A Multi-Centered, Randomized, Blinded, Placebo-Controlled, Serial-Cohort, Multiple Ascending Dose Study of the Safety, Tolerability, Pharmacokinetics and Efficacy of BG00010 (Neublastin) in Subjects with Sciatica

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Spinal cord and nerve root disorders
Study type	Interventional

Summary

ID

NL-OMON35890

Source
ToetsingOnline

Brief title
Multiple Ascending Dose Study of BG00010 in Subjects With Sciatica

Condition

- Spinal cord and nerve root disorders

Synonym
low back pain, sciatica

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Glial cell line-derived neurotrophic factor (GDNF), Multiple-Dose, Neuropathic pain, Sciatica

Outcome measures

Primary outcome

Primary endpoints:

-the number and proportion of subjects with Adverse Events (AEs)

-the type and severity of AEs

-changes in clinical laboratory measurements

-pharmacokinetic (PK) parameters

Secondary outcome

Secondary endpoints:

-the incidence of anti-BG00010 antibodies

-changes in pain as measured by a Likert numerical pain rating scale and the

VAS of the SF-MPQ

Exploratory endpoints:

-Intra Epidermal Nerve Fiber Density (IENFD) in both affected and unaffected

leg to assess for change

-changes in pain thresholds as determined by longitudinal nociceptive testing

(electrical and mechanical pain, and cold pressor testing)

Study description

Background summary

BG00010 is a protein that interacts with sensory neurons in the peripheral nervous system to alleviate neuropathic pain. BG00010 is being developed as a treatment for conditions like sciatica that are associated with neuropathic pain. This study expands on a previous study, which is a single ascending dose (SAD) study in sciatica subjects, and will be the second study of BG00010 in humans.

Study objective

The primary objective of the study is to evaluate the safety, tolerability, and pharmacokinetic (PK) profile of 3 intravenous (IV) injections of BG00010 given on 2 fixed schedules; weekly and as frequently as every 48 hours (but no more than 3 times per week). Secondary objectives of this study in this study population are to explore the repeated-dose immunogenicity of BG00010 and the potential of BG00010 to reduce pain following multiple dose administration.

Study design

This will be a phase 1, randomized, blinded, placebo controlled, serial-cohort study in sciatica subjects that will examine 2 dose schedules: Part I (once weekly) and Part II (up to 3 times weekly).

Intervention

4 ascending IV doses will be examined (50, 150, 400, and 800 µg/kg). Dose escalation will first occur in Part I (the once weekly group). Once escalation is complete up to 800 µg/kg, or a maximum tolerated dose (MTD) is determined, then the frequency of dosing will be increased (Part II). Subjects in both Part I and Part II will receive no more than 3 IV injections of study drug.

Study burden and risks

Side-effects that are reported after use of BG00010 are headache, itchiness, rash, feeling warm and pain in legs or arms. An immune reaction to BG00010 is possible. Within animal studies, transient neuronal vacuolation was observed at the highest dose levels. No exceptional severe adverse drug reactions are expected and burden/inconvenience for the subjects are considered relatively

mild. Development of BG00010 could constitute an additional therapeutic tool for the treatment of sciatica.

Contacts

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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. Must give written informed consent and any authorizations required by local law (e.g., Protected Health Information).
2. Must be aged 18 to 85 years old, inclusive, at the time of informed consent.
3. Must have a diagnosis of unilateral sciatica, determined by the Investigator including pain radiating down the leg following a dermatome, suggesting L4, L5, or S1 nerve root involvement. Sciatica symptoms must be present for 3 or more months prior to the Screening Visit.
4. Must rate their pain at >=40 mm on the 100 mm VAS of the SF-MPQ at the Screening and

Baseline Visits.
5. All male subjects and all female subjects of child-bearing potential must practice effective contraception during the study and be willing and able to continue contraception for 2 months after their last dose of study treatment.

Exclusion criteria

Medical History
1. History of malignancy or clinically relevant (as determined by the Investigator) allergies; and/or cardiac, endocrinologic, hematologic, hepatic, immunologic, metabolic, urologic, pulmonary, neurologic (not related to sciatica), dermatologic, rheumatic/joint, psychiatric, renal, and/or other major disease.
2. History of severe pain as judged by the investigator, other than that caused by sciatica, during the 3 months prior to their screening visit
3. Signs or symptoms of peripheral neuropathy, other than symptoms of sciatica during the 3 months prior to screening
4. History of severe allergic or anaphylactic drug-related reactions.
5. Major surgery within the 3 months prior to the Screening Visit or planned sciatica surgery within 6 months of the Screening Visit.
6. Current generalized myalgia.
7. Fever (body temperature >38°C) or symptomatic viral or bacterial infection within 2 weeks prior to the Baseline Visit.
8. Laboratory value at the Screening or Baseline Visits that is outside the normal range, unless it is judged by the Investigator as not clinically relevant after appropriate evaluation.
9. Serum Creatinine clearance >1.5 x upper limit of normal (ULN).
10. History of or positive screening test for hepatitis C infection (defined as positive for hepatitis C virus antibody [HCVAb]), hepatitis B infection (defined as positive for hepatitis B surface antigen [HBsAg] and/or positive for hepatitis B core antibody [HBcAb] at Screening), or positive for human immunodeficiency virus (HIV) antibody. Subjects who are HBsAg negative and HBcAb positive are allowed to participate if they are positive for HBsAb IgG (see the Centers for Disease Control and Prevention's interpretation of the hepatitis B serology panel; Appendix 28).
11. Clinically relevant abnormal electrocardiogram (ECG, 12-lead) at the Screening or Baseline Visits, as determined by the Investigator. Subjects who have a marked prolongation of the QT corrected (QTc) interval (i.e., repeated demonstration of a QTc interval >450 msec for females or >430 msec for males) at the Screening or Baseline Visits will not be allowed to enroll into the study.;Treatment History
12. Previous participation in a study with neurotrophic factors.
13. Participation in a study with another investigational drug or approved therapy for investigational use within the 3 months prior to the Baseline Visit.
14. Any immunization/vaccination within 1 month prior to the Baseline Visit.
15. Treatment with any prescription medication and/or over the-counter products such as herbal supplements, unless the dose has been stabilized prior to the Baseline Visit. Selective serotonin reuptake inhibitor, selective noradrenaline reuptake inhibitor, and tricyclic antidepressant doses must be stable for 4 weeks prior to the Baseline Visit. Gabapentin and

pregabalin doses must be stable for 1 week prior to the Baseline Visit. ;Miscellaneous
16. Female subjects who are pregnant or currently breastfeeding, or who have a positive pregnancy test result at the Screening or Baseline Visits.
17. Relevant history of illicit drug or alcohol abuse (as determined by the Investigator) within 1 year of the Screening Visit. Subjects who have a positive urine drug test at the Screening or Baseline Visits may be enrolled at the discretion of the Investigator.
18. Blood donation (1 unit or more) within 1 month prior to the Screening Visit.
19. Smoke >5 cigarettes per day.
20. Current enrollment in any other study.
21. Any alcohol use within 24 hours prior to dosing on Day 01.
22. Vigorous exercise (i.e., greater than 30 minutes of aerobic exercise) within 48 hours prior to dosing on Day 01.
23. Unwillingness or inability to comply with the requirements of this protocol, including the presence of any condition (physical, mental, or social) that is likely to affect the subject's returning for follow-up visits on schedule.
24. Other unspecified reasons that, in the opinion of the Investigator or Biogen Idec Inc. (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):	30-06-2011
Enrollment:	56
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	NA
Generic name:	Neublastin

Ethics review

Approved WMO Date:	30-05-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-06-2011
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-07-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	11-08-2011
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-01-2012
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-01-2012
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-03-2012

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-03-2012
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-07-2012
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	EUCTR2011-000681-35-NL
CCMO	NL36767.056.11