Clinical trial results:
A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of BIIB074 in Subjects With Neuropathic Pain From Lumbosacral Radiculopathy

Summary

EudraCT number	2015-004775-78
Trial protocol	LV GB CZ SK AT ES NL BE FR RO BG LT IT
Global end of trial date	06 August 2018

Results information

Result version number	v1 (current)
This version publication date	22 August 2019
First version publication date	22 August 2019

Trial information

Trial identification

Sponsor protocol code	1014802-203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02935608
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	250 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	06 August 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	06 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to evaluate the efficacy of 2 dose regimens of BIIB074 on neuropathic pain in subjects with pain from lumbosacral radiculopathy (PLSR).

Protection of trial subjects:

Written informed consent was obtained from each subject or subject's legally authorized representative (e.g., parent or legal guardian), as applicable, prior to evaluations performed for eligibility. Subjects or the subject's legally authorized representative were given adequate time to review the information in the informed consent/assent and were allowed to ask, and have answered, questions concerning all portions of the conduct of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 October 2016
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	12 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Bulgaria: 108
Country: Number of subjects enrolled	Slovakia: 70
Country: Number of subjects enrolled	Czech Republic: 69
Country: Number of subjects enrolled	Serbia: 51
Country: Number of subjects enrolled	Georgia: 50
Country: Number of subjects enrolled	Spain: 19
Country: Number of subjects enrolled	Romania: 16
Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	Latvia: 13
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Estonia: 1
Country: Number of subjects enrolled	Italy: 1
Worldwide total number of subjects	424
EEA total number of subjects	323

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)	360
From 65 to 84 years	64
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study was conducted from 31 October 2016 to 06 Aug 2018 in Austria, Belgium, Bulgaria, Czech Republic, Estonia, France, Georgia, Italy, Latvia, Netherlands, Romania, Serbia, Slovakia, Spain, United Kingdom.

Pre-assignment

Screening details:

A total of 502 subjects were enrolled in the study and 425 were randomised. Of which, 424 subjects received study treatment and 383 subjects completed the study.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

All subjects received placebo tablets (matched to BIIB074) orally twice daily (BID), in placebo run-in period (14 days). Subjects randomized to placebo in the double-blind (DB) blind period received placebo tablets (matched to BIIB074) orally BID for up to 12 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to BIIB074 tablets taken orally BID for up to 12 weeks during the DB period.

Arm title	BIIB074 200 milligram (mg) BID

Arm description:

All subjects received placebo tablets (matched to BIIB074) orally BID in placebo run-in period (14 days). Subjects received BIIB074 200mg tablets orally BID for up to 12 weeks during the DB period.

Arm type	Experimental
Investigational medicinal product name	BIIB074
Investigational medicinal product code	
Other name	Vixotrigine
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

BIIB074 200mg tablets orally BID for up to 12 weeks during the DB period.

Arm title	BIIB074 350 mg BID

Arm description:

All subjects received placebo tablets (matched to BIIB074) orally BID in placebo run-in period (14 days). Subjects received BIIB074 350mg tablets orally BID for up to 12 weeks during the DB period.

Arm type	Experimental

Investigational medicinal product name	BIIB074
Investigational medicinal product code	
Other name	Vixotrigine
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

BIIB074 350mg tablets orally BID for up to 12 weeks during the DB period.

Number of subjects in period 1	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID
Started	142	140	142
Completed	127	129	127
Not completed	15	11	15
Other	4	-	1
Adverse event	1	4	3
Investigator decision	-	-	1
Lost to follow-up	-	1	-
Consent withdrawn	10	6	10

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
All subjects received placebo tablets (matched to BIIB074) orally twice daily (BID), in placebo run-in period (14 days). Subjects randomized to placebo in the double-blind (DB) blind period received placebo tablets (matched to BIIB074) orally BID for up to 12 weeks.	
Reporting group title	BIIB074 200 milligram (mg) BID
Reporting group description:	
All subjects received placebo tablets (matched to BIIB074) orally BID in placebo run-in period (14 days). Subjects received BIIB074 200mg tablets orally BID for up to 12 weeks during the DB period.	
Reporting group title	BIIB074 350 mg BID
Reporting group description:	
All subjects received placebo tablets (matched to BIIB074) orally BID in placebo run-in period (14 days). Subjects received BIIB074 350mg tablets orally BID for up to 12 weeks during the DB period.	

Reporting group values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID
Number of subjects	142	140	142
Age Categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	53.1	52.1	52.8
standard deviation	± 11.16	± 10.65	± 9.58
Gender Categorical			
Units: Subjects			
Female	86	92	92
Male	56	48	50

Reporting group values	Total		
Number of subjects	424		
Age Categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		
Gender Categorical			
Units: Subjects			
Female	270		
Male	154		

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

All subjects received placebo tablets (matched to BIIB074) orally twice daily (BID), in placebo run-in period (14 days). Subjects randomized to placebo in the double-blind (DB) blind period received placebo tablets (matched to BIIB074) orally BID for up to 12 weeks.

Reporting group title	BIIB074 200 milligram (mg) BID

Reporting group description:

All subjects received placebo tablets (matched to BIIB074) orally BID in placebo run-in period (14 days). Subjects received BIIB074 200mg tablets orally BID for up to 12 weeks during the DB period.

Reporting group title	BIIB074 350 mg BID

Reporting group description:

All subjects received placebo tablets (matched to BIIB074) orally BID in placebo run-in period (14 days). Subjects received BIIB074 350mg tablets orally BID for up to 12 weeks during the DB period.

Primary: Change from Baseline to Double-Blind (DB) Week 12 in Weekly Average of Daily Neuropathic Pain Score

End point title	Change from Baseline to Double-Blind (DB) Week 12 in Weekly Average of Daily Neuropathic Pain Score

End point description:

The subjects rated their average neuropathic pain score scores over 24 hours using the 11-point pain intensity numerical rating scale (PI-NRS) where 0= No pain and 10= Pain as bad as you can imagine. A negative change from Baseline indicates an improvement. The primary analysis is based on the intent-to-treat (ITT) population which includes all randomised subjects who took at least one dose of randomised study treatment.

End point type	Primary

End point timeframe:

Baseline (Week 2), DB Week 12

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	139[1]	142	
Units: score on a scale				
least squares mean (standard error)	-1.75 (± 0.181)	-1.50 (± 0.177)	-1.81 (± 0.176)	

Notes:

[1] - Number of subjects analysed is number of subjects with data available for analysis.

Statistical analyses

Statistical analysis title	Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID

Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.314
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.24
upper limit	0.74

Statistical analysis title	Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.797
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	0.43

Secondary: Percentage of Subjects with 50% Neuropathic Pain Reduction Response at DB Week 12

End point title	Percentage of Subjects with 50% Neuropathic Pain Reduction Response at DB Week 12

End point description:

Daily neuropathic pain score is used to capture the subject's average neuropathic pain scores and low back pain scores over 24 hours on 11-point pain intensity numerical rating scale (PI-NRS). Each item is rated on a scale where 0= No pain and 10= Pain as bad as you can imagine. The percentage of subjects with 50% pain reduction from baseline are tallied. The ITT population included all randomised subjects who took at least one dose of randomised study treatment.

End point type	Secondary

End point timeframe:

DB Week 12

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	140	142	
Units: percentage of subjects				
number (not applicable)	22.5	20.0	20.4	

Statistical analyses

Statistical analysis title	Placebo v BIIB074 200 mg BID
Statistical analysis description:	
Analysis was based on logistic regression adjusted for treatment, prior back surgery (yes/no), NSAIDs ongoing at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.525
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.46
upper limit	1.48

Statistical analysis title	Placebo v BIIB074 350 mg BID
Statistical analysis description:	
Analysis was based on logistic regression adjusted for treatment, prior back surgery (yes/no), NSAIDs ongoing at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.669
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	1.56

Secondary: Percentage of Subjects with 30% Neuropathic Pain Reduction Response at DB Week 12

End point title	Percentage of Subjects with 30% Neuropathic Pain Reduction Response at DB Week 12

End point description:

Daily neuropathic pain score is used to capture the subject's average neuropathic pain scores and low back pain scores over 24 hours on 11-point pain intensity numerical rating scale (PI-NRS). Each item is rated on a scale where 0= No pain and 10= Pain as bad as you can imagine. The percentage of subjects with 30% pain reduction from baseline are tallied. The ITT population included all randomised subjects who took at least one dose of randomised study treatment.

End point type	Secondary

End point timeframe:

DB Week 12

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	140	142	
Units: percentage of subjects				
number (not applicable)	40.1	34.3	33.8	

Statistical analyses

Statistical analysis title	Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on logistic regression adjusted for treatment, prior back surgery (yes/no), NSAIDs ongoing at
randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.248
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	1.23

Statistical analysis title	Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on logistic regression adjusted for treatment, prior back surgery (yes/no), NSAIDs ongoing at
randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.277
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.47
upper limit	1.24

Secondary: Change from Baseline in Weekly Average of the Daily Neuropathic Pain Score at Each Visit

End point title	Change from Baseline in Weekly Average of the Daily Neuropathic Pain Score at Each Visit

End point description:

Daily neuropathic pain score is used to capture the subject's average neuropathic pain scores and low back pain scores over 24 hours on 11-point pain intensity numerical rating scale (PI-NRS). Each item is rated on a scale where 0= No pain and 10= Pain as bad as you can imagine. The ITT population included all randomised subjects who took at least one dose of randomised study treatment.

End point type	Secondary

End point timeframe:

Baseline (Week 2), DB Week 1, DB Week 2, DB Week 3, DB Week 4, DB Week 5, DB Week 6, DB Week 7, DB Week 8, DB Week 9, DB Week 10, DB Week 11

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	139[2]	142	
Units: score on a scale				
least squares mean (standard error)				
Change at DB Week 1	-0.30 (± 0.082)	-0.36 (± 0.083)	-0.42 (± 0.082)	
Change at DB Week 2	-0.48 (± 0.098)	-0.59 (± 0.099)	-0.64 (± 0.098)	
Change at DB Week 3	-0.77 (± 0.117)	-0.77 (± 0.117)	-0.93 (± 0.117)	
Change at DB Week 4	-0.97 (± 0.125)	-0.88 (± 0.125)	-1.09 (± 0.125)	
Change at DB Week 5	-1.16 (± 0.136)	-1.03 (± 0.136)	-1.40 (± 0.135)	

Change at DB Week 6	-1.25 (± 0.144)	-1.05 (± 0.144)	-1.53 (± 0.143)	
Change at DB Week 7	-1.42 (± 0.152)	-1.08 (± 0.151)	-1.59 (± 0.150)	
Change at DB Week 8	-1.50 (± 0.157)	-1.19 (± 0.157)	-1.69 (± 0.155)	
Change at DB Week 9	-1.64 (± 0.165)	-1.34 (± 0.162)	-1.75 (± 0.161)	
Change at DB Week 10	-1.62 (± 0.170)	-1.39 (± 0.166)	-1.78 (± 0.165)	
Change at DB Week 11	-1.66 (± 0.176)	-1.41 (± 0.172)	-1.77 (± 0.171)	

Notes:

[2] - Number of subjects analysed is number of subjects with data available for analysis.

Statistical analyses

Statistical analysis title	DB Week 1: Placebo v BIIB074 200 mg BID
Statistical analysis description:	
DB Week 1: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	-0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.28
upper limit	0.18

Statistical analysis title	DB Week 1: Placebo v 350 mg BID
Statistical analysis description:	
DB Week 1: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	0.11

Statistical analysis title	DB Week 2: Placebo v BIIB074 200 mg BID
Statistical analysis description:	
DB Week 2: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.38
upper limit	0.16

Statistical analysis title	DB Week 2: Placebo v BIIB074 350 mg BID
Statistical analysis description:	
DB Week 2: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	0.11

Statistical analysis title	DB Week 3: Placebo v BIIB074 200 mg BID
Statistical analysis description:	
DB Week 3: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.33
upper limit	0.32

Statistical analysis title	DB Week 3: Placebo v BIIB074 350 mg BID
Statistical analysis description:	
DB Week 3: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.49
upper limit	0.16

Statistical analysis title	DB Week 4: Placebo v BIIB074 200 mg BID
Statistical analysis description:	
DB Week 4: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	0.43

Statistical analysis title	DB Week 4: Placebo v BIIB074 350 mg BID
Statistical analysis description:	
DB Week 4: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	-0.12

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.47
upper limit	0.22

Statistical analysis title	DB Week 5: Placebo v BIIB074 200 mg BID
Statistical analysis description:	
DB Week 5: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	0.13
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.25
upper limit	0.5

Statistical analysis title	DB Week 5: Placebo v BIIB074 350 mg BID
Statistical analysis description:	
DB Week 5: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.13

Statistical analysis title	DB Week 6: Placebo v BIIB074 200 mg BID
Statistical analysis description:	
DB Week 6: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region(Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 200 milligram (mg) BID

Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.6

Statistical analysis title	DB Week 6: Placebo v BIIB074 350 mg BID

Statistical analysis description:

DB Week 6: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.68
upper limit	0.12

Statistical analysis title	DB Week 7: Placebo v BIIB074 200 mg BID

Statistical analysis description:

DB Week 7: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region(Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.08
upper limit	0.76

Statistical analysis title	DB Week 7: Placebo v BIIB074 350 mg BID

Statistical analysis description:

DB Week 7: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	0.25

Statistical analysis title	DB Week 8: Placebo v BIIB074 200 mg BID

Statistical analysis description:

DB Week 8: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.12
upper limit	0.74

Statistical analysis title	DB Week 8: Placebo v BIIB074 350 mg BID

Statistical analysis description:

DB Week 8: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	-0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.62
upper limit	0.24

Statistical analysis title	DB Week 9: Placebo v BIIB074 200 mg BID
Statistical analysis description:	
DB Week 9: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	0.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.14
upper limit	0.76

Statistical analysis title	DB Week 9: Placebo v BIIB074 350 mg BID
Statistical analysis description:	
DB Week 9: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.56
upper limit	0.34

Statistical analysis title	DB Week 10: Placebo v BIIB074 200 mg BID
Statistical analysis description:	
DB Week 10: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	0.24

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	0.7

Statistical analysis title	DB Week 10: Placebo v BIIB074 350 mg BID
Statistical analysis description:	
DB Week 10: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.61
upper limit	0.31

Statistical analysis title	DB Week 11: Placebo v BIIB074 200 mg BID
Statistical analysis description:	
DB Week 11: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	0.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.22
upper limit	0.72

Statistical analysis title	DB Week 11: Placebo v BIIB074 350 mg BID
Statistical analysis description:	
DB Week 11: ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.	
Comparison groups	Placebo v BIIB074 350 mg BID

Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Least squares mean difference
Point estimate	-0.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.59
upper limit	0.37

Secondary: Change from Baseline to DB Week 12 in Weekly Average of Daily Low Back Pain Score

End point title	Change from Baseline to DB Week 12 in Weekly Average of Daily Low Back Pain Score

End point description:

The subjects rated their average low back pain score scores over 24 hours using the 11-point pain intensity numerical rating scale (PI-NRS) where 0= No pain and 10= Pain as bad as you can imagine. A negative change from Baseline indicates an improvement. The analysis is based on the ITT population which includes all randomised subjects who took at least one dose of randomised study treatment.

End point type	Secondary

End point timeframe:

Baseline (Week 2), DB Week 12

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	139[3]	142	
Units: score on a scale				
least squares mean (standard error)	-0.94 (± 0.164)	-0.74 (± 0.162)	-1.03 (± 0.163)	

Notes:

[3] - Number of subjects analysed is number of subjects with data available for analysis.

Statistical analyses

Statistical analysis title	Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID

Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.695
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.55
upper limit	0.36

Statistical analysis title	Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	281
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.403
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.26
upper limit	0.65

Secondary: Number of Subjects with Patient Global Impression of Change (PGIC) Responder at DB Week 12

End point title	Number of Subjects with Patient Global Impression of Change (PGIC) Responder at DB Week 12

End point description:

PGIC is a 7-point scale depicting a subject's rating of overall improvement using a range of responses from 1 (very much improved) to 7 (very much worse). The data represented the number of subjects who had answered 'very much improved' or 'much improved' on the PGIC questionnaire. The ITT population included all randomised subjects who took at least one dose of randomised study treatment.

End point type	Secondary

End point timeframe:

DB Week 12

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	140	142	
Units: subjects				
number (not applicable)	35	30	35	

Statistical analyses

Statistical analysis title	Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on logistic regression adjusted for treatment, prior back surgery (yes/no), NSAIDs ongoing at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.997
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	1.72

Statistical analysis title	Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on logistic regression adjusted for treatment, prior back surgery (yes/no), NSAIDs ongoing at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.434
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.45
upper limit	1.41

Secondary: Change from Baseline on the Oswestry Disability Index up to DB Week 12

End point title	Change from Baseline on the Oswestry Disability Index up to DB Week 12

End point description:

Disability at the day measured by Oswestry Disability index (ODI). Each of the ten items in the ODI has six statements from which subjects are requested to select one. This allows scoring from 0-5 for each item, where 0 represents no pain and 5 worst pain. A maximum score of 50 is possible. A negative change indicates no disability. The ITT population included all randomised subjects who took at least one dose of randomised study treatment.

End point type	Secondary

End point timeframe:

Baseline (Week 2), DB Week 12

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	135[4]	136[5]	135[6]	
Units: score on a scale				
least squares mean (standard error)	-6.85 (± 1.039)	-6.31 (± 1.020)	-6.24 (± 1.030)	

Notes:

[4] - Number of subjects analysed is number of subjects with data available for analysis.

[5] - Number of subjects analysed is number of subjects with data available for analysis.

[6] - Number of subjects analysed is number of subjects with data available for analysis.

Statistical analyses

Statistical analysis title	Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	271
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.711
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.3
upper limit	3.38

Statistical analysis title	Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.68
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.26
upper limit	3.47

Secondary: Change from Baseline in the Weekly Average of the Daily Sleep Interference Score up to DB Week 12

End point title	Change from Baseline in the Weekly Average of the Daily Sleep Interference Score up to DB Week 12

End point description:

Daily sleep interference score is assessed using electronic diaries using an 11-point numeric rating scale (NRS) ranging from 0 (pain does not interfere with sleep) to 10 (pain completely interferes with sleep, unable to sleep). The sleep interference NRS is a tool sleep numerical rating scale how leg pain interfered with their sleep quality. A negative change indicates minimal or no interference in sleep. The ITT population included all randomised subjects who took at least one dose of randomised study treatment.

End point type	Secondary

End point timeframe:

Baseline (Week 2), DB Week 12

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	141[7]	138[8]	141[9]	
Units: score on a scale				
least squares mean (standard error)	-1.46 (± 0.173)	-1.27 (± 0.174)	-1.55 (± 0.176)	

Notes:

[7] - Number of subjects analysed is number of subjects with data available for analysis.

[8] - Number of subjects analysed is number of subjects with data available for analysis.

[9] - Number of subjects analysed is number of subjects with data available for analysis.

Statistical analyses

Statistical analysis title	Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	279
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.458
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.3
upper limit	0.66

Statistical analysis title	Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.716
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.57
upper limit	0.39

Secondary: Change from Baseline in the Brief Pain Inventory (BPI) –Interference index up to DB Week 12

End point title	Change from Baseline in the Brief Pain Inventory (BPI) –Interference index up to DB Week 12

End point description:

BPI measures how much pain has interfered with seven daily activities, including general activity, walking, work, mood, enjoyment of life, relations with others, and sleep. Each activity is rated on a scale of 0 (does not interfere) to 10 (completely interferes). The BPI - Interference index was calculated as the mean of the seven interference scores. If more than 3 of the 7 scores are missing, then the BPI – Interference Index will be set to missing. A negative score indicates no interference. The ITT population included all randomised subjects who took at least one dose of randomised study

treatment.

End point type	Secondary

End point timeframe:

Baseline (Week 2), DB Week 12

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140[10]	137[11]	135[12]	
Units: score on a scale				
least squares mean (standard error)	-1.25 (± 0.147)	-1.19 (± 0.145)	-1.37 (± 0.145)	

Notes:

[10] - Number of subjects analysed is number of subjects with data available for analysis.

[11] - Number of subjects analysed is number of subjects with data available for analysis.

[12] - Number of subjects analysed is number of subjects with data available for analysis.

Statistical analyses

Statistical analysis title	Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.767
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.34
upper limit	0.46

Statistical analysis title	Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID

Number of subjects included in analysis	275
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.545
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.53
upper limit	0.28

Secondary: Change from Baseline in the BPI – Pain index to DB Week 12

End point title	Change from Baseline in the BPI – Pain index to DB Week 12

End point description:

BPI items 3-6 ask subjects to assess their pain at its "worst", "least", "average" and "right now", respectively. Each item is rated on a scale of 0 (no pain) to 10 (pain as bad as you can imagine). The BPI – Pain Index is calculated as the mean of the scores from items 3-6, and is set to missing if any of items 3-6 are missing. A negative change indicates no pain. The ITT population included all randomised subjects who took at least one dose of randomised study treatment.

End point type	Secondary

End point timeframe:

Baseline (Week 2), DB Week 12

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	140[13]	137[14]	135[15]	
Units: score on a scale				
least squares mean (standard error)	-1.40 (± 0.146)	-1.43 (± 0.147)	-1.58 (± 0.148)	

Notes:

[13] - Number of subjects analysed is number of subjects with data available for analysis.

[14] - Number of subjects analysed is number of subjects with data available for analysis.

[15] - Number of subjects analysed is number of subjects with data available for analysis.

Statistical analyses

Statistical analysis title	Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID

Number of subjects included in analysis	277
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.889
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.43
upper limit	0.37

Statistical analysis title	Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	275
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.399
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.58
upper limit	0.23

Secondary: Change from Baseline on the EuroQoL 5-Dimension 5-Level (EQ- 5D-5L) Questionnaire Health Index to DB Week 12

End point title	Change from Baseline on the EuroQoL 5-Dimension 5-Level (EQ- 5D-5L) Questionnaire Health Index to DB Week 12

End point description:

The EQ-5D questionnaire is a brief, generic health-related quality of life assessment (HRQOL) that can also be used to incorporate subject preferences into health economic evaluations. The EQ-5D-5L descriptive system comprises the following 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression and as overall health on a visual analogue scale from 0 to 100 where 0 represents the "best health you can imagine" and 100 represents the "worst health you can imagine". A positive change indicates worst health. The ITT population included all randomised subjects who took at least one dose of randomised study treatment.

End point type	Secondary

End point timeframe:

Baseline (Week 2), DB Week 12

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	135[16]	136[17]	135[18]	
Units: score on a scale				
least squares mean (standard error)	0.06 (± 0.009)	0.05 (± 0.010)	0.06 (± 0.010)	

Notes:

[16] - Number of subjects analysed is number of subjects with data available for analysis.

[17] - Number of subjects analysed is number of subjects with data available for analysis.

[18] - Number of subjects analysed is number of subjects with data available for analysis.

Statistical analyses

Statistical analysis title	Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	271
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.542
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.03
upper limit	0.02

Statistical analysis title	Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	270
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.741
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.02
upper limit	0.03

Secondary: Change from Baseline to DB Week 12 in the Short Form 36 (SF-36) Questionnaire

End point title	Change from Baseline to DB Week 12 in the Short Form 36 (SF-36) Questionnaire

End point description:

36-Item Short Form Health Survey (SF-36) Version 2 is a general health-related quality of life survey, with a 1-week recall period. It is composed of 36 items. These items are grouped into 8 scales: physical functioning, role physical, bodily pain, general health, vitality, social functioning, role emotional, mental health, physical component score (PCS) and mental component score. All of the scales are scored 1-100, with higher scores indicating better health. The ITT population included all randomised subjects who took at least one dose of randomised study treatment. Here, "n" signifies the number of subjects with data available for analysis at specified timepoint.

End point type	Secondary

End point timeframe:

Baseline (Week 2), DB Week 12

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	140	142	
Units: score on a scale				
least squares mean (standard error)				
Physical Functioning (n=133,135,134)	8.68 (± 1.472)	8.08 (± 1.459)	7.16 (± 1.468)	
Role Physical (n=132,135,134)	8.23 (± 1.536)	6.70 (± 1.521)	6.92 (± 1.522)	
Bodily Pain (n=132,135,134)	9.56 (± 1.355)	8.95 (± 1.341)	10.66 (± 1.345)	
General Health (n=133,135,134)	4.44 (± 1.209)	2.13 (± 1.200)	4.71 (± 1.203)	
Vitality (n=132,135,134)	5.52 (± 1.204)	5.34 (± 1.189)	5.19 (± 1.194)	
Social Functioning (n=132,135,134)	6.09 (± 1.670)	4.90 (± 1.652)	4.54 (± 1.656)	
Role Emotional (n=132,135,134)	6.43 (± 1.692)	4.48 (± 1.674)	2.78 (± 1.675)	
Mental Health (n=132,135,134)	4.53 (± 1.120)	3.28 (± 1.111)	4.02 (± 1.111)	
Physical Component Score (n=132,135,134)	3.43 (± 0.553)	3.09 (± 0.547)	3.51 (± 0.549)	
Mental Component Score (n=132,135,134)	2.17 (± 0.649)	1.59 (± 0.643)	1.30 (± 0.643)	

Statistical analyses

Statistical analysis title	Physical Functioning: Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use

at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.772
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.67
upper limit	3.47

Statistical analysis title	Physical Functioning: Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.463
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-1.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.62
upper limit	2.56

Statistical analysis title	Role Physical: Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.482
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-1.52

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.79
upper limit	2.74

Statistical analysis title	Role Physical: Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.546
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-1.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.56
upper limit	2.94

Statistical analysis title	Bodily Pain: Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.749
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.36
upper limit	3.14

Statistical analysis title	Bodily Pain: Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.562
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	1.11
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.64
upper limit	4.86

Statistical analysis title	General Health: Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.177
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-2.31
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.66
upper limit	1.05

Statistical analysis title	General Health: Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.874
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	0.27

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.08
upper limit	3.62

Statistical analysis title	Vitality: Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.916
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.51
upper limit	3.15

Statistical analysis title	Vitality: Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.847
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.66
upper limit	3.01

Statistical analysis title	Social Functioning: Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.613
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-1.19
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.81
upper limit	3.43

Statistical analysis title	Social Functioning: Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.51
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.17
upper limit	3.07

Statistical analysis title	Role Emotional: Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.415
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-1.95

Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.64
upper limit	2.74

Statistical analysis title	Role Emotional: Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.126
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-3.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-8.33
upper limit	1.03

Statistical analysis title	Mental Health: Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.429
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-1.25
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.37
upper limit	1.86

Statistical analysis title	Mental Health: Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.747
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.61
upper limit	2.59

Statistical analysis title	PCS: Placebo v BIIB074 200 mg BID

Statistical analysis description:

ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs ongoing at randomization (yes/no),
region (Eastern/Western Europe) and baseline SF-36 parameter.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.656
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.88
upper limit	1.18

Statistical analysis title	PCS: Placebo v BIIB074 350 mg BID

Statistical analysis description:

ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs ongoing at randomization (yes/no),
region (Eastern/Western Europe) and baseline SF-36 parameter.

Comparison groups	Placebo v BIIB074 350 mg BID

Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.924
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.46
upper limit	1.61

Statistical analysis title	Mental Component Score:Placebo v BIIB074 200mg BID
Statistical analysis description:	
ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs ongoing at randomization (yes/no), region (Eastern/Western Europe) and baseline SF-36 parameter.	
Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.527
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.58
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.38
upper limit	1.22

Statistical analysis title	Mental Component Score:Placebo v BIIB074 350mg BID
Statistical analysis description:	
ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs ongoing at randomization (yes/no), region (Eastern/Western Europe) and baseline SF-36 parameter.	
Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.341
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.87

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.66
upper limit	0.92

Secondary: Amount of Rescue Medication Used

End point title	Amount of Rescue Medication Used

End point description:

The amount of rescue medication used per day during the double-blind (DB) period will be calculated as the total dosage recorded divided by the total number of days with a recorded rescue medication use (including the days with a record of 0 tablet) during the DB period. The ITT population included all randomised subjects who took at least one dose of randomised study treatment.

End point type	Secondary

End point timeframe:

Baseline (Week 2) up to Day 125

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	140	142	
Units: dosage/day				
least squares mean (standard error)	377.37 (± 49.055)	447.54 (± 49.405)	356.33 (± 49.052)	

Statistical analyses

Statistical analysis title	Placebo v BIIB074 200 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 200 milligram (mg) BID
Number of subjects included in analysis	282
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.314
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	70.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-66.7
upper limit	207.04

Statistical analysis title	Placebo v BIIB074 350 mg BID

Statistical analysis description:

Analysis was based on ANCOVA model adjusted for treatment, prior back surgery (yes/no), NSAIDs use at randomization (yes/no), region (Eastern/Western Europe) and baseline neuropathic pain score.

Comparison groups	Placebo v BIIB074 350 mg BID
Number of subjects included in analysis	284
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.762
Method	ANCOVA
Parameter estimate	Least squares mean difference
Point estimate	-21.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-157.42
upper limit	115.32

Secondary: Number of Subjects with Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Subjects with Treatment-Emergent Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

An AE was any untoward medical occurrence in subjects who received study drug without regard to possibility of causal relationship. SAE was an AE resulting in any of the following outcomes or deemed significant for any other reason: death; initial or prolonged inpatient hospitalization; life-threatening experience (immediate risk of dying); persistent or significant disability/incapacity; congenital anomaly. Treatment-emergent were events after first dose of study drug that were absent before treatment or that worsened relative to pretreatment state. AEs included both serious and non-serious. The safety population included all subjects who were randomised and received at least 1 dose of study treatment in the double-blind period.

End point type	Secondary

End point timeframe:

AEs: Baseline (Week 2) up to Day 125; SAEs: Screening up to Day 125

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	140	142	
Units: subjects				
number (not applicable)				
AEs	36	34	40	
SAEs	1	2	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects With Clinically Relevant Abnormalities in Vital Signs

End point title	Number of Subjects With Clinically Relevant Abnormalities in Vital Signs

End point description:

Abnormal vital signs were determined by the following criteria: temperature >38°C and an increase from pre-dose of at least 1°C; pulse >100 beat per minute (bpm) and an increase from baseline of more than 20 bpm, or <50 bpm and a decrease from baseline of more than 20 bpm; systolic blood pressure >160 mmHg and an increase from baseline of more than 40 mmHg, or <90 mmHg and a decrease from baseline of more than 30 mmHg; diastolic blood pressure >100 mmHg and an increase from pre-dose of more than 30 mmHg, or <45 mmHg and a decrease from pre-dose of more than 20 mmHg; respiration rate >25 breaths per minute, or <10 breaths per minute. The safety population included all subjects who were randomised and received at least 1 dose of study treatment in the double-blind period.

End point type	Secondary

End point timeframe:

Baseline up to Day 125

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	140	142	
Units: subjects				
number (not applicable)				
Temperature	0	0	0	
Pulse	0	1	1	
Systolic blood pressure	0	0	0	
Diastolic blood pressure	0	0	0	
Respiration Rate	1	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Abnormal Significant 12-Lead Electrocardiogram (ECG) Values

End point title	Number of Subjects with Abnormal Significant 12-Lead Electrocardiogram (ECG) Values

End point description:

The safety population included all subjects who were randomised and received at least 1 dose of study

treatment in the double-blind period.

End point type	Secondary

End point timeframe:

Baseline (Week 2) up to Day 125

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	140	142	
Units: subjects				
number (not applicable)	0	0	1	

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Subjects with Clinically Significant Laboratory Test Abnormalities

End point title	Number of Subjects with Clinically Significant Laboratory Test Abnormalities

End point description:

The safety population included all subjects who were randomised and received at least 1 dose of study treatment in the double-blind period.

End point type	Secondary

End point timeframe:

Baseline (Week 2) up to Day 125

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	140	142	
Units: subjects				
number (not applicable)	0	0	0	

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Suicidal Ideation or Behavior Based on Columbia-Suicide Severity Rating Scale (C-SSRS) Score

End point title	Percentage of Subjects with Suicidal Ideation or Behavior

	Based on Columbia-Suicide Severity Rating Scale (C-SSRS) Score

End point description:

The C-SSRS is an assessment tool that evaluates suicidal ideation and behavior. C-SSRS data are collected at each clinic visit. Suicidal ideation events include: (1) Wish to be dead, (2) Nonspecific active thoughts, (3) Active ideation: method, but no intent or plan, (4) Active ideation: method and intent, but no plan; (5) Active ideation: method, intent, and plan. Suicidal behaviour events include (6) actual attempt, (7) Interrupted attempt, (8) Aborted attempt, (9) Preparatory acts or behavior, (10) Suicide behavior, and (11) Suicide. All suicide-related events based on C-SSRS data will be listed only for subjects with YES response to any question. Here, SI/B = Suicidal ideation or behavior and b/w = between. The safety population included all subjects who were randomised and received at least 1 dose of study treatment in the double-blind period.

End point type	Secondary

End point timeframe:

Screening (=<28 days before Day 1) up to Day 125

End point values	Placebo	BIIB074 200 milligram (mg) BID	BIIB074 350 mg BID	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	142	139[19]	139[20]	
Units: percentage of subjects				
number (not applicable)				
Screening: SI/B	2.8	0.7	2.2	
B/w screening&first randomized dose:SI/B	1.4	0	0.7	
Randomization visit: SI/B	2.1	0	0.7	
During the DB period: SI/B	2.1	0	0.7	
Follow-up: SI/B	0	0	0	

Notes:

[19] - Number of subjects analysed is number of subjects with data available for analysis.

[20] - Number of subjects analysed is number of subjects with data available for analysis.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
Day 1 (Week 2) up to through the follow-up visit (Day 129)	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
All subjects received placebo matched to BIIB074 tablets twice daily (BID), in placebo run-in period (14 days) and orally on Day 1 (Week 0); Day 15 (Week 2); Day 29 (Week 4); Day 43 (Week 6); and Day 71 (Week 10).	
Reporting group title	BIIB074 350 mg
Reporting group description:	
All subjects received placebo tablets (matched to BIIB074) orally BID in placebo run-in period (14 days). Subjects received BIIB074 350mg tablets orally BID for up to 12 weeks.	
Reporting group title	BIIB074 200 mg
Reporting group description:	
All subjects received placebo tablets (matched to BIIB074) orally BID in placebo run-in period (14 days). Subjects received BIIB074 200mg tablets orally BID for up to 12 weeks.	

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: No non-serious adverse event occurred in the 5% threshold in any of the reporting arms.

Serious adverse events	Placebo	BIIB074 350 mg	BIIB074 200 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 142 (0.70%)	1 / 142 (0.70%)	2 / 140 (1.43%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Injury, poisoning and procedural complications			
Alcohol poisoning			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	1 / 140 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 142 (0.00%)	1 / 142 (0.70%)	0 / 140 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	1 / 140 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	1 / 140 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcoholism			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	1 / 140 (0.71%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 142 (0.70%)	0 / 142 (0.00%)	0 / 140 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Placebo	BIIB074 350 mg	BIIB074 200 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 142 (0.00%)	0 / 142 (0.00%)	0 / 140 (0.00%)

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
03 March 2016	• Clarification was added to clinic procedures and laboratory tests for safety assessments, eligibility criteria, prohibited medications, and treatment compliance, and to the timing of interim sample size re-estimation. • Information on serotonin syndrome was added, as requested by the Food and Drug Administration (FDA).
28 July 2016	• The maximum dose of paracetamol/acetaminophen in prolonged therapy was reduced from 3 g/day to 2.5 g/day and a restriction to the duration of prolonged therapy to no more than 5 out of 7 consecutive days was added; an associated exclusion and withdrawal criteria were also added. • The number of contraceptives to be used for highly effective contraception was reduced from 2 to 1 (thereafter stated as "effective contraception"). • Changes to the withdrawal criteria and inclusion and exclusion criteria were made to consolidate the protocol across different countries. • Changes were made to ensure any event of seizure was considered medically significant and, hence, reported as an SAE.
05 May 2017	• The nonclinical safety information included under "Profile of Previous Experience" was updated. • Alcohol and drug screen, study treatment administration, and drug accountability were added as assessments to the Unscheduled Visit. • The exclusion criteria were updated to exclude concomitant use of medications that are P-glycoprotein substrates with a narrow therapeutic index, prohibit the concomitant use of all cytochrome P450 3A4 and uridine 5'-diphosphoglucuronosyltransferase inducers and inhibitors, and allow the enrollment of individuals already receiving disability payments for PLSR. • Instructions were added for managing subjects who experienced a suspected treatment-induced rash. • An unblinded administrative interim analysis was added to enable planning of the Phase 3 program for PLSR.
23 May 2017	• A clarification was provided that the pregnancy of a female partner would not impact the study status of a male subject either at Screening or during his participation in the study. • The eligibility criteria were updated to clarify the definition of a positive test result for Hepatitis B at Screening.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported