ECTRIMS
EUROPEAN COMMITTEE FOR TREATMENT AND RESEARCH IN MULTIPLE SCLEROSIS

Day 3

ECTRIMS 2021 Congress Reporting

Clinical

Free Communication 5: Progression

Friday, 15 October 15:00 – 16:00 CEST
Speakers: Angelo Bellinvia, Carmen Tur, Alessandro Cagol, Synne Brune, Jerry S. Wolinsky
Chairs: Christiane Schmied, Zsolt Illes

Conclusion: Progression independent of relapse activity (PIRA) is more common in patients who are older at time of MS onset and should be identified and treated early to minimise disability accrual. Long-term results continue to support early and continuous ocrelizumab treatment results in more favourable disability progression outcomes.

What's New: In a real-world study of patients with early relapsing MS, PIRA accounted for two-thirds of disability-worsening events overall, although relapse-associated worsening (RAW) events were more frequent than PIRA events in patients with paediatric-onset MS. An analysis of the Barcelona inception cohort found that early PIRA (within 5 years of clinically isolated syndrome [CIS]) was associated with poor long-term prognosis and was more common in patients that were older at the time of CIS. Furthermore, an analysis of the Swiss MS Cohort study found that increased brain atrophy rates in patients with PIRA were at a similar level to patients with focal inflammatory activity.

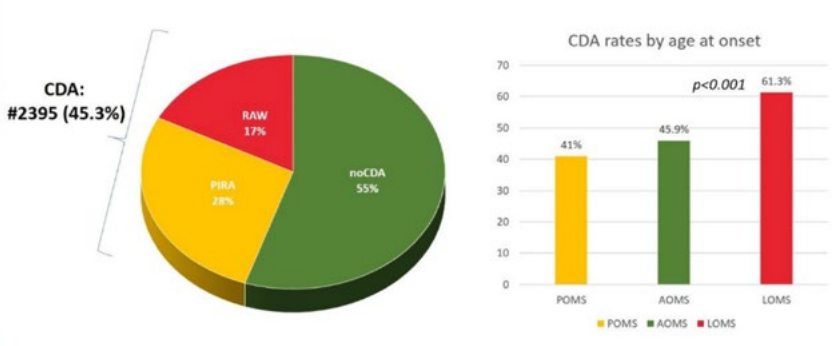
Eight-year follow-up data from the ORATORIO open-label extension study of patients with primary progressive MS treated with ocrelizumab show that earlier, continuous treatment with ocrelizumab results in more favourable confirmed disability progression outcomes. Patients that initiated ocrelizumab 3–5 years earlier than patients switching from placebo had a significantly reduced risk of first CDP-EDSS (Expanded Disability Status Scale [EDSS] score increase from baseline of ≥1 point if baseline EDSS ≤5.5 or ≥0.5 points if baseline EDSS >5.5) and rate of repeated CDP-EDSS.

Composite PIRA measures that include EDSS and other tests to detect disability worsening, combined with MRI activity analysis, could be useful in the research setting to better characterise these patients.

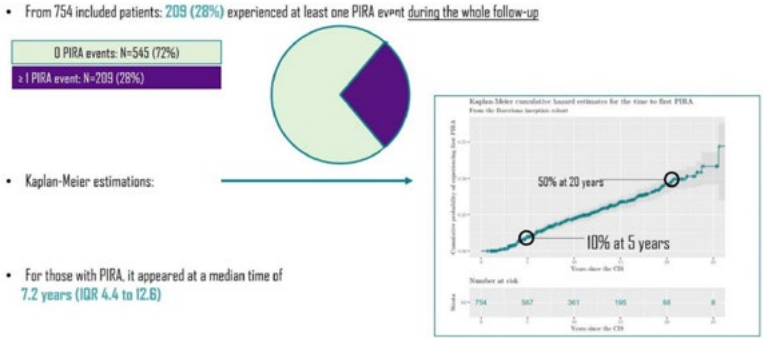
An initial investigation into serum neurofilament light chain concentration in MS suggests that this measurement may be useful as a biomarker for disease progression.

Background: The two mechanisms of disability accrual in MS are RAW and PIRA. Although PIRA is mainly responsible for irreversible disability accrual, the incidence of PIRA in the early stages of the disease has not been investigated previously.

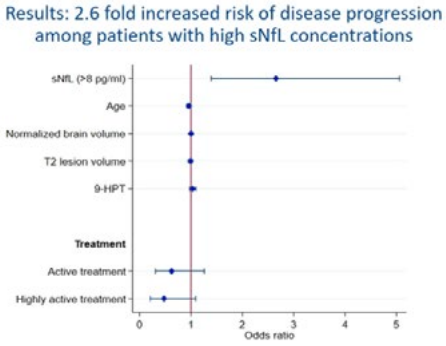
Results: CDA Events
(Bellinvia presentation)



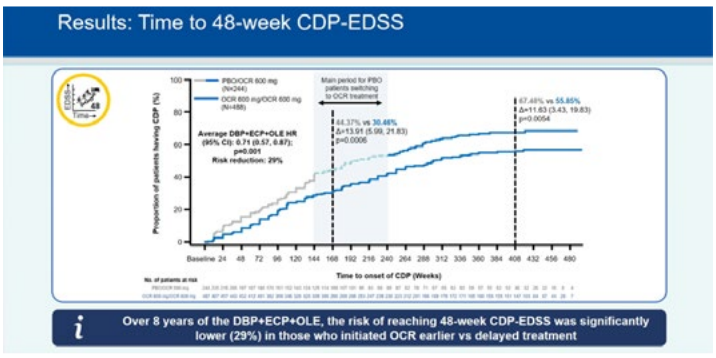
Results: CDA Events
(Tur presentation)



(Brune presentation)



(Wolinsky presentation)



Clinical

Scientific Session 12: Patients' perspectives

Friday, 15 October 12:00 – 13:30 CEST

Speakers: Patricia K. Coyle, Daniel Golan, Mar Tintoré, Stephen Krieger, Jeremy Hobart, Ka Hoo Lam

Chairs: Maria Pia Amato, Oscar Fernandez-Fernandez

Conclusion: Patient-reported outcomes (PROs) provide additional data to clinical assessments and can show differences between patients and their physicians in their general health status and importance of symptoms. Digital solutions, such as smartphone apps, can increase the frequency and convenience of PRO measurement. The COVID-19 pandemic greatly reinforced the value of telemedicine and opened up the potential use of computers in MS therapy.

What's New: Regarding PROs in clinical research, the Symbol Digit Modalities Test is considered the quickest and easiest screening test for cognitive dysfunction.

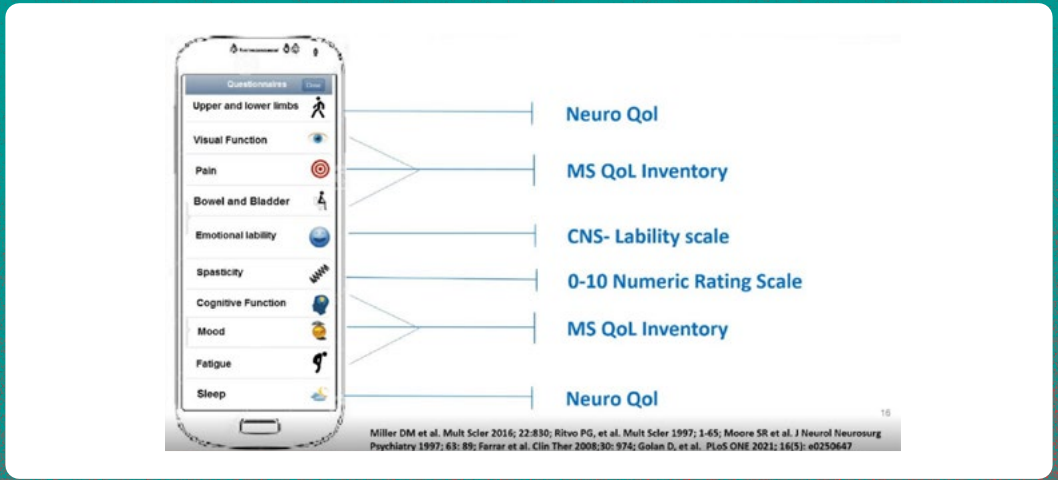
In clinical practice, worsening PROs can alert the physician not only to reassess disease activity and treatment, but also to address issues with anxiety, depression and social support dynamics. The increasing availability and use of electronic techniques to capture PROs will provide valuable data without adding to physician burden, and studies have shown that patients have good adherence to smartphone-based diaries for longitudinal collection of PRO data. Smartphone-adapted versions of patient-reported cognition and walking function measures have shown equivalence to their clinical counterparts, with improved detection of changes due to more frequent assessment.

The Barcelona Baseline Risk Score categorises patients as green, orange or red at disease onset based on patient characteristics and clinical measures. Patients in the red category had a 98% chance of developing McDonald 2017 criteria at 10 years. They also had higher stigma, worse perception of limb function and worse cognitive performance than the orange and green risk groups. A proof-of-concept study found that item banks are a promising basis for developing a high-quality PRO measure of upper limb function in MS.

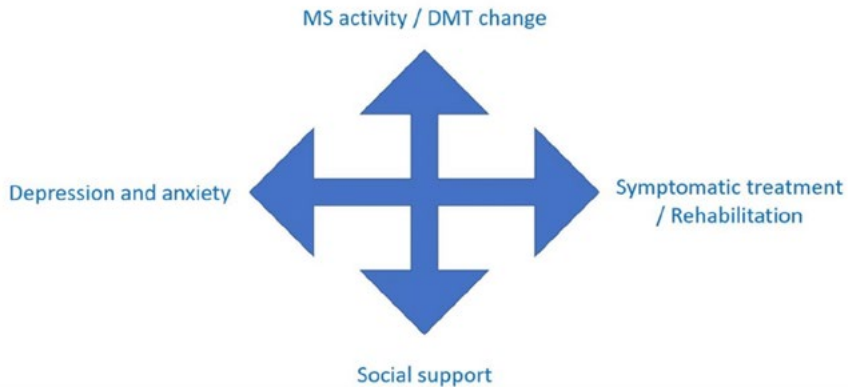
Patients with MS and an Expanded Disability Status Scale score of 0 ('neurologically normal') were found to perform worse than healthy volunteers on a number of standard tests including the timed 25-foot walk and Nine-Hole Peg Test, indicating the importance of subclinical burden.

Background: The use of PROs is becoming more frequent in clinical trials and in clinical practice, with many practitioners feeling that PROs offer the best way to evaluate MS symptoms and quality of life.

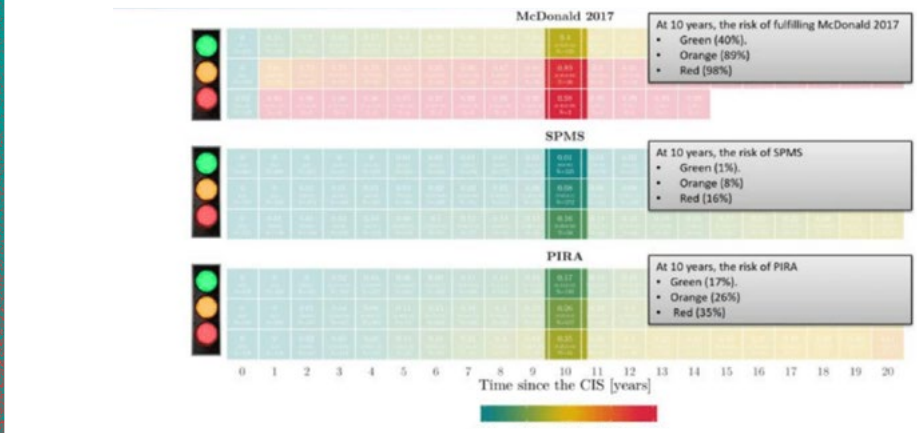
(Golan presentation)



Considerations in case of worsening PROs
(Golan presentation)



Results: Part 1:
LONGITUDINAL clinical trajectories according to BRS
(Tintore presentation)



Pathogenesis

Scientific Session 13: B-cells responses in MS: phenotypes and interactions

Friday, 15 October 12:00 – 13:30 CEST

Speakers: Simon Fillatreau, Bibiana Bielekova, Meike Mitsdoerffer, Marvin M. van Luijn, Marie Freier, Mihir Kakara

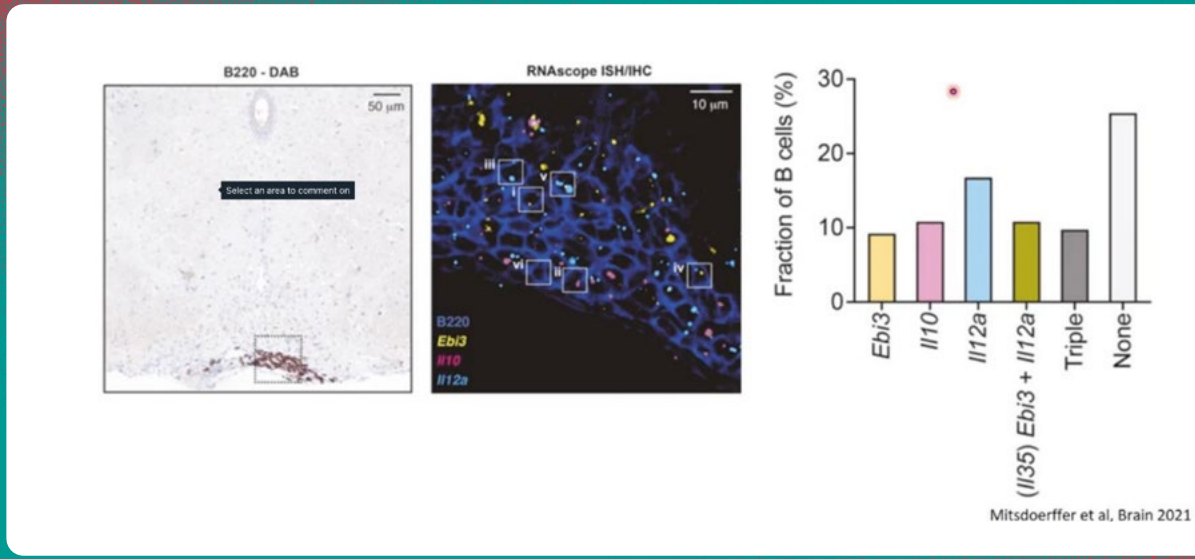
Chairs: Mireia Sospedra Ramos, Amit Bar-Or

Conclusion: B-cells in meningeal B-cell aggregates (MEBAGS) produce anti-inflammatory cytokines and might play a regulatory role during chronic inflammation in the meningeal compartment. B-cells expressing CXCR3 are more prone to infiltrate the brain and differentiate into antibody secreting cells than other B-cells. It is likely that the functional dysregulation of B-cells in the cerebrospinal fluid results in compartmentalisation of inflammation to central nervous system (CNS) tissue that might contribute to reduced efficacy of current disease-modifying treatments. SARS-CoV-2 mRNA vaccination is recommended for patients receiving B-cell-depleting therapy because of robust CD4+ and CD8+ responses; however, it may be best to maximise the time between vaccination and both the previous and next dose of MS treatment.

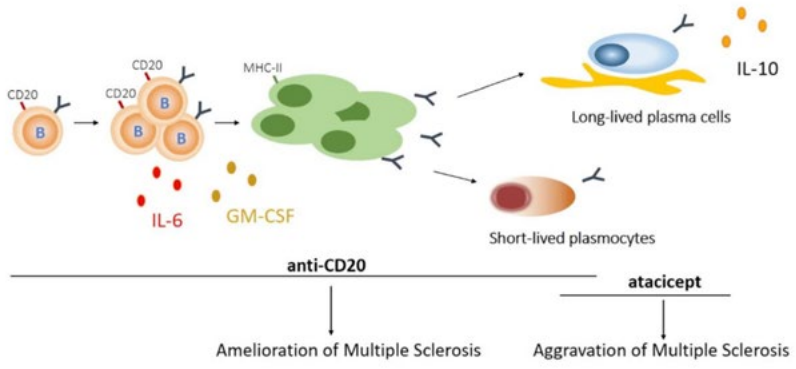
What's New: The absence of alfa4-integrins on myelin oligodendrocyte glycoprotein (MOG)-specific T- or B-cells or the elimination of B-cells inhibits formation of meningeal B-cell aggregates and increases severe CNS inflammation and disease progression in preclinical models of MS. Alfa-AQP4 and alfa-MOG IgG antibodies found in patients with neuromyelitis optica spectrum (NMO) and MOG antibody-associated disease (MOGAD) opsonise CNS antigen in preclinical models, fostering protein update by human antigen-presenting cells. Patients receiving B-cell-depleting therapy have attenuated antibody and antigen-specific memory B-cell responses to SARS-CoV-2 mRNA vaccines that are correlated with time from last anti-CD20 infusion; however, CD4+ T-cell and antigen-specific CD4 T-cell responses are robust, although mildly attenuated, and antigen-specific CD8+ T-cell responses are robust and mildly augmented.

Background: B-cells and antibody-secreting cells, including plasmablasts and plasma cells, play a role in progression of MS and the presence of meningeal B-cells has been associated with a more severe disease course in patients with MS. However, some plasma cells can produce anti-inflammatory cytokines that are protective against MS, indicating the complex relationship of cellular responses in this disease. B-cells and B-cell-secreted antibodies also have a role in progression of other CNS demyelinating disorders. Patients receiving B-cell-depleting (anti-CD20) therapy may be at increased risk of SARS-CoV-2 infection and may have attenuated antibody responses to vaccines against the virus.

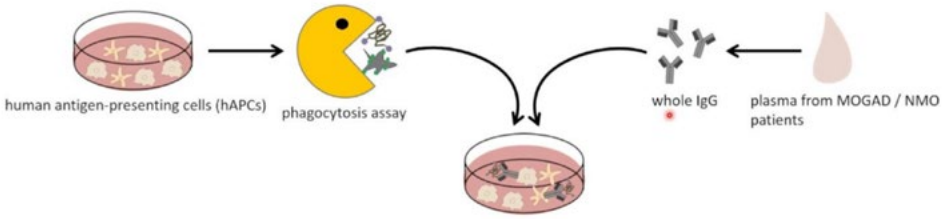
B cells in MEBAGs produce immunomodulatory cytokines
(Mitsdoerffer presentation)



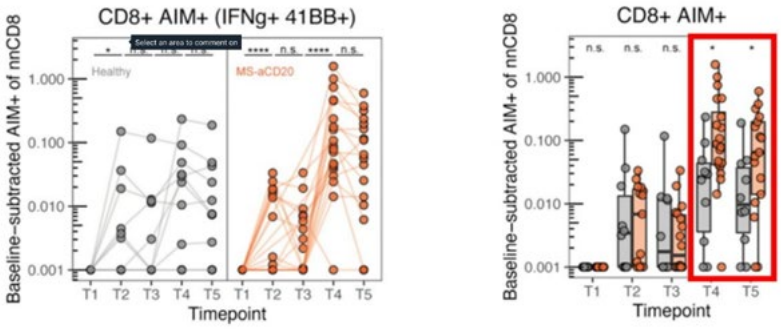
Relevence of cytokine production by B cell subsets for therapy
(Fillatreau presentation)



Investigating the opsonizing capacity of a-MOG antibodies in MOGAD patients
(Freier presentation)



Antigen-specific CD8 T-cells
(Kakara presentation)



Pathogenesis

Scientific Session 16: Gut microbiome – much ado about nothing?

Friday, 15 October 15:00 – 16:30 CEST

Speakers: Anne-Katrin Pröbstel, Stephanie Tankou, Thomas Korn, Xiaoyuan Zhou, A.L. Bruijstens, Martin Diebold

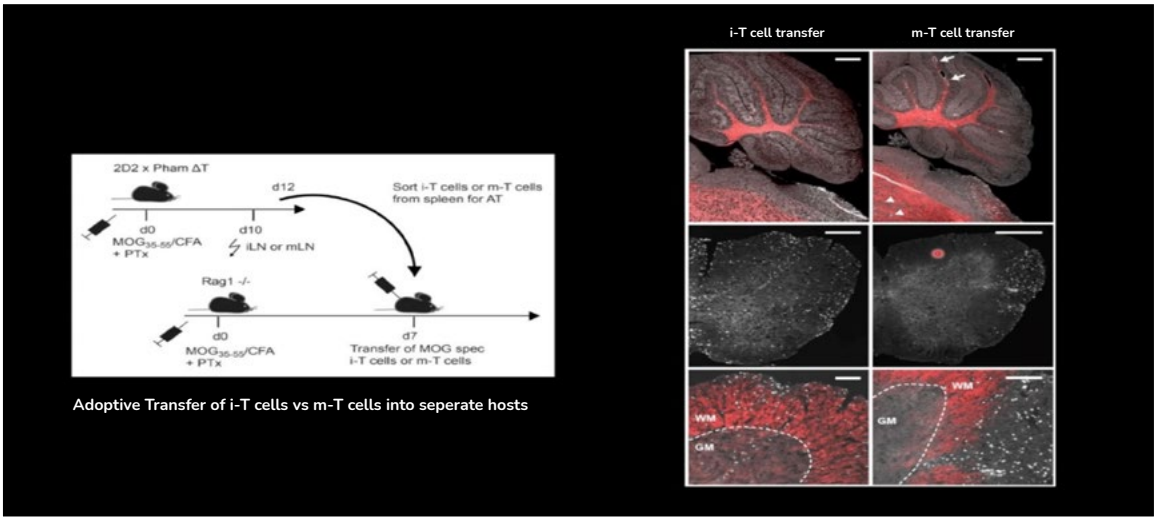
Chairs: Paulus Rommer, Gabriele C. De Luca

Conclusion: Peripheral T-cells have been identified that may be targetable for specific central nervous system (CNS) pathologies. The microbiome of patients with MS differs from that of controls and may be modulated by disease-modifying treatments (DMTs), dietary interventions and more investigational interventions such as probiotics, microbial-derived products, antibiotics and faecal microbiota transplant. However, in paediatric patients with MS, no specific MS-related microbiota have been identified. Pre-treatment microbiome composition might predict the development of dimethyl fumarate (DMF)-associated lymphopenia.

What's New: Alterations in the gut microbiome in patients with MS are (1) associated with increased phytate degradation and increased carboxylate metabolism, and (2) may be corrected by certain DMTs and dietary changes, potentially altering neuroinflammation. T-cells from skin and mesenteric lymph nodes are distinct and cannot be classified by T-helper cell lineage; these T-cells migrate to the CNS differentially, with skin-derived T-cell grey-matter recruitment driven by CXCR6. In paediatric patients with MS, the gut microbiome does not differ from that of healthy controls; however, obesity is associated with differences in the overall composition and presence of individual microbes. Treatment with DMF does not affect the overall alfa diversity of the gut microbiome, but alters levels of specific strains. The overall microbiome composition is not correlated with the efficacy of DMF, but is moderately corelated with lymphopenia, as a result of differences in glycolysis between patients and the contribution of multiple specific microbiota strains.

Background: The gut microbiome modulates the immune system and neurodevelopment. Specific alterations in the gut microbiome are associated with MS, MS progression and DMTs such as DMF. The microbiome can alter the peripheral T-cell balance to a more proinflammatory phenotype that contributes to neuroinflammation, whereas gut-originating immunoglobulin-A-producing B-cells can regulate gut homeostasis and microbiota composition, as well as promoting neuroinflammation. Autoreactive T-cells can be primed in peripheral lymph nodes before migration to the CNS.

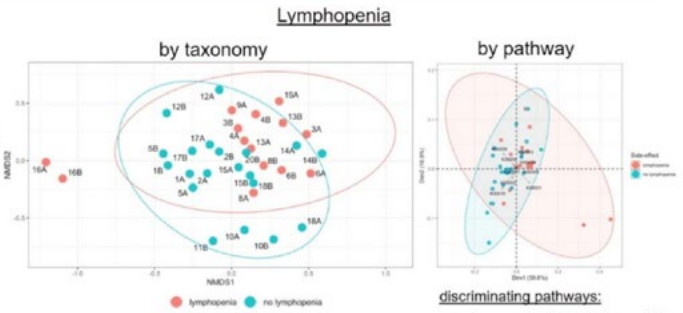
Functional phenotpyes of i-T cells and m-T cells in the CNS
(Korn presentation)



Adoptive Transfer of i-T cells vs m-T cells into seperate hosts

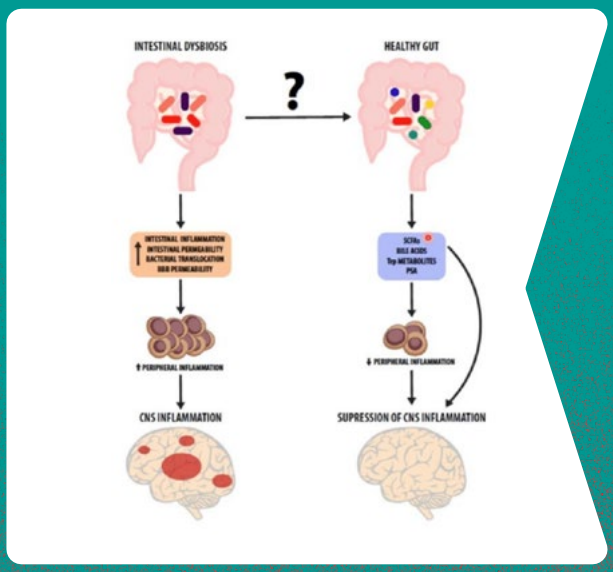
Correlation with Lymphopenia
(Diebold presentation)

- Moderate discrimination of overall microbiome composition regarding lymphopenia
- Reconstruction of affected KEGG orthologs and metabolic pathways using PICRUSt 2.0: Metabolic alterations affecting glycolysis mainly observed in patients with lymphopenia

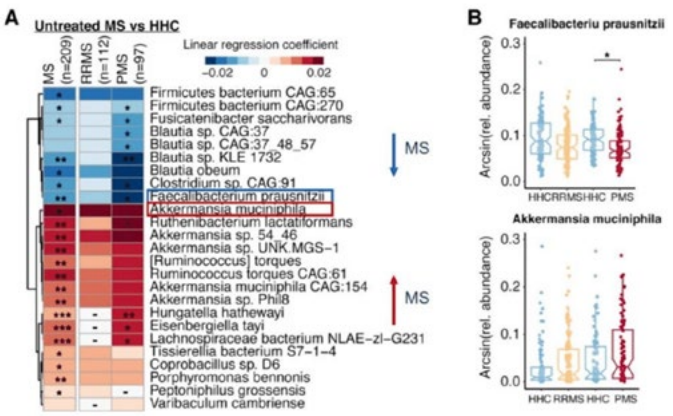


discriminating pathways:
- glycogen and starch degradation
- pentose phosphate pathway
- pyruvate degradation

The gut microbiome as a therapeutic target
(Tankou presentation)



Git mircobiome was altered in untreated MS versus HHC
(Zhou presentation)



Imaging & Non-Imaging

Scientific Session 14: Advanced MRI methods for assessing changes in brain metabolism and tissue structure

Friday, 15 October 12:00 – 13:30 CEST

Speakers: Wolfgang Bogner, Maria Assunta Rocca, Laura Lacruz-Ballester, Olwen C. Murphy, Ceren Tozlu, Alessandro d'Ambrosio

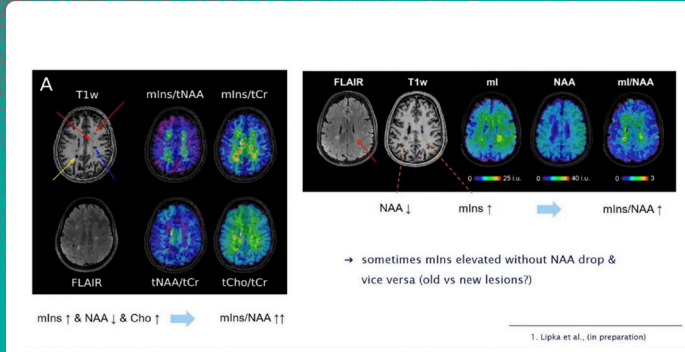
Chairs: Stefan Ropele, Hugo Vrenken

Conclusion: Magnetic resonance spectroscopic imaging (MRSI) may be used to detect a number of promising biomarkers in MS pathology. Improved magnetic resonance imaging (MRI) techniques have increased the knowledge of white matter damage and repair mechanisms. Spinal cord T2 lesions have been identified as a strong predictor of progression from clinically isolated syndrome (CIS) to secondary progressive MS. Finally, trans-synaptic degeneration appears to be a pathway of neurodegeneration in MS.

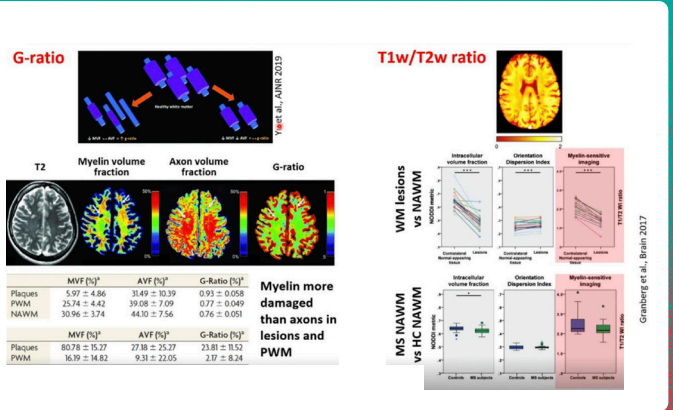
What's New: Myo-inositol (mIns) detected by MRSI has been identified as a potential biomarker for early lesion development and n-acetyl aspartate (NAA) may indicate later expansion of lesions. Magnetisation transfer (MTR) has been reported to drop during demyelination in white matter lesions and increase during remyelination. Other advanced techniques include myelin water imaging (MWI) to detect progressive myelin damage and neurite orientation dispersion and density imaging (NODDI) to detect axonal damage. The occurrence and number of T2 lesions in the spinal cord at time of CIS were significantly higher in patients that converted to secondary progressive MS than patients who converted to relapsing remitting MS or who did not convert. Indicators of trans-synaptic degeneration were observed in patients with MS after acute optic neuritis (AON), including reductions in retinal layer thickness and brain substructure atrophy. Functional connectivity networks estimated from standard MRI scans using deep learning were found to outperform functional connectivity networks observed with advanced MRI. Furthermore, the application of machine learning to MRI scans was shown to predict cognitive impairment and identified that changes in other brain structures may be more relevant than white matter lesion volume.

Background: The spectrum generated by MRSI has the potential to be used for biomarker detection of lesion development in MS, and structural and functional connectivity measured with other advanced techniques may be biomarkers for clinical disability. Pathology of MS has heterogenous effects on brain white matter and includes both demyelination and remyelination. Brain MRI T2 lesions at CIS are a well-known risk factor for developing secondary progressive MS. Trans-synaptic degeneration may occur in MS but has not been clearly observed *in vivo*.

Two relapsing-remitting MS sample cases
(Bogner presentation)



WM lesions and NAWM / Grading
(Rocca presentation)



Imaging & Non-Imaging

Young Scientific Investigators' Session 3: Imaging

Friday, 15 October 15:00 – 16:00 CEST

Speakers: Elia Sechi, Alberto Calvi, Andrea Lazzarotto, Frederike Cosima Oertel, Rosa Cortese

Chairs: Nevin Shalaby, Katie K. H. Chan

Conclusion: Recent developments in imaging techniques and analytical methodology provide new opportunities for earlier diagnosis and more precise disease monitoring in MS and other demyelinating diseases. Furthermore, there is increased understanding of the mechanisms of disease onset and progression, which may help to guide future drug development.

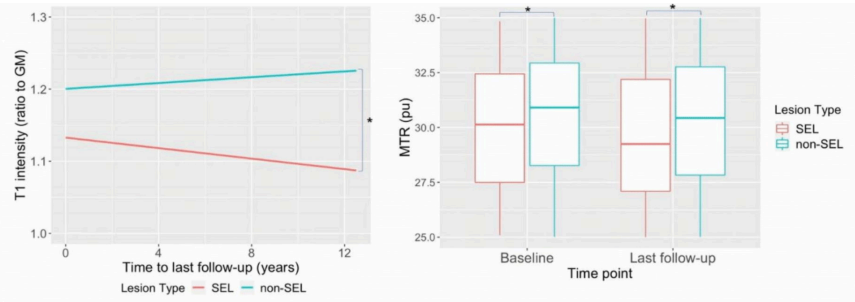
What's New: T2 lesions resolve more frequently in myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) than MS, and black holes are uncommon in MOGAD. Longitudinal retinal optical coherence tomography found no evidence of subclinical retinal neurodegeneration in MOGAD; however, there was a prolonged influence of optic neuritis on neuroaxonal loss.

Slowly expanding lesions (SELs) represent approximately 30% of all T2 lesions in relapse-onset MS, and are associated with increased disability progression. Long-term follow-up revealed that SELs can be detected for up to 12 years.

The Magnetic Resonance Imaging in Multiple Sclerosis (Magnims) study used the MRI magnetisation transfer ratio to assess myelin content in patients with different forms of MS versus healthy controls. Changes in cortical myelin content were found to be very heterogenous in all forms of MS, and cortical remyelination prevents short-term cortical atrophy and protects against clinical progression in early MS.

Background: The evolution of MRI lesions may be important for diagnosis and understanding differences in pathogenesis between demyelinating diseases. In MS, SELs are more common in progressive disease and represent a novel biomarker. The inflammatory demyelinating disease MOGAD is a distinct condition from MS, with patients often presenting with optic neuritis.

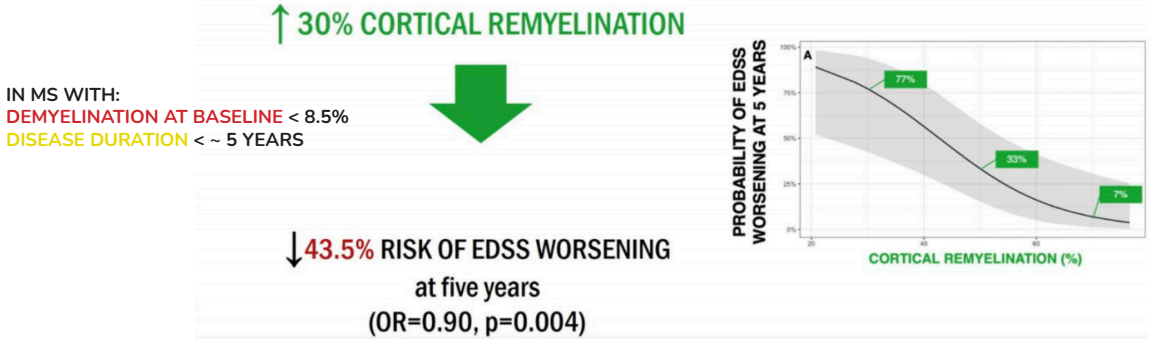
Results: T1 & MTR Analysis
(Calvi presentation)



SELs showed a longitudinal decrease in T1 intensity and lower MTR at baselline and last follow-up vs non-SELs

*p<0.001, mixed-effects models adjusted for age, gender, time to follow-up, T2 lesion volume, T2 lesion volume change

Cortical Remyelination protects from clinical progression in early MS
(Lazzarotto presentation)



Biomarkers/Translational Therapy

Scientific Session 15: Neurorehabilitation in MS – delete old views and see new ways

Friday, 15 October 12:00 – 13:30 CEST

Speakers: Ulrik Dalgas, Barbara Seebacher, Morten Riemenschneider, Brian Sandroff, Jacqueline Nicholas, Rainer Ehling

Chairs: Hanneke Hulst, Alan J. Thompson

Conclusion: Exercise and motor imagery are established as effective tools for neurorehabilitation in MS. New and promising neurorehabilitative strategies are also under development, building on these existing approaches and exploring new avenues to compensate for functional deficits and to address complications such as spasticity.

What's New: A selection of original papers presented during this session highlighted important new research being undertaken in the field of neurorehabilitation in MS.

Results from the Early Multiple MS Exercise Study (EMSES) have highlighted the potential disease-modifying and neuroprotective efficacy of exercise therapy early in the disease course of MS. This study enrolled 84 patients ≤2 years since relapsing remitting MS diagnosis, randomised to either supervised exercise group therapy or health education (control). The exercise group showed a greater increase in aerobic capacity, and the annualised relapse rate was almost half that of the control group (0.12 versus 0.23), although the difference in incidence-rate-ratio was not significant.

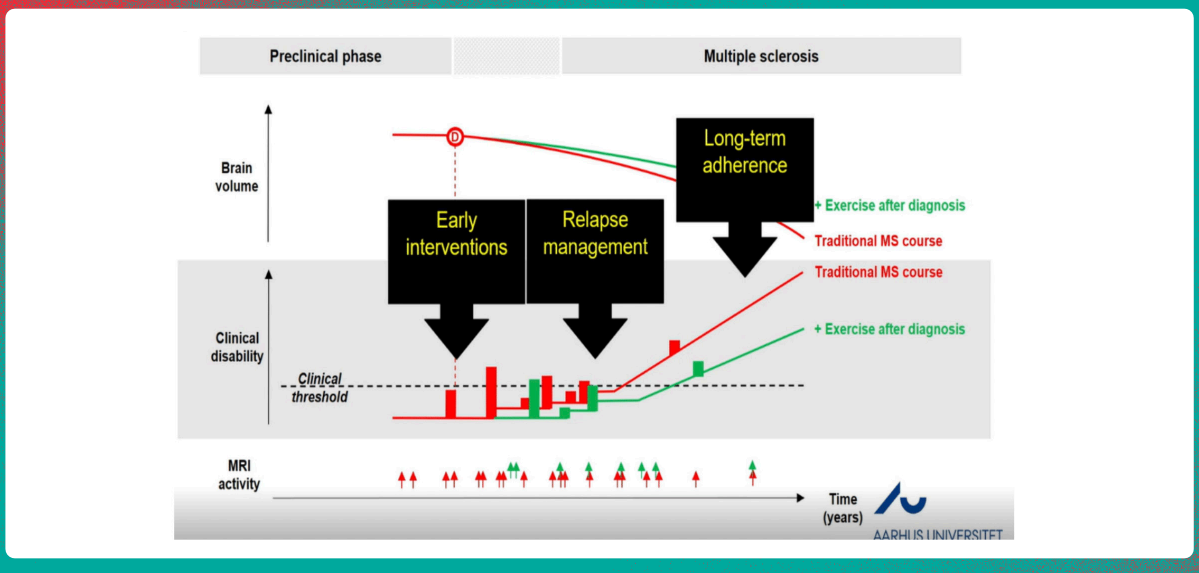
Analysis of baseline data from the multisite CogEx randomised controlled trial (RCT) indicated that cardiorespiratory fitness and free-living physical activity were not associated with better cognitive performance in patients with progressive MS. These findings highlight the importance of examining other exercise-related mechanisms of action for improving cognition and brain health in progressive MS.

Nabiximols oromucosal spray is a botanical mixture containing plant-derived cannabinoids and other ingredients. Analysis of data from two pivotal RCTs has shown that nabiximols confer a measurable benefit on spastic muscle tone in MS, as assessed by the Modified Ashworth Scale (MAS) measurements in relevant muscle groups. In these studies, nabiximols were generally well tolerated, with dizziness being the most common adverse event.

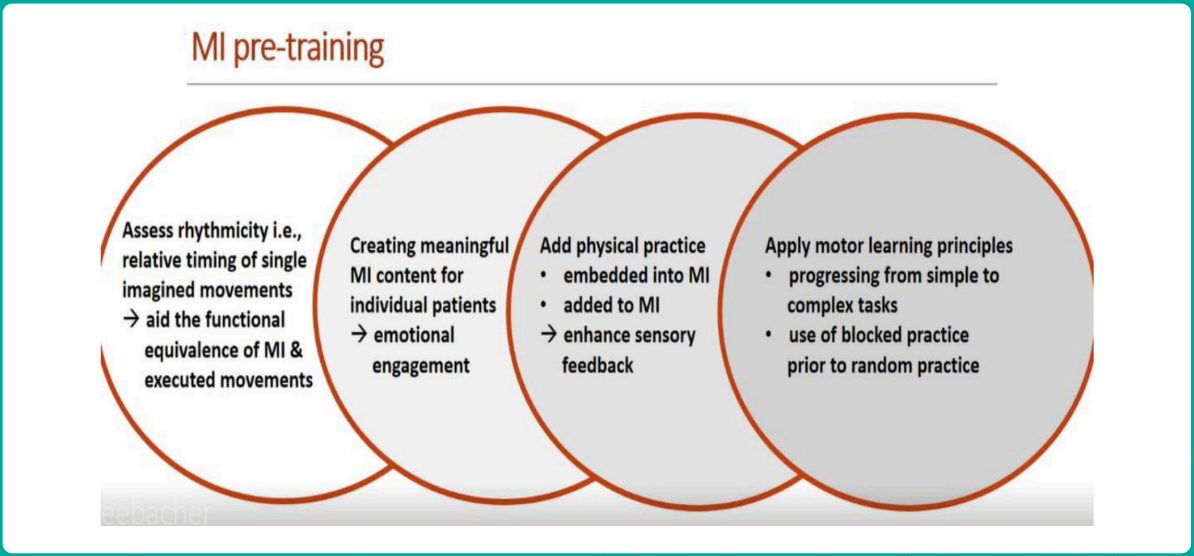
Findings from a randomised, controlled, multicentre trial of 94 patients have demonstrated the successful long-term management of spasticity in people with MS using a software app to maximise adherence to an exercise rehabilitation program. Self-training with the individualised MS spasticity app was effective in sustaining improvements from inpatient rehabilitation for 12 weeks, with high adherence.

Background: The accumulated evidence from multiple studies has shown that exercise in MS is safe and potent, with no significant side effects. Exercise is an important symptomatic treatment at all disease stages and may have disease-modifying effects, suggesting that greater emphasis should be placed on its preventative effects. Motor imagery (MI) is another approach to neurorehabilitation in MS, which involves the mental rehearsal of movements without their actual execution. MI success can be maximised by focusing on more dexterous and frequently used body parts and by the concomitant use of external rhythmic auditory or visual cues.

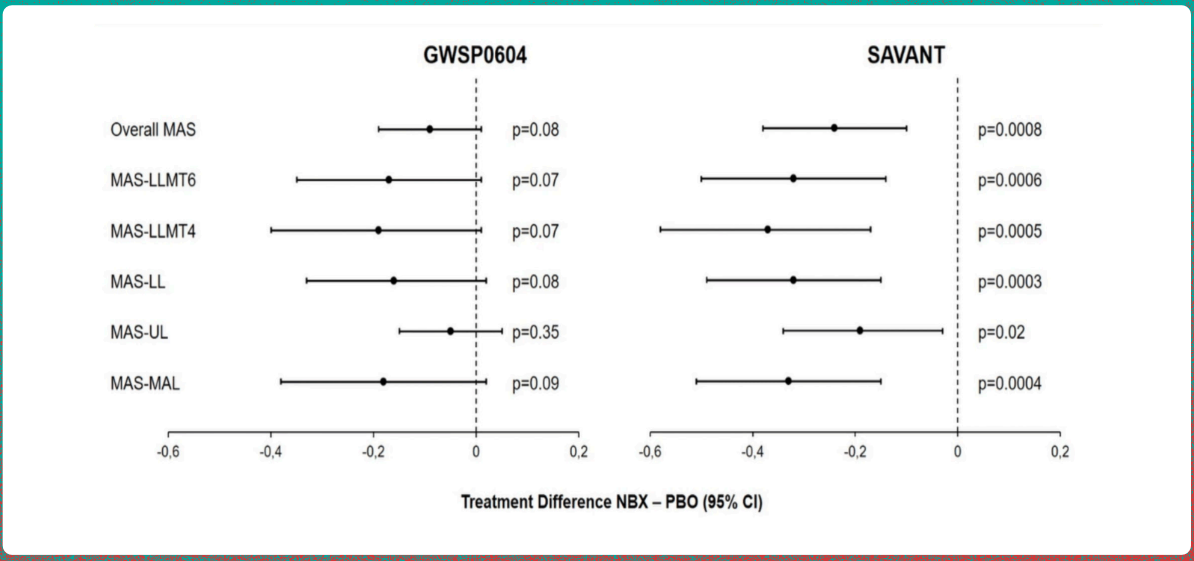
Challenges and directions
(Dalgas presentation)



A tentative framework: What can be done?
(Seebacher presentation)



Treatment Difference (NBX - PBO)
(Nicholas presentation)



Biomarkers/Translational Therapy

ECTRIMS-EAN Session

Friday, 15 October 15:00 – 16:30 CEST

Speakers: Sandra Vukusic, Susana Otero-Romero, Mauricio Farez, Simón Cárdenas-Robledo, Xavier Montalban

Chairs: Massimo Filippi, Mar Tintoré, Maria Pia Amato, Celia Oreja-Guevara

Conclusion: Patients with MS should continue to receive influenza, pneumococcal, local/travel vaccines and eventually yearly boosters of COVID-19 vaccines in line with national recommendations on immunisation programmes. Vaccination should be considered early in the MS management algorithm, before initiation of immunosuppressants whenever possible.

What's New: As a result of a joint effort between ECTRIMS/EAN, the first European consensus on vaccination in MS patients has been developed, and recommendations are expected to be published soon. ECTRIMS/EAN has also developed a position statement for immunisation against COVID-19 in MS patients, available as a web-based Q&A format document on the ECTRIMS and EAN websites.

EAN/ECTRIMS guidelines on the treatment of patients with MS have been updated and include the following recommendations:

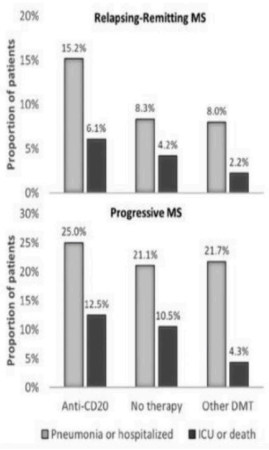
- Offer interferon (IFN) or glatiramer acetate (GA) to patients with clinically isolated syndrome (CIS) highly suggestive of MS and an abnormal magnetic resonance imaging (MRI) with lesions suggestive of MS who do not fulfil criteria for MS (Topic 1).
- For patients with relapsing-remitting MS, offer treatment with IFN beta-1b, IFN beta-1a, pegIFN beta-1a, GA, teriflunomide, dimethyl fumarate, cladribine, fingolimod, ozanimod, ponesimod, natalizumab, alemtuzumab, ocrelizumab or ofatumumab (Topic 1).
- For patients with secondary progressive MS (SPMS) with evidence of inflammatory activity (relapses and/or MRI activity) offer treatment with siponimod (Topic 1).
- For SPMS without evidence of inflammatory activity, particularly in young patients and those in whom progression has started recently, consider treatment with siponimod or anti-CD20 monoclonal antibodies (Topic 1).
- Consider ocrelizumab for patients with primary progressive MS, particularly early and active (clinically and/or radiologically) disease (Topic 1).
- Consider choosing a higher efficacy disease-modifying drug (DMD) early on, according to disease activity (either clinically or on MRI) and patient particulars (Topic 2).
- Offer a more efficacious drug to patients treated with DMDs who show evidence of disease activity (Topic 3).
- In the stable patient (clinically and on MRI) who shows no safety or tolerability issues, consider continuing treatment with DMDs taking into account patient circumstances (Topic 4).

Background: The available evidence indicates that MS patients do not seem to develop more severe forms of COVID-19 compared with healthy controls, although patients with greater disability receiving anti-CD20 treatment or with recent steroid use are at higher risk. So far, no specific contraindications have been reported for any vaccines in MS patients. Vaccinations in general are considered safe for patients with MS and do not modify disease activity/progression; however, live attenuated vaccines are contraindicated with immunosuppressants.

Are patients with MS at higher risk of COVID-19 or having more serious form of the disease?

(Farez presentation)

- Treatment with IFNs or GA do not increase the risk of getting the infection or worsen the clinical course of COVID-19 disease.
- Fingolimod, teriflunomide, natalizumab and dimethyl fumarate do not seem to negatively affect SARSCoV- 2 infection.
- Several studies showing anti-CD20 antibodies and steroid pulses confering an increased risk of COVID-19.



Recommended Vaccines
(Otero-Romero presentation)

1. **Routine vaccination schedule** for the general population
2. **Influenza and pneumococcal vaccination** if immunosuppression or significant disability
3. **Human papillomavirus vaccine** in women and men, independently of their age if treatment with alemtuzumab, S1P, cladribine or anti-CD20
4. **Herpes zoster inactivated vaccine** in patients over 50 years of age if treatment with cladribine, alemtuzumab, S1P, natalizumab or anti-CD20
5. **Hepatitis B vaccine** in non-immune in patients if treatment with anti-CD20

EAN / ECTRIMS guidelines development group
(Montalban presentation)

Working Group

Chairs
Xavier Montalban (Spain) & Maria Pia Amato (Italy)

Working group

Kerstin Hellwig (Germany)
Alan Thompson (UK)
Sandra Vukusic (France)

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Biomarkers/Translational Therapy

Scientific Session 18: Late Breaking News

Friday, 15th October 16:45 – 17:45 CEST

Speakers: Gabriel Bsteh, Sifat Sharmin, Hanneke Hulst, Koji Shinoda, Hardeep Kataria, Alexandra Nicaise

Chairs: Samia Khoury, Heinz Wiendl

Conclusion: Knowledge and understanding in MS continues to grow with exciting new research into risk prediction, cellular profiling and translational experiments.

What's New: An Australian, multicentre, prospective cohort study involving ~600 participants assessed the humoral immune response and safety of SARS-CoV-2 vaccines in MS patients and healthy controls. Vaccination was found to be safe and humoral responses in MS were generally excellent. Responses were reduced in patients receiving anti-CD20 therapy and sphingosine-1-phosphate receptor modulators, but the majority still developed antibodies.

Evidence from a multi-national registry (MSBase) has identified early predictors of disability in paediatric MS. First-year clinico-demographic characteristics found to be predictive of disability worsening included: MS symptoms presenting later in childhood; higher disability; frequent relapses; a greater number of relapses with incomplete recovery and pyramidal, visual or cerebellum symptoms. Complete recovery from first relapse, presence of brainstem relapses in the first year and persistent treatment with high-efficacy disease-modifying therapies (DMTs) were favourable for disease prognosis.

11C Flumazenil positron emission tomography has been validated for use in MS and has been shown to have clinical applicability in patients with cognitive impairment. Higher gamma aminobutyric acid (GABA) receptor binding was seen in cognitively preserved versus impaired patients, and K1 and VT values were altered differently in different stages of cognitive impairment.

A cellular profiling study involving two independent cohorts of MS patients treated with ocrelizumab showed that, as expected, anti-CD20 therapy depleted the majority of circulating B-cells as well as CD20-expressing T-cells. For both CD4+ and CD8+ T-cells, the cells removed were preferentially effector memory, pro-inflammatory cytokine-producing and CNS-trafficking T-cells. Results also implicated CD20dimCD8+ T-cells leaving the circulation as an early step in the development of new MS disease activity.

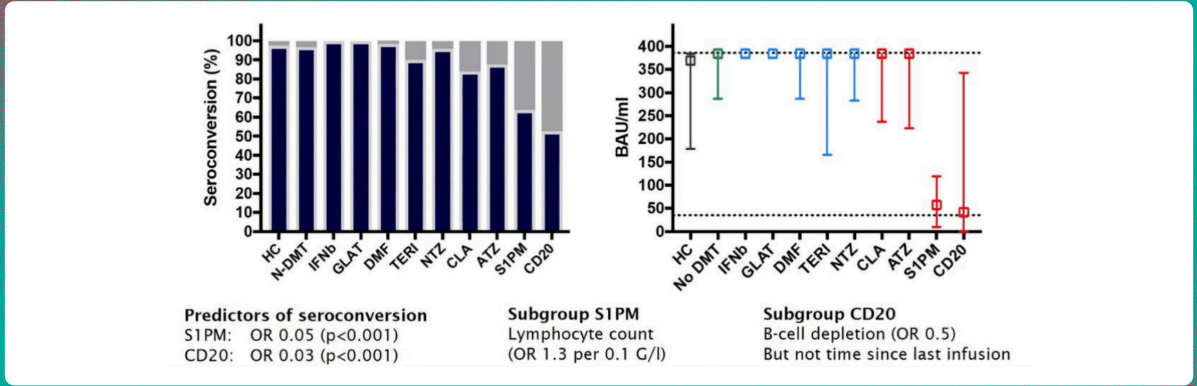
Neuregulin-1 (Nrg-1) is an important growth factor with roles in inflammation modulation and remyelination, which is being investigated as a potential therapeutic in MS. Nrg-1 is depleted in the brain lesions of MS patients but has been shown to ameliorate experimental autoimmune encephalomyelitis disease deficits and preserve axons and accelerate remyelination in animal models. It also promotes myelin debris metabolism and expression of cholesterol exporters in the microglia, and enhances oligodendrocyte precursor cell (OPC) maturation.

Research has documented a decline of neural stem cell (NSC) resilience in MS. A disease-associated phenotype was found in NSCs from patients with progressive MS compared to age-matched controls. This effect was reminiscent of cellular ageing/senescence and loss of resilience that occurs over time and initiates the transition to the progressive MS disease state. Associated phenotypic differences included cell cycling and transcriptomic/epigenetic changes.

Background: The late-breaking news sessions showcase cutting-edge new research findings in the field of MS.

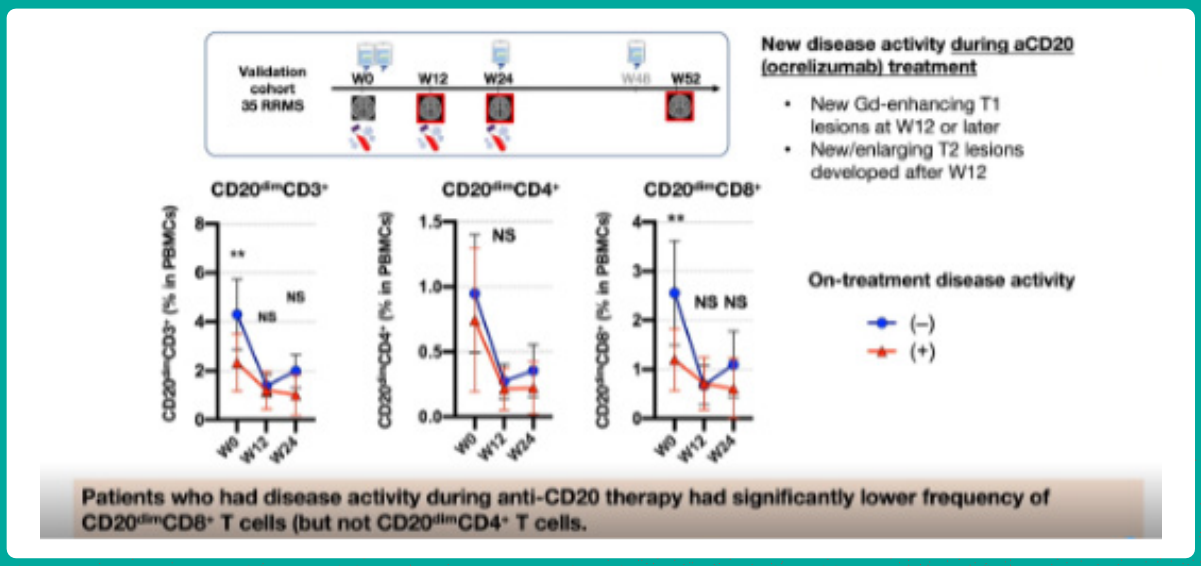
Seroconversion and antibody titer and DMTs

(Bsteh presentation)



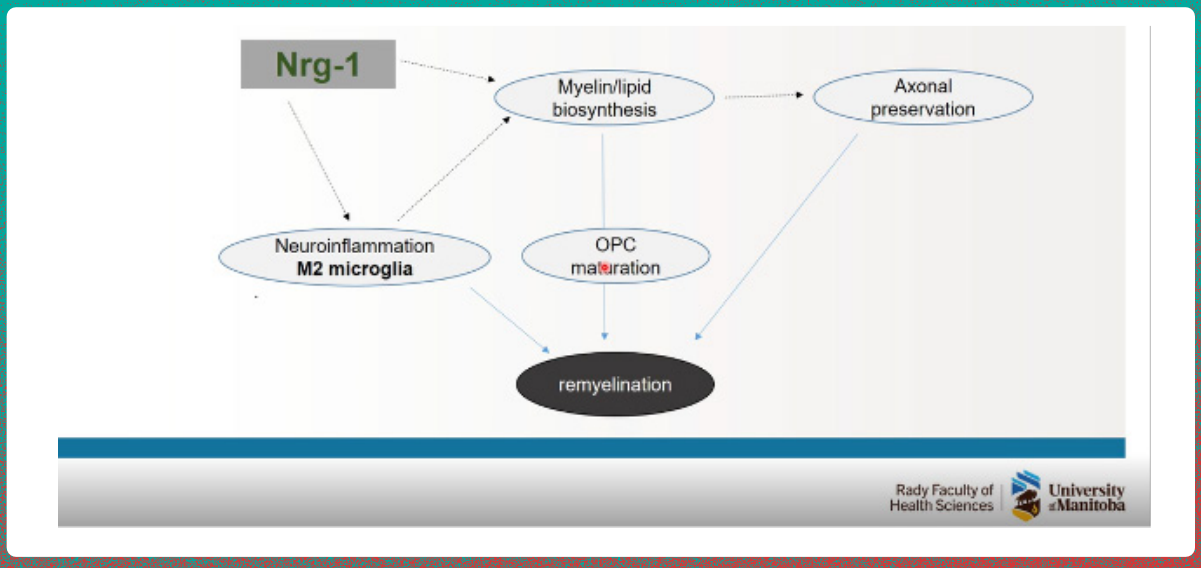
Disease activity early after aCD20 initiation associated with lower baseline CD20^{dim}CD8^{+} (not CD4^{+}) T cell frequencies

(Shinoda presentation)



Possible mechanisms of Nrg-1 in remyelination in MS

(Kataria presentation)



Biomarkers/Translational Therapy

Plenary Session 2: Awards, ECTRIMS Honorary Members, Charcot Lecture and ECTRIMS 2021 Highlights

Friday, 15th October 18:00 – 19:00 CEST

Speakers: Alan J. Thompson, Lou Brundin, Ruth Ann Marrie, Roland Wiest, Martin Kerschensteiner, Bernard Uitehaag

Chairs: Maria Pia Amato, Mar Tintoré, Thomas Berger

Conclusion: The ECTRIMS 2021 annual congress involved a total of 9000 participants and 200 speakers from 100 countries, and showcased approximately 1700 original abstracts. The focus for the 2021 programme was translation of neuropathological and immunopathogenetic insights, including new body fluid and imaging-based biomarkers. ECRIMS continues to move towards the vision of achieving personalised treatment for MS patients by adopting a broader holistic view of both management and care-giving.

What's New:

Awards. 2021 Charcot award: Alan Thompson; ECTRIMS Honorary Member: Bernhard Hemmer; ECTRIMS Young Investigator Awards: Melanie Eschborn, Gabriel Bsteh; ECTRIMS Poster Awards: Paolo Preziosa, Mattias Bronge, Zoe Yolanthe Germieke Jocelyn van Lierop, Izanne Roos, Marta Pengo; MSIF Young Investigator Award: Giacomo Boffa.

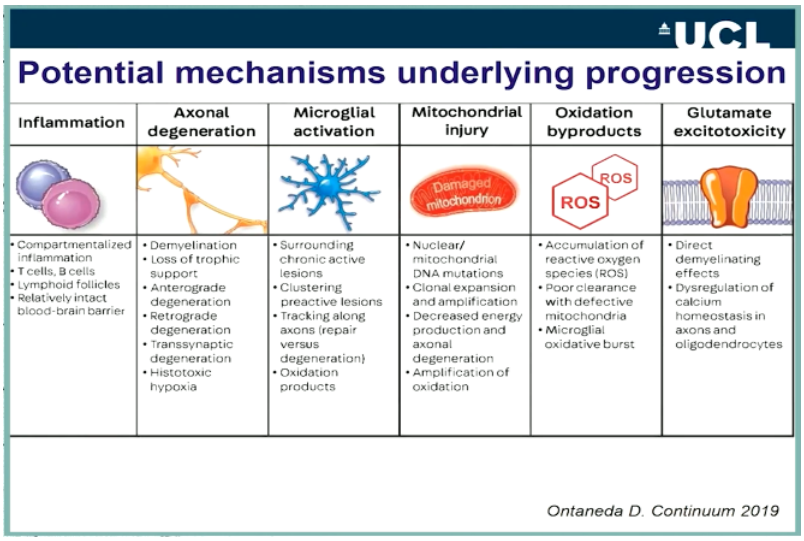
Clinical Highlights included identification of genes (e.g. TWNT9B) and comorbidities that increase risk of relapse and disability progression in MS. Progression independent of relapse activity (PIRA) has emerged as an area of intense research, with time spend on disease-modifying therapy (DMT) shown to lower PIRA risk. In the COVID-19 domain, studies have revealed a suboptimal antibody response in patients on B-cell depleting therapies and identified key risk factors for severe COVID-19 outcomes in MS populations.

Scientific Highlights included new research targeting disease-relevant cellular interactions in the CNS and further dissection of the role of microglia cells which are found in white and grey matter lesion borders and appear to be a site for lymphocyte interactions. Microglial cells instruct CNS damage and repair with a dual role for complement, while microglia-oligodendrocyte interactions can modulate remyelination. Important advances in MS imaging have come in the form of clinical magnetic resonance imaging (MRI), molecular imaging and the use of ultra-high field MR.

EAN/ECTRIMS have unveiled two important projects: Updated EAN/ECTRIMS treatment guidelines for MS and new vaccination consensus recommendations.

Background: The focus for the 2021 Charcot lecture was progressive MS which affects an estimated 1 to 1.5 million patients worldwide. Progressive MS has moved 'centre stage' in recent years due to new treatments and increased international research focus. Understanding of the underlying pathological mechanisms of progression has advanced and it is now recognised that these processes begin early in the disease process. Timely intervention is therefore critical before compensatory cognitive mechanisms are lost and the impact of ageing becomes more pronounced. Future treatments in progressive MS are focusing not just on immune modification, but exciting new areas such as neuroprotection and remyelination.

Potential mechanisms underlying progression
(Thompson presentation)



Immune modification
(Thompson presentation)