An Open-Label, Multicenter, Multinational Study to Assess the Effect of Long Term Prolonged Release Fampridine (BIIB041) 10 mg Twice Daily on Quality of Life as Reported by Subjects with Multiple Sclerosis

Published: 03-11-2011
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Primary: The primary objective of the study is to assess the effect of long term treatment with prolonged release fampridine 10 mg twice daily on the physical component scale (PCS) of the Short Form (36) Health Status Questionnaire (SF 36) as...

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

Summary

ID

NL-OMON37416

Source
ToetsingOnline

Brief title
ENABLE 218MS403

Condition

- Central nervous system infections and inflammations

Synonym
Plaques in central nervous system

Research involving

Human

Sponsors and support

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

Intervention

Keyword: Fampridine, Multiple Sclerosis, Phase 4

Outcome measures

Primary outcome

• Change from baseline in the PCS of the SF 36 measured over Months 3, 6, 9, and 12 among subjects who respond to treatment with prolonged release fampridine.

Secondary outcome

• Comparison of the change from baseline in the PCS of the SF 36 measured over Months 3, 6, 9, and 12 among subjects who respond to treatment with prolonged release fampridine and those who do not.

• Change from baseline in additional QoL measures over Months 3, 6, 9, and 12 among responders as well as comparisons in change from baseline between responders and non responders:

- Total and mental component scale (MCS) of the SF 36

- Multiple Sclerosis Impact Scale (MSIS 29) Physical and Psychological Score

- EuroQoL descriptive system of health-related quality of life states consisting of 5 dimensions (questionnaire; EQ 5D)

- Work Productivity and Activity Impairment (WPAI) Specific Health Problem (SHP) questionnaire

• Change in QoL measures among responders stratified by disease type.

• Change in QoL measures between responders and non responders not taking

additional MS therapy.

• Safety of prolonged-release fampridine will be assessed by:

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

adverse events (SAEs)

Study description

Background summary

Walking impairment is a prominent manifestation of MS. With the exception of anti spasticity agents, no functional modifying therapies are currently available to treat walking impairment. Walking disability has also been ranked by both MS patients and neurologists as having the greatest negative impact on quality of life (QoL). This was demonstrated by an increase in walking speed. Fampridine has also been approved under the brand name Fampyra* in Australia (May 2011) and in the European Union (EU; July 2011). Approval in the EU is *conditional approval,* which means that further evidence on this medicinal product is awaited, in particular about prolonged released fampridine*s benefits beyond its effects on walking speed and with respect to early identification of responders.

Study objective

Primary:
The primary objective of the study is to assess the effect of long term treatment with prolonged release fampridine 10 mg twice daily on the physical component scale (PCS) of the Short Form (36) Health Status Questionnaire (SF 36) as reported by treatment responders.
Secondary:
The secondary objectives of this study are as follows:
•Compare the change in the PCS of the SF 36 between treatment responders and non responders (treatment discontinued at Week 4).
•Evaluate change from baseline in additional QoL measures among treatment responders as well as changes from baseline in treatment responders versus non responders.
•Assess the safety and tolerability of prolonged release fampridine 10 mg twice

daily.

Study design

A multicenter, open label study to assess subject QoL as reported by responders to long term treatment with prolonged release fampridine 10 mg twice daily. Subjects classified as non responders (those who did not meet criteria for continued fampridine treatment in this study) at Week 4 will stop treatment but will continue to provide QoL data for comparative purposes.

Intervention

Open label run-in period of 4 weeks to assess treatment response:
All eligible subjects will receive prolonged release fampridine 10 mg orally twice daily for 4 weeks.
Observational period of 44 weeks (Treatment or No Treatment during Weeks 5 48):
• Group 1 (Treatment, Weeks 5-48): Subjects who improved in overall score on the MS Walking Scale (MSWS 12) at the 4 week on treatment visit of the run in period over baseline AND who have both on treatment T25FWs (Week 2 and Week 4) > mean pretreatment T25FW, will be considered treatment responders in this study and will continue to receive prolonged release fampridine 10 mg twice daily for the next 44 weeks. It is estimated that approximately 300 subjects will qualify for Group 1.
• Group 2 (No Treatment, Weeks 5 48): Subjects who do not meet the above criteria will be considered non responders in this study. It is estimated that approximately 500 subjects will be offered the opportunity to continue study participation via quarterly QoL assessments.

Study burden and risks

The PR fampridine dose and regimen to be used in this study will be 10 mg twice daily, given orally, which is the commercially approved dose/regimen in the EU. Phase 3 studies have demonstrated that the effect of PR fampridine with respect to an improvement in T25FW was observed 2 to 4 weeks after initiation of therapy allowing for the early identification of responders to therapy. Responders to treatment will be identified at week 4 based on objective (Timed 25 foot walk, T25FW) and subjective MS walking scale score (MSWS-12).
PR fampridine 10 mg twice daily has been well tolerated in clinical studies to date. Of the adverse events (AEs) observed in the placebo-controlled studies, 94% were assessed as either mild or moderate in intensity and rarely caused withdrawal of treatment.
Based on the current benefit/risk profile of PR fampridine, the potential benefit of treatment in responders to therapy is likely to outweigh any risks of treatment at the proposed dose and regimen. Physical burden to patients is limited to a one time blood collected. Furthermore are several questionnaire

used and walking ability assessed.

Contacts

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Scientific
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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. Male or female subjects, 18 to 75 years old, inclusive, at the time of informed consent.
2. Must have a diagnosis of primary progressive, secondary progressive, progressive remitting, or relapsing remitting MS per revised McDonald Committee criteria as defined by Lublin and Reingold of at least 3 months duration.
3. Have a walking impairment as determined by the Investigator.
4. Able to perform the T25FW test with or without a walking aid.
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.

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.
4.Subject needs to take medicinal products that are inhibitors of organic cation transporter 2 (OCT2 [e.g., cimetidine]).
5.Previous exposure to fampridine.

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-02-2012
Enrollment:	90
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Fampyra
Generic name:	fampridine
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	03-11-2011
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-01-2012
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-02-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	29-03-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-04-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-04-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	15-05-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO	

Date:	16-05-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	31-05-2012
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	17-01-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-01-2013
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2011-003507-38-NL
CCMO	NL38261.060.11