The evolution of infusion therapy for Parkinson’s Disease
Translating clinical progress into personalised solutions

Britannia-sponsored virtual symposium
Monday 21 June 2021, 13:45–14:45, Vienna Room

Agenda

Welcome & introductions: Device-aided therapies for PD – current landscape and goals of treatment
K Ray Chaudhuri (UK) – Symposium Chair

Developments in levodopa infusion therapies - less is more
Dag Nyholm (Sweden)

The patient experience – generating data to improve outcomes
Tobias Warnecke (Germany)

Developments in apomorphine infusion therapy - recent data and new insights
Werner Poewe (Austria)

Followed by an audience Q&A with the faculty - please join us and have your say!

Join our symposium to learn about the latest developments in device-aided therapies for Parkinson’s disease and how they can benefit patients

Company products will be discussed during the symposium. Prescribing information can be found on pages 6 and 7. Please note that registration conditions for LECIGON® differ internationally, so it may not be registered in your country of origin. Please consult your local prescribing information before initiating treatment.
Welcome & introduction

Device-aided therapies for PD – current landscape and goals of treatment

K Ray Chaudhuri, UK – Symposium Chair

Professor Chaudhuri will introduce the esteemed international faculty who will each bring you up to date on key developments in research or clinical practice with device-aided therapies for Parkinson’s disease and demonstrate how this progress can help provide personalised care for patients as well as practical benefits for healthcare teams.

To set the scene for the presentations, Professor Chaudhuri will review:

- The rationale for device-aided therapies – what’s the real benefit?
- Transitioning from oral medications – when is the right time?
- The patient experience – what do patients want from their treatment?
- Recent advances in device-aided therapies – the need for evidence-based and patient-centred treatment options.
Developments in levodopa infusion therapies – less is more

Dag Nyholm, Sweden

Professor Nyholm will provide an overview of the latest device-aided therapy option for patients with Parkinson's disease – a novel trigel for intestinal infusion comprising levodopa, carbidopa and entacapone – which has already been used successfully to treat patients with PD in Sweden and several other European countries.

- The clinical evidence – efficacy, safety and practical use.1,2

- What are the advantages compared with standard levodopa–carbidopa infusion – for healthcare teams and for patients?

- Which patients would be suitable and who would not be suitable?

- What is the procedure for transitioning patients from oral medications or other device-aided therapies?

- Review of real patient case studies.

The patient experience – generating data to improve outcomes

Tobias Warnecke, Germany

For any therapeutic intervention, the generation of registry is an invaluable source of real-world information to support controlled clinical trial data. Professor Warnecke will outline plans for the ELEGANCE study: a prospective, observational study of levodopa–carbidopa–entacapone infusion.

- ELEGANCE: Global Long-Term Registry on Efficacy and Safety of LECIGON in Patients with Advanced Parkinson's Disease in Routine Care.

- A multinational study across 18 countries.

- Patient outcomes will be observed over 24 months:
  - Analysis of long-term efficacy and safety in a routine care setting
  - Analysis of patient quality of life and healthcare resource utilisation.
Developments in apomorphine infusion therapy – recent data and new insights

Werner Poewe, Austria

Subcutaneous apomorphine infusion is currently the least invasive device-aided therapy option. As a key investigator of the TOLEDO randomised, controlled trial of apomorphine infusion, Professor Poewe will review the recently-published long-term safety and efficacy data from the open-label phase of this trial as well as ongoing studies that support the long-standing clinical experience with this product.

• Results from the TOLEDO trial\textsuperscript{1,2} – what do they tell us about long-term use of apomorphine infusion?

• The EARLY-pump study (NCT02864004) – evaluating the timing of apomorphine infusion initiation.

• Meeting the challenges of the COVID-19 pandemic – remote initiation of apomorphine infusion.

Consult Summary of Product Characteristics before prescribing.

**Indications** Treatment of motor fluctuations ("on-off" phenomena) in patients with Parkinson's disease which are not sufficiently controlled by oral anti-Parkinson medication.

**Dosage and Administration** Apomorphine hydrochloride is administered subcutaneously either as an intermittent bolus injection or by continuous subcutaneous infusion. Apomorphine should be initiated in the controlled environment of a specialist clinic. The patient should be supervised/assisted during treatment by an experienced neurologist (e.g. neurologist). The patient's treatment with levodopa, with or without dopamine agonists, should be optimised before starting APO-go® treatment. The appropriate dose for each patient is established by incremental dosing schedules. For bolus injection it is suggested to start with 1 mg of apomorphine (0.1 ml) during a hypokinetic or 'off' period. If no response or an inadequate response is obtained after 30 minutes, a second dose of 2 mg is injected and the patient is observed for a further 30 minutes. The dosage may be increased by incremental injections with at least a forty minute interval between succeeding injections, until a satisfactory motor response is obtained. Patients who have shown a good 'on' period response during the initiation stage of apomorphine therapy, but whose on-off control remains unsatisfactory using intermittent injections, or who require many and frequent injections (more than 10 per day), may be commenced on or transferred to continuous subcutaneous infusion by minipump and/or syringe driver.

Continuous infusion is started at a rate of 1 mg apomorphine HCl (0.1 ml) per hour then increased according to the individual response. Increases in the infusion rate should not exceed 0.5 mg per hour at intervals of not less than 4 hours. Hourly infusion rates may range between 1 mg and 4 mg (0.1 ml and 0.4 ml), equivalent to 0.015 - 0.06 mg/kg/hour. Infusions should run for waking hours only. Patients treated with apomorphine will usually need to start domperidone at least two days prior to initiation of therapy. The domperidone dose should be titrated to the lowest effective dose and discontinued as soon as possible. Before the decision to initiate domperidone and apomorphine treatment, risk factors for QT interval prolongation in the individual patient should be carefully assessed to ensure that the benefit outweighs the risk. The optimal dosage of apomorphine HCl has to be determined on an individual patient basis; individual bolus injections should not exceed 10 mg and the total daily dose should not exceed 100 mg. Do not use if the solution has turned green. The solution should be inspected visually prior to use. Only clear, colourless and particle free solution should be used. Apomorphine must not be used via the intravenous route.

**Contraindications** Children and adolescents (up to 18 years of age). Known hypersensitivity to apomorphine or any excipients of the medicinal product. Respiratory depression, dementia, psychotic disease or hepatic insufficiency. Intermittent apomorphine HCl treatment is not suitable for patients who have an "on" response to levodopa which is marred by hypokalaemia. Apomorphine HCl has to be determined on an individual patient basis; individual bolus injections should not exceed 10 mg and the total daily dose should not exceed 100 mg. Do not use if the solution has turned green. The solution should be inspected visually prior to use. Only clear, colourless and particle free solution should be used. Apomorphine must not be used via the intravenous route.

**Precautions** Use with caution in patients with renal, pulmonary or cardiovascular disease, or who are prone to nausea or vomiting. Apomorphine may produce hypotension, exercise care in patients with cardiac disease or who are taking vasoactive drugs. Neuropsychiatric disturbances may be exacerbated by apomorphine. Apomorphine has been associated with somnolence and episodes of sudden sleep onset (e.g. somnolence on driving at night). Haematology tests should be undertaken at regular intervals as haemolytic anaemia and thrombocytopenia have been reported. Monitor patients for the development of impulse control disorders. Dose reduction/tapered discontinuation should be considered if such symptoms develop. Dopamine dysregulation Syndrome (DDS) is an addictive disorder resulting in excessive use of the product seen in some patients treated with apomorphine; patients and caregivers should be warned of the potential risk of developing DDS. Apomorphine may have the potential for QT prolongation, exercised caution when treating patients at risk for torsades de pointes arrhythmia. Risk factors for use with domperidone include serious underlying heart conditions such as congestive cardiac failure, severe hepatic impairment or significant electrolyte disturbance. An ECG should be performed prior to treatment with domperidone, during the treatment initiation phase and as clinically indicated thereafter to monitor prolongation of QT interval. Patients should report possible cardiac symptoms; palpitations, syncope, or near-syncope and clinical changes that could lead to hypokalaemia, e.g. gastroenteritis or initiation of diuretic therapy. At each medical visit, risk factors should be re-evaluated. Apomorphine has been associated with local subcutaneous effects that can be sometimes reduced by rotation of injection sites in order to avoid nodularity and induration. Contains sodium metabisulphite which may rarely cause severe allergic reactions and bronchospasm.

**Side Effects:** Very common: Hallucinations and injection site reactions. Common: Neuropsychiatric disturbances, somnolence, transient sedation, dizziness, yawning, nausea and vomiting. Rarely, injection site necrosis and ulceration have been reported. Severe drug-induced dyskinesias during "on" periods may require discontinuation. Postural hypotension is usually transient and infrequent. Positive Coombs' tests, haemyolytic anaemia and thrombocytopenia have been reported. Eosinophilia occurs rarely. Dopamine agonists, including apomorphine, may cause impulse control disorders such as pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating or compulsive eating. Rarely, allergic reactions (including anaphylaxis and bronchospassm) due to sodium metabisulphite. Symptoms of overdose like excessive emesis, respiratory depression, hypotension and bradycardia may be treated empirically.

Prescribers should consult the Summary of Product Characteristics in relation to other adverse reactions.

**Presentation and Basic NHS Cost** APO-go® pens (disposable multiple injection system) contain apomorphine hydrochloride 10 mg/ml, as follows: 30 mg in 3 ml – basic NHS cost £123.91 per carton of 5 pens. APO-go® Pre-filled syringes contain apomorphine hydrochloride 5 mg/ml, as follows: 50 mg in 10 ml – basic NHS cost £73.31 per carton of 5 syringes. APO-go® ampoules contain apomorphine hydrochloride 10 mg/ml as follows: 50 mg in 5 ml – basic NHS cost £73.31 per carton of 5 ampoules.

**Marketing Authorisation Numbers:**
- APO-go® Ampoules: PL 04483/0072
- APO-go® Pen: PL 04483/0073
- APO-go® Pre Filled Syringes: PL 04483/0074

**Legal Category** POM

**SmPC Revision Date** January 2020

**API Revision date** May 2021

Marketing Authorisation Holder in the UK: Britannia Pharmaceuticals, 200 Longwater Avenue, Green Park, Reading, Berkshire, RG2 6GP

Full prescribing information and further information is available from Britannia Pharmaceuticals at medinfo@britannia-pharm.com or 0808 196 8585.

Adverse events should be reported. Reporting forms and information can be found at https://yellowcard.mhra.gov.uk/ or search for MHRA Yellow Card in the Google Play or Apple App Store. Adverse events should also be reported to Britannia Pharmaceuticals Ltd at dso@britannia-pharm.com or 0808 196 8585.
FACHKURZINFORMATION: Lecigimon 20 mg/ml + 5 mg/ml + 20 mg/ml Gel zur intestinalen Anwendung.