Clinical trial results:
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)

Summary

EudraCT number	2012-000368-90
Trial protocol	BE GB NL IT
Global end of trial date	08 August 2013

Results information

Result version number	v1 (current)
This version publication date	04 February 2016
First version publication date	06 August 2015

Trial information

Trial identification

Sponsor protocol code	218MS205

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	225 Binney Street, Cambridge, United States, 02142
Public contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com
Scientific contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com

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	08 August 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	08 August 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives of this study were as follows:

-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, and subjects' global impression of change in walking

-to evaluate the safety and tolerability of prolonged-release fampridine

Protection of trial subjects:

Written informed consent was obtained from each subject prior to evaluations being performed for eligibility. Subjects were given adequate time to review the information in the informed consent and were allowed to ask, and have answered, questions concerning all portions of the conduct of the study. Through the informed consent process each subject was made aware of the purpose of the study, the procedures, the benefits and risks of the study, the discomforts and the precautions taken. Any side effects or other health issues occurring during the study were followed up by the study doctor. Subjects were able to stop taking part in the study at any time without giving any reason.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	30 August 2012
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	Netherlands: 17
Country: Number of subjects enrolled	Sweden: 19
Country: Number of subjects enrolled	United Kingdom: 18
Country: Number of subjects enrolled	Belgium: 20
Country: Number of subjects enrolled	Italy: 31
Country: Number of subjects enrolled	Canada: 27
Worldwide total number of subjects	132
EEA total number of subjects	105

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)	126
From 65 to 84 years	6
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment/enrollment was at a single investigational site in The Netherlands.

Pre-assignment

Screening details:

This study included a 14-day screening period.

Period 1

Period 1 title	Double-blind period + 2-week Follow-up (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Blinding implementation details:

All subjects and study staff, including the Neurologist, were blinded to the subject treatment assignments.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo tablet twice daily (BID)

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

Dosage and administration details:

Study treatment was to be dispensed by a pharmacist or appropriately qualified staff, and only to subjects enrolled in this study. Staff were to refer to the Directions for Handling and Administration for specific instructions about handling, preparation, administration, and disposal of study treatment.

Arm title	Fampridine 10 mg BID

Arm description:

Prolonged-release fampridine 10 mg tablet BID

Arm type	Experimental
Investigational medicinal product name	fampridine
Investigational medicinal product code	BIIB041
Other name	Fampyra, fampridine-PR
Pharmaceutical forms	Prolonged-release tablet
Routes of administration	Oral use

Dosage and administration details:

Study treatment was to be dispensed by a pharmacist or appropriately qualified staff, and only to subjects enrolled in this study. Staff were to refer to the Directions for Handling and Administration for specific instructions about handling, preparation, administration, and disposal of study treatment.

Number of subjects in period 1	Placebo	Fampridine 10 mg BID
Started	64	68
Completed	51	56
Not completed	13	12
Consent withdrawn by subject	1	2
Not specified	6	3
Adverse event	5	6
Lack of efficacy	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo tablet twice daily (BID)	
Reporting group title	Fampridine 10 mg BID
Reporting group description:	
Prolonged-release fampridine 10 mg tablet BID	

Reporting group values	Placebo	Fampridine 10 mg BID	Total
Number of subjects	64	68	132
Age categorical Units: Subjects			
18 to 19 years	0	0	0
20 to 29 years	0	2	2
30 to 39 years	11	8	19
40 to 49 years	20	23	43
50 to 59 years	22	26	48
>= 60 years	11	9	20
Age continuous Units: years			
arithmetic mean	49.8	49.8	
standard deviation	± 9.28	± 8.69	-
Gender categorical Units: Subjects			
Female	33	38	71
Male	31	30	61

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description: Placebo tablet twice daily (BID)	
Reporting group title	Fampridine 10 mg BID
Reporting group description: Prolonged-release fampridine 10 mg tablet BID	

Primary: Change From Baseline to Mean On-treatment (Weeks 2 to 24) on the Multiple Sclerosis Walking Scale-12 (MSWS-12)

End point title	Change From Baseline to Mean On-treatment (Weeks 2 to 24) on the Multiple Sclerosis Walking Scale-12 (MSWS-12)

End point description:

The MSWS-12 is a 12-item questionnaire that asks subjects to rate limitations of their mobility due to multiple sclerosis (MS) during the preceding 2 weeks on a 5-point scale (from 1= not at all to 5= extremely). The higher the score, the greater the degree of limitation in walking caused by MS. A negative change indicates an improvement in walking. For each subject, the mean change from baseline to on-treatment was calculated. As the distribution of between-subject changes from baseline were not normally distributed, the median change from baseline and corresponding 95% confidence interval (CI) were calculated for each treatment group. Treatment groups were compared using median differences and corresponding 95% CI, which were calculated using non-parametric methods. Missing data were imputed by last observation carried forward (LOCF) method. Intention to treat (ITT) population: all treated subjects.

End point type	Primary

End point timeframe:

Baseline (mean of Screening and Day 1 visits) up to Week 24 (mean of Weeks 2, 4, 8, 12, 16, 20 and 24 [or early termination] visits)

End point values	Placebo	Fampridine 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	68		
Units: units on a scale				
median (confidence interval 95%)	-2.89 (-5.36 to 1.04)	-6.92 (-11.61 to -1.64)		

Statistical analyses

Statistical analysis title	Estimate of median difference

Statistical analysis description:

Estimate of median difference: fampridine minus placebo. Median difference and corresponding non-parametric 95% CI determined from all possible differences between the two treatment groups.

Comparison groups	Placebo v Fampridine 10 mg BID

Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Median difference (net)
Point estimate	-3.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.59
upper limit	1.19

Primary: Percentage Change From Baseline to Mean On-treatment (Weeks 2 to 24) on the Timed Up and Go (TUG)

End point title	Percentage Change From Baseline to Mean On-treatment (Weeks 2 to 24) on the Timed Up and Go (TUG)

End point description:

TUG was presented using speed in meters per second (m/s), derived by dividing 6 meters by the time (in seconds) required to complete the walk. At each study visit, there were 2 trials of the TUG; the speed for any particular study visit was calculated as the average of the speeds for trial 1 and trial 2. If either trial was missing, then the speed for that visit was the speed from the completed trial. For each subject, the mean change from baseline to on-treatment was calculated. As the distribution of between-subject changes from baseline were not normally distributed, the median change from baseline and corresponding 95% confidence interval were calculated for each treatment group. Treatment groups were compared using median differences and corresponding 95% CI, which were calculated using non-parametric methods. Missing data were imputed by LOCF method. ITT population: all treated subjects.

End point type	Primary

End point timeframe:

Baseline (mean of Screening and Day 1 visits) up to Week 24 (mean of Weeks 2, 4, 8, 12, 16, 20 and 24 [or early termination] visits)

End point values	Placebo	Fampridine 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63[1]	68		
Units: percentage change				
median (confidence interval 95%)	3.49 (-2.81 to 9.63)	12.26 (7.58 to 19.35)		

Notes:

[1] - subjects in the ITT population with data available at baseline and on-treatment

Statistical analyses

Statistical analysis title	Estimate of median difference

Statistical analysis description:

Estimate of median difference: fampridine minus placebo. Median difference and corresponding non-parametric 95% CI determined from all possible differences between the two treatment groups.

Comparison groups	Placebo v Fampridine 10 mg BID

Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Median difference (net)
Point estimate	9.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	2.05
upper limit	16.48

Primary: Change From Baseline to Mean On-treatment (Weeks 2 to 24) on the Berg Balance Scale (BBS)

End point title	Change From Baseline to Mean On-treatment (Weeks 2 to 24) on the Berg Balance Scale (BBS)

End point description:

The BBS test comprises 14 balance-related tasks scored from 0 (unable to perform) to 4 (able to perform independently). The BBS is the sum of scores across these tasks and ranges from 0 (poor balance) to 56 (good balance). A positive change on the BBS indicates an improvement in balance. For each subject, the mean change from baseline to on-treatment was calculated. As the distribution of between-subject changes from baseline were not normally distributed, the median change from baseline and corresponding 95% CI were calculated for each treatment group. Treatment groups were compared using median differences and corresponding 95% CI, which were calculated using non-parametric methods. Missing data were imputed by LOCF method. ITT population: all treated subjects.

End point type	Primary

End point timeframe:

Baseline (mean of Screening and Day 1 visits) up to Week 24 (Weeks 2, 4, 8, 12, 16, 20 and 24 [or early termination] visits)

End point values	Placebo	Fampridine 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63[2]	68		
Units: units on a scale				
median (confidence interval 95%)	1.71 (0.57 to 2.93)	2.93 (2.14 to 4.14)		

Notes:

[2] - subjects in the ITT population with data available at baseline and on-treatment

Statistical analyses

Statistical analysis title	Estimate of median difference

Statistical analysis description:

Estimate of median difference: fampridine minus placebo. Median difference and corresponding non-parametric 95% CI determined from all possible differences between the two treatment groups.

Comparison groups	Placebo v Fampridine 10 mg BID

Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Median difference (net)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	2.93

Primary: Change From Baseline to Mean On-treatment (Weeks 2 to 24) on the Multiple Sclerosis Impact Scale-29 (MSIS-29) Physical Impact Score

End point title	Change From Baseline to Mean On-treatment (Weeks 2 to 24) on the Multiple Sclerosis Impact Scale-29 (MSIS-29) Physical Impact Score

End point description:

MSIS-29 is a subject-completed questionnaire comprising 29 questions measuring the physical (questions 1 to 20) and psychological (questions 21 to 29) impact of MS. For a particular visit, the MSIS-29 physical subscale score was calculated by summing the 20 items and transforming to a scale with a range of 0 (no impact of MS) to 100 (extreme impact of MS). A negative change indicates an improvement in function. For each subject, the mean change from baseline to on-treatment was calculated. As the distribution of between-subject changes from baseline were not normally distributed, the median change from baseline and corresponding 95% CI were calculated for each treatment group. Treatment groups were compared using median differences and corresponding 95% CI, which were calculated using non-parametric methods. Missing data were imputed by LOCF method. ITT population: all treated subjects.

End point type	Primary

End point timeframe:

Baseline (mean of Screening and Day 1 visits) up to Week 24 (mean of Weeks 2, 4, 8, 12, 16, 20 and 24 [or early termination] visits)

End point values	Placebo	Fampridine 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	68		
Units: units on a scale				
median (confidence interval 95%)	-2.19 (-5.27 to 1.25)	-4.96 (-10 to -1.07)		

Statistical analyses

Statistical analysis title	Estimate of median difference

Statistical analysis description:

Estimate of median difference: fampridine minus placebo. Median difference and non-parametric CI determined from all possible differences between the two treatment groups.

Comparison groups	Placebo v Fampridine 10 mg BID

Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Median difference (net)
Point estimate	-3.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-7.68
upper limit	0.98

Primary: Change from Baseline to Mean On-treatment (Weeks 4 to 24) in EuroQoL Descriptive System of Health-related Quality of Life States Consisting of 5 Dimensions (EQ-5D) Visual Analogue Scale (VAS)

End point title	Change from Baseline to Mean On-treatment (Weeks 4 to 24) in EuroQoL Descriptive System of Health-related Quality of Life States Consisting of 5 Dimensions (EQ-5D) Visual Analogue Scale (VAS)

End point description:

The EQ-5D is a generic quality of life instrument that comprises 5 questions and a VAS. The VAS ranges from 0 (worst imagined health state) to 100 (best imagined health state). A positive change indicates an improvement in health state. An analysis of covariance (ANCOVA) with adjustment for baseline values was used to calculate least squares means and corresponding 95% CI for each treatment group, as well as the least squares mean differences and corresponding 95% CI. No imputation for missing data was performed. ITT population: all treated subjects.

End point type	Primary

End point timeframe:

Baseline (Day 1), up to Week 24 (mean of Weeks 4, 8, 12, 16, 20 and 24 [or early termination] visits)

End point values	Placebo	Fampridine 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63	68		
Units: units on a scale				
least squares mean (confidence interval 95%)	-0.42 (-3.75 to 2.91)	0.13 (-3.07 to 3.34)		

Statistical analyses

Statistical analysis title	Least squares mean difference

Statistical analysis description:

Least squares mean difference: calculated from an ANCOVA model with adjustment for baseline value.

Comparison groups	Placebo v Fampridine 10 mg BID

Number of subjects included in analysis	131
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	least squares mean difference
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.07
upper limit	5.18

Primary: Change from Baseline to Mean On-treatment (Weeks 4 to 24) in EQ-5D Utility Score

End point title	Change from Baseline to Mean On-treatment (Weeks 4 to 24) in EQ-5D Utility Score

End point description:

The EQ-5D is a generic quality of life instrument that comprises 5 questions and a VAS. Questions address mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. A score of 1 (no problem) to 5 (severe problem) are possible responses. A summary utility index value was calculated for subjects with non-missing data for each of the 5 questions at a visit. EQ-5D utility score ranges from -0.594 (worst health state) to 1.000 (best health state). A positive change indicates an improvement in utility score. An ANCOVA with adjustment for baseline values was used to calculate least squares means and corresponding 95% CI for each treatment group, as well as the least squares mean differences and corresponding 95% CI. No imputation for missing data was performed. ITT population: all treated subjects.

End point type	Primary

End point timeframe:

Baseline (Day 1) up to Week 24 (Mean of Weeks 4, 8, 12, 16, 20, and 24 [or early termination] visits)

End point values	Placebo	Fampridine 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	68		
Units: units on a scale				
least squares mean (confidence interval 95%)	-0.0271 (-0.0655 to 0.0112)	-0.0046 (-0.0419 to 0.0326)		

Statistical analyses

Statistical analysis title	Least squares mean difference

Statistical analysis description:

Least squares mean difference: calculated from an ANCOVA model with adjustment for baseline value.

Comparison groups	Placebo v Fampridine 10 mg BID

Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	least squares mean of difference
Point estimate	0.0225
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.031
upper limit	0.076

Primary: Percentage of Subjects With an Improvement on the Patient Global Impression of Change (PGIC) at Week 2

End point title	Percentage of Subjects With an Improvement on the Patient Global Impression of Change (PGIC) at Week 2[3]

End point description:

The PGIC is a global assessment of the subject's impression of how the study drug affected their overall walking during the preceding 7 days. The assessment is scored on a 7-point scale (1=very much worse, 2=much worse, 3=slightly worse, 4=unchanged, 5=slightly improved, 6=much improved, 7=very much improved). The number and proportion of subjects with an improvement (i.e., a score of 5, 6, or 7) at Week 2 were calculated. ITT population: all treated subjects with PGIC data available at Week 2.

End point type	Primary

End point timeframe:

Week 2

Notes:

[3] - 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: Descriptive data were collected for this endpoint.

End point values	Placebo	Fampridine 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	61	68		
Units: percentage of subjects				
number (not applicable)	26	46		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Treatment-emergent Adverse Events (TEAEs)

End point title	Number of Subjects With Treatment-emergent Adverse Events (TEAEs)[4]

End point description:

A TEAE was defined as any AE with an onset date that was on or after the first dose of study drug or any pre-existing condition that worsened in severity after the first dose of study drug. Safety population: all subjects who were randomized and received at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

Screening Visit (14 ± 3 days before Day 1) through Week 26; 2-Week (14 ± 3 days) Post-Dosing/End of

Study Visit; serious adverse events (AEs) collected from signing of informed consent form, AEs collected from first dose of study treatment.

Notes:

[4] - 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: Descriptive data were collected for this endpoint.

End point values	Placebo	Fampridine 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	68		
Units: subjects				
Subjects with an event	49	51		
Subjects with a moderate or severe event	24	26		
Subjects with a severe event	4	7		
Subjects with a related event	9	15		
Subjects with a serious event	5	2		
Subjects with event leading to dose interruption	4	5		
Subjects discontinuing treatment due to an event	5	7		
Subjects withdrawing from study due to an event	5	6		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Notable Changes in Hematology, Blood Chemistry, and Urinalysis

End point title	Number of Subjects With Notable Changes in Hematology, Blood Chemistry, and Urinalysis[5]

End point description:

The following laboratory tests were performed: hematology: hemoglobin, hematocrit, red blood cell count, white blood cell count (with differential), and platelet count; blood chemistry: sodium, potassium, chloride, total bilirubin, alkaline phosphatase, alanine aminotransferase, aspartate aminotransferase, lactate dehydrogenase, gamma-glutamyl transferase, blood urea nitrogen, creatinine, and bicarbonate; urinalysis: color, appearance, leukocyte esterase, specific gravity, pH, protein, glucose, blood, ketones, microscopy, and urine culture (if necessary to rule out infection); estimated creatinine clearance (using the Cockcroft-Gault formula); pregnancy testing for all female subjects of childbearing potential. Safety population: all subjects who were randomized and received at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

Screening Visit (14±3 days before Day 1) through Week 26; 2-Week (14±3 days) Post-Dosing/End of Study Visit

Notes:

[5] - 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: Descriptive data were collected for this endpoint.

End point values	Placebo	Fampridine 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	68		
Units: subjects				
Subjects with notable changes in hematology	0	0		
Subjects with notable changes in blood chemistry	0	0		
Subjects with notable changes in urinalysis	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects With Abnormalities in Vital Signs

End point title	Number of Subjects With Abnormalities in Vital Signs[6]

End point description:

Vital signs included supine systolic and diastolic blood pressure, pulse, and body temperature. The subject was to rest quietly for 5 minutes prior to blood pressure measurements. Safety population: all subjects who were randomized and received at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

Screening Visit (14 ± 3 days before Day 1) through Week 26; 2-Week (14 ± 3 days) Post-Dosing/End of Study Visit

Notes:

[6] - 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: Descriptive data were collected for this endpoint.

End point values	Placebo	Fampridine 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	68		
Units: subjects				
Temperature > 38 C	0	0		
Temperature increase from baseline of >= 1 C	4	5		
Pulse rate > 120 beats per minute (bpm)	0	0		
Pulse rate > 20 bpm increase from baseline	6	7		
Pulse rate < 50 bpm	1	0		
Pulse rate > 20 bpm decrease from baseline	1	2		
Systolic blood pressure (SBP) > 180 mmHg	0	0		
SBP > 40 mmHg increase from baseline	0	0		
SBP < 90 mmHg	1	1		
SBP > 30 mmHg decrease from baseline	5	2		
Diastolic blood pressure (DBP) > 105 mmHg	0	1		
DBP > 30 mmHg increase from baseline	3	0		

DBP < 50 mmHg	1	1		
DBP > 20 mmHg decrease from baseline	9	4		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Subjects with Abnormal Electrocardiogram (ECG) Findings When Normal at Baseline

End point title	Number of Subjects with Abnormal Electrocardiogram (ECG) Findings When Normal at Baseline[7]

End point description:

ECG (12-lead reads) were performed after the subject had been resting quietly for at least 5 minutes. Safety population: all subjects who were randomized and received at least 1 dose of study treatment with a normal baseline ECG reading.

End point type	Primary

End point timeframe:

Screening Visit (14±3 days before Day 1) through Week 26; 2-Week (14±3 days) Post-Dosing/End of Study Visit

Notes:

[7] - 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: Descriptive data were collected for this endpoint.

End point values	Placebo	Fampridine 10 mg BID		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	44	49		
Units: subjects				
Abnormal, not an AE	4	4		
Abnormal, AE	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Screening Visit (14 ± 3 days before Day 1) through Week 26; 2-Week (14 ± 3 days) Post-Dosing/End of Study Visit; serious AEs collected from signing of informed consent form, AEs collected from first dose of study treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Placebo

Reporting group description:

Placebo tablet BID

Reporting group title	Fampridine 10 mg BID

Reporting group description:

Prolonged-release fampridine 10 mg BID

Serious adverse events	Placebo	Fampridine 10 mg BID	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 64 (7.81%)	2 / 68 (2.94%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Nervous system disorders			
Multiple sclerosis relapse			
subjects affected / exposed	1 / 64 (1.56%)	2 / 68 (2.94%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraparesis			
subjects affected / exposed	1 / 64 (1.56%)	1 / 68 (1.47%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal neuralgia			
subjects affected / exposed	1 / 64 (1.56%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Constipation			

subjects affected / exposed	1 / 64 (1.56%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 64 (1.56%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 64 (1.56%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Stress			
subjects affected / exposed	1 / 64 (1.56%)	0 / 68 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	Fampridine 10 mg BID	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 64 (59.38%)	35 / 68 (51.47%)	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	8 / 64 (12.50%)	4 / 68 (5.88%)	
occurrences (all)	13	6	
Nervous system disorders			
Balance disorder			
subjects affected / exposed	1 / 64 (1.56%)	6 / 68 (8.82%)	
occurrences (all)	1	8	
Dizziness			
subjects affected / exposed	1 / 64 (1.56%)	4 / 68 (5.88%)	
occurrences (all)	1	5	
Headache			

subjects affected / exposed	5 / 64 (7.81%)	5 / 68 (7.35%)	
occurrences (all)	9	5	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 64 (6.25%)	4 / 68 (5.88%)	
occurrences (all)	4	4	
Gait disturbance			
subjects affected / exposed	2 / 64 (3.13%)	5 / 68 (7.35%)	
occurrences (all)	2	5	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	3 / 64 (4.69%)	4 / 68 (5.88%)	
occurrences (all)	3	7	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 64 (6.25%)	4 / 68 (5.88%)	
occurrences (all)	4	5	
Back pain			
subjects affected / exposed	3 / 64 (4.69%)	6 / 68 (8.82%)	
occurrences (all)	3	6	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	9 / 64 (14.06%)	11 / 68 (16.18%)	
occurrences (all)	10	12	
Influenza			
subjects affected / exposed	4 / 64 (6.25%)	2 / 68 (2.94%)	
occurrences (all)	4	2	
Urinary tract infection			
subjects affected / exposed	12 / 64 (18.75%)	6 / 68 (8.82%)	
occurrences (all)	17	6	

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