with A53T-PD cases, in a 3:1 ratio (i.e. 3 iPD and 3 controls for every A53T-PD case). The logistic regression model for the matching score used the age and age of onset (in the case of iPD) as independent variables, and it was fed in a nearest neighbor matching algorithm.
Results: Serum NfL data were available for 18 A53T-PD cases. Consequently, 54 iPD and 54 controls were selected by the matching algorithm. NfL levels were increased in A53T-PD (13.8 pg/mL) in comparison with iPD (7.56 pg/mL) and healthy controls (8.01 pg/mL) (overall $p=0.010$).
Conclusion: The increase in serum NfL points to a more aggressive neurodegenerative process in A53T-PD compared to iPD.
Disclosure: This study was funded by the Michael J Fox Foundation through the Write Now initiative.

LBN_04 | Efficacy and safety of efgartigimod as an add-on therapy in patients with NMOSD and MOGAD

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Background and Aims: Neuromyelitis optica spectrum disorders (NMOSD) and myelin oligodendrocyte glycoprotein associated disease (MOGAD) are autoimmune antibody mediated diseases. Efgartigimod is a neonatal Fc receptor targeting therapeutic, causing antibody titers reduction. The efficacy and safety of efgartigimod added with intravenous methylprednisolone (IVMP) in NMOSD and MOGAD patients was assessed in this study.
Methods: Patients diagnosed with NMOSD or MOGAD were enrolled. Efgartigimod was administered intravenously 10 mg/kg×4 doses or 20 mg/kg×2 doses. Expanded disability status scores (EDSS), serum immunoglobulin G (IgG) levels and pathogenic antibody titers were evaluated before and after therapy.
Results: In total, 27 adult patients were enrolled, 13 patients were treated with IVMP plus efgartigimod, comparable 14 controls treated with IVMP alone. Efgartigimod group achieved better outcome with EDSS reduction by 1.3 ± 0.6, compared with control group (0.5 ± 0.5). Meanwhile, serum IgG levels in efgartigimod treated group decreased by 69.8% after therapy, and nine patients (69.2%) showed antibody titers reduction. Moreover, the EDSS and antibody titers decreased more rapidly and largely in intensive therapy cohort (20 mg/kg×2).

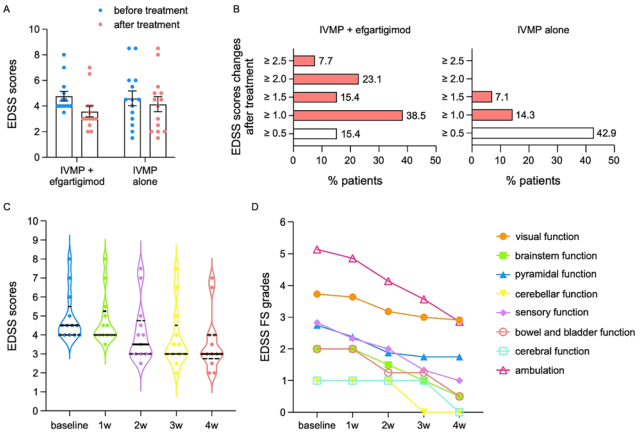

FIGURE 1 The changes of EDSS scores in IVMP plus efgartigimod group and in IVMP alone group before and after treatment.

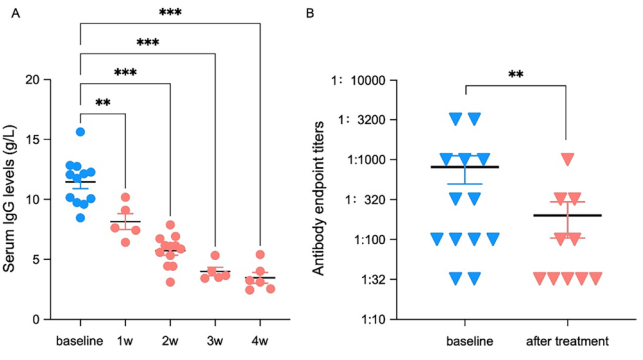

FIGURE 2 Levels of serum IgG and serum pathogenic antibody titers at baseline and after treatment of efgartigimod in NMOSD and MOGAD patients.

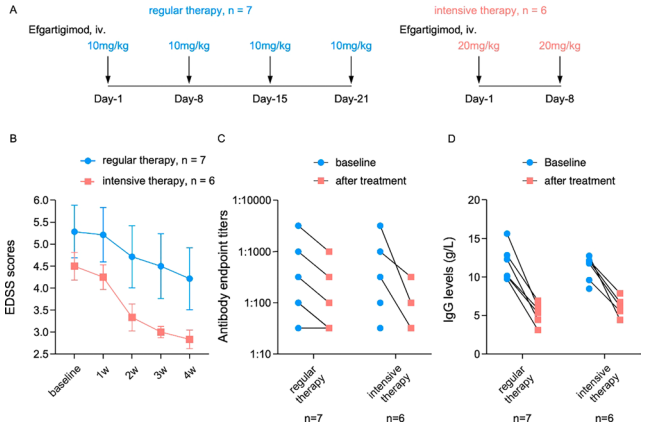

FIGURE 3 The efficacy of efgartigimod in regular and intensive therapy cohort.

Conclusion: Efgartigimod add-on therapy was beneficial and tolerable in patients with NMOSD and MOGAD in acute phase.
Disclosure: Nothing to disclose.

LBN_05 | Detection of misfolded TDP-43 in CSF of genetic FTD and FTD/ALS patients at both presymptomatic and symptomatic stages

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Background and Aims: Seed amplification assays (SAAs) have shown promising results in detecting misfolded TDP-43 in cerebrospinal fluid (CSF) of patients with genetic FTD with TDP-43 pathology. However, there are no data available on SAA analysis of CSF from subjects in the presymptomatic phase of the disease.
Methods: We tested TDP-43 seeding activity in CSF of 32 patients carrying pathogenic GRN mutations, C9orf72 expansion and MAPT mutations, 14 presymptomatic carriers and 12 controls (subjects without neurodegenerative disorders). Truncated

recombinant TDP-43 protein has been used as a SAA reaction substrate. We also used Single Molecule Array technology for measuring the neurofilament light chain (NfL) levels in the entire cohort.

Results: We found a seeding activity in in 67% of TDP-43-linked symptomatic patients, with a specificity of 93%. A half of presymptomatic subjects tested positive, most of them GRN carriers. Interestingly, among TDP-43_SAA positive presymptomatic individuals, two GRN carriers underwent phenoconversion. Furthermore, presymptomatic individuals who tested positive for TDP-43_SAA had also higher levels of NfL compared to TDP-43 negative individuals.

Conclusion: We confirm the presence of seeding activity for TDP-43 in the CSF of symptomatic patients with genetic forms of TDP-43 pathology. However, what is particularly intriguing is our demonstration that this seeding activity is also detectable in presymptomatic disease stages, mostly in GRN mutation carriers. We also suggest a possible link between positive TDP-43_SAA and conversion to the symptomatic phase.

Disclosure: The work was supported by the project JPND – MINDFACE – MIcroglial early Neuroinflammatory Dysfunction in Frontotemporal Dementia and Amyotrophic Lateral Sclerosis due to C9orf72 repeat Expansions (Coordinator, Prof Van Swieten). Paola Caroppo has received funding from Italian Ministry of Health.

LBN_06 | Early Versus Delayed Add-on Therapy in Generalised Myasthenia Gravis: A Multicentre Real-World Cohort Study

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Background and Aims: Generalised myasthenia gravis (gMG) is an autoimmune disorder marked by fluctuating skeletal muscle weakness due to antibodies targeting the neuromuscular junction. Although many patients respond to standard immunosuppression, a substantial subgroup experiences persistent symptoms or medication-related toxicity. Recently approved add-on therapies – complement component 5 inhibitors (C5IT) and neonatal Fc receptor (FcRn) antagonists – offer new treatment avenues. However, the optimal timing of therapy escalation remains unclear.

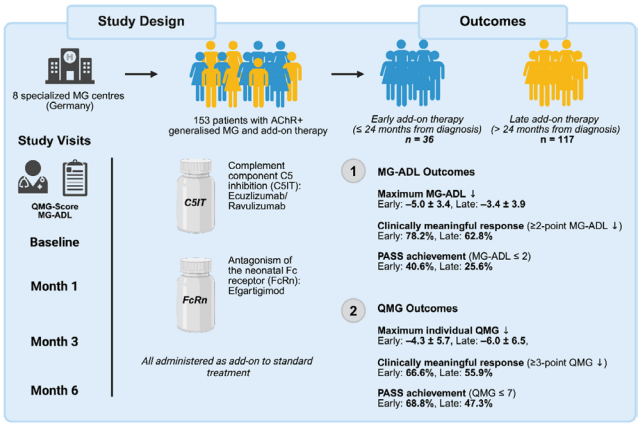

FIGURE 1 Study overview.

Methods: In this multicentre, retrospective cohort study, 153 patients with acetylcholine receptor antibody-positive gMGs were treated at eight specialised German centres with either C5IT (eculizumab or ravulizumab) or FcRn antagonism (efgartigimod). Patients were grouped based on whether treatment began within ($n=36$) or after ($n=117$) 24 months of diagnosis. Disease severity was assessed at baseline and at 1, 3, and 6 months using the Myasthenia Gravis Activities of Daily Living (MG-ADL) and Quantitative Myasthenia Gravis (QMG) scores. Primary outcome was maximum MG-ADL improvement. Secondary endpoints included clinically meaningful response (≥2-point MG-ADL reduction), PASS (MG-ADL ≤2), MSE (MG-ADL ≤1), and QMG-based response (≥3-point reduction).

Results: Early-treated patients showed greater improvements: 78.2% vs. 62.8% achieved MG-ADL response; 40.6% vs. 25.6% reached PASS; 21.9% vs. 18.0% met MSE; and 66.6% vs. 55.9% showed QMG response. QMG worsening occurred in 6.3% (early) vs. 16.2% (late).

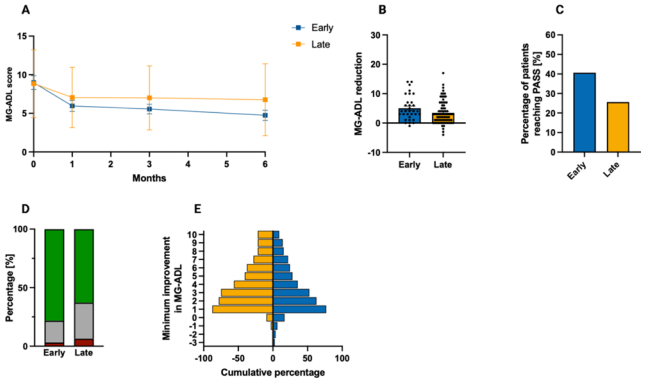

FIGURE 2 MG-ADL outcomes in patients undergoing early versus late treatment escalation.

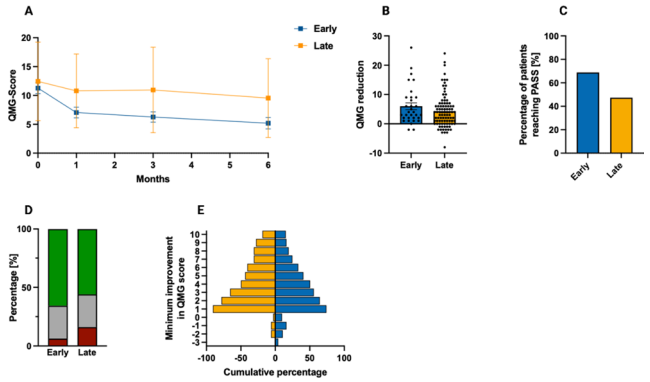

FIGURE 3 QMG outcomes in patients undergoing early versus late treatment escalation.

Conclusion: Early initiation of add-on therapy was associated with more favourable outcomes, supporting a time-sensitive treatment approach in gMG.
Disclosure: Nothing to disclose.

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