Clinical trial results:
Prolonged-release oral Fampridine in Multiple Sclerosis: effects on clinical, neurophysiological and quantified gait analysis parameters. A cross-over, double-blinded, placebo-controlled study.

Summary

EudraCT number	2012-005076-34
Trial protocol	BE
Global end of trial date	29 September 2015

Results information

Result version number	v1 (current)
This version publication date	03 April 2021
First version publication date	03 April 2021

Trial information

Trial identification

Sponsor protocol code	BEL-FMP-12-10325

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Cliniques universitaires Saint-Luc
Sponsor organisation address	Avenue Hippocrate 10, Brussels, Belgium, 1200
Public contact	Souraya ElSankari, Cliniques Universitaires Saint-Luc, Neurologie, 00 3227641932, souraya.elsankari@uclouvain.be
Scientific contact	Souraya ElSankari, Cliniques Universitaires Saint-Luc, Neurologie, 00 3227641932, souraya.elsankari@uclouvain.be

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 September 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 September 2015
Global end of trial reached?	Yes
Global end of trial date	29 September 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to assess the effect of treatment with prolonged-release fampridine 10 mg twice, on the quantified gait analysis parameters (kinematics, dynamics, mechanical work).

Protection of trial subjects:

All observed adverse events regardless of treatment group or suspected relationship to the IP were reported.

Background therapy:

Patients meeting the inclusion criteria first underwent a 4-week run-in period during which they were treated by 10 mg PR-fampridine twice a day, to test for the responder status. A responder was defined as a 10% improvement at the timed 25-foot walk test (T25fWT) and any improvement in the multiple sclerosis walking scale (MSWS-12) at the end of the 4-week run-in period. Non-responders were subsequently excluded from the study. Responders then underwent a 2-week wash-out period before entering the main phase of the study. Included participants were randomly allocated (1:1 ratio) by a computer software to receive either 6 weeks of PR-fampridine (Fampyra®, Biogen; 10mg b.i.d.) followed by a 2-week wash-out period and a 6-week course of placebo (manufactured to appear identical to Fampyra), or the other way-round. Participants, therapists and assessors were blinded to the condition. Participants were assessed before (w6) and after (w12) the first treatment period and again before (w14) and after the second period (w20).

Evidence for comparator:

This is a blinded placebo controlled cross-over study aiming to assess the effects of IP on patients reported outcomes and gait analysis.

Actual start date of recruitment	01 January 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Belgium: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0

Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	24
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between February 2013 and April 2015, 39 patients from the MS consultation of the neurology department of our institution Cliniques Universitaires Saint Luc were selected for inclusion. After 4 weeks, fifteen patients were considered non-responding and withdrawn from the rest of the study. . Only 24 patients were included and randomized.

Pre-assignment

Screening details:

Patients with McDonald's criteria were eligible if they were between 18 and 65 years of age, had a subjective complaint of inability to walk, and had an EDSS score of 6 or less.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Assessor

Blinding implementation details:

According to GCP rules.

Arms

Arm title	Fampyra versus Placebo

Arm description:

10 Randomized to receive IP during the first phase and placebo during 2nd phase
14 placebo treatment during first phase, then cross over after wash out period, and IP treated

Arm type	Cross over
Investigational medicinal product name	Fampridine
Investigational medicinal product code	BIIB041
Other name	
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

2 pills per day

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2 pills per day

Number of subjects in period 1	Fampyra versus Placebo
Started	24
Completed	23
Not completed	1
Patient convenience	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	24	24	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	24	24	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
arithmetic mean	46		
standard deviation	± 10	-	
Gender categorical Units: Subjects			
Female	12	12	
Male	12	12	

End points

End points reporting groups

Reporting group title	Fampyra versus Placebo

Reporting group description:

10 Randomized to receive IP during the first phase and placebo during 2nd phase
14 placebo treatment during first phase, then cross over after wash out period, and IP treated

Primary: External work change under treatment

End point title	External work change under treatment[1]

End point description:

The primary endpoint was to indicate a difference in Wext under treatment with PR-fampridine versus placebo. The expected minimal detectable change15 was assumed to be 15% for the primary endpoint.

End point type	Primary

End point timeframe:

6 weeks

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: For each outcome, repeated measures ANCOVAs were applied, with the treatment being the explicative variable and the within-subject differences between baselines (prePR-fampridine and prePlacebo) being the covariate.16Intention-to-treat (ITT) analysis was performed, including all participants assessed at w6. For missing data, the 'last observation carried forward' strategy was applied.

End point values	Fampyra versus Placebo			
Subject group type	Reporting group			
Number of subjects analysed	23			
Units: J.kg-1.m-1				
number (not applicable)	-0.04			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Adverse events were screened at each visit (screening, start and end of both phases A and B), from first patient inclusion and until the last patient end of study visit.

Adverse event reporting additional description:

No adverse event were reported in our population. Patients screened but non included were excluded because they were considered as non responders according to protocol definition.

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	3.0

Reporting groups

Reporting group title	Fampyra versus Placebo

Reporting group description:

*IP (Fampridine) treatment during first phase, then cross over after wash out period, and placebo treated
*Placebo treatment during first phase, then cross over after wash out period, and IP treated

Serious adverse events	Fampyra versus Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Fampyra versus Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 23 (0.00%)		

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: There were no adverse events during the randomisation period

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported