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Efficacy and safety of orally inhaled apomorphine in patients with Parkinson's disease

Submission date 17/12/2008	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 16/02/2009	**Overall study status** Completed	
Last Edited 17/05/2016	**Condition category** Nervous System Diseases	

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
VR040/2/008

Study information

Scientific Title
A phase IIb randomised, double-blind, placebo-controlled, parallel-group study investigating the efficacy and safety of inhaled apomorphine in patients with "on-off" or "wearing-off" effects associated with Parkinson's disease

Study objectives
Apomorphine administered by injection or subcutaneous pump is approved for the treatment of disabling motor fluctuations that persist in PD patients, despite treatment with levodopa and/or oral dopamine agonists. Inhaled apomorphine is expected to present a more rapid clinical effect achieved via a convenient and non-invasive route of administration. Treatment consistency will be improved, allowing accurate and precise dose setting, thereby minimising peak-dose dyskinesia incidence. Based upon inhaled apomorphine bioavailability, an improved risk/benefit profile may be established, resulting in a reduced need to administer concomitant domperidone medication.

Ethics approval required
Old ethics approval format

Ethics approval(s)
A favourable opinion was given by Scottish A Research Ethics Committee on 12/11/2008 and by Ricerca Biomedica dell'Universita Degli Studi Gabriele D'Annunzio e della Asl di Chieti, Italy on 27 /11/2008. Approval is pending from Ethics Committee of the Dept. of Human Medicine, Philipps University, Marburg, Germany.

Study design
Randomised double-blind placebo-controlled parallel-group study

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Parkinson's disease

Interventions

During an In-Clinic dosing period patients will be titrated to their optimal delivered dose of Apomorphine HCl or placebo based on tolerance and efficacy, for up to 6 weeks. During the At-Home dosing period, patients will take their study medication for the treatment of sudden "on-off" or "wearing-off" episodes up to 5 times per day for 4 weeks at his or her optimal dose as determined during the In-Clinic dosing period. Patients will be followed-up for a further 3 weeks.

Intervention Type
Drug

Phase
Phase II

Drug/device/biological/vaccine name(s)
Apomorphine

Primary outcome measure
Change in "off" time per day compared with the baseline value derived from the three-consecutive-day patient diary card information completed prior to visit 1 and prior to visits 5 and 6 during the At-Home dosing period and the maximum change in total UPDRS III score from pre-dose to post-dose during the In-Clinic dosing titration period.

Secondary outcome measures
1. Proportion of "off" events per day aborted by study treatment
2. Interval between dose administration and onset of "on" state
3. Period from onset of "on" state to return to an "off" state
4. Mean daily duration in "on" without dyskinesias
5. Mean daily duration in "on" with non-troublesome dyskinesias
6. Mean daily duration in "on" with troublesome dyskinesias
7. Time taken for the study medication to start working and the period of time when the study medication was working
8. Mean number of "off" episodes per day
9. Mean daily period in "off" state
10. Mean daily period in any "on" state
11. Mean daily period asleep

Safety parameters:
12. Incidence of treatment-emergent AEs
13. Changes in laboratory tests and physical examination
14. Changes in vital signs, ECG, forced vital capacity (FVC)/FEV1

All measured from screening to the end-of-treatment or close out visit.

Overall study start date
15/01/2009

Completion date
15/11/2009

Eligibility

Key inclusion criteria
1. Male and female patients between the ages of 30 and 90 years
2. A clinical diagnosis of PD of at least 5 years duration
3. Fulfilled Steps 1 and 2 of the UK Brain Bank Criteria
4. Classified as Hoehn and Yahr Stage II - IV in "on" state
5. Have suffered from motor fluctuations associated with fluctuating idiopathic PD and a minimum of a 2-hour average daily "off" time
6. Showed dopaminergic responsiveness as defined by equal to or more than 30% change (reduction) in Unified Parkinson's Disease Rating Scale (UPDRS III) score compared to the pre-dose value
7. Optimised on oral therapy, including levodopa not greater than 1500 mg/day (in combination with decarboxylase inhibitors) at least 30 days before screening
8. Receiving (for at least 30 days), or have received in the past, but discontinued due to adverse events (AEs), at least one of the following types of medications:
8.1. Dopamine agonist
8.2. Catechol-o-methyltransferase inhibitor
8.3. Monoamine oxidase B inhibitor
9. Understand (with carer assistance) their daily medications

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
66 patients

Key exclusion criteria
1. Very serious or advanced disease
2. Dyskinesias rated as severe, i.e. equal to 2 in Item 32 of the UPDRS IV assessment and equal to 2 in Item 33 of the UPDRS IV assessment, at screening
3. Previous intolerance or allergy to apomorphine or any of its constituents, or any previous significant historic complication from oral dopamine agonist (DA) therapy
4. Pregnant or lactating females, and patients with known human immunodeficiency virus or active chronic hepatitis B or C infection
5. Any clinically significant abnormality or finding from examination, tests, or history that may compromise patient safety, specifically any history of renal or hepatic impairment
6. Relevant electrocardiogram (ECG) abnormalities
7. Forced expiratory volume in one second (FEV1) equals 65% predicted
8. Evidence of orthostatic or persistent arterial hypotension
9. Hypertension
10. Cancer
11. Those taking certain prohibited medications or anabolic steroids or antipsychotics (some exceptions apply)
12. Those taking 5HT3 antagonists or clozapine
13. History of drug or alcohol abuse
14. Current, or a history of, hypersensitivity to domperidone, pituitary tumour (prolactinoma), or

gastrointestinal blockage or haemorrhage
15. Known non-responders to apomorphine treatment for "off" episodes, e.g. in previous challenge tests or trials

Date of first enrolment
15/01/2009

Date of final enrolment
15/11/2009

Locations

Countries of recruitment
Germany

Italy

Scotland

United Kingdom

Study participating centre
Southern General Hospital
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Sponsor information

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Sponsor type
Industry

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Funder(s)

Funder type
Industry

Funder Name
Vectura Limited (UK)

Results and Publications

Publication and dissemination plan
Not provided at time of registration

Intention to publish date

Individual participant data (IPD) sharing plan

IPD sharing plan summary
Not provided at time of registration