A Multicenter, Randomized, Double-Blind, Placebo-Controlled Exploratory Study to Assess the Effect of Treatment With Prolonged-Release Fampridine (BIIB041) 10 mg Twice Daily on Walking Ability and Balance in Subjects with Multiple Sclerosis (MOBILE)

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The objectives of this study in MS subjects treated with prolonged-release fampridine 10 mg twice daily compared with subjects treated with placebo are: - To assess the effect of prolonged-release fampridine over 24 weeks on the following parameters...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Central nervous system infections and inflammations
Study type	Interventional

Summary

ID

NL-OMON37170

Source
ToetsingOnline

Brief title
MOBILE

Condition

- Central nervous system infections and inflammations

Synonym
MS

Research involving
Human

Sponsors and support

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

Intervention

Keyword: balance, multiple sclerosis, prolonged-release fampridine, walking ability

Outcome measures

Primary outcome

- Change from baseline in self-assessed walking disability up to Week 24 as reported on the MSWS-12.

- Change from baseline in balance up to Week 24 as assessed by the BBS and the TUG.

- Change from baseline in subjective impression of well-being (MS-related quality of life [QoL]) up to Week 24 as measured by the MSIS-29 physical subscale and the EuroQoL descriptive system of health-related quality of life states consisting of 5 dimensions (EQ-5D [The EuroQol Group 1990]).

- Subjects* global impression of change in walking as reported on the PGIC scale.

- Safety of prolonged-release fampridine as assessed by the following:

* the number and proportion of subjects with adverse events (AEs) and serious AEs (SAEs)

* clinical laboratory parameters

* vital signs

* physical examination

* assessment of electrocardiograms (ECGs)

Secondary outcome

N/A

Study description

Background summary

Prolonged-release fampridine has been well tolerated in clinical studies to date. Study 218MS205 will assess the effect of prolonged-release fampridine 10 mg twice daily on MS patients* self-assessed walking disability by using the Multiple Sclerosis Walking Scale-12 (MSWS-12), and on balance by means of the Timed Up and Go (TUG) and the Berg Balance Scale (BBS), to further support prolonged-release fampridine*s impact on overall walking disability. This study will explore the effect of treatment on walking measured by the MSWS-12 to further elucidate the clinical relevance of changes over 6-month treatment duration.

The change over time on the MSWS-12 will be related to change on the Multiple Sclerosis Impact Scale-29 (MSIS-29)-physical subscale [Hobart et al, 2001; Hobart et al, 2005] and to a patient global impression of change (PGIC) scale. The MSIS-29 consists of 2 subscales assessing the patients' perspective of their physical (20 questions) and psychological (9 questions) well-being, respectively, and has been explicitly developed for MS [Hobart et al, 2001; Hobart et al, 2005]. The PGIC scale consists of a question (7-point scale) about the perceived impact of the treatment effect on overall walking ability.

An improvement in balance would constitute additional evidence of impact on walking in patients with MS induced balance disturbance; to this end, subjects in this study will also be assessed on the TUG test [Podsiadlo and Richardson 1991; Schoppen et al, 1999; Shumway-Cook et al, 2000; Cattaneo et al, 2006] and the BBS [Berg and Wood-Dauphinee 1992; Riddle and Stratford 1999; Cattaneo et al, 2006; Cattaneo et al, 2007; Blum and Korner-Bitensky 2008; Gijbels et al, 2010]. This exploratory study will further validate the usefulness of these assessments in interventional MS studies.

Study objective

The objectives of this study in MS subjects treated with prolonged-release fampridine 10 mg twice daily compared with subjects treated with placebo are:

- To assess the effect of prolonged-release fampridine over 24 weeks on the

following parameters to explore endpoints for the Phase 3 study:
* self-assessed walking disability
* dynamic and static balance
* subjective impression of well-being subjects* global impression of change in walking

- To evaluate the safety and tolerability of prolonged-release fampridine.

Study design

A prospective, multicenter, randomized, placebo-controlled study with a 24-week double-blind treatment period.

Intervention

Patients will be asked to take either prolonged release fampridine or placebo twice daily (every 12 hours) for 24 weeks.
Furthermore patients will be asked to complete a diary and some questionnaires and perfom some walking and balace tests.

Study burden and risks

Study 218MS205 is considered justified to address clinically important questions about the benefits of fampridine while its use within the registered indication does not pose any new or unknown risk to the patients on overall walking ability. The Sponsor concludes that this study supports a positive benefit risk profile.

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

To be eligible to participate in this study, candidates must meet the following eligibility criteria at the Screening Visit or at the timepoint specified in the individual eligibility criterion listed:
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. Male or female subjects must be 18 to 70 years old, inclusive, at the time of informed consent.
3. Must have a diagnosis of primary-progressive, secondary-progressive, progressive-remitting, or relapsingremitting MS per revised McDonald Committee criteria ([McDonald et al, 2001; Polman et al, 2005] as defined by Lublin and Reingold [Lublin and Reingold 1996]; Section 22.2; Appendix B) of at least 3-month duration.
4. EDSS 4 to 7
5. Female subjects of childbearing potential must practice effective contraception during the study and be willing and able to continue contraception for 30 days after their last dose of study treatment. For further details of contraceptive requirements for this study, please refer to Section 15.5.3.
6. Subjects must be able to understand and comply with the requirements of the protocol.

Exclusion criteria

1.Known allergy to pyridine-containing substances or to any of the inactive ingredients in the prolonged-release fampridine tablet.
2.Any history of seizure, epilepsy, or other convulsive disorder, with the exception of febrile seizures in childhood.
3. An estimated CrCl of <80 mL/minute (using the Cockcroft-Gault formula).
4.Known history of Human Immunodeficiency Virus, hepatitis C, or hepatitis B. Subjects who

have evidence of prior hepatitis infection that has been serologically confirmed as resolved based on previous testing documented in the subjects* medical history are not excluded from study participation.
5.History of malignant disease including solid tumors and hematologic malignancies (with the exception of basal cell and squamous cell carcinomas of the skin that have been completely excised and are considered cured) within the 5 years prior to the Screening Visit, or at any time during the screening period.
6.Onset of MS exacerbation within the 60 days prior to the Screening Visit, or at any time during the screening period.
7.History of any major surgical intervention (with the exception of skin biopsy) within the 30 days prior to the Screening Visit, or at any time during the screening period.
8.Any non-MS-related condition or factor (as determined by the Investigator) that is likely to interfere with walking ability including, but not limited to, previous major surgery of the foot, leg, or hip; any significant trauma; or known peripheral neuropathy of the lower limb.
9.Presence of pulmonary disease including, but not limited to, chronic obstructive pulmonary disease that could impede the subject*s daily activities (as determined by the Investigator)10.Presence of any psychiatric disorder, including clinical depression, that is likely to interfere with the subject*s participation in the study (as determined by the Investigator).
11.Uncontrolled hypertension (as determined by the Investigator) at the Screening Visit, any time during the screening period, or Day 1.
12.History of any clinically significant endocrinologic, hematologic, immunologic, metabolic, urologic, neurologic (except for MS, but including events indicative of a potentially lower seizure threshold), dermatologic, or other major disease (as determined by the Investigator).
13.Clinically significant abnormal laboratory values (as determined by the Investigator).
14.A Body Mass Index *40.
15. Use of off-label MS treatment including rituximab, alemtuzumab, daclizumab, or antibody (except natalizumab) within the 3 months prior to the Screening Visit, or any time during the screening period, or scheduled use during study participation.
16.Use of mitoxantrone or cyclophosphamide within the 3 months prior to the Screening Visit, or any time during the screening period, or scheduled use during study participation.
17.Initiation of natalizumab treatment or any change in the subject*s dose or regimen of natalizumab, within the 3 months prior to the Screening Visit, or at any time during the screening period.
18. Initiation of treatment with, or any change in the subject*s dose or regimen of, interferon *-1b, interferon *-1a, fingolimod, or glatiramer acetate within the 30 days prior to the Screening Visit, or at any time during the screening period.
19.Pulsed steroid treatment within the 60 days prior to the Screening Visit, or at any time during the screening period.
20.Any change in the subject*s medication dose or regimen for the treatment of fatigue or depression within the 30 days prior to the Screening Visit, or at any time during the screening period.
21. Any change in prophylactic treatment for pain with antidepressants or anticonvulsants prescribed for this purpose within 30 days prior to the Screening Visit, or at any time during the screening period.
22.Any change in the subject*s dose or regimen of antispastic agents within the 7 days prior to the Screening Visit, or at any time during the screening period.

23. Treatment with an investigational drug or approved therapy for investigational use within the 30 days (or 7 half-lives, whichever is longer) prior to the Screening Visit, or at any time during the screening period.
24.Treatment with 4-AP or 3,4-diaminopyridine (DAP) in any formulation within the 30 days prior to the Screening Visit, or at any time during the screening period
25.History of drug or alcohol abuse (as defined by the Investigator) within the 2 years prior to the Screening Visit, or at any time during the screening period.
26.Female subjects who are currently pregnant or who are considering becoming pregnant while participating in the study. Female subjects of childbearing potential who have a positive pregnancy test at either the Screening Visit or Day 1 may not participate in this study
27.Female subjects who are currently breastfeeding.
28.Inability to comply with study requirements.
29.Current enrollment in any other drug, biological, device, or clinical study.
30.Previous participation in this study.
31.Any other reason, in the opinion of the Investigator, which would disqualify the subject from participation in this study or make the subject unsuitable for enrollment

Study design

Design

Study phase:	2
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):	13-11-2012
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine

Brand name:	Fampyra
Generic name:	Fampridine

Ethics review

Approved WMO Date:	06-08-2012
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	28-09-2012
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	02-10-2012
Application type:	First submission
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)
Approved WMO Date:	09-04-2013
Application type:	Amendment
Review commission:	METC Z: Zuyderland-Zuyd (Heerlen)

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	EUCTR2012-000368-90-NL
ClinicalTrials.gov	NCT01597297
CCMO	NL40921.096.12