A Randomized, Blinded, Placebo-Controlled, Single Ascending Dose Study of the Safety, Tolerability, and Pharmacokinetics of BIIB033 in Healthy Adult Volunteers

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The primary objective of the study is to evaluate the safety and tolerability of single-dose IV infusion of BIIB033 administered to healthy adult volunteers.Secondary objectives of this study are:* assess the single dose PK profile of BIIB033 *...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Demyelinating disorders
Study type	Interventional

Summary

ID

NL-OMON32724

Source
ToetsingOnline

Brief title
Safety, Tolerability, and Pharmacokinetics of BIIB033 in Healthy Adults

Condition

- Demyelinating disorders

Synonym
demyelination, MS

Research involving
Human

Sponsors and support

Primary sponsor: Biogen
Source(s) of monetary or material Support: Biogen Idec

Intervention

Keyword: BIIB033, Multiple sclerosis, Phase I, Safety

Outcome measures

Primary outcome

Primary study parameters:

* incidence of adverse events (AEs)

* incidence of serious adverse events (SAEs)

* clinical laboratory assessments and vital signs

* other safety measures: physical, neurological and retinal examinations, electrocardiogram (ECG), brain magnetic resonance imaging (MRI), visual evoked potentials (VEP), somatosensory evoked potentials (SSEP) and electroencephalogram (EEG).

Secondary outcome

Secondary study parameters:

* serum BIIB033 concentrations and PK parameters: area under the concentration curve (AUC), maximum (peak) serum concentration (Cmax,), time to maximum serum concentration (Tmax), elimination half life (t*), clearance (Cl), and volume of distribution (Vd)

* incidence of anti-BIIB033 serum antibodies

* exploratory biomarker profiles in blood, urine and CSF (selected cohorts)

Study description

Background summary

BIIB033 is an investigational product being developed to promote remyelination in patients with multiple sclerosis (MS). This Phase 1 study will evaluate the safety, tolerability and pharmacokinetic (PK) profile from a range of BIIB033 doses administered by intravenous (IV) infusion. Since this is the first in human study with BIIB033, the study will be conducted in healthy adult volunteers to allow for assessment of study objectives under normal conditions, and to prevent the potential confounding effects of comorbidities and concomitant medications that are common in MS subjects.

Study objective

The primary objective of the study is to evaluate the safety and tolerability of single-dose IV infusion of BIIB033 administered to healthy adult volunteers.

Secondary objectives of this study are:
* assess the single dose PK profile of BIIB033
* explore the single dose immunogenicity of BIIB033
* explore potential biomarkers of BIIB033 activity

Study design

Approximately 64 subjects are planned to be enrolled in the study. Total number will depend on number of cohorts enrolled.
Up to 8 single-dose cohorts (n = 8 subjects per cohort, 6 on active drug and 2 on placebo) are planned as follows:
* Cohort 1: 0.1 mg/kg BIIB033 or placebo
* Cohort 2: 0.3 mg/kg BIIB033 or placebo
* Cohort 3: 1.0 mg/kg BIIB033 or placebo
* Cohort 4: 3.0 mg/kg BIIB033 or placebo
* Cohort 5: 10.0 mg/kg BIIB033 or placebo
* Cohort 6: 30.0 mg/kg BIIB033 or placebo
* Cohort 7: 60.0 mg/kg BIIB033 or placebo
* Cohort 8: 100.0 mg/kg BIIB033 or placebo

Staggered Subject Dosing: The first 2 subjects within each cohort will be assigned to receive either active or placebo and they will be dosed both on the first day. Additional subjects will not be dosed until the Investigator has reviewed safety assessments conducted through 24 hours post dose. The remaining subjects will be dosed at least 2 hours apart to allow review of safety assessments conducted up to 2 hours post dose. No more than 2 subjects

will be dosed per day.

Intervention

A single dose will be administered intravenously:

* Cohort 1: 0.1 mg/kg BIIB033 or placebo
* Cohort 2: 0.3 mg/kg BIIB033 or placebo
* Cohort 3: 1.0 mg/kg BIIB033 or placebo
* Cohort 4: 3.0 mg/kg BIIB033 or placebo
* Cohort 5: 10.0 mg/kg BIIB033 or placebo
* Cohort 6: 30.0 mg/kg BIIB033 or placebo
* Cohort 7: 60.0 mg/kg BIIB033 or placebo
* Cohort 8: 100.0 mg/kg BIIB033 or placebo

Study burden and risks

Side effects from safety assessments: physical, neurological and retinal examinations, electrocardiogram (ECG), brain magnetic resonance imaging (MRI), visual evoked potentials (VEP), somatosensory evoked potentials (SSEP) and electroencephalogram (EEG).
Results from serology (HIV, etc).

Contacts

Public
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Scientific
Biogen

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Ability to understand the purpose and risks of the study and provide signed and dated informed consent and authorization to use protected health information (PHI) in accordance with national and local subject privacy regulations.
2. Aged 25 to 55 years, inclusive, at the time of informed consent.
3. Must be in good health as determined by the Investigator, based on medical history and screening evaluations.
4. Must have a BMI of 18 to 30 kg/m2, inclusive. (Note: subjects enrolled into any dose level less than 1 mg/kg must have a body weight of at least 60 kg.)
5. All male subjects must practice effective contraception during the study and be willing and able to continue contraception for at least 6 months after their dose of study treatment. Females of childbearing potential, unless postmenopausal or surgically sterile, are not allowed to enter the study.

Exclusion criteria

1. History of any clinically significant cardiac, endocrinologic, hematologic, hepatic, immunologic, metabolic, urologic, pulmonary, neurologic, dermatologic, psychiatric, renal, or other major disease, as determined by the Investigator.
2. Clinically significant abnormal clinical laboratory test values, as determined by the Investigator, or any values for alanine aminotransferase (ALT), aspartate aminotransferase (AST), bilirubin, or creatinine that are above the upper limit of normal, any values for platelets or hemoglobin that are below the lower limit of normal, or any clinically significant out of normal range values for white blood cells.
3. Clinically significant (as determined by the Investigator) 12 lead ECG abnormalities, including corrected QT interval using Bazett*s correction method of >450 msec for males and >470 msec for females.
4. (For selected cohorts) Any history of lumbar surgery for any reason (e.g., hernia), or contraindications to having an LP, including prominent chronic back pain or prominent scoliosis, or a refractory or prolonged headache or other complication after the screening LP that does not resolve within 5 days with conservative treatment. Note: All post LP symptoms must have resolved prior to randomization.

5. Any contraindications to having a brain MRI.
6. History of severe allergic or anaphylactic reactions.
7. Subjects who have plans to undergo elective procedures/surgeries at any time during the study through the Follow-Up visits.
8. Known history of or positive test result for human immunodeficiency virus.
9. Known history of or positive test result for HCVAb, HBcAb, or HBsAg.
10. Serious infection (e.g., pneumonia, septicemia) as determined by the Investigator within the 3 months prior to Day -1.
11. Fever or bacterial, or viral infection (including upper respiratory tract infection) within 2 weeks prior to Day -1.
12. Treatment with any prescription medication within the 28 days prior to Day -1.
13. Treatment with any over-the-counter products, including herbal and/or alternative health preparations and procedures within the 14 days prior to Day -1. (Intermittent treatment with paracetamol [*1000 mg/day] and/or ibuprofen [*400 mg/day] is permitted.)
14. Current enrollment in any other drug, biologic, device, or clinical study, or treatment with an investigational drug or approved therapy for investigational use within 30 days (or 5 half lives, whichever is longer) prior to Day -1.
15. Any live or attenuated immunization/vaccination within 1 month prior to the study drug infusion or planned to occur during the study period.
16. Blood donation (1 unit or more) within 1 month prior to Screening.
17. History of alcohol or substance abuse (as determined by the Investigator), a positive urine drug/alcohol test at Screening or Day -1, or alcohol use within 48 hours prior to Day -1.
18. Inability to comply with study requirements.
19. Vigorous exercise (as determined by the Investigator) within 48 hours prior to the study drug infusion.
20. Regular use of any tobacco product within 3 months prior to Day -1.
21. Other unspecified reasons that, in the opinion of the Investigator or Biogen Idec, make the subject unsuitable for enrollment.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	25-01-2010
Enrollment:	64
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	BIIB033
Generic name:	NA

Ethics review

Approved WMO Date:	17-12-2009
Application type:	First submission
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	13-01-2010
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	26-05-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Approved WMO Date:	08-07-2010
Application type:	Amendment
Review commission:	CCMO: Centrale Commissie Mensgebonden Onderzoek (Den Haag)
Not approved Date:	20-07-2010

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2009-016730-28-NL
CCMO	NL30671.040.09