Clinical trial results:
A Randomized, Double-Blind, Parallel-Group, Placebo-Controlled Study to Assess the Efficacy, Safety, Tolerability, and Pharmacokinetics of BIIB033 in Subjects with First Episode of Acute Optic Neuritis

Summary

EudraCT number	2011-006291-39
Trial protocol	SE BE DE CZ GB HU ES IT DK
Global end of trial date	21 October 2014

Results information

Result version number	v1 (current)
This version publication date	24 March 2016
First version publication date	24 March 2016

Trial information

Trial identification

Sponsor protocol code	215ON201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01721161
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	21 October 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	21 October 2014
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 BIIB033 in subjects with their first episode of unilateral acute optic neuritis (AON). The secondary objective of this study in this population was to assess the safety, tolerability, and pharmacokinetics (PK) of BIIB033.

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.

Following study treatment administration, subjects were required to remain at the study site for 1 hour for monitoring of any unexpected infusion reactions. Medications for the treatment of severe hypersensitivity reactions (e.g., epinephrine for subcutaneous injections, diphenhydramine for IV injection) were available for immediate use.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	21 December 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	Germany: 22
Country: Number of subjects enrolled	Spain: 14
Country: Number of subjects enrolled	Italy: 11
Country: Number of subjects enrolled	Australia: 9
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Sweden: 5
Country: Number of subjects enrolled	Czech Republic: 4
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	United Kingdom: 3
Country: Number of subjects enrolled	Canada: 2
Country: Number of subjects enrolled	Denmark: 2
Worldwide total number of subjects	82
EEA total number of subjects	71

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)	82
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Subject eligibility for the study was determined within 28 days prior to Day -1. The daily course of IV methylprednisolone was completed before administration of the first dose of study treatment on Day 1/baseline.

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	Investigator, Subject

Blinding implementation details:

This was a randomized, double-blinded, parallel-group, placebo-controlled study.
All study staff were blinded to the subject treatment assignments (BIIB033 or placebo) with the exception of the unblinded Pharmacist or designee who was responsible for preparing the study treatments, the unblinded Pharmacy Monitor, and the study staff responsible for the analysis of the PK data.

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo via IV infusion once every 4 weeks for 20 weeks (a total of 6 doses)

Arm type	Placebo
Investigational medicinal product name	sterile normal saline (0.9% sodium chloride for IV administration)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects who were randomized to placebo were dosed at 6 study visits (every 4 weeks for 20 weeks: Day 1/baseline, Week 4, Week 8, Week 12, Week 16, and Week 20) by IV infusion.

Arm title	BIIB033

Arm description:

BIIB033 100 mg/kg via IV infusion once every 4 weeks for 20 weeks (a total of 6 doses)

Arm type	Experimental
Investigational medicinal product name	BIIB033
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intravenous use

Dosage and administration details:

All subjects were dosed at the Day 1/baseline Visit. Subsequent doses were administered once every 4 weeks for a total of 6 doses. Dosing schedule for each subject was as follows: Day 1/baseline, Week 4, Week 8, Week 12, Week 16, and Week 20.

Number of subjects in period 1	Placebo	BIIB033
Started	41	41
Completed	37	34
Not completed	4	7
Consent withdrawn by subject	1	1
Adverse event, non-fatal	2	3
Not Specified	-	1
Lost to follow-up	1	2

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo via IV infusion once every 4 weeks for 20 weeks (a total of 6 doses)	
Reporting group title	BIIB033
Reporting group description:	
BIIB033 100 mg/kg via IV infusion once every 4 weeks for 20 weeks (a total of 6 doses)	

Reporting group values	Placebo	BIIB033	Total
Number of subjects	41	41	82
Age categorical Units: Subjects			
Age Continuous | Units: years			
arithmetic mean	32.4	31.8	
standard deviation	± 8.85	± 7.17	-
Gender, Male/Female Units: participants			
Female	31	27	58
Male	10	14	24
Affected eye Units: Subjects			
Right eye	19	25	44
Left eye	22	16	38
FF-VEP conduction block in the affected eye at baseline			
FF-VEP=full-field visual evoked potentials			
Units: Subjects			
FF-VEP conduction block	5	10	15
No FF-VEP conduction block	36	31	67
Days from first AON symptom to first dose			
First dose given, on average, 2 weeks after completion of high-dose (1 g daily for 3 to 5 days) IV methylprednisolone treatment.			
Units: days			
arithmetic mean	24.6	23.6	
standard deviation	± 3.4	± 4	-
Days from confirmed AON diagnosis to first dose Units: days			
arithmetic mean	19.2	18.7	
standard deviation	± 4.9	± 4.7	-
FF-VEP latency in the fellow eye at baseline Units: ms			
arithmetic mean	101.7	102.7	
standard deviation	± 5.25	± 6.4	-

RGCL/IPL thickness in the affected eye at baseline			
RGCL/IPL=retinal ganglion cell layer/inner plexiform retinal layer. n=38 in the placebo group and n=40 in the anti-LINGO-1 group, total n=78.			
Units: microns			
arithmetic mean	66	63.8	
standard deviation	± 6.9	± 7.4	-
Brain Gd+ lesions before first dose			
Gd+=gadolinium-enhancing. n=38 in each group, total n=76.			
Units: lesions			
arithmetic mean	0.5	0.2	
standard deviation	± 1.6	± 1	-
Volume of brain T2 lesions before first dose			
n=38 in each group, total n=76.			
Units: mL			
arithmetic mean	1.09	1.09	
standard deviation	± 1.32	± 1.9	-

End points

End points reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo via IV infusion once every 4 weeks for 20 weeks (a total of 6 doses)	
Reporting group title	BIIB033
Reporting group description:	
BIIB033 100 mg/kg via IV infusion once every 4 weeks for 20 weeks (a total of 6 doses)	

Primary: Change in Full-field Visual Evoked Potential (FF-VEP) Latency at Week 24: Intent-to-treat (ITT) Population	
End point title	Change in Full-field Visual Evoked Potential (FF-VEP) Latency at Week 24: Intent-to-treat (ITT) Population
End point description:	
Adjusted mean change in optic nerve conduction velocity (NCV) at Week 24 for the affected eye from the baseline of unaffected fellow eye as determined by FF-VEP. Adjusted for the baseline latency of fellow eye.	
End point type	Primary
End point timeframe:	
Baseline, Week 24	

End point values	Placebo	BIIB033		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	41		
Units: msec				
arithmetic mean (standard error)	20.83 (± 2.53)	17.34 (± 2.53)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BIIB033
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3337
Method	ANCOVA
Parameter estimate	Difference
Point estimate	-3.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	-10.61
upper limit	3.65

Primary: Change in FF-VEP Latency at Week 24: Per-protocol Population

End point title	Change in FF-VEP Latency at Week 24: Per-protocol Population

End point description:

Adjusted mean change in optic nerve conduction velocity (NCV) at Week 24 for the affected eye from the baseline of unaffected fellow eye as determined by FF-VEP. Adjusted for the baseline latency of fellow eye.

End point type	Primary

End point timeframe:

Baseline, Week 24

End point values	Placebo	BIIB033		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	33		
Units: msec				
arithmetic mean (standard error)	22.24 (± 2.61)	14.69 (± 2.72)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BIIB033
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0504
Method	ANCOVA
Parameter estimate	Difference
Point estimate	-7.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.12
upper limit	0.01

Secondary: Percentage Change in Spectral-domain Optical Coherence Tomography (SD-OCT) Average Retinal Nerve Fiber Layer (RNFL) Thickness at Week 24: ITT Population

End point title	Percentage Change in Spectral-domain Optical Coherence Tomography (SD-OCT) Average Retinal Nerve Fiber Layer (RNFL) Thickness at Week 24: ITT Population

End point description:

Adjusted mean percentage change in thickness of the RNFL at Week 24 for the affected eye from the baseline of unaffected fellow eye as determined by SD-OCT. Percentage change is calculated as

(affected eye - baseline of fellow eye)/baseline of fellow eye*100. Adjusted for the baseline RNFL thickness.

End point type	Secondary
End point timeframe:	
Baseline, Week 24	

End point values	Placebo	BIIB033		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	41		
Units: percentage change				
arithmetic mean (standard error)	-11.77 (± 2.08)	-15.66 (± 2.03)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BIIB033
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1868
Method	ANCOVA
Parameter estimate	Difference
Point estimate	-3.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	-9.7
upper limit	1.92

Secondary: Percentage Change in SD-OCT Average RNFL Thickness at Week 24: Per-protocol Population

End point title	Percentage Change in SD-OCT Average RNFL Thickness at Week 24: Per-protocol Population

End point description:

Adjusted mean percentage change in thickness of the RNFL at Week 24 for the affected eye from the baseline of unaffected fellow eye as determined by SD-OCT. Percentage change is calculated as (affected eye - baseline of fellow eye)/baseline of fellow eye*100. Adjusted for the baseline RNFL thickness.

End point type	Secondary
End point timeframe:	
Baseline, Week 24	

End point values	Placebo	BIIB033		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	35	33		
Units: percentage change				
arithmetic mean (standard error)	-12.22 (± 2.26)	-16.98 (± 2.33)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BIIB033
Number of subjects included in analysis	68
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1488
Method	ANCOVA
Parameter estimate	Difference
Point estimate	-4.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-11.26
upper limit	1.74

Secondary: Change in SD-OCT Average Retinal Ganglion Cell Layer/Inner Plexiform Retinal Layer (RGCL/IPL) at Week 24: ITT Population

End point title	Change in SD-OCT Average Retinal Ganglion Cell Layer/Inner Plexiform Retinal Layer (RGCL/IPL) at Week 24: ITT Population

End point description:

Adjusted mean change in thicknesses of the RGCL/IPL at Week 24 for the affected eye from the baseline of unaffected fellow eye as determined by segmentation of SD-OCT. Adjusted for the baseline RGCL/IPL thickness.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	BIIB033		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	41		
Units: µm				
arithmetic mean (standard deviation)	-9.9 (± 1.2)	-11.05 (± 1.18)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BIIB033
Number of subjects included in analysis	81
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4975
Method	ANCOVA
Parameter estimate	Difference
Point estimate	-1.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.51
upper limit	2.21

Secondary: Change in SD-OCT Average RGCL/IPL at Week 24: Per-protocol Population

End point title	Change in SD-OCT Average RGCL/IPL at Week 24: Per-protocol Population

End point description:

Adjusted mean change in thicknesses of the RGCL/IPL at Week 24 for the affected eye from the baseline of unaffected fellow eye as determined by segmentation of SD-OCT. Adjusted for the baseline RGCL/IPL thickness.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	BIIB033		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	33		
Units: µm				
arithmetic mean (standard deviation)	-10.17 (± 1.29)	-11.93 (± 1.35)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v BIIB033
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3505
Method	ANCOVA
Parameter estimate	Difference
Point estimate	-1.76
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.5
upper limit	1.98

Secondary: Change in Low-contrast Letter Acuity (LCLA) at Week 24: ITT Population

End point title	Change in Low-contrast Letter Acuity (LCLA) at Week 24: ITT Population

End point description:

Adjusted mean change in LCLA at Week 24 from baseline as determined by 1.25% and 2.5% low contrast Sloan letter charts, adjusted for the baseline LCLA value. The fellow eye is the reference eye for the inter-eye asymmetry. The range for LCLA assessment is 0-60.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	BIIB033		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	39		
Units: letters on a chart				
arithmetic mean (standard deviation)				
LCLA 1.25% chart	8.1 (± 1.8)	6.5 (± 1.9)		
LCLA 2.5% chart	11.9 (± 2)	11 (± 2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

LCLA 1.25% chart

Comparison groups	Placebo v BIIB033

Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5371
Method	ANCOVA
Parameter estimate	Difference
Point estimate	-1.6
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.9
upper limit	3.6

Statistical analysis title	Statistical Analysis 2
Statistical analysis description:	
LCLA 2.5% chart	
Comparison groups	Placebo v BIIB033
Number of subjects included in analysis	80
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7741
Method	ANCOVA
Parameter estimate	Difference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.5
upper limit	4.9

Secondary: Change in LCLA at Week 24: Per-protocol Population

End point title	Change in LCLA at Week 24: Per-protocol Population

End point description:

Adjusted mean change in LCLA at Week 24 from baseline as determined by 1.25% and 2.5% low contrast Sloan letter charts, adjusted for the baseline LCLA value. The fellow eye is the reference eye for the inter-eye asymmetry. The range for LCLA assessment is 0-60.

End point type	Secondary

End point timeframe:

Baseline, Week 24

End point values	Placebo	BIIB033		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	33		
Units: letters on a chart				
arithmetic mean (standard error)				
LCLA 1.25% chart	7.2 (± 1.8)	6 (± 2)		
LCLA 2.5% chart	11.6 (± 2)	10.8 (± 2.2)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: LCLA 1.25% chart	
Comparison groups	Placebo v BIIB033
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6645
Method	ANCOVA
Parameter estimate	Difference
Point estimate	-1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.6
upper limit	4.3

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: LCLA 2.5%	
Comparison groups	Placebo v BIIB033
Number of subjects included in analysis	69
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8015
Method	ANCOVA
Parameter estimate	DIfference
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-6.7
upper limit	5.2

Secondary: Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Number of Participants With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

An AE was any untoward medical occurrence that did not necessarily have a causal relationship with this treatment. An SAE was any untoward medical occurrence that at any dose: resulted in death; in the view of the Investigators, placed the subject at immediate risk of death (a life-threatening event); however, this did not include an event that, had it occurred in a more severe form, might have caused death; required inpatient hospitalization or prolongation of existing hospitalization; resulted in persistent or significant disability/incapacity; resulted in a congenital anomaly/birth defect; any other medically important event that, in the opinion of the Investigators, could have jeopardized the subject or may have required intervention to prevent one of the other outcomes listed in the definition above.

End point type	Secondary

End point timeframe:

32 weeks

End point values	Placebo	BIIB033		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	41	41		
Units: participants				
Participants with an event	34	34		
Participants with a moderate or severe event	22	21		
Participants with a severe event	2	3		
Participants with a related event	8	14		
Participants with a serious event	2	5		
Participants with a related serious event	0	3		
Participants discontinuing treatment due to event	1	3		
Participants withdrawing from study due to event	2	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of BIIB033 Concentration

End point title	Summary of BIIB033 Concentration[1]

End point description:

One pre-dose pharmacokinetic (PK) sample and 1 post-dose PK sample (approximately between 1 and 3 hours after the end of IV infusion) were collected for all participants on Day 1 and at Weeks 4 through 20 (every 4 weeks). Additionally, only 1 PK sample was collected at Week 24 and Week 32. (There was no dosing on Week 24 and Week 32, so only one blood sample for BIIB033 concentration was taken.) Samples collected at early termination visits were treated as predose samples for the next scheduled visit.

End point type	Secondary

End point timeframe:

Up to 32 weeks

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: PK values are not reported for the placebo group as no study drug was taken.

End point values	BIIB033			
Subject group type	Reporting group			
Number of subjects analysed	41			
Units: µg/mL				
median (full range (min-max))				
Baseline predose; n=41	0 (0 to 3.22)			
Baseline postdose; n=40	2030 (1370 to 3200)			
Week 4 predose; n=41	375 (14.6 to 2960)			
Week 4 postdose; n=37	2350 (368 to 3590)			
Week 8 predose; n=38	537 (32.7 to 1130)			
Week 8 postdose; n=36	2585 (550 to 4220)			
Week 12 predose; n=36	622 (39.9 to 3230)			
Week 12 postdose; n=34	2695 (542 to 4240)			
Week 16 predose; n=35	593 (173 to 1320)			
Week 16 postdose; n=34	2500 (1560 to 4590)			
Week 20 predose; n=37	673 (107 to 4760)			
Week 20 postdose; n=35	2530 (366 to 3990)			
Week 24; n=37	624 (4.3 to 1060)			
Week 32; n=33	82.7 (2.56 to 339)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs were monitored from administration of first dose of study treatment through to Week 32 visit. SAEs were monitored from signing of the Informed Consent Form (ICF) through to Week 32 visit.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	BIIB033 100 mg/kg

Reporting group description:

BIIB033 100 mg/kg via IV infusion once every 4 weeks for 20 weeks (a total of 6 doses)

Reporting group title	Placebo

Reporting group description:

Placebo via IV infusion once every 4 weeks for 20 weeks (a total of 6 doses)

Serious adverse events	BIIB033 100 mg/kg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 41 (12.20%)	2 / 41 (4.88%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events			
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 41 (2.44%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cytomegalovirus test positive			
subjects affected / exposed	0 / 41 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Multiple sclerosis			

subjects affected / exposed	0 / 41 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis relapse			
subjects affected / exposed	1 / 41 (2.44%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic neuritis			
subjects affected / exposed	1 / 41 (2.44%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	2 / 41 (4.88%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Liver disorder			
subjects affected / exposed	1 / 41 (2.44%)	0 / 41 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Viral pericarditis			
subjects affected / exposed	0 / 41 (0.00%)	1 / 41 (2.44%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	BIIB033 100 mg/kg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 41 (65.85%)	25 / 41 (60.98%)	
Nervous system disorders			
Dysaesthesia			

subjects affected / exposed	3 / 41 (7.32%)	2 / 41 (4.88%)	
occurrences (all)	3	3	
Headache			
subjects affected / exposed	11 / 41 (26.83%)	11 / 41 (26.83%)	
occurrences (all)	25	18	
Multiple sclerosis			
subjects affected / exposed	1 / 41 (2.44%)	3 / 41 (7.32%)	
occurrences (all)	1	3	
Paraesthesia			
subjects affected / exposed	4 / 41 (9.76%)	0 / 41 (0.00%)	
occurrences (all)	5	0	
Uhthoff's phenomenon			
subjects affected / exposed	3 / 41 (7.32%)	6 / 41 (14.63%)	
occurrences (all)	3	6	
Visual field defect			
subjects affected / exposed	3 / 41 (7.32%)	0 / 41 (0.00%)	
occurrences (all)	3	0	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	6 / 41 (14.63%)	5 / 41 (12.20%)	
occurrences (all)	7	5	
Eye disorders			
Colour blindness acquired			
subjects affected / exposed	3 / 41 (7.32%)	2 / 41 (4.88%)	
occurrences (all)	3	2	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 41 (12.20%)	3 / 41 (7.32%)	
occurrences (all)	7	3	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 41 (7.32%)	1 / 41 (2.44%)	
occurrences (all)	6	1	
Infections and infestations			
Influenza			

subjects affected / exposed	2 / 41 (4.88%)	3 / 41 (7.32%)	
occurrences (all)	2	3	
Nasopharyngitis			
subjects affected / exposed	12 / 41 (29.27%)	13 / 41 (31.71%)	
occurrences (all)	15	20	
Upper respiratory tract infection			
subjects affected / exposed	3 / 41 (7.32%)	2 / 41 (4.88%)	
occurrences (all)	5	3	

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