Clinical trial results:
A Dose-Frequency Blinded, Multicenter, Extension Study to Determine the Long Term Safety and Efficacy of PEGylated Interferon Beta-1a (BIIB017) in Subjects with Relapsing Multiple Sclerosis

Summary

EudraCT number	2010-024477-39
Trial protocol	LV BE DE ES BG EE GB GR CZ
Global end of trial date	02 October 2015

Results information

Result version number	v2 (current)
This version publication date	29 January 2017
First version publication date	14 October 2016
Version creation reason	• Correction of full data set Added minor description clarifications

Trial information

Trial identification

Sponsor protocol code	105MS302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01332019
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	225 Binney Street, Cambridge, Massachusetts, 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	02 October 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	02 October 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to evaluate the long-term safety and tolerability of BIIB017 in subjects originally treated in Study 105MS301 who continued BIIB017 treatment. The secondary objective of this study was to describe the long-term MS outcomes in subjects originally treated in Study 105MS301 who continued BIIB017 treatment.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 April 2011
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	Czech Republic: 24
Country: Number of subjects enrolled	United States: 22
Country: Number of subjects enrolled	Peru: 20
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	Mexico: 17
Country: Number of subjects enrolled	Georgia: 16
Country: Number of subjects enrolled	Colombia: 13
Country: Number of subjects enrolled	Estonia: 13
Country: Number of subjects enrolled	New Zealand: 12
Country: Number of subjects enrolled	Canada: 9
Country: Number of subjects enrolled	France: 9
Country: Number of subjects enrolled	Netherlands: 9
Country: Number of subjects enrolled	United Kingdom: 8
Country: Number of subjects enrolled	Greece: 7
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Latvia: 6

Country: Number of subjects enrolled	Croatia: 4
Country: Number of subjects enrolled	Chile: 1
Country: Number of subjects enrolled	Poland: 312
Country: Number of subjects enrolled	Ukraine: 134
Country: Number of subjects enrolled	India: 108
Country: Number of subjects enrolled	Serbia: 104
Country: Number of subjects enrolled	Russian Federation: 89
Country: Number of subjects enrolled	Bulgaria: 50
Country: Number of subjects enrolled	Romania: 39
Country: Number of subjects enrolled	Germany: 27
Worldwide total number of subjects	1077
EEA total number of subjects	532

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)	1077
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Study 105MS302 (NCT01332019) is an extension study and includes participants previously randomized to Study 105MS301 (NCT00906399). Only participants in Study 105MS301 who completed the study treatment and visit schedule through Week 96 were eligible for entry into this study.

Pre-assignment

Screening details:

Participants continued BIIB017 at the same dosage regimen they were following during treatment year 2 of Study 105MS301: BIIB017 125 µg subcutaneously (SC) every 2 weeks (Q2W) or every 4 weeks (Q4W). A major change in study design was introduced in Amendment 3 of the protocol, which switched all ongoing subjects dosing Q4W to dosing Q2W.

Pre-assignment period milestones

Number of subjects started	1077
Number of subjects completed	1076

Pre-assignment subject non-completion reasons

Reason: Number of subjects	Subject was not dosed: 1

Period 1

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

Blinding implementation details:

Dose frequency (Q2W or Q4W) was blinded in this study, and the study was also rater-blinded (separate study personnel were assigned to conduct efficacy assessments and treat subjects) to protect against perceived dose-frequency unblinding of subjects' treatment assignments. When Amendment 3 took effect, the study became open-label although the dose frequency was not unblinded.

Arms

Are arms mutually exclusive?	Yes
Arm title	BIIB017 Q4W

Arm description:

125 µg BIIB017 administered by SC injection Q4W for at least 2 years and up to 4 years.

Arm type	Experimental
Investigational medicinal product name	PEGylated Interferon Beta-1a
Investigational medicinal product code	BIIB017
Other name	Plegridy, PEG IFN β-1a
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Study treatment was administered by SC self-injection into the skin. Subjects could inject study treatment into the thigh, abdomen, or arms.

Arm title	BIIB017 Q2W

Arm description:

125 µg BIIB017 administered by SC injection Q2W for at least 2 years and up to 4 years.

Arm type	Experimental

Investigational medicinal product name	PEGylated Interferon Beta-1a
Investigational medicinal product code	BIIB017
Other name	Plegridy, PEG IFN β-1a
Pharmaceutical forms	Solution for injection
Routes of administration	Subcutaneous use

Dosage and administration details:

Study treatment was administered by SC self-injection into the skin. Subjects could inject study treatment into the thigh, abdomen, or arms.

Number of subjects in period 1[1]	BIIB017 Q4W	BIIB017 Q2W
Started	529	547
Completed	417	425
Not completed	112	122
Adverse event, serious fatal	2	1
Physician decision	4	3
Consent withdrawn by subject	73	71
Adverse event, non-fatal	13	22
NotSpecified	16	18
Lost to follow-up	4	7

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: As shown in the "pre-assignment period milestones," 1077 subjects started in this study and 1 subject was not dosed.

Baseline characteristics

Reporting groups	
Reporting group title	BIIB017 Q4W
Reporting group description:	
125 µg BIIB017 administered by SC injection Q4W for at least 2 years and up to 4 years.	
Reporting group title	BIIB017 Q2W
Reporting group description:	
125 µg BIIB017 administered by SC injection Q2W for at least 2 years and up to 4 years.	

Reporting group values	BIIB017 Q4W	BIIB017 Q2W	Total
Number of subjects	529	547	1076
Age Categorical Units: Subjects			
20-29 years	131	107	238
30-39 years	165	180	345
40-49 years	150	172	322
50-59 years	80	83	163
60-65 years	3	5	8
Age Continuous Units: years			
arithmetic mean	38.1	38.7	
standard deviation	± 9.95	± 9.59	-
Gender, Male/Female Units: Subjects			
Female	378	397	775
Male	151	150	301

End points

End points reporting groups

Reporting group title	BIIB017 Q4W
Reporting group description:	
125 µg BIIB017 administered by SC injection Q4W for at least 2 years and up to 4 years.	
Reporting group title	BIIB017 Q2W
Reporting group description:	
125 µg BIIB017 administered by SC injection Q2W for at least 2 years and up to 4 years.	

Primary: Number of Participants Experiencing Adverse Events (AEs) Serious AEs, and Discontinuations Due to AEs

End point title	Number of Participants Experiencing Adverse Events (AEs) Serious AEs, and Discontinuations Due to AEs[1]

End point description:

AE: any untoward medical occurrence that did not necessarily have a causal relationship with study treatment. SAE: any untoward medical occurrence that at any dose: resulted in death; in the view of the Investigator, placed the subject at immediate risk of 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 Investigator, could have jeopardized the subject or may have required intervention to prevent 1 of the other outcomes listed in the definition above. Data collected after Amendment 3 took effect were excluded for subjects enrolled into study 105MS302 on every 4 week dosing, but not excluded for subjects enrolled on every 2 week dosing. For subjects who switched to alternative MS medications, data after switch and 14 days after last dose of study treatment are excluded.

End point type	Primary

End point timeframe:

up to 4 years

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics are presented for this endpoint, per protocol.

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: participants				
Any event	471	478		
Moderate or severe event	343	348		
Severe event	74	73		
Event related to study treatment	400	399		
Serious event	113	90		
Discontinuing study treatment due to an event	18	26		
Withdrawing from study due to an event	14	23		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Potentially Clinically Significant Hematology Laboratory Abnormalities

End point title	Number of Participants With Potentially Clinically Significant Hematology Laboratory Abnormalities[2]

End point description:

Data collected after Amendment 3 took effect were excluded for subjects enrolled into study 105MS302 on every 4 week dosing,
but not excluded for subjects enrolled on every 2 week dosing.

End point type	Primary

End point timeframe:

up to 4 years

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics are presented for this endpoint, per protocol.

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	528	547		
Units: participants				
White blood cells < 3.0*10^9/L	28	86		
White blood cells ≥ 16.0*10^9/L	13	4		
Lymphocytes < 0.8*10^9/L	41	62		
Lymphocytes < 0.5*10^9/L	2	7		
Lymphocytes > 12*10^9/L	0	0		
Segmented neutrophils ≤ 1*10^9/L	8	16		
Segmented neutrophils < 1.5*10^9/L	31	84		
Segmented neutrophils ≥ 12*10^9/L	18	5		
Total absolute neutrophils ≤ 1*10^9/L	8	15		
Total absolute neutrophils < 1.5*10^9/L	31	83		
Total absolute neutrophils ≥ 12*10^9/L	18	5		
Red blood cells ≤ 3.3*10^12/L	1	7		
Red blood cells ≥ 6.8*10^12/L	0	0		
Hemoglobin ≤ 100 g/L	33	35		
Platelet count ≤ 100*10^9/L	3	11		
Platelet count ≥ 600*10^9/L	2	2		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Shifts From Baseline: Liver Function Laboratory Values

End point title	Number of Participants With Shifts From Baseline: Liver Function Laboratory Values[3]

End point description:

Shift to low includes normal to low, high to low, and unknown to low. Shift to high includes normal to high, low to high, and unknown to high. For participants who switched to alternative MS medications,

data after switch and 14 days after last dose of study treatment are excluded. Data collected after Amendment 3 took effect were excluded for subjects enrolled into study 105MS302 on every 4 week dosing, but not excluded for subjects enrolled on every 2 week dosing. ALT=alanine aminotranferase; AST=aspartate aminotransferase; GGT=gamma-glutamyl transferase.

End point type	Primary

End point timeframe:

Baseline (BIIB017 Treatment Baseline from Study 105MS301) up to 4 years

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics are presented for this endpoint, per protocol.

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: participants				
ALT: shift to low; n=528, 546	3	3		
ALT: shift to high; n=487, 497	119	153		
AST: shift to low; n=528, 546	10	8		
AST: shift to high; n=514, 530	75	110		
Total bilirubin: shift to low; n=512, 517	94	76		
Total bilirubin: shift to high; n=511, 535	22	16		
GGT: shift to low; n=529, 545	16	6		
GGT: shift to high; n=512, 528	73	97		
Alkaline phosphatase: shift to low; n=522, 543	4	5		
Alkaline phosphatase: shift to high; n=516, 536	28	26		
Lactate dehydrogenase: shift to low; n=529, 547	0	0		
Lactate dehydrogenase: shift to high; n=524, 541	18	30		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Shifts From Baseline: Kidney Function and Other Blood Chemistry

End point title	Number of Participants With Shifts From Baseline: Kidney Function and Other Blood Chemistry[4]

End point description:

Shift to low includes normal to low, high to low, and unknown to low. Shift to high includes normal to high, low to high, and unknown to high. For participants who switched to alternative MS medications, data after switch and 14 days after last dose of study treatment are excluded. Data collected after Amendment 3 took effect were excluded for subjects enrolled into Study 105MS302 on every 4 week dosing, but not excluded for subjects enrolled on every 2 week dosing. TSH=thyroid stimulating hormone.

End point type	Primary

End point timeframe:

Baseline (BIIB017 Treatment Baseline from Study 105MS301) up to 4 years

Notes:

[4] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics are presented for this endpoint, per protocol.

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: participants				
Blood urea nitrogen: shift to low; n=529, 546	0	1		
Blood urea nitrogen: shift to high; n=527, 543	16	20		
Creatinine: shift to low; n=529, 547	0	1		
Creatinine: shift to high; n=528, 545	15	8		
Bicarbonate: shift to low; n=523, 540	49	64		
Bicarbonate: shift to high; n=529, 544	0	0		
Sodium: shift to low; n=529, 546	0	3		
Sodium: shift to high; n=524, 544	39	46		
Potassium: shift to low; n=527, 544	13	21		
Potassium: shift to high; n=528, 546	17	20		
Chloride: shift to low; n=529, 546	1	2		
Chloride: shift to high; n=528, 547	0	3		
Glucose: shift to low; n=522, 539	54	51		
Glucose: shift to high; n=506, 513	304	311		
TSH: shift to low; n=515, 533	47	30		
TSH: shift to high; n=518, 539	37	55		

Statistical analyses

No statistical analyses for this end point

Primary: Number of Participants With Shifts From Baseline: Urinalysis

End point title	Number of Participants With Shifts From Baseline: Urinalysis[5]

End point description:

Shift to low includes normal to low, high to low, and unknown to low. Shift to high/positive includes normal to high/positive, low to high/positive, negative to high/positive, and unknown to high/positive. For participants who switched to alternative MS medications, data after switch and 14 days after last dose of study treatment are excluded. Data collected after Amendment 3 took effect were excluded for subjects enrolled into Study 105MS302 on every 4 week dosing, but not excluded for subjects enrolled on every 2 week dosing. Pos=positive; RBC=red blood cells; WBC=white blood cells.

End point type	Primary

End point timeframe:

Baseline (BIIB017 Treatment Baseline from Study 105MS301) up to 4 years

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive statistics are presented for this endpoint, per protocol.

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: participants				
Specific gravity: shift to low; n=525, 545	2	1		
Specific gravity: shift to high/pos; n=528,547	13	3		
pH: shift to low; n=529, 547	0	0		
pH: shift to high/pos; n=528, 547	6	4		
Color: shift to high/pos; n=516, 529	33	36		
Blood: shift to high/pos; n=469, 495	159	167		
Glucose: shift to high/pos; n=521, 542	28	25		
Ketones: shift to high/pos; n=510, 530	64	73		
Protein: shift to high/pos; n=380, 391	270	277		
RBC: shift to high/pos; n=419, 402	110	106		
WBC: shift to high/pos; n=472, 495	116	130		
Bilirubin: shift to high/pos; n=529, 547	0	1		
Nitrite: shift to high/pos; n=508, 519	84	94		
Urobilinogen: shift to high/pos; n=529, 546	7	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Annualized Relapse Rate (ARR)

End point title	Annualized Relapse Rate (ARR)

End point description:

Relapses are defined as new or recurrent neurologic symptoms not associated with fever or infection, lasting at least 24 hours, and accompanied by new objective neurological findings upon examination by the examining neurologist. The annualized relapse rate is calculated as the total number of relapses occurred during the period for all subjects, divided by the total number of subject-years followed in the period.

End point type	Secondary

End point timeframe:

up to 4 years

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: relapses per person-years				
number (confidence interval 95%)	0.189 (0.154 to 0.231)	0.142 (0.114 to 0.177)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Based on negative binomial regression for each treatment group, with adjustment for EDSS (<4 vs. >=4), relapse rate (based on 1 year before 105MS301 and 105MS301), and age (<40 vs. >=40) at 105MS302 baseline.

Comparison groups	BIIB017 Q4W v BIIB017 Q2W
Number of subjects included in analysis	1076
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0203 [6]
Method	negative binomial regression
Parameter estimate	rate ratio
Point estimate	0.755
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.595
upper limit	0.957

Notes:

[6] - q2w/q4w

Secondary: Percentage of Participants Who Relapsed

End point title	Percentage of Participants Who Relapsed

End point description:

Relapses are defined as new or recurrent neurologic symptoms not associated with fever or infection, lasting at least 24 hours, and accompanied by new objective neurological findings upon examination by the examining neurologist. New or recurrent neurologic symptoms that occur less than 30 days following the onset of a relapse were considered part of the same relapse. Participants who did not experience a relapse prior to switching to alternative MS medications, withdrew from study, or Amendment 3 (A3) took effect were censored at the time of switch/withdrawal/A3 effective date.

End point type	Secondary

End point timeframe:

Up to 4 years

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: percentage of participants				
Did not relapse	71	77		
Relapsed	29	23		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

q2w/q4w

Comparison groups	BIIB017 Q4W v BIIB017 Q2W
Number of subjects included in analysis	1076
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0201 [7]
Method	Cox proportion hazards model
Parameter estimate	Hazard ratio (HR)
Point estimate	0.75
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	0.96

Notes:

[7] - Based on Cox proportion hazards model, adjusted for EDSS (<4 vs >= 4), age (<40 vs >=40), relapse rate (based on 1 year before 105MS301 and 105MS301), and gadolinium (Gd) enhancing lesions (presence vs. absence) at 105MS302 baseline.

Secondary: Number of New or Newly Enlarging T2 Hyperintense Lesions

End point title	Number of New or Newly Enlarging T2 Hyperintense Lesions

End point description:

The total number of new or newly enlarging T2 hyperintense lesions (from Study 105MS302 Baseline) as assessed by magnetic resonance imaging (MRI). Observed data after participants switched to alternative MS medications or after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Week 48, Week 96

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	481	493		
Units: lesions				
arithmetic mean (standard deviation)				
Week 48; n=481, 493	4.4 (± 8.19)	1.9 (± 4.5)		
Week 96; n=411, 407	8.9 (± 16.64)	3.9 (± 9.37)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 48

Comparison groups	BIIB017 Q4W v BIIB017 Q2W

Number of subjects included in analysis	974
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [8]
Method	negative binomial regression
Parameter estimate	lesion mean ratio
Point estimate	0.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.41
upper limit	0.63

Notes:

[8] - Lesion mean ratio (95% CI) and p-value for comparison between the every 2 weeks group and the every 4 weeks group, based on negative binomial regression, adjusted for 105MS302 baseline number of T2 lesions.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Week 96

Comparison groups	BIIB017 Q4W v BIIB017 Q2W
Number of subjects included in analysis	974
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [9]
Method	negative binomial regression
Parameter estimate	lesion mean ratio
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	0.62

Notes:

[9] - Lesion mean ratio (95% CI) and p-value for comparison between the every 2 weeks group and the every 4 weeks group, based on negative binomial regression, adjusted for 302 baseline number of T2 lesions.

Secondary: Number of New Active Lesions

End point title	Number of New Active Lesions

End point description:

The number of new active lesions as assessed by MRI. Observed data after participants switched to alternative MS medications or after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Week 48, Week 96

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: lesions				
arithmetic mean (standard deviation)				
Week 48; n=481, 493	4.4 (± 8.25)	2 (± 4.62)		
Week 96; n=411, 406	9 (± 16.88)	3.9 (± 9.47)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description: Week 48	
Comparison groups	BIIB017 Q4W v BIIB017 Q2W
Number of subjects included in analysis	1076
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [10]
Method	negative binomial regression
Parameter estimate	lesion mean ratio
Point estimate	0.54
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	0.68

Notes:

[10] - Lesion mean ratio (95% CI) and p-value for comparison between the every 2 weeks group and the every 4 weeks group, based on negative binomial regression, adjusted for 105MS302 baseline number of Gd lesions.

Statistical analysis title	Statistical Analysis 2
Statistical analysis description: Week 96	
Comparison groups	BIIB017 Q4W v BIIB017 Q2W
Number of subjects included in analysis	1076
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [11]
Method	negative binomial regression
Parameter estimate	lesion mean ratio
Point estimate	0.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	0.71

Notes:

[11] - Lesion mean ratio (95% CI) and p-value for comparison between the every 2 weeks group and the every 4 weeks group, based on negative binomial regression, adjusted for 105MS302 baseline number of Gd lesions.

Secondary: Number of New T1 Hypointense Lesions

End point title	Number of New T1 Hypointense Lesions

End point description:

The total number of new T1 hypointense lesions as assessed by MRI.

End point type	Secondary

End point timeframe:

Week 48, Week 96

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: lesions				
arithmetic mean (standard deviation)				
Week 48; n=481, 493	1.4 (± 3.02)	0.8 (± 2.18)		
Week 96; n=411, 406	2.8 (± 5.92)	1.5 (± 4.14)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 48

Comparison groups	BIIB017 Q4W v BIIB017 Q2W
Number of subjects included in analysis	1076
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [12]
Method	Regression, Logistic

Notes:

[12] - p-value for comparison between the every 2 weeks group and the every 4 weeks group, based on multiple logit regression, adjusted for 302 baseline number of T1 lesions.

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Week 96

Comparison groups	BIIB017 Q4W v BIIB017 Q2W
Number of subjects included in analysis	1076
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [13]
Method	Regression, Logistic

Notes:

[13] - p-value for comparison between the every 2 weeks group and the every 4 weeks group, based on multiple logit regression, adjusted for 302 baseline number of T1 lesions.

Secondary: Number of Gd-Enhancing Lesions

End point title	Number of Gd-Enhancing Lesions

End point description:

The number of Gd-enhancing lesions as assessed by MRI. Observed data after participants switched to alternative MS medications or after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Baseline (start of 105MS302), Week 48, Week 96

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: lesions				
arithmetic mean (standard deviation)				
Baseline; n=528, 543	0.6 (± 1.85)	0.2 (± 1.07)		
Week 48; n=481, 493	0.7 (± 2.07)	0.2 (± 1.42)		
Week 96; n=411, 407	0.8 (± 2.59)	0.2 (± 0.89)		

Statistical analyses

Statistical analysis title	Statistical Analysis 2

Statistical analysis description:

Week 96

Comparison groups	BIIB017 Q4W v BIIB017 Q2W
Number of subjects included in analysis	1076
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0026 [14]
Method	Regression, Logistic

Notes:

[14] - p-value for comparison between the every 2 weeks group and the every 4 weeks group, based on multiple logit regression, adjusted for 302 baseline number of Gd-enhancing lesion.

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Week 48

Comparison groups	BIIB017 Q4W v BIIB017 Q2W

Number of subjects included in analysis	1076
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0012 [15]
Method	Regression, Logistic

Notes:

[15] - p-value for comparison between the every 2 weeks group and the every 4 weeks group, based on multiple logit regression, adjusted for 302 baseline number of Gd-enhancing lesion.

Secondary: Volume of T2 Hyperintense Lesions

End point title	Volume of T2 Hyperintense Lesions

End point description:

The volume of T2 hyperintense lesions as assessed by MRI. Observed data after participants switched to alternative MS medications or after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Baseline (start of 105MS302), Week 48, Week 96

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: cm^3				
arithmetic mean (standard deviation)				
Baseline; n=528, 543	11.4742 (± 13.55811)	9.9678 (± 11.41807)		
Week 48; n=481, 493	11.7421 (± 13.91774)	9.8335 (± 11.05029)		
Week 96; n=411, 407	12.0257 (± 13.91056)	9.9487 (± 10.97208)		

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of T1 Hypointense Lesions

End point title	Volume of T1 Hypointense Lesions

End point description:

The volume of T1 hypointense lesions as assessed by MRI. Observed data after participants switched to alternative MS medications or after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Baseline (start of 105MS302), Week 48, Week 96

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: cm^3				
arithmetic mean (standard deviation)				
Baseline; n=528, 543	3.9869 (± 6.29557)	3.632 (± 5.47465)		
Week 48; n=481, 493	4.3062 (± 6.92839)	3.6529 (± 5.19027)		
Week 96; n=411, 407	4.3171 (± 6.70107)	3.7494 (± 5.21314)		

Statistical analyses

No statistical analyses for this end point

Secondary: Volume of Gd-Enhancing Lesions

End point title	Volume of Gd-Enhancing Lesions

End point description:

The volume of Gd-enhancing lesions as assessed by MRI. Observed data after participants switched to alternative MS medications or after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Baseline (start of 105MS302), Week 48, Week 96

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: cm^3				
arithmetic mean (standard deviation)				
Baseline; n=528, 543	0.0911 (± 0.30013)	0.0348 (± 0.17344)		
Week 48; n=481, 493	0.1172 (± 0.42762)	0.0477 (± 0.31479)		
Week 96; n=411, 407	0.1346 (± 0.5058)	0.0357 (± 0.14976)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change of Whole Brain Volume

End point title	Percentage Change of Whole Brain Volume

End point description:

Percentage change of whole brain volume as assessed by MRI. Observed data after participants switched to alternative MS medications or after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Baseline (start of 105MS302), Week 48, Week 96

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: percentage change				
arithmetic mean (standard deviation)				
Change at Week 48; n=402, 418	-0.522 (± 0.6205)	-0.453 (± 0.8127)		
Change at Week 96; n=365, 358	-0.835 (± 1.0785)	-0.788 (± 1.1912)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Expanded Disability Status Scale (EDSS)

End point title	Change from Baseline in Expanded Disability Status Scale (EDSS)

End point description:

Change from Baseline in disability as measured by the Expanded Disability Status Scale (EDSS). The EDSS measures
the disability status of people with multiple sclerosis on a scale that ranges from 0 to 10. The range of main categories
include (0) = normal neurologic exam; to (5) = ambulatory without aid or rest for 200 meters; disability severe enough to
impair full daily activities; to (10) = death due to MS. Data after participants switched to alternative MS medications or
after Amendment 3 took effect are excluded

End point type	Secondary

End point timeframe:

Baseline (start of 105MS302), Weeks 12, 24, 48, 72, 96, 120, 144, 168

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline; n=516, 535	2.43 (± 1.346)	2.35 (± 1.299)		
Change at Week 12; n=503, 524	0.02 (± 0.388)	0 (± 0.45)		
Change at Week 24; n=500, 519	0.02 (± 0.449)	0 (± 0.486)		
Change at Week 48; n=488, 497	0.08 (± 0.564)	0.03 (± 0.51)		
Change at Week 72; n=468, 484	0.13 (± 0.629)	0.06 (± 0.484)		
Change at Week 96; n=429, 446	0.15 (± 0.618)	0.09 (± 0.563)		

Change at Week 120; n=187, 205	0.19 (± 0.7)	0.1 (± 0.538)		
Change at Week 144; n=90, 98	0.23 (± 0.72)	0.1 (± 0.587)		
Change at Week 168; n=21, 25	0.24 (± 0.889)	0.18 (± 0.454)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Sustained Disability Progression

End point title	Time to Sustained Disability Progression

End point description:

Estimated proportion of participants with progression and time to progression based on the Kaplan-Meier product limit method. Sustained disability progression is defined as: at least a 1.0 point increase on the EDSS from baseline EDSS ≥ 1.0 that is sustained for 24 weeks, or at least a 1.5 point increase on the EDSS from baseline EDSS = 0 that is sustained for 24 weeks. The EDSS measures the disability status of people with multiple sclerosis on a scale that ranges from 0 to 10. The range of main categories include (0) = normal neurologic exam; to (5) = ambulatory without aid or rest for 200 meters; disability severe enough to impair full daily activities; to (10) = death due to MS. Participants were censored at the time of withdrawal/switch/A3 effective date if they withdrew from study, switched to alternative MS medication, or Amendment 3 took effect without a progression.

End point type	Secondary

End point timeframe:

Weeks 12, 24, 28, 72, 96, 120, 144, 168

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	63[16]	38[17]		
Units: proportion of participants				
number (not applicable)				
Progressed at 12 weeks	0.023	0.007		
Progressed at 24 weeks	0.046	0.023		
Progressed at 48 weeks	0.079	0.045		
Progressed at 72 weeks	0.103	0.057		
Progressed at 96 weeks	0.115	0.069		
Progressed at 120 weeks	0.147	0.085		
Progressed at 144 weeks	0.161	0.096		
Progressed at 168 weeks	99999	99999		

Notes:

[16] - Subjects who experienced disability progression. 99999=was not calculated (under 30 subjects).

[17] - Subjects who experienced disability progression. 99999=was not calculated (under 30 subjects).

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	BIIB017 Q4W v BIIB017 Q2W

Number of subjects included in analysis	101
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006 [18]
Method	Cox Proportional Hazards model
Parameter estimate	Cox proportional hazard
Point estimate	0.57
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.38
upper limit	0.85

Notes:

[18] - Based on Cox Proportional Hazards model, adjusted for 105MS302 baseline EDSS and age (<40 vs >=40).

Secondary: Change From Baseline in Symbol Digit Modalities Test (SDMT)

End point title	Change From Baseline in Symbol Digit Modalities Test (SDMT)

End point description:

SDMT is a screening test for cognitive impairment. Participants are given 90 seconds in which to pair specific numbers
with given geometric figures using a key. Scores range from 0 (worst) to 110 (best).

End point type	Secondary

End point timeframe:

Baseline (start of 105MS302), Weeks 24, 48, 72, 96, 120, 144, 168

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline; n=523, 543	52.134 (± 17.7653)	52.744 (± 17.6994)		
Change at Week 24; n=508, 530	-0.313 (± 8.5862)	-1.106 (± 8.1292)		
Change at Week 48; n=493, 509	-0.365 (± 9.3557)	-0.864 (± 8.6059)		
Change at Week 72; n=472, 489	-0.625 (± 8.8037)	-1.012 (± 8.5038)		
Change at Week 96; n=435, 450	-0.34 (± 8.7817)	-0.231 (± 9.3148)		
Change at Week 120; n=190, 203	-1.305 (± 8.9248)	-1.099 (± 9.5425)		
Change at Week 144; n=88, 96	-1.727 (± 7.79)	-0.906 (± 10.8367)		
Change at Week 168; n=21, 25	-4 (± 10.4403)	-3.84 (± 13.4712)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Multiple Sclerosis Impact Scale (MSIS)-29 Physical Score

End point title	Change from Baseline in Multiple Sclerosis Impact Scale (MSIS)-29 Physical Score

End point description:

The 29-item MSIS-29 is a disease-specific participant-reported outcome measure that has been developed and validated to examine the physical and psychological impact of MS from a patient's perspective; it measures 20 physical items and 9 psychological items. Responses use a 5-point Likert scale range from 1 to 5. All questions are to be answered. The physical well being assessment portion of the MSIS-29 consists of 20 questions in which subjects rate the impact of MS on their day-to-day life during the past two weeks from 1=no impact to 5=extreme impact for a total score of 20-100. A lower total score indicates less physically-related impact while a higher total score indicates greater physically-related impact on a participant's functioning. Observed data after subjects switched to alternative MS medications or after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Baseline (start of 105MS302), Weeks 24, 48, 72, 96, 120, 144, 168

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline; n=527, 544	20.494 (± 19.829)	20.218 (± 19.0264)		
Change at Week 24; n=513, 534	-0.152 (± 9.3332)	0.552 (± 10.0147)		
Change at Week 48; n=498, 510	0.462 (± 10.7054)	0.545 (± 10.6342)		
Change at Week 72; n=474, 491	0.937 (± 11.5682)	0.684 (± 12.469)		
Change at Week 96; n=437, 452	1.471 (± 10.8997)	1.19 (± 11.4005)		
Change at Week 120; n=193, 205	2.654 (± 14.2983)	0.116 (± 10.4382)		
Change at Week 144; n=88, 98	0.327 (± 10.5888)	0.051 (± 12.1417)		
Change at Week 168; n=20, 26	2.25 (± 7.3292)	-0.288 (± 13.5615)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in 12-Item Short Form Health Survey (SF-12) Mental Component Scale (MCS)

End point title	Change from Baseline in 12-Item Short Form Health Survey (SF-12) Mental Component Scale (MCS)

End point description:

The SF-12 is a multipurpose short form survey with 12 questions, all selected from the SF-36 Health Survey. The
questions were combined, scored, and weighted to create two scales that provide glimpses into mental and physical
functioning and overall health-related-quality of life. MCS computed using the scores of 12 questions and range from 0
to 100, where a 0 score indicates the lowest level of health and 100 indicates the highest level of health. Observed data
after participants switched to alternative MS medications or after Amendment 3 took effect are exclu

End point type	Secondary

End point timeframe:

Baseline (start of 105MS302), Weeks 24, 48, 72, 96, 120, 144, 168

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline; n=527, 544	47.803 (± 10.2111)	48.591 (± 10.3624)		
Change at Week 24; n=514, 535	0.396 (± 7.5967)	-0.734 (± 8.3567)		
Change at Week 48; n=498, 510	0.409 (± 8.4442)	-0.69 (± 8.3903)		
Change at Week 72; n=474, 491	0.242 (± 9.3223)	-0.162 (± 9.0676)		
Change at Week 96; n=437, 452	-0.141 (± 9.4833)	0.014 (± 8.8856)		
Change at Week 120; n=193, 205	-1.223 (± 10.4664)	0.616 (± 7.5313)		
Change at Week 144; n=88, 98	0.346 (± 8.6814)	0.11 (± 8.0301)		
Change at Week 168; n=20, 26	-0.451 (± 8.8575)	0.294 (± 9.7505)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in SF-12 Physical Component Score (PCS)

End point title	Change from Baseline in SF-12 Physical Component Score (PCS)

End point description:

The SF-12 is a multipurpose short form survey with 12 questions, all selected from the SF-36 Health Survey. The questions were combined, scored, and weighted to create two scales that provide glimpses into mental and physical functioning and overall health-related-quality of life. PCS was computed using the scores of 12 questions and range from 0 to 100, where a 0 score indicates the lowest level of health and 100 indicates the highest level of health. Observed data after participants switched to alternative MS medications or after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Baseline (start of 105MS302), Weeks 24, 48, 72, 96, 120, 144, 168

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: units on a scale				
arithmetic mean (standard deviation)				
105MS302 Baseline; n=527, 544	45.154 (± 9.4474)	44.902 (± 9.9312)		
Change at Week 24; n=514, 535	0.138 (± 6.0841)	0.337 (± 5.7878)		
Change at Week 48; n=498, 510	-0.351 (± 6.1785)	0.214 (± 5.8377)		
Change at Week 72; n=474, 491	-0.27 (± 6.6319)	-0.169 (± 6.3824)		
Change at Week 96; n=437, 452	-0.15 (± 6.6971)	-0.138 (± 6.4453)		
Change at Week 120; n=193, 205	-0.118 (± 7.8826)	0.021 (± 6.1354)		
Change at Week 144; n=88, 98	-0.256 (± 5.7252)	0.118 (± 6.783)		
Change at Week 168; n=20, 26	-1.558 (± 7.6525)	0.152 (± 7.5206)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change form Baseline in Euro Quality of Life (EQ-5D) Index Score

End point title	Change form Baseline in Euro Quality of Life (EQ-5D) Index Score

End point description:

The EQ-5D is a participant-answered questionnaire scoring 5 dimensions: mobility, self-care, usual activities, pain/discomfort and anxiety/depression. Scores of 1, 2, or 3 are possible responses for each of 5 questions (1=no problems, 2=some problems, 3=severe problems). A scoring formula developed by the EuroQol Group is then used to assign utility values for each participant's Health State Profile. A summary index score (EQ-5D index score) is derived from the 5 questions by conversion with this scoring formula and a table of scores. EQ-5D Summary Index values ranged from -0.6 (worst health state) to 1.00 (perfect health state). Observed data after participants switched to alternative MS medications or after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Baseline (start of 105MS302), Weeks 24, 48, 72, 96, 120, 144, 168

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline; n=527, 544	0.76 (± 0.23)	0.76 (± 0.23)		
Change at Week 24; n=514, 534	0 (± 0.159)	0 (± 0.171)		
Change at Week 48; n=498, 510	-0.01 (± 0.159)	0 (± 0.171)		
Change at Week 72; n=472, 491	-0.01 (± 0.158)	0 (± 0.179)		
Change at Week 96; n=436, 452	-0.01 (± 0.156)	-0.01 (± 0.195)		
Change at Week 120; n=193, 205	-0.02 (± 0.19)	0 (± 0.165)		
Change at Week 144; n=88, 98	0 (± 0.169)	0.01 (± 0.166)		
Change at Week 168; n=21, 26	0 (± 0.08)	0.02 (± 0.137)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change Form Baseline in EQ-5D Visual Analogue Scale (VAS)

End point title	Change Form Baseline in EQ-5D Visual Analogue Scale (VAS)

End point description:

The EQ-5D VAS records the participant's self-rated health on a scale from 0-100 where 100 is the 'best imaginable
health state' and 0 is the 'worst imaginable health state.' The scale was normalized to a scale of 0 to 1, with higher
values indicating a better health state. Observed data after participants switched to alternative MS medications or after
Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Baseline (start of 105MS302), Weeks 24, 48, 72, 96, 120, 144, 168

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: units on a scale				
arithmetic mean (standard deviation)				
Baseline; n=527, 542	77.07 (± 17.623)	77.33 (± 18.348)		
Change at Week 24; n=511, 532	-0.22 (± 11.411)	-0.98 (± 12.064)		
Change at Week 48; n=498, 508	-0.81 (± 12.828)	-0.93 (± 12.719)		
Change at Week 72; n=472, 490	-0.59 (± 12.735)	-1.89 (± 15.27)		
Change at Week 96; n=436, 450	-1.1 (± 14.266)	-2.2 (± 14.095)		

Change at Week 120; n=193, 204	-0.47 (± 12.714)	-0.88 (± 12.793)		
Change at Week 144; n=88, 97	-0.31 (± 14.247)	-0.87 (± 14.865)		
Change at Week 168; n=21, 26	1.38 (± 14.925)	0.46 (± 12.602)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of Relapses Requiring Intravenous (IV) Steroid Use

End point title	Number of Relapses Requiring Intravenous (IV) Steroid Use

End point description:

Observed data after participants switched to alternative MS medications or after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

up to 4 years

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: relapses	217	181		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of MS-Related Hospitalizations

End point title	Number of MS-Related Hospitalizations

End point description:

Observed data after participants switched to alternative MS medications or after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

up to 4 years

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529	547		
Units: hospitalizations	113	81		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subject-Reported Treatment Satisfaction: How Tolerable or Intolerable Do You Find the Medication?

End point title	Summary of Subject-Reported Treatment Satisfaction: How Tolerable or Intolerable Do You Find the Medication?

End point description:

Subjects completed a Treatment Satisfaction Questionnaire composed of a range of 14 questions regarding the subject's perception of treatment satisfaction at the end of each year of treatment. For the question "How tolerable or intolerable do you find the medication?" answers were numerically rated from 1 (extremely intolerable) to 10 (extremely tolerable). Data after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Year 1, Year 2, Year 3

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529[19]	547[20]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Year 1; n=482, 496	6.8 (± 2.36)	7 (± 2.21)		
Year 2; n=425, 430	7.2 (± 2.28)	7.1 (± 2.27)		
Year 3; n=82, 88	7.5 (± 2.46)	7.3 (± 2.17)		

Notes:

[19] - n=subjects with an assessment at given timepoint.

[20] - n=subjects with an assessment at given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subject-Reported Treatment Satisfaction: How Convenient or Inconvenient Is It to Take Your Medication as Instructed?

End point title	Summary of Subject-Reported Treatment Satisfaction: How Convenient or Inconvenient Is It to Take Your Medication as Instructed?

End point description:

Subjects completed a Treatment Satisfaction Questionnaire composed of a range of 14 questions regarding the subject's perception of treatment satisfaction at the end of each year of treatment. For the question "How convenient or inconvenient is it to take your medication as instructed?" answers were numerically rated from 1 (extremely inconvenient) to 10 (extremely convenient). Data after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Year 1, Year 2, Year 3

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529[21]	547[22]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Year 1; n=482, 496	8.2 (± 2.09)	8 (± 2.12)		
Year 2; n=426, 430	8.3 (± 1.98)	8.2 (± 2.05)		
Year 3; n=82, 88	8.3 (± 2.05)	8 (± 2.08)		

Notes:

[21] - n=subjects with an assessment at given timepoint.

[22] - n=subjects with an assessment at given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subject-Reported Treatment Satisfaction: How Convenient or Inconvenient Is It to Take Your Medication Every 2 Weeks?

End point title	Summary of Subject-Reported Treatment Satisfaction: How Convenient or Inconvenient Is It to Take Your Medication Every 2 Weeks?

End point description:

Subjects completed a Treatment Satisfaction Questionnaire composed of a range of 14 questions regarding the subject’s perception of treatment satisfaction at the end of each year of treatment. For the question "How convenient or inconvenient is it to take your medication every 2 weeks?" answers were numerically rated from 1 (extremely inconvenient) to 10 (extremely convenient). Data after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Year 1, Year 2, Year 3

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529[23]	547[24]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Year 1; n=482, 496	8.4 (± 2.02)	8.4 (± 1.99)		
Year 2; n=426, 430	8.6 (± 1.93)	8.4 (± 2.06)		
Year 3; n=82, 88	8.6 (± 2)	8.5 (± 1.79)		

Notes:

[23] - n=subjects with an assessment at given timepoint.

[24] - n=subjects with an assessment at given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subject-Reported Treatment Satisfaction: Overall, How Satisfied or Dissatisfied Are You With This Medication?

End point title	Summary of Subject-Reported Treatment Satisfaction: Overall, How Satisfied or Dissatisfied Are You With This Medication?

End point description:

Subjects completed a Treatment Satisfaction Questionnaire composed of a range of 14 questions regarding the subject's perception of treatment satisfaction at the end of each year of treatment. For the question "Overall, how satisfied or dissatisfied are you with this medication?" answers were numerically rated from 1 (extremely dissatisfied) to 10 (extremely satisfied). Data after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Year 1, Year 2, Year 3

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529[25]	547[26]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Year 1; n=482, 496	7.9 (± 2.04)	8.1 (± 1.97)		
Year 2; n=426, 430	8.2 (± 2.04)	8.3 (± 2)		
Year 3; n=82, 88	8.2 (± 2)	8.6 (± 1.6)		

Notes:

[25] - n=subjects with an assessment at given timepoint.

[26] - n=subjects with an assessment at given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subject-Reported Treatment Satisfaction: How Satisfied or Dissatisfied Are You With the Injection Frequency (Every 2 Weeks)?

End point title	Summary of Subject-Reported Treatment Satisfaction: How Satisfied or Dissatisfied Are You With the Injection Frequency (Every 2 Weeks)?

End point description:

Subjects completed a Treatment Satisfaction Questionnaire composed of a range of 14 questions regarding the subject's perception of treatment satisfaction at the end of each year of treatment. For the question "How satisfied or dissatisfied are you with the injection frequency (every 2 weeks)?" answers were numerically rated from 1 (extremely dissatisfied) to 10 (extremely satisfied). Data after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Year 1, Year 2, Year 3

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529[27]	547[28]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Year 1; n=482, 496	8.4 (± 1.92)	8.3 (± 1.98)		
Year 2; n=426, 430	8.5 (± 1.89)	8.3 (± 2.07)		
Year 3; n=82, 88	8.7 (± 1.99)	8.6 (± 1.59)		

Notes:

[27] - n=subjects with an assessment at given timepoint.

[28] - n=subjects with an assessment at given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subject-Reported Treatment Satisfaction: How Likely Would You Be to Continue to Use This Medication?

End point title	Summary of Subject-Reported Treatment Satisfaction: How Likely Would You Be to Continue to Use This Medication?

End point description:

Subjects completed a Treatment Satisfaction Questionnaire composed of a range of 14 questions regarding the subject's perception of treatment satisfaction at the end of each year of treatment. For the question "How likely would you be to continue to use this medication?" answers were numerically rated from 1 (extremely unlikely) to 10
(extremely likely). Data after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Year 1, Year 2, Year 3

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529[29]	547[30]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Year 1; n=482, 496	8.5 (± 2.11)	8.6 (± 2)		
Year 2; n=426, 430	8.1 (± 2.67)	8.3 (± 2.58)		
Year 3; n=82, 88	8.5 (± 2.39)	8.8 (± 2)		

Notes:

[29] - n=subjects with an assessment at given timepoint.

[30] - n=subjects with an assessment at given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subject-Reported Treatment Satisfaction: This Medication Enables Me to Focus More on Myself and My Family Rather Than My MS.

End point title	Summary of Subject-Reported Treatment Satisfaction: This Medication Enables Me to Focus More on Myself and My Family Rather Than My MS.

End point description:

Subjects completed a Treatment Satisfaction Questionnaire composed of a range of 14 questions regarding the subject's perception of treatment satisfaction at the end of each year of treatment. For the statement "This Medication Enables Me to Focus More on Myself and My Family Rather Than My MS," answers were numerically rated from 1 (strongly disagree) to 10 (strongly agree). Data after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Year 1, Year 2, Year 3

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529[31]	547[32]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Year 1; n=482, 496	7.3 (± 2.52)	7.8 (± 2.21)		
Year 2; n=426, 430	7.8 (± 2.35)	7.8 (± 2.31)		
Year 3; n=82, 88	8 (± 2.44)	8.3 (± 2)		

Notes:

[31] - n=subjects with an assessment at given timepoint.

[32] - n=subjects with an assessment at given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subject-Reported Treatment Satisfaction: This Medication Makes It Easy For Me to Carry Out My Daily Responsibilities.

End point title	Summary of Subject-Reported Treatment Satisfaction: This Medication Makes It Easy For Me to Carry Out My Daily Responsibilities.

End point description:

Subjects completed a Treatment Satisfaction Questionnaire composed of a range of 14 questions regarding the subject's perception of treatment satisfaction at the end of each year of treatment. For the statement "This medication makes it easy for me to carry out my daily responsibilities (ie, going to work, doing household chores or caring for my family)," answers were numerically rated from 1 (strongly disagree) to 10 (strongly agree). Data after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Year 1, Year 2, Year 3

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529[33]	547[34]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Year 1; n=482, 496	7.4 (± 2.44)	7.7 (± 2.33)		
Year 2; n=426, 429	7.8 (± 2.32)	7.7 (± 2.35)		
Year 3; n=82, 88	7.9 (± 2.57)	8.3 (± 2.07)		

Notes:

[33] - n=subjects with an assessment at given timepoint.

[34] - n=subjects with an assessment at given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subject-Reported Treatment Satisfaction: The Twice a Month Dosing Makes It More Convenient for Me to Travel/Vacation.

End point title	Summary of Subject-Reported Treatment Satisfaction: The Twice a Month Dosing Makes It More Convenient for Me to Travel/Vacation.

End point description:

Subjects completed a Treatment Satisfaction Questionnaire composed of a range of 14 questions regarding the subject's perception of treatment satisfaction at the end of each year of treatment. For the statement "The twice a month dosing makes it more convenient for me to travel/vacation," answers were numerically rated from 1 (strongly disagree) to 10 (strongly agree). Data after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Year 1, Year 2, Year 3

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529[35]	547[36]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Year 1; n=482, 496	8.2 (± 2.21)	8.2 (± 2.13)		
Year 2; n=426, 430	8.3 (± 2.2)	8.2 (± 2.21)		
Year 3; n=82, 88	8.6 (± 1.97)	8.5 (± 1.86)		

Notes:

[35] - n=subjects with an assessment at given timepoint.

[36] - n=subjects with an assessment at given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subject-Reported Treatment Satisfaction: The Twice a Month Dosing Enables Me to Be More Spontaneous and Flexible.

End point title	Summary of Subject-Reported Treatment Satisfaction: The Twice a Month Dosing Enables Me to Be More Spontaneous and Flexible.

End point description:

Subjects completed a Treatment Satisfaction Questionnaire composed of a range of 14 questions regarding the subject's perception of treatment satisfaction at the end of each year of treatment. For the statement "The twice a month dosing enables me to be more spontaneous and flexible," answers were numerically rated from 1 (strongly disagree) to 10 (strongly agree). Data after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Year 1, Year 2, Year 3

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529[37]	547[38]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Year 1; n=482, 496	8.1 (± 2.2)	8.2 (± 2.09)		
Year 2; n=426, 430	8.3 (± 2.12)	8.2 (± 2.12)		
Year 3; n=82, 88	8.5 (± 2.17)	8.4 (± 1.93)		

Notes:

[37] - n=subjects with an assessment at given timepoint.

[38] - n=subjects with an assessment at given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subject-Reported Treatment Satisfaction: This Medication Improves My Self-Confidence and Self-Reliance.

End point title	Summary of Subject-Reported Treatment Satisfaction: This Medication Improves My Self-Confidence and Self-Reliance.

End point description:

Subjects completed a Treatment Satisfaction Questionnaire composed of a range of 14 questions regarding the subject’s perception of treatment satisfaction at the end of each year of treatment. For the statement "This medication improves my self-confidence and self-reliance," answers were numerically rated from 1 (strongly disagree) to 10 (strongly agree). Data after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Year 1, Year 2, Year 3

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529[39]	547[40]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Year 1; n=482, 496	7.5 (± 2.47)	7.7 (± 2.29)		
Year 2; n=426, 429	7.9 (± 2.5)	7.9 (± 2.31)		
Year 3; n=82, 88	8.1 (± 2.45)	8.4 (± 1.98)		

Notes:

[39] - n=subjects with an assessment at given timepoint.

[40] - n=subjects with an assessment at given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subject-Reported Treatment Satisfaction: I Am Satisfied With the Dosing Frequency of This Medication.

End point title	Summary of Subject-Reported Treatment Satisfaction: I Am Satisfied With the Dosing Frequency of This Medication.

End point description:

Subjects completed a Treatment Satisfaction Questionnaire composed of a range of 14 questions regarding the subject's perception of treatment satisfaction at the end of each year of treatment. For the statement "I am satisfied with the dosing frequency (2 times per month) of this medication" answers were numerically rated from 1 (strongly disagree) to 10 (strongly agree). Data after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Year 1, Year 2, Year 3

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529[41]	547[42]		
Units: units on a scale				
arithmetic mean (standard deviation)				
Year 1; n=482, 496	8.4 (± 1.98)	8.5 (± 1.94)		
Year 2; n=425, 430	8.7 (± 1.83)	8.5 (± 2.06)		
Year 3; n=82, 88	8.8 (± 1.87)	8.7 (± 1.81)		

Notes:

[41] - n=subjects with an assessment at given timepoint.

[42] - n=subjects with an assessment at given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subject-Reported Treatment Satisfaction: Over the Past 4 Weeks, Did You Miss Any of Your Injections?

End point title	Summary of Subject-Reported Treatment Satisfaction: Over the Past 4 Weeks, Did You Miss Any of Your Injections?

End point description:

Subjects completed a Treatment Satisfaction Questionnaire composed of a range of 14 questions regarding the subject's perception of treatment satisfaction at the end of each year of treatment. For the question "Over the past 4 weeks, did you miss any of your injections?" answer choices were given as "none missed," "miss 1 injection," or "miss 2 injections." Data after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Year 1, Year 2, Year 3

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529[43]	547[44]		
Units: subjects				
Year 1: none missed; n=482, 493	474	487		
Year 1: 1 missed; n=482, 493	8	4		
Year 1: 2 missed; n=482, 493	0	2		
Year 2: none missed; n=426, 429	422	426		
Year 2: 1 missed; n=426, 429	3	2		
Year 2: 2 missed; n=426, 429	1	1		
Year 3: none missed; n=81, 88	79	86		
Year 3: 1 missed; n=81, 88	0	1		
Year 3: 2 missed; n=81, 88	2	1		

Notes:

[43] - n=subjects with an assessment at given timepoint.

[44] - n=subjects with an assessment at given timepoint.

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Subject-Reported Treatment Satisfaction: Main Reason for Missed Injections

End point title	Summary of Subject-Reported Treatment Satisfaction: Main Reason for Missed Injections

End point description:

Subjects completed a Treatment Satisfaction Questionnaire composed of a range of 14 questions regarding the subject’s perception of treatment satisfaction at the end of each year of treatment. For the question "Main reason for missed injections?" answer choices were given as "medication side effects," "injection pain," "forget to take medication," "tired of taking injections," "don't think medication is working," or "other." Data after Amendment 3 took effect are excluded.

End point type	Secondary

End point timeframe:

Year 1, Year 2, Year 3

End point values	BIIB017 Q4W	BIIB017 Q2W		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	529[45]	547[46]		
Units: subjects				
Year 1: medication side effects; n=8, 6	0	1		
Year 1: injection pain; n=8, 6	0	0		
Year 1: forget to take medication; n=8, 6	2	1		
Year 1: tired of taking injections; n=8, 6	0	0		
Year 1: don't think medication is working; n=8, 6	0	0		
Year 1: other; n=8, 6	6	4		
Year 2: medication side effects; n=4, 3	1	1		
Year 2: injection pain; n=4, 3	0	0		
Year 2: forget to take medication; n=4, 3	1	1		

Year 2: tired of taking injections; n=4, 3	0	0		
Year 2: don't think medication is working; n=4, 3	0	0		
Year 2: other; n=4, 3	2	1		
Year 3: medication side effects; n=3, 2	0	0		
Year 3: injection pain; n=3, 2	0	0		
Year 3: forget to take medication; n=3, 2	0	0		
Year 3: tired of taking injections; n=3, 2	1	1		
Year 3: don't think medication is working; n=3, 2	0	0		
Year 3: other; n=3, 2	2	1		

Notes:

[45] - n=subjects with an assessment who missed at least 1 injection at given timepoint.

[46] - n=subjects with an assessment who missed at least 1 injection at given timepoint.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

up to 4 years

Adverse event reporting additional description:

All treatment-emergent events are presented. (An event was considered to be treatment emergent if it had an onset date on or after the date of first study treatment or if it was present prior to start of study treatment and subsequently worsened.)

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	BIIB017 Q2W

Reporting group description:

125 µg BIIB017 administered by SC injection Q2W for at least 2 years and up to 4 years.

Reporting group title	BIIB017 Q4W

Reporting group description:

125 µg BIIB017 administered by SC injection Q4W for at least 2 years and up to 4 years.

Serious adverse events	BIIB017 Q2W	BIIB017 Q4W	
Total subjects affected by serious adverse events			
subjects affected / exposed	91 / 547 (16.64%)	114 / 529 (21.55%)	
number of deaths (all causes)	1	2	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial adenocarcinoma			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangioma			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ovarian adenoma			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	2 / 547 (0.37%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Hysterectomy			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyst			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Adenomyosis			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical dysplasia			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menorrhagia			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metrorrhagia			
subjects affected / exposed	1 / 547 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	2 / 547 (0.37%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			

Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Bipolar 1 disorder			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Catatonia			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test abnormal			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb traumatic amputation			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 547 (0.00%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Thermal burn			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 547 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiomyopathy			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve prolapse			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	0 / 547 (0.00%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Nervous system disorders			
Epilepsy			
subjects affected / exposed	3 / 547 (0.55%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial neuralgia			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Ischaemic stroke			
subjects affected / exposed	2 / 547 (0.37%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar infarction			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
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	57 / 547 (10.42%)	83 / 529 (15.69%)	
occurrences causally related to treatment / all	1 / 86	1 / 117	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis			
subjects affected / exposed	2 / 547 (0.37%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Secondary progressive multiple sclerosis			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	2 / 547 (0.37%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic stroke			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			

subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uhthoff's phenomenon			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Heterophoria			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Colitis			
subjects affected / exposed	1 / 547 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Cholelithiasis			
subjects affected / exposed	2 / 547 (0.37%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis toxic			
subjects affected / exposed	1 / 547 (0.18%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis contact			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus ureteric			
subjects affected / exposed	1 / 547 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Endocrine disorders			
Autoimmune thyroiditis			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basedow's disease			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Bone cyst			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myositis			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	1 / 547 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Osteonecrosis			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patellofemoral pain syndrome			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometritis			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster oticus			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious thyroiditis			

subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis bacterial			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pharyngitis			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	0 / 547 (0.00%)	2 / 529 (0.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			

subjects affected / exposed	1 / 547 (0.18%)	1 / 529 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 547 (0.18%)	0 / 529 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 547 (0.00%)	1 / 529 (0.19%)	
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	BIIB017 Q2W	BIIB017 Q4W	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	438 / 547 (80.07%)	435 / 529 (82.23%)	
Nervous system disorders			
Hypoaesthesia			
subjects affected / exposed	28 / 547 (5.12%)	31 / 529 (5.86%)	
occurrences (all)	48	86	
Headache			
subjects affected / exposed	161 / 547 (29.43%)	152 / 529 (28.73%)	
occurrences (all)	2409	1658	
Paraesthesia			
subjects affected / exposed	20 / 547 (3.66%)	31 / 529 (5.86%)	
occurrences (all)	52	48	
Multiple sclerosis relapse			
subjects affected / exposed	130 / 547 (23.77%)	155 / 529 (29.30%)	
occurrences (all)	208	246	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	45 / 547 (8.23%)	64 / 529 (12.10%)	
occurrences (all)	318	441	

Chills			
subjects affected / exposed	58 / 547 (10.60%)	70 / 529 (13.23%)	
occurrences (all)	565	527	
Fatigue			
subjects affected / exposed	52 / 547 (9.51%)	40 / 529 (7.56%)	
occurrences (all)	297	155	
Injection site erythema			
subjects affected / exposed	224 / 547 (40.95%)	222 / 529 (41.97%)	
occurrences (all)	7819	3621	
Influenza like illness			
subjects affected / exposed	234 / 547 (42.78%)	234 / 529 (44.23%)	
occurrences (all)	6506	4105	
Injection site pain			
subjects affected / exposed	34 / 547 (6.22%)	38 / 529 (7.18%)	
occurrences (all)	162	215	
Injection site pruritus			
subjects affected / exposed	34 / 547 (6.22%)	24 / 529 (4.54%)	
occurrences (all)	521	134	
Pyrexia			
subjects affected / exposed	132 / 547 (24.13%)	147 / 529 (27.79%)	
occurrences (all)	2228	1765	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	34 / 547 (6.22%)	25 / 529 (4.73%)	
occurrences (all)	146	47	
Psychiatric disorders			
Depression			
subjects affected / exposed	26 / 547 (4.75%)	27 / 529 (5.10%)	
occurrences (all)	32	30	
Insomnia			
subjects affected / exposed	19 / 547 (3.47%)	27 / 529 (5.10%)	
occurrences (all)	41	39	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	57 / 547 (10.42%)	53 / 529 (10.02%)	
occurrences (all)	233	192	

Arthralgia			
subjects affected / exposed	52 / 547 (9.51%)	49 / 529 (9.26%)	
occurrences (all)	535	322	
Myalgia			
subjects affected / exposed	67 / 547 (12.25%)	65 / 529 (12.29%)	
occurrences (all)	1020	781	
Pain in extremity			
subjects affected / exposed	55 / 547 (10.05%)	52 / 529 (9.83%)	
occurrences (all)	204	166	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	49 / 547 (8.96%)	68 / 529 (12.85%)	
occurrences (all)	79	122	
Upper respiratory tract infection			
subjects affected / exposed	34 / 547 (6.22%)	18 / 529 (3.40%)	
occurrences (all)	47	24	
Urinary tract infection			
subjects affected / exposed	53 / 547 (9.69%)	51 / 529 (9.64%)	
occurrences (all)	70	75	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 December 2011	The BDI-II questionnaire was added as an additional safety assessment to monitor depression, which is a known side effect of interferon. The BDI-II is the same questionnaire that was used in Study 301 to monitor depression. The MES was added to the study activity chart to provide information on rebound effects in subjects who prematurely discontinued BIIB017 treatment. The MES added to Study 302 was the same as that offered in Study 301.
24 July 2014	The protocol was amended to remove the Q4W dosing group from the study. All subjects will now receive BIIB017 Q2W.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported