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A randomised, double-blind, placebo-controlled, dose-escalation study of multiple doses of BIIB014 administered orally in subjects with early Parkinson's disease

Submission date 19/03/2007	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 30/08/2007	**Overall study status** Completed	
Last Edited 01/02/2019	**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
NCT00442780

Secondary identifying numbers

204-PD-203 (BIIB014)

Study information

Scientific Title
A randomised, double-blind, placebo-controlled, dose-escalation study of multiple doses of BIIB014 administered orally in subjects with early Parkinson's disease

Acronym
MOBILE

Study objectives
To establish a safe and tolerable dose range for future studies of BIIB014 in subjects with early-stage Parkinsons Disease (PD).

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approvals pending from the following ethics committees as of 10/08/2007:
1. Czech Republic: Multicentric Ethic Committee (MEC)
2. Israel:
2.1. Ethics Committee of Tel-Aviv Sourasky Medical Centre
2.2. Ethics Committee of Sheba Medical Centre
2.3. Ethics Committee of Rabin Medical Centre
3. Poland: Bioethic Committee at Okregowa Izba Lekarska in Krakow
4. Serbia:
4.1. Ethics Committee of Clinical Centre of Serbia
4.2. Ethics Committee of Military Medical Academy

Study design
Randomised, double-blind, placebo-controlled, multicentre, dose escalation, multiple dose study.

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Not specified

Study type(s)
Treatment

Participant information sheet

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

Interventions
Subjects will be randomised to receive either BIIB014 or placebo orally in one of the following sequentially enrolled cohorts:
Cohort 1: 8 subjects receive 10 mg BIIB014 and 2 subjects receive placebo for a total of 8 weeks
Cohort 2: 8 subjects receive 30 mg BIIB014 and 2 subjects receive placebo for a total of 8 weeks
Cohort 3: 8 subjects receive 30 mg BIIB014 for 1 week, followed by 100 mg of BIIB014 for 7 weeks; 2 subjects receive placebo
Cohort 4: 8 subjects receive 100 mg BIIB014 and 2 subjects receive placebo for a total of 8 weeks

No maximum tolerated dose was identified in Phase 1. An alternative 50 mg BIIB014 dose may be explored if 100 mg BIIB014 in Cohort 3 is not tolerated.

Intervention Type
Drug

Phase
Not Specified

Drug/device/biological/vaccine name(s)
BIIB014

Primary outcome measure
To assess the preliminary safety and tolerability of multiple oral doses of BIIB014 when administered to subjects with early-stage PD, carried out throughout the study.

Secondary outcome measures
1.To estimate pharmacokinetic (PK) parameters of BIIB014 and its N-acetyl metabolite in subjects with early-stage PD, carried out throughout the study
2.To explore the activity of BIIB014 when administered to subjects with early-stage PD. This will be assessed by the Unified Parkinson's Disease Rating Scale (UPDRS) throughout the study, and the Hoehn and Yahr staging at days 8, 15, 29, 43, 57 and 71 and the Clinical Global Impression scale (CGI) at days 29, 57 and 71.

Overall study start date
01/06/2007

Completion date
01/04/2008

Eligibility

Key inclusion criteria
1. Must give written informed consent and any authorisations required by local law
2. Must be 30 years or older at the time of informed consent
3. Must carry a diagnosis of idiopathic Parkinsons disease, without any other known or suspected cause of parkinsonism, according to the UK Parkinsons Disease Society Brain Bank Clinical Diagnostic Criteria. Initial diagnosis of PD must have been made within the 5 years prior to Screening with at least two or more of the following cardinal signs being present: bradykinesia, resting tremor, rigidity, and postural instability.
4. Must be Modified Hoehn and Yahr Stage 1 to 2.5 inclusive

5. Must have a Unified Parkinson's Disease Rating Scale (UPDRS) motor score (Part III) of greater or equal to 10
6. For subjects receiving an anticholinergic agent and/or MAO-B inhibitor, must have been on a stable dose of that medication for at least 4 weeks prior to Day 1. Subjects must be willing and able to maintain this dosing regimen throughout their participation in the study and must be willing and able to refrain from any other PD medication throughout their participation in the study.
7. Male and female subjects of child-bearing potential must be willing to practice effective birth control for the duration of the study. Female subjects must be one of the following:
7.1. Postmenopausal for at least 12 months, as confirmed by the patient's Obstetrician /Gynecologist (OB/GYN) or medical records
7.2. Surgically sterile (i.e., no uterus or no ovaries; females who have tubal ligation [tubes tied or cut] are not considered surgically sterile)
7.3. Willing to use 2 acceptable forms of birth control (i.e., barrier and spermicide, intrauterine device and barrier or spermicide, or birth control pill and barrier or spermicide). Male subjects with partners of child-bearing potential must use barrier contraception in addition to a second method of contraception used by their female partners. Male subjects should be advised to abstain from sexual intercourse with pregnant women or use condoms. Male and female subjects must be willing and able to continue contraception for 2 months after their last dose of study treatment. Female subjects of childbearing potential must have a negative pregnancy test result at both the Screening Visit and the Day 1 Visit.

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
40

Key exclusion criteria
1. Has a Mini Mental State Examination (MMSE) score less than 26 (the MMSE is provided in the Study Reference Manual)
2. History or clinical features (such as impaired downward gaze, prominent axial rigidity, gait initiation failure, autonomic dysfunction, etc.) consistent with an atypical parkinsonian syndrome
3. Any significant non-PD central nervous system disorder, including history of cerebrovascular disease, epilepsy, mass brain lesion, chronic inflammatory brain disease, or other neurological condition
4. Any significant AXIS I psychiatric disease as defined by the Diagnostic and Statistical Manual of Mental Disorders, 4th edition-Revised (DSM IV-TR, American Psychiatric Association, 2000)
5. History of cognitive (e.g., cognitive slowing, bradyphrenia) or neuropsychiatric conditions.
6. History of surgical intervention for PD (pallidotomy, thalamotomy, deep brain stimulation, etc.)
7. History of L-DOPA-induced motor or non-motor complication
8. History of malignancy
9. History of severe allergic or anaphylactic reactions to any drug
10. History of human immunodeficiency virus (HIV)

11. Positive for hepatitis C antibody and/or positive for hepatitis B surface antigen (HBsAg)
12. Serious infection (e.g., pneumonia, septicaemia) within 4 weeks prior to Day 1
13. Clinically significant renal dysfunction (serum creatinine greater than 2.0 mg/dL [greater than 178 mmol/L])
14. Abnormal laboratory results as follows:
14.1. Aspartate aminotransferase (AST), alanine aminotransferase (ALT), total bilirubin, gamma-glutamyl transferase (GGT) levels greater than 1.5 x upper limit of normal (ULN)
14.2. Serum lipase greater than ULN
14.3. White blood cell count (WBC) less than 4,000 cells/mm^3
14.4. Haemoglobin less than 10 g/dL, or any other abnormal laboratory value that could interfere with the assessment of safety
15. HbA1c greater than 7.0%
16. A positive G6PD assay. Subjects with a family history of G6PD (including immediate family members [first degree relatives] diagnosed with sickle cell anaemia or deaths due to neonatal jaundice) and subjects with a history of haemolytic anaemia or severe hemolysis are also to be excluded from the study.
17. Clinically significant (as determine by the Investigator) electrocardiogram (ECG) (12-lead) abnormalities including QTc interval greater than 500 Msec for males and greater than 450 Msec for females
18. Supine (measured at least 5 minutes after resting) or standing (measured 2 minutes after changing from a supine to a standing position) blood pressure (BP) of greater than 140 or less than 90 mmHg systolic or greater than 90 or less than 40 mmHg diastolic on two consecutive occasions at least 15 minutes apart
19. Orthostatic hypotension as defined by a decrease in systolic BP of greater than 20 mmHg or in diastolic BP of greater than 10 mmHg measured 2 minutes after changing from a supine to standing position (the mean of three independent sets of vital signs, taken at least 15 minutes apart at the screening visit, will determine eligibility)
20. Clinically significant hypertension, cardiac, gastrointestinal, renal, pulmonary, haematopoietic (including drug-induced haemolytic anaemia), endocrine, hepatic, immunologic, metabolic, urologic, pulmonary, dermatologic, and/or other major disease (as determined by the Investigator)

Treatment History
21. Treatment with L-DOPA/carbidopa or L-DOPA/benzerazide for more than 6 cumulative months at any time since subject's initial diagnosis of PD
22. Treatment with any of the following within the 3 months prior to day 1: antipsychotics, reserpine, flunarizine, cinnarizine, MAO-A inhibitors, anticonvulstants, or alpha methyl dopa
23. For subjects receiving treatment with non-centrally acting anti-hypertensive agents (e.g., beta blockers, angiotensin converting enzyme [ACE] inhibitors, calcium channel blockers, or diuretics), any change in dosing (i.e., start or discontinuation of treatment, or change in dose and /or frequency) within the 3 months prior to day 1
24. Participation in any other investigational drug study within the 4 weeks prior to screening or within 5 half-lives of the investigational treatment, whichever is longer
25. Treatment with any of the following within the 4 weeks prior to day 1:
25.1. L-DOPA/carbidopa or L-DOPA/benzerazide
25.2. Any dopamine agonist
25.3. Any centrally-acting dopamine antagonists including, quetiapine, clozapine, and risperidol
25.4. Amantadine
25.5. Methylphenidate
25.6. Amphetamines
25.7. Norepinephrine reuptake inhibitors, and/or
25.8. COMT inhibitors

26. For subjects receiving central nervous system (CNS) active therapy (e.g., sedatives, hypnotics, antidepressants, anxyolitics), any change in dosing (i.e., start or discontinuation of treatment, or change in dose and/or frequency) within the 4 weeks prior to day 1
27. Use of oestrogen-containing depot or intrauterine contraceptives or second-generation oestrogen-containing oral contraceptives within the 4 weeks prior to day 1
28. Any change in dosing (i.e., start or discontinuation of treatment, or change in dose and/or frequency) within the 4 weeks prior to day 1 for any of the following:
28.1. Maintenance or prophylactic therapy for stable medical conditions
28.2. Approved contraceptives
28.3. Approved over-the-counter medications
28.4. Approved alternative health preparations and procedures

Miscellaneous:
29. Female subjects who are pregnant or are planning to become pregnant within the 6 months following study entry, or who are currently breastfeeding
30. History of drug or alcohol abuse as defined by the DSM IV-TR (American Psychiatric Association, 2000) within 1 year prior to day 1
31. Donation of blood or plasma in excess of 500 mL within 3 months of day 1
32. Caffeine intake within the 24 hours prior to day 1
33. Unwillingness or inability to comply with the requirements of the protocol including the presence of any condition (physical, mental, or social) that is likely to affect the subject's ability to comply with the protocol
34. Any other reasons that, in the opinion of the Investigator and/or the Sponsor, the subject is determined to be unsuitable for enrolment in this study

Date of first enrolment
01/06/2007

Date of final enrolment
01/04/2008

Locations

Countries of recruitment
Czech Republic

Israel

Poland

Serbia

United States of America

Study participating centre
Gilmore O'Neill
Cambridge
United States of America
02142

Sponsor information

Organisation
Biogen Idec Ltd (USA)

Sponsor details
14 Cambridge Center
Cambridge
United States of America
02142

Sponsor type
Industry

ROR
https://ror.org/02jqkb192

Funder(s)

Funder type
Industry

Funder Name
Biogen Idec Ltd (USA)

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