Clinical trial results:
A Multicenter, Randomized, Double-Blind, Placebo-Controlled Study, with an Active-Treatment Dose-Blinded Period, to Evaluate the Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of BIIB054 in Subjects with Parkinson's Disease

Summary

EudraCT number	2016-004610-95
Trial protocol	GB AT DE FR ES IT
Global end of trial date	29 April 2021

Results information

Result version number	v1 (current)
This version publication date	02 April 2022
First version publication date	02 April 2022

Trial information

Trial identification

Sponsor protocol code	228PD201

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03318523
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	250 Binney Street, Cambridge, United States, 02142
Public contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com
Scientific contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 April 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 April 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the clinical efficacy of BIIB054 via dose response using the change from baseline in Movement Disorder Society-Unified Parkinson's Disease Rating Scale (MDS-UPDRS) total score.
The secondary objectives of the study are to evaluate the dose-related safety of BIIB054, to evaluate the clinical efficacy of BIIB054 via MDS-UPDRS total score, to assess the pharmacokinetic (PK) profile of BIIB054, to evaluate the clinical efficacy of BIIB054 based on MDS-UPDRS subparts, to evaluate the pharmacodynamic effects of BIIB054 on the integrity of nigrostriatal dopaminergic nerve terminals and to evaluate the immunogenicity of BIIB054.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	10 January 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 167
Country: Number of subjects enrolled	Italy: 70
Country: Number of subjects enrolled	Spain: 48
Country: Number of subjects enrolled	Germany: 18
Country: Number of subjects enrolled	France: 19
Country: Number of subjects enrolled	Israel: 12
Country: Number of subjects enrolled	United Kingdom: 12
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	Austria: 3
Worldwide total number of subjects	357
EEA total number of subjects	158

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)	232
From 65 to 84 years	125
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 75 investigational sites from 10 January 2018 to 29 April 2021.

Pre-assignment

Screening details:

Subjects with Parkinson's Disease(PD) were randomised to receive placebo or BIIB054 250/1250/3500 milligrams(mg) for Year 1 in Placebo-Controlled(PC) Period. After Year 1, those on placebo [delayed start (DS)] received BIIB054 250/1250/3500 mg, and others on BIIB054 in Year 1 continued to receive same dose until Week 96 visit.

Period 1

Period 1 title	PC Period: Up to Year 1
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	PC Period: Placebo

Arm description:

Subjects received BIIB054-matching placebo, intravenous (IV) infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

Arm type	Placebo
Investigational medicinal product name	BIIB054-matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB054-matching placebo administered via IV infusion, on Day 1 and then every 4 weeks for Year 1.

Arm title	PC Period: BIIB054 250 mg (Early Start)

Arm description:

Subjects received BIIB054, 250 milligrams (mg), IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

Arm type	Experimental
Investigational medicinal product name	BIIB054
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB054 250 mg administered via IV infusion, on Day 1 and then every 4 weeks for Year 1.

Arm title	PC Period: BIIB054 1250 mg (Early Start)

Arm description:

Subjects received BIIB054, 1250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

Arm type	Experimental

Investigational medicinal product name	BIIB054
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB054 1250 mg administered via IV infusion, on Day 1 and then every 4 weeks for Year 1.

Arm title	PC Period: BIIB054 3500 mg (Early Start)

Arm description:

Subjects received BIIB054, 3500 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

Arm type	Experimental
Investigational medicinal product name	BIIB054
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB054 3500 mg administered via IV infusion, on Day 1 and then every 4 weeks for Year 1.

Number of subjects in period 1	PC Period: Placebo	PC Period: BIIB054 250 mg (Early Start)	PC Period: BIIB054 1250 mg (Early Start)
Started	100	55	102
Completed	96	53	100
Not completed	4	2	2
Adverse Event	1	-	2
Consent Withdrawn	3	2	-

Number of subjects in period 1	PC Period: BIIB054 3500 mg (Early Start)
Started	100
Completed	96
Not completed	4
Adverse Event	-
Consent Withdrawn	4

Period 2

Period 2 title	DBE Period:Year 2 to EOS (Up to 3 Years)
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	DBE Period: Placebo to BIIB054 250 mg (DS)

Arm description:

Subjects received BIIB054 250 mg, IV infusion from Year 2 up to end of study (EOS) (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.

Arm type	Experimental
Investigational medicinal product name	BIIB054
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB054 250 mg administered via IV infusion, once every 4 weeks, from Year 2 up to EOS (approximately 3 years).

Arm title	DBE Period: Placebo to BIIB054 1250 mg (DS)

Arm description:

Subjects received BIIB054 1250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.

Arm type	Experimental
Investigational medicinal product name	BIIB054
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB054 1250 mg administered via IV infusion, once every 4 weeks, from Year 2 up to EOS (approximately 3 years).

Arm title	DBE Period: Placebo to BIIB054 3500 mg (DS)

Arm description:

Subjects received BIIB054 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.

Arm type	Experimental
Investigational medicinal product name	BIIB054
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB054 3500 mg administered via IV infusion, once every 4 weeks, from Year 2 up to EOS (approximately 3 years).

Arm title	DBE Period: BIIB054 250 mg (Early Start)

Arm description:

Subjects received BIIB054 250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 250 mg in the PC period were included in this arm.

Arm type	Experimental
Investigational medicinal product name	BIIB054
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB054 250 mg administered via IV infusion, once every 4 weeks, from Year 2 up to EOS (approximately 3 years).

Arm title	DBE Period: BIIB054 1250 mg (Early Start)

Arm description:

Subjects received BIIB054 1250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 1250 mg in the PC period were included in this arm.

Arm type	Experimental
Investigational medicinal product name	BIIB054
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB054 1250 mg administered via IV infusion, once every 4 weeks, from Year 2 up to EOS (approximately 3 years).

Arm title	DBE Period: BIIB054 3500 mg (Early Start)

Arm description:

Subjects received BIIB054 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 3500 mg in the PC period were included in this arm.

Arm type	Experimental
Investigational medicinal product name	BIIB054
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB054 3500 mg administered via IV infusion, once every 4 weeks, from Year 2 up to EOS (approximately 3 years).

Number of subjects in period 2[1]	DBE Period: Placebo to BIIB054 250 mg (DS)	DBE Period: Placebo to BIIB054 1250 mg (DS)	DBE Period: Placebo to BIIB054 3500 mg (DS)
Started	20	37	39
Number of Subjects Dosed	20	37	39
Completed	0	0	0
Not completed	20	37	39
Adverse Event	1	-	-
Death	-	-	-
Not Specified	1	-	-
Investigator Decision	-	1	-
Study Terminated by Sponsor	17	36	39
Consent Withdrawn	1	-	-

Number of subjects in period 2	DBE Period: BIIB054 250 mg (Early Start)	DBE Period: BIIB054 1250 mg (Early	DBE Period: BIIB054 3500 mg (Early

[1]		Start)	Start)
Started	52	100	96
Number of Subjects Dosed	52	100	94
Completed	0	0	0
Not completed	52	100	96
Adverse Event	1	-	2
Death	-	-	1
Not Specified	2	3	-
Investigator Decision	-	-	-
Study Terminated by Sponsor	48	94	91
Consent Withdrawn	1	3	2

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: 345 subjects completed the PC Period, out of which only 344 subjects entered in DBE Period. 1 subject from PC Period did not enter DBE Period.

Baseline characteristics

Reporting groups	
Reporting group title	PC Period: Placebo
Reporting group description:	
Subjects received BIIB054-matching placebo, intravenous (IV) infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.	
Reporting group title	PC Period: BIIB054 250 mg (Early Start)
Reporting group description:	
Subjects received BIIB054, 250 milligrams (mg), IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.	
Reporting group title	PC Period: BIIB054 1250 mg (Early Start)
Reporting group description:	
Subjects received BIIB054, 1250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.	
Reporting group title	PC Period: BIIB054 3500 mg (Early Start)
Reporting group description:	
Subjects received BIIB054, 3500 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.	

Reporting group values	PC Period: Placebo	PC Period: BIIB054 250 mg (Early Start)	PC Period: BIIB054 1250 mg (Early Start)
Number of subjects	100	55	102
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	61.0	61.3	59.2
standard deviation	± 8.39	± 9.24	± 8.48
Gender Categorical Units: subjects			
Female	28	16	29
Male	72	39	73
Race Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	0	0	3
Black or African American	0	0	1
White	96	53	92
Unknown or Not Reported	4	2	6
Ethnicity Units: Subjects			
Hispanic or Latino	3	1	1
Not Hispanic or Latino	96	54	101
Unknown or Not Reported	1	0	0
Baseline Movement Disorder Society Sponsored Revision of the Unified PD Rating Scale Total Score			
Movement Disorder Society Sponsored Revision of the Unified PD Rating Scale (MDS-UPDRS) is multimodal scale assessing impairment and disability consisting of 4 parts. Part I: non-motor			

experiences of daily living and has 2 components (13 questions[Q], Range[R] 0-52). Part II: motor experiences of daily living (13 Q, R 0-52). Part III: motor signs of PD and was administered by rater (33 Q, R 0-132). Numeric score for each question is between 0-4; 0=Normal,1=Slight,2=Mild,3=Moderate,4=Severe. MDS-UPDRS Total Score=sum of Parts I, II, and III (R 0-236). Higher score=more severe symptoms of PD.			
Units: score on a scale			
arithmetic mean	31.9	31.9	32.9
standard deviation	± 12.41	± 12.25	± 12.58
Baseline MDS-UPDRS Subpart I Score			
MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. It is separated into 4 subscales: Part I assessed non-motor experiences of daily living and has 2 components (Range 0-52). Part IA contained 6 questions and were assessed by the examiner (Range 0-24). Part IB contained 7 questions on non-motor experiences of daily living which were completed by the subject (Range 0-28). For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD.			
Units: score on a scale			
arithmetic mean	4.3	3.3	4.8
standard deviation	± 3.50	± 2.74	± 3.99
Baseline MDS-UPDRS Subpart II Score			
MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part II assessed motor experiences of daily living (Range 0-52). It contained 13 questions completed by the subject. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD.			
Units: score on a scale			
arithmetic mean	5.4	5.0	5.3
standard deviation	± 3.87	± 3.30	± 3.66
Baseline MDS-UPDRS Subpart III Score			
MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part III assessed the motor signs of Parkinson's Disease (PD) and was administered by the rater (Range 0-132). Part III contained 33 scores based on 18 items. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD.			
Units: score on a scale			
arithmetic mean	22.2	23.5	22.8
standard deviation	± 9.31	± 9.38	± 8.69
Baseline Total Striatum Striatal Binding Ratio (SBR)			
Number analysed is the number of subjects analysed for this study specific baseline measure: PC Period: Placebo (100), PC Period: BIIB054 250 mg (Early Start) (55), PC Period: BIIB054 1250 mg (Early Start) (102) and PC Period: BIIB054 3500 mg (Early Start) (99).			
Units: striatal binding ratio			
arithmetic mean	1.295	1.409	1.342
standard deviation	± 0.3177	± 0.3875	± 0.3197
Baseline Total Putamen SBR			
Number analysed is the number of subjects analysed for this study specific baseline measure: PC Period: Placebo (100), PC Period: BIIB054 250 mg (Early Start) (55), PC Period: BIIB054 1250 mg (Early Start) (102) and PC Period: BIIB054 3500 mg (Early Start) (99).			
Units: striatal binding ratio			
arithmetic mean	1.255	1.388	1.291
standard deviation	± 0.3429	± 0.4294	± 0.3269
Baseline Total Caudate SBR			
Number analysed is the number of subjects analysed for this study specific baseline measure: PC Period: Placebo (100), PC Period: BIIB054 250 mg (Early Start) (55), PC Period: BIIB054 1250 mg (Early Start) (102) and PC Period: BIIB054 3500 mg (Early Start) (99).			
Units: striatal binding ratio			
arithmetic mean	1.336	1.433	1.397
standard deviation	± 0.3279	± 0.3751	± 0.3417

Reporting group values	PC Period: BIIB054 3500 mg (Early Start)	Total	
Number of subjects	100	357	
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	59.3		
standard deviation	± 9.92	-	
Gender Categorical Units: subjects			
Female	34	107	
Male	66	250	
Race Units: Subjects			
American Indian or Alaska Native	2	2	
Asian	3	6	
Black or African American	0	1	
White	84	325	
Unknown or Not Reported	11	23	
Ethnicity Units: Subjects			
Hispanic or Latino	6	11	
Not Hispanic or Latino	94	345	
Unknown or Not Reported	0	1	
Baseline Movement Disorder Society Sponsored Revision of the Unified PD Rating Scale Total Score			
Movement Disorder Society Sponsored Revision of the Unified PD Rating Scale (MDS-UPDRS) is multimodal scale assessing impairment and disability consisting of 4 parts. Part I: non-motor experiences of daily living and has 2 components (13 questions[Q], Range[R] 0-52). Part II: motor experiences of daily living (13 Q, R 0-52). Part III: motor signs of PD and was administered by rater (33 Q, R 0-132). Numeric score for each question is between 0-4; 0=Normal,1=Slight,2=Mild,3=Moderate,4=Severe. MDS-UPDRS Total Score=sum of Parts I, II, and III (R 0-236). Higher score=more severe symptoms of PD.			
Units: score on a scale			
arithmetic mean	32.6		
standard deviation	± 13.46	-	
Baseline MDS-UPDRS Subpart I Score			
MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. It is separated into 4 subscales: Part I assessed non-motor experiences of daily living and has 2 components (Range 0-52). Part IA contained 6 questions and were assessed by the examiner (Range 0-24). Part IB contained 7 questions on non-motor experiences of daily living which were completed by the subject (Range 0-28). For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD.			
Units: score on a scale			
arithmetic mean	4.3		
standard deviation	± 3.60	-	
Baseline MDS-UPDRS Subpart II Score			
MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part II assessed motor experiences of daily living (Range 0-52). It contained 13 questions completed by the subject. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD.			
Units: score on a scale			

arithmetic mean	5.5		
standard deviation	± 4.30	-	
Baseline MDS-UPDRS Subpart III Score			
MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part III assessed the motor signs of Parkinson's Disease (PD) and was administered by the rater (Range 0-132). Part III contained 33 scores based on 18 items. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD.			
Units: score on a scale			
arithmetic mean	22.9		
standard deviation	± 8.86	-	
Baseline Total Striatum Striatal Binding Ratio (SBR)			
Number analysed is the number of subjects analysed for this study specific baseline measure: PC Period: Placebo (100), PC Period: BIIB054 250 mg (Early Start) (55), PC Period: BIIB054 1250 mg (Early Start) (102) and PC Period: BIIB054 3500 mg (Early Start) (99).			
Units: striatal binding ratio			
arithmetic mean	1.351		
standard deviation	± 0.3495	-	
Baseline Total Putamen SBR			
Number analysed is the number of subjects analysed for this study specific baseline measure: PC Period: Placebo (100), PC Period: BIIB054 250 mg (Early Start) (55), PC Period: BIIB054 1250 mg (Early Start) (102) and PC Period: BIIB054 3500 mg (Early Start) (99).			
Units: striatal binding ratio			
arithmetic mean	1.286		
standard deviation	± 0.3627	-	
Baseline Total Caudate SBR			
Number analysed is the number of subjects analysed for this study specific baseline measure: PC Period: Placebo (100), PC Period: BIIB054 250 mg (Early Start) (55), PC Period: BIIB054 1250 mg (Early Start) (102) and PC Period: BIIB054 3500 mg (Early Start) (99).			
Units: striatal binding ratio			
arithmetic mean	1.416		
standard deviation	± 0.3643	-	

End points

End points reporting groups

Reporting group title	PC Period: Placebo
Reporting group description:	
Subjects received BIIB054-matching placebo, intravenous (IV) infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.	
Reporting group title	PC Period: BIIB054 250 mg (Early Start)
Reporting group description:	
Subjects received BIIB054, 250 milligrams (mg), IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.	
Reporting group title	PC Period: BIIB054 1250 mg (Early Start)
Reporting group description:	
Subjects received BIIB054, 1250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.	
Reporting group title	PC Period: BIIB054 3500 mg (Early Start)
Reporting group description:	
Subjects received BIIB054, 3500 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.	
Reporting group title	DBE Period: Placebo to BIIB054 250 mg (DS)
Reporting group description:	
Subjects received BIIB054 250 mg, IV infusion from Year 2 up to end of study (EOS) (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.	
Reporting group title	DBE Period: Placebo to BIIB054 1250 mg (DS)
Reporting group description:	
Subjects received BIIB054 1250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.	
Reporting group title	DBE Period: Placebo to BIIB054 3500 mg (DS)
Reporting group description:	
Subjects received BIIB054 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.	
Reporting group title	DBE Period: BIIB054 250 mg (Early Start)
Reporting group description:	
Subjects received BIIB054 250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 250 mg in the PC period were included in this arm.	
Reporting group title	DBE Period: BIIB054 1250 mg (Early Start)
Reporting group description:	
Subjects received BIIB054 1250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 1250 mg in the PC period were included in this arm.	
Reporting group title	DBE Period: BIIB054 3500 mg (Early Start)
Reporting group description:	
Subjects received BIIB054 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 3500 mg in the PC period were included in this arm.	
Subject analysis set title	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects who received BIIB054-matching placebo in Year 1 followed by BIIB054 250 mg or 1250 mg or 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) were pooled in this arm.	
Subject analysis set title	PC Period: Early Start BIIB054 250 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received BIIB054, 250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.	
Subject analysis set title	PC Period: Early Start BIIB054 1250 mg

Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received BIIB054, 1250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in PC Period.	
Subject analysis set title	PC Period: Early Start BIIB054 3500 mg
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received BIIB054, 3500 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in PC Period.	
Subject analysis set title	BIIB054 250 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects received BIIB054, 250 mg, IV infusion, from Day 1 up to EOS (approximately 3 years).	
Subject analysis set title	BIIB054 1250 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects received BIIB054, 1250 mg, IV infusion, from Day 1 up to EOS (approximately 3 years).	
Subject analysis set title	BIIB054 3500 mg
Subject analysis set type	Sub-group analysis
Subject analysis set description:	
Subjects received BIIB054, 3500 mg, IV infusion, from Day 1 up to EOS (approximately 3 years).	
Subject analysis set title	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled)
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects who received BIIB054-matching placebo in Year 1 followed by BIIB054 250 mg or 1250 mg or 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) were pooled in this arm.	
Subject analysis set title	PC Period: Early Start BIIB054 250 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received BIIB054, 250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.	
Subject analysis set title	PC Period: Early Start BIIB054 1250 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received BIIB054, 1250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in PC Period.	
Subject analysis set title	PC Period: Early Start BIIB054 3500 mg
Subject analysis set type	Safety analysis
Subject analysis set description:	
Subjects received BIIB054, 3500 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in PC Period.	
Subject analysis set title	PC Period: Placebo
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received BIIB054-matching placebo, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.	
Subject analysis set title	PC Period: BIIB054 250 mg (Early Start)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
Subjects received BIIB054, 250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.	
Subject analysis set title	PC Period: BIIB054 1250 mg (Early Start)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects received BIIB054, 1250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in PC Period.

Subject analysis set title	PC Period: BIIB054 3500 mg (Early Start)
Subject analysis set type	Intention-to-treat

Subject analysis set description:

Subjects received BIIB054, 3500 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in PC Period.

Primary: Change From Baseline in Movement Disorder Society Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Total Score (Sum of Parts I, II, and III) at Week 52

End point title	Change From Baseline in Movement Disorder Society Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Total Score (Sum of Parts I, II, and III) at Week 52

End point description:

MDS-UPDRS is multimodal scale assessing impairment and disability consisting of 4 parts. Part I assessed non-motor experiences of daily living and has 2 components (Range [R] 0-52). Part IA: 6 questions (Qs) assessed by examiner (R 0-24). Part IB: 7 Qs completed by subject (R 0-28). Part II assessed motor experiences of daily living (R 0-52). It contained 13 Qs completed by subject. Part III assessed motor signs of PD and was administered by rater (R 0-132). Part III contained 33 scores based on 18 items. Numeric score for each question is between 0-4, where 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. MDS-UPDRS Total Score=sum of Parts I, II, and III (R 0-236). A higher score indicated more severe symptoms of PD. ITT Population. The mean values reported are the adjusted mean values.

End point type	Primary

End point timeframe:

Baseline, Week 52

End point values	PC Period: Placebo	PC Period: BIIB054 250 mg (Early Start)	PC Period: BIIB054 1250 mg (Early Start)	PC Period: BIIB054 3500 mg (Early Start)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	53[1]	29[2]	57[3]	51[4]
Units: score on a scale				
arithmetic mean (standard error)	10.78 (± 1.490)	10.48 (± 1.951)	11.29 (± 1.446)	10.86 (± 1.518)

Notes:

[1] - Number of subjects analysed were subjects analysed for this endpoint.

[2] - Number of subjects analysed were subjects analysed for this endpoint.

[3] - Number of subjects analysed were subjects analysed for this endpoint.

[4] - Number of subjects analysed were subjects analysed for this endpoint.

Statistical analyses

Statistical analysis title	Week 52: Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% confidence interval (CI), and p-value were based on a mixed model for repeated measures (MMRM) model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period: BIIB054 250 mg (Early Start) v PC Period: Placebo

Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8976
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.3
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.888
upper limit	4.287

Statistical analysis title	Week 52: Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 1250 mg (Early Start)
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.796
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.31
upper limit	4.312

Statistical analysis title	Week 52: Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 3500 mg (Early Start)
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9695
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.08

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.805
upper limit	3.956

Primary: Change From Baseline in Movement Disorder Society Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Total Score (Sum of Parts I, II, and III) at Week 72

End point title	Change From Baseline in Movement Disorder Society Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS) Total Score (Sum of Parts I, II, and III) at Week 72

End point description:

MDS-UPDRS is multimodal scale assessing impairment and disability consisting of 4 parts. Part I assessed non-motor experiences of daily living and has 2 components (Range [R] 0-52). Part IA: 6 questions (Qs) assessed by examiner (R 0-24). Part IB: 7 Qs completed by subject (R 0-28). Part II assessed motor experiences of daily living (R 0-52). It contained 13 Qs completed by subject. Part III assessed motor signs of PD and was administered by rater (R 0-132). Part III contained 33 scores based on 18 items. Numeric score for each question is between 0-4, where 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. MDS-UPDRS Total Score=sum of Parts I, II, and III (R 0-236). Higher score=severe symptoms of PD. ITT Population. As prespecified in protocol, data for delayed start BIIB054 were pooled from Placebo/BIIB054 250/1250/3500 mg for analysis of this endpoint. The mean values reported=adjusted mean values.

End point type	Primary

End point timeframe:

Baseline, Week 72

End point values	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled)	PC Period: Early Start BIIB054 250 mg	PC Period: Early Start BIIB054 1250 mg	PC Period: Early Start BIIB054 3500 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	68[5]	32[6]	62[7]	64[8]
Units: score on a scale				
arithmetic mean (standard error)	7.11 (± 1.476)	6.83 (± 2.032)	8.66 (± 1.496)	6.94 (± 1.508)

Notes:

[5] - Number of subjects analysed were subjects analysed for this endpoint.

[6] - Number of subjects analysed were subjects analysed for this endpoint.

[7] - Number of subjects analysed were subjects analysed for this endpoint.

[8] - Number of subjects analysed were subjects analysed for this endpoint.

Statistical analyses

Statistical analysis title	Week 72: Pooled Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg
Number of subjects included in analysis	100
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9093
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.035
upper limit	4.483

Statistical analysis title	Week 72: Pooled Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg
Number of subjects included in analysis	130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4327
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	1.55
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.336
upper limit	5.44

Statistical analysis title	Week 72: Pooled Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg

Number of subjects included in analysis	132
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.933
Method	Mixed Model with repeated Measures
Parameter estimate	Difference
Point estimate	-0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.051
upper limit	3.719

Secondary: Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point description:

An AE is any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. An SAE is any untoward medical occurrence that at any dose, results in death; in the view of the investigator places the subject at immediate risk of death; requires inpatient hospitalisation or prolongation of existing hospitalisation; results in persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; is a medically important event. The safety population was defined as all subjects who received at least one dose of study treatment (BIIB054).

End point type	Secondary

End point timeframe:

Up to 3 years

End point values	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled)	PC Period: Early Start BIIB054 250 mg	PC Period: Early Start BIIB054 1250 mg	PC Period: Early Start BIIB054 3500 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	96	55	102	100
Units: percentage of subjects				
number (not applicable)				
AEs	77.1	85.5	89.2	93.0
SAEs	8.3	10.9	8.8	12.0

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in MDS-UPDRS Total Score (Sum of Parts I, II, and III) at Week 96

End point title	Change From Baseline in MDS-UPDRS Total Score (Sum of Parts I, II, and III) at Week 96

End point description:

MDS-UPDRS is multimodal scale assessing impairment and disability consisting of 4 parts. Part I assessed non-motor experiences of daily living and has 2 components (Range [R] 0-52). Part IA: 6 questions (Qs) assessed by examiner (R 0-24). Part IB: 7 Qs completed by subject (R 0-28). Part II assessed motor experiences of daily living (R 0-52). It contained 13 Qs completed by subject. Part III assessed motor signs of PD and was administered by rater (R 0-132). Part III contained 33 scores based on 18 items. Numeric score for each question is between 0-4, where 0=Normal, 1=Slight, 2=Mild, 3=Moderate, 4=Severe. MDS-UPDRS Total Score=sum of Parts I, II, and III (R 0-236). Higher score=Severe symptoms of PD. ITT population. As prespecified in protocol, data for delayed start BIIB054 were pooled from Placebo/BIIB054 250/1250/3500 mg for analysis of this endpoint. The mean values reported are the adjusted mean values.

End point type	Secondary

End point timeframe:

Baseline, Week 96

End point values	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled)	PC Period: Early Start BIIB054 250 mg	PC Period: Early Start BIIB054 1250 mg	PC Period: Early Start BIIB054 3500 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	67[9]	28[10]	62[11]	59[12]
Units: score on a scale				
arithmetic mean (standard error)	7.88 (± 1.616)	8.28 (± 2.317)	8.71 (± 1.628)	8.87 (± 1.659)

Notes:

[9] - Number of subjects analysed were subjects analysed for this endpoint.

[10] - Number of subjects analysed were subjects analysed for this endpoint.

[11] - Number of subjects analysed were subjects analysed for this endpoint.

[12] - Number of subjects analysed were subjects analysed for this endpoint.

Statistical analyses

Statistical analysis title	Week 96: Pooled Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg
Number of subjects included in analysis	95
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8828
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.41

Confidence interval	
level	95 %
sides	2-sided
lower limit	-5.013
upper limit	5.825

Statistical analysis title	Week 96: Pooled Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg
Number of subjects included in analysis	129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7019
Method	Mixed Model for Repeated Measure
Parameter estimate	Difference
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.458
upper limit	5.128

Statistical analysis title	Week 96: Pooled Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg
Number of subjects included in analysis	126
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6519
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.323
upper limit	5.301

Secondary: Serum Concentration of BIIB054

End point title	Serum Concentration of BIIB054

End point description:

The pharmacokinetic (PK) population was defined as all subjects in the ITT population who had at least one measurable BIIB054 concentration in serum or cerebrospinal fluid (CSF). The 'n' signifies the number of subjects analysed at the specified time point. ‘99999’ signifies that mean and SD were non-determinable.

End point type	Secondary

End point timeframe:

Pre-dose and 1 hour post-dose of Baseline, Weeks 4, 8, 12, 16, 24, 32, 36, 44, 52, 60, 68, 84, 96, 120 and 144

End point values	BIIB054 250 mg	BIIB054 1250 mg	BIIB054 3500 mg	
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	
Number of subjects analysed	75	139	139	
Units: micrograms per millilitre (ug/mL)				
arithmetic mean (standard deviation)				
Baseline (Pre-dose) (n=48,95,92)	0 (± 0)	7.47 (± 51.281)	0.01 (± 0.065)	
Baseline (1 Hour Post-dose) (n=62,121,114)	75.02 (± 15.829)	374.79 (± 86.004)	1137.28 (± 335.336)	
Week 4 (Pre-dose) (n=46,95,91)	20.37 (± 5.004)	95.36 (± 27.882)	306.20 (± 95.257)	
Week 4 (1 Hour Post-dose) (n=47,94,91)	97.09 (± 19.711)	468.56 (± 190.589)	1354.19 (± 364.468)	
Week 8 (Pre-dose) (n=63,125,122)	29.73 (± 8.371)	169.79 (± 68.025)	495.79 (± 153.357)	
Week 8 (1 Hour Post-dose) (n=64,127,122)	103.69 (± 26.964)	543.91 (± 143.212)	1591.57 (± 465.798)	
Week 12 (Pre-dose) (n=50,97,96)	36.76 (± 11.830)	195.16 (± 51.020)	580.43 (± 185.761)	
Week 12 (1 Hour Post-dose) (n=54,99,97)	112.61 (± 27.378)	569.41 (± 141.250)	1632.29 (± 459.839)	
Week 16 (Pre-dose) (n=51,99,98)	40.82 (± 11.421)	201.33 (± 73.451)	642.06 (± 194.288)	
Week 16 (1 Hour Post-dose) (n=50,99,98)	117.08 (± 27.401)	614.85 (± 186.892)	1739.98 (± 506.346)	
Week 24 (Pre-dose) (n=54,98,94)	43.31 (± 12.906)	235.69 (± 84.454)	724.60 (± 228.295)	
Week 24 (1 Hour Post-dose) (n=46,90,87)	125.79 (± 36.695)	664.26 (± 209.251)	1867.92 (± 470.283)	
Week 32 (Pre-dose) (n=11,19,24)	42.69 (± 13.486)	260.35 (± 104.397)	772.75 (± 299.703)	
Week 32 (1 Hour Post-dose) (n=15,25,28)	139.00 (± 34.758)	626.16 (± 164.497)	1985.71 (± 497.545)	
Week 36 (Pre-dose) (n=51,100,96)	45.77 (± 11.867)	262.80 (± 85.052)	819.83 (± 328.774)	
Week 36 (1 Hour Post-dose) (n=51,100,95)	123.67 (± 29.536)	665.60 (± 145.235)	1916.84 (± 543.373)	
Week 44 (Pre-dose) (n=3,5,7)	58.17 (± 22.774)	280.40 (± 116.590)	858.43 (± 349.573)	

Week 44 (1 Hour Post-dose) (n=3,5,8)	143.33 (± 41.004)	582.40 (± 194.431)	2066.25 (± 579.555)	
Week 52 (Pre-dose) (n=49,98,82)	46.70 (± 19.343)	232.08 (± 87.529)	787.35 (± 341.229)	
Week 52 (1 Hour Post-dose) (n=35,74,64)	114.59 (± 25.913)	645.36 (± 264.270)	1920.78 (± 479.511)	
Week 60 (Pre-dose) (n=42,86,84)	43.41 (± 15.973)	254.52 (± 88.446)	724.77 (± 314.854)	
Week 60 (1 Hour Post-dose) (n=41,83,80)	122.55 (± 29.374)	657.94 (± 149.654)	1905.43 (± 494.136)	
Week 68 (Pre-dose) (n=2,3,2)	706.25 (± 966.969)	202.33 (± 34.210)	1362.50 (± 533.866)	
Week 68 (1 Hour Post-dose) (n=2,3,2)	171.50 (± 44.548)	576.33 (± 85.290)	2305.00 (± 1025.305)	
Week 84 (Pre-dose) (n=28,50,42)	47.00 (± 15.535)	255.54 (± 81.407)	746.43 (± 249.770)	
Week 84 (1 Hour Post-dose) (n=38,60,52)	134.91 (± 33.035)	648.62 (± 120.163)	1942.02 (± 501.095)	
Week 96 (Pre-dose) (n=11,18,16)	41.25 (± 15.345)	274.56 (± 71.718)	654.70 (± 262.926)	
Week 96 (1 Hour Post-dose) (n=10,20,16)	122.00 (± 29.527)	682.30 (± 123.653)	1822.50 (± 475.682)	
Week 120 (Pre-dose) (n=6,6,7)	34.98 (± 12.042)	279.00 (± 99.499)	727.29 (± 116.793)	
Week 120 (1 Hour Post-dose) (n=6,6,7)	119.67 (± 15.629)	769.83 (± 279.182)	1717.14 (± 320.037)	
Week 144 (Pre-dose) (n=0,1,0)	99999 (± 99999)	365.00 (± 99999)	99999 (± 99999)	
Week 144 (1 Hour Post-dose) (n=0,1,0)	99999 (± 99999)	721.00 (± 99999)	99999 (± 99999)	

Statistical analyses

No statistical analyses for this end point

Secondary: Change From Baseline in MDS-UPDRS Subpart I Score at Week 52

End point title	Change From Baseline in MDS-UPDRS Subpart I Score at Week 52

End point description:

MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part I assessed non-motor experiences of daily living and has 2 components (Range 0-52). Part IA contained 6 questions and were assessed by the examiner (Range 0-24). Part IB contained 7 questions on non-motor experiences of daily living which were completed by the subject (Range 0-28). For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. The ITT population was defined as all randomised subjects who received at least one dose of study treatment (BIIB054 or placebo). The mean values reported are the adjusted mean values.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	PC Period: Placebo	PC Period: BIIB054 250 mg (Early Start)	PC Period: BIIB054 1250 mg (Early Start)	PC Period: BIIB054 3500 mg (Early Start)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	53[13]	29[14]	57[15]	51[16]
Units: score on a scale				
arithmetic mean (standard error)	1.43 (± 0.436)	0.90 (± 0.570)	1.56 (± 0.423)	1.65 (± 0.446)

Notes:

[13] - Number of subjects analysed were subjects analysed for this endpoint.

[14] - Number of subjects analysed were subjects analysed for this endpoint.

[15] - Number of subjects analysed were subjects analysed for this endpoint.

[16] - Number of subjects analysed were subjects analysed for this endpoint.

Statistical analyses

Statistical analysis title	Week 52: Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 250 mg (Early Start)
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4327
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.851
upper limit	0.794

Statistical analysis title	Week 52: Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 1250 mg (Early Start)
Number of subjects included in analysis	110
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8155
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.13

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.965
upper limit	1.225

Statistical analysis title	Week 52: Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 3500 mg (Early Start)
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7015
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.899
upper limit	1.334

Secondary: Change From Baseline in MDS-UPDRS Subpart I Score at Weeks 72 and 96

End point title	Change From Baseline in MDS-UPDRS Subpart I Score at Weeks 72 and 96

End point description:

MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part I assessed non-motor experiences of daily living and has 2 components (Range 0-52). Part IA contained 6 questions and were assessed by the examiner (Range 0-24). Part IB contained 7 questions on non-motor experiences of daily living which were completed by the subject (Range 0-28). For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. The ITT population was defined as all randomised subjects who received at least one dose of study treatment (BIIB054 or placebo). As prespecified in the protocol, the data for the delayed start BIIB054 were pooled from Placebo/BIIB054 250/1250/3500 mg for the analysis of this endpoint. The 'n' signifies number of subjects analysed at the specified time point. The mean values reported are the adjusted mean values.

End point type	Secondary

End point timeframe:

Baseline, Weeks 72 and 96

End point values	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled)	PC Period: Early Start BIIB054 250 mg	PC Period: Early Start BIIB054 1250 mg	PC Period: Early Start BIIB054 3500 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	100	55	102	100
Units: score on a scale				
arithmetic mean (standard error)				
Change from Baseline at Week 72 (n=68,32,62,64)	1.65 (± 0.395)	0.61 (± 0.538)	1.73 (± 0.402)	1.63 (± 0.405)
Change from Baseline at Week 96 (n=67,28,62,59)	1.95 (± 0.398)	1.69 (± 0.568)	1.93 (± 0.403)	1.72 (± 0.414)

Statistical analyses

Statistical analysis title	Week 72: Pooled Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1038
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.276
upper limit	0.213

Statistical analysis title	Week 72: Pooled Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg

Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8689
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.09
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.933
upper limit	1.103

Statistical analysis title	Week 72: Pooled Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.982
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.026
upper limit	1.003

Statistical analysis title	Week 96: Pooled Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg

Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.693
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.563
upper limit	1.04

Statistical analysis title	Week 96: Pooled Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9606
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.053
upper limit	1.001

Statistical analysis title	Week 96: Pooled Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg

Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6512
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.24
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.269
upper limit	0.794

Secondary: Change From Baseline in MDS-UPDRS Subpart II Score at Week 52

End point title	Change From Baseline in MDS-UPDRS Subpart II Score at Week 52

End point description:

MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part II assessed motor experiences of daily living (Range 0-52). It contained 13 questions completed by the subject. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. The ITT population was defined as all randomised subjects who received at least one dose of study treatment (BIIB054 or placebo). The mean values reported are the adjusted mean values.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	PC Period: Placebo	PC Period: BIIB054 250 mg (Early Start)	PC Period: BIIB054 1250 mg (Early Start)	PC Period: BIIB054 3500 mg (Early Start)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	54[17]	29[18]	58[19]	51[20]
Units: score on a scale				
arithmetic mean (standard error)	3.17 (± 0.473)	2.72 (± 0.621)	3.16 (± 0.460)	3.01 (± 0.486)

Notes:

[17] - Number of subjects analysed were subjects analysed for this endpoint.

[18] - Number of subjects analysed were subjects analysed for this endpoint.

[19] - Number of subjects analysed were subjects analysed for this endpoint.

[20] - Number of subjects analysed were subjects analysed for this endpoint.

Statistical analyses

Statistical analysis title	Week 52: Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 250 mg (Early Start)
Number of subjects included in analysis	83
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5497
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.889
upper limit	1.007

Statistical analysis title	Week 52: Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 1250 mg (Early Start)
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.998
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.2
upper limit	1.197

Statistical analysis title	Week 52: Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 3500 mg (Early Start)

Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8069
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.374
upper limit	1.07

Secondary: Change From Baseline in MDS-UPDRS Subpart II Score at Weeks 72 and 96

End point title	Change From Baseline in MDS-UPDRS Subpart II Score at Weeks 72 and 96

End point description:

MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part II assessed motor experiences of daily living (Range 0-52). It contained 13 questions completed by the subject. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. The ITT population was defined as all randomised subjects who received at least one dose of study treatment (BIIB054 or placebo). As prespecified in the protocol, the data for the delayed start BIIB054 were pooled from (Placebo/BIIB054 250/1250/3500 mg) for the analysis of this endpoint. The 'n' signifies number of subjects analysed at the specified time point. The mean values reported are the adjusted mean values.

End point type	Secondary

End point timeframe:

Baseline, Weeks 72 and 96

End point values	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled)	PC Period: Early Start BIIB054 250 mg	PC Period: Early Start BIIB054 1250 mg	PC Period: Early Start BIIB054 3500 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	100	55	102	100
Units: score on a scale				
arithmetic mean (standard error)				
Change from Baseline at Week 72 (n=69,33,62,64)	1.83 (± 0.491)	1.62 (± 0.672)	2.36 (± 0.497)	1.68 (± 0.503)
Change from Baseline at Week 96 (n=67,28,62,60)	1.87 (± 0.529)	1.33 (± 0.762)	2.39 (± 0.533)	2.22 (± 0.541)

Statistical analyses

Statistical analysis title	Week 72: Pooled Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7968
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.21
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.786
upper limit	1.372

Statistical analysis title	Week 72: Pooled Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4211
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.766
upper limit	1.827

Statistical analysis title	Week 72: Pooled Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time

interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8166
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.15
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.448
upper limit	1.143

Statistical analysis title	Week 96: Pooled Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5535
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.53
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.31
upper limit	1.24

Statistical analysis title	Week 96: Pooled Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg

Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4654
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.52
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.881
upper limit	1.922

Statistical analysis title	Week 96: Pooled Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6184
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.051
upper limit	1.763

Secondary: Change From Baseline in MDS-UPDRS Subpart III Score at Week 52

End point title	Change From Baseline in MDS-UPDRS Subpart III Score at Week 52

End point description:

MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part III assessed the motor signs of PD and was administered by the rater (Range 0-132). Part III contained 33 scores based on 18 items. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. The ITT population was defined as all randomised subjects who received at least one dose of study treatment (BIIB054 or placebo). The mean values reported are the adjusted mean values.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	PC Period: Placebo	PC Period: BIIB054 250 mg (Early Start)	PC Period: BIIB054 1250 mg (Early Start)	PC Period: BIIB054 3500 mg (Early Start)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	53[21]	29[22]	58[23]	51[24]
Units: score on a scale				
arithmetic mean (standard error)	6.10 (± 1.083)	6.69 (± 1.419)	6.76 (± 1.046)	6.20 (± 1.104)

Notes:

[21] - Number of subjects analysed were subjects analysed for this endpoint.

[22] - Number of subjects analysed were subjects analysed for this endpoint.

[23] - Number of subjects analysed were subjects analysed for this endpoint.

[24] - Number of subjects analysed were subjects analysed for this endpoint.

Statistical analyses

Statistical analysis title	Week 52: Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 250 mg (Early Start)
Number of subjects included in analysis	82
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7274
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.742
upper limit	3.925

Statistical analysis title	Week 52: Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 1250 mg (Early Start)

Number of subjects included in analysis	111
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6385
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.094
upper limit	3.411

Statistical analysis title	Week 52: Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, baseline MDS-UPDRS score, baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 3500 mg (Early Start)
Number of subjects included in analysis	104
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9467
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.718
upper limit	2.91

Secondary: Change From Baseline in MDS-UPDRS Subpart III Score at Weeks 72 ad 96

End point title	Change From Baseline in MDS-UPDRS Subpart III Score at Weeks 72 ad 96

End point description:

MDS-UPDRS is a multimodal scale assessing impairment and disability consisting of 4 parts. Part III assessed the motor signs of PD and was administered by the rater (Range 0-132). Part III contained 33 scores based on 18 items. For each question a numeric score was assigned between 0-4, where 0 = Normal, 1 = Slight, 2 = Mild, 3 = Moderate, 4 = Severe. A higher score indicated more severe symptoms of PD. The ITT population was defined as all randomised subjects who received at least one dose of study treatment (BIIB054 or placebo). As prespecified in the protocol, the data for the delayed start BIIB054 were pooled from (Placebo/BIIB054 250/1250/3500 mg) for the analysis of this endpoint. The 'n' signifies number of subjects analysed at the specified time point. The mean values reported are the adjusted mean values.

End point type	Secondary

End point timeframe:
Baseline, Weeks 72 and 96

End point values	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled)	PC Period: Early Start BIIB054 250 mg	PC Period: Early Start BIIB054 1250 mg	PC Period: Early Start BIIB054 3500 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	100	55	102	100
Units: score on a scale				
arithmetic mean (standard error)				
Change from Baseline at Week 72 (n=68,32,62,64)	3.64 (± 1.027)	4.48 (± 1.404)	4.49 (± 1.038)	3.69 (± 1.048)
Change from Baseline at Week 96 (n=67,28,62,60)	4.49 (± 1.174)	5.14 (± 1.679)	4.39 (± 1.180)	5.17 (± 1.201)

Statistical analyses

Statistical analysis title	Week 72: Pooled Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg
Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6112
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.423
upper limit	4.114

Statistical analysis title	Week 72: Pooled Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time

interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg
Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9673
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.608
upper limit	2.719

Statistical analysis title	Week 72: Pooled Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.527
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.806
upper limit	3.52

Statistical analysis title	Week 96: Pooled Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 250 mg

Number of subjects included in analysis	155
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7455
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.65
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.274
upper limit	4.569

Statistical analysis title	Week 96: Pooled Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 1250 mg
Number of subjects included in analysis	202
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9506
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.192
upper limit	2.997

Statistical analysis title	Week 96: Pooled Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with delayed start group, 95% CI, and p-value were based on an MMRM model, with change from baseline in MDS-UPDRS score as dependent variable and with fixed effects of treatment group, time, treatment group-by-time interaction, region, PD subtype, prior use of PD medication, corresponding baseline MDS-UPDRS score, corresponding baseline MDS-UPDRS by time interaction, baseline striatum SBR values and baseline striatum SBR value by time interaction.

Comparison groups	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled) v PC Period: Early Start BIIB054 3500 mg

Number of subjects included in analysis	200
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6643
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.69
Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.422
upper limit	3.794

Secondary: Change From Baseline in Striatal Binding Ratio (SBR) in the Putamen as Measured by Single-Photon Emission Computed Tomography (SPECT) Imaging of the Dopamine Transporter (DaT) at Week 52

End point title	Change From Baseline in Striatal Binding Ratio (SBR) in the Putamen as Measured by Single-Photon Emission Computed Tomography (SPECT) Imaging of the Dopamine Transporter (DaT) at Week 52

End point description:

SBR in the putamen as measured by SPECT imaging of the dopamine transporter (DaT) with 123^I-ioflupane (DaTscan™). The pharmacodynamic population was defined as a subset of the ITT population with at least 1 post-baseline pharmacodynamic measurement. The mean values reported are the adjusted mean values.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	PC Period: Placebo	PC Period: BIIB054 250 mg (Early Start)	PC Period: BIIB054 1250 mg (Early Start)	PC Period: BIIB054 3500 mg (Early Start)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	91	52	97	84
Units: SBR				
arithmetic mean (standard error)	-0.093 (± 0.0151)	-0.098 (± 0.0199)	-0.102 (± 0.0146)	-0.125 (± 0.0155)

Statistical analyses

Statistical analysis title	Week 52: Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 250 mg (Early Start)
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8274
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.005
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0548
upper limit	0.0438

Statistical analysis title	Week 52: Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 1250 mg (Early Start)
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.6671
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.009
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0504
upper limit	0.0323

Statistical analysis title	Week 52: Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 3500 mg (Early Start)

Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1313
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.033
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0751
upper limit	0.0098

Secondary: Change From Baseline in SBR in the Striatum as Measured by SPECT Imaging of the DaT at Week 52

End point title	Change From Baseline in SBR in the Striatum as Measured by SPECT Imaging of the DaT at Week 52

End point description:

SBR in the striatum as measured by SPECT imaging of the DaT with 123^I-ioflupane (DaTscan™). The pharmacodynamic population was defined as a subset of the ITT population with at least 1 post-baseline pharmacodynamic measurement. The mean values reported are the adjusted mean values.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	PC Period: Placebo	PC Period: BIIB054 250 mg (Early Start)	PC Period: BIIB054 1250 mg (Early Start)	PC Period: BIIB054 3500 mg (Early Start)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	91	52	97	84
Units: SBR				
arithmetic mean (standard error)	-0.081 (± 0.0145)	-0.090 (± 0.0191)	-0.081 (± 0.0140)	-0.108 (± 0.0148)

Statistical analyses

Statistical analysis title	Week 52: Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 250 mg (Early Start)

Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7079
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.009
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0562
upper limit	0.0382

Statistical analysis title	Week 52: Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 1250 mg (Early Start)
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9835
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.04
upper limit	0.0392

Statistical analysis title	Week 52: Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 3500 mg (Early Start)
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1869
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.027

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0682
upper limit	0.0134

Secondary: Change From Baseline in SBR in the Caudate as Measured by SPECT Imaging of the DaT at Week 52

End point title	Change From Baseline in SBR in the Caudate as Measured by SPECT Imaging of the DaT at Week 52

End point description:

SBR in the caudate as measured by SPECT imaging of the DaT with 123^I-ioflupane (DaTscan™). The pharmacodynamic population was defined as a subset of the ITT population with at least 1 post-baseline pharmacodynamic measurement. The mean values reported are the adjusted mean values.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	PC Period: Placebo	PC Period: BIIB054 250 mg (Early Start)	PC Period: BIIB054 1250 mg (Early Start)	PC Period: BIIB054 3500 mg (Early Start)
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	91	52	97	84
Units: SBR				
arithmetic mean (standard error)	-0.067 (± 0.0166)	-0.075 (± 0.0219)	-0.060 (± 0.0161)	-0.089 (± 0.0171)

Statistical analyses

Statistical analysis title	Week 52: Placebo vs BIIB054 250 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 250 mg (Early Start)
Number of subjects included in analysis	143
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7585
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.008

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0625
upper limit	0.0456

Statistical analysis title	Week 52: Placebo vs BIIB054 1250 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 1250 mg (Early Start)
Number of subjects included in analysis	188
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7808
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	0.006
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0391
upper limit	0.052

Statistical analysis title	Week 52: Placebo vs BIIB054 3500 mg

Statistical analysis description:

Adjusted mean, difference with placebo, 95% CI, and p-value were based on an MMRM model, with change from baseline in DaT/SPECT parameter as dependent variable and with fixed effects of treatment group, region, time, treatment group-by-time interaction, baseline MDS-UPDRS part I+II+III total score, baseline MDS-UPDRS part I+II+III total score by time interaction, baseline DaT/SPECT values and baseline DaT/SPECT by time interaction.

Comparison groups	PC Period: Placebo v PC Period: BIIB054 3500 mg (Early Start)
Number of subjects included in analysis	175
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3532
Method	Mixed Model for Repeated Measures
Parameter estimate	Difference
Point estimate	-0.022
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.0691
upper limit	0.0248

Secondary: Percentage of Subjects With Anti-BIIB054 Antibodies in the Serum

End point title	Percentage of Subjects With Anti-BIIB054 Antibodies in the Serum

End point description:

The analysis population for immunogenicity was defined as all subjects in the safety population. As prespecified in the protocol, the data for the delayed start BIIB054 were pooled from Placebo/BIIB054 250/1250/3500 mg for the analysis of this endpoint.

End point type	Secondary

End point timeframe:

Up to Week 144

End point values	PC Period:Placebo to BIIB054 250/1250/3500 mg (DS-Pooled)	PC Period: Early Start BIIB054 250 mg	PC Period: Early Start BIIB054 1250 mg	PC Period: Early Start BIIB054 3500 mg
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	96	55	100	99
Units: percentage of subjects				
number (not applicable)	0	1.8	0	0

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 3 years

Adverse event reporting additional description:

Safety Population included all subjects who received at least one dose of the study treatment (BIIB054 250 mg, 1250 mg, 3500 mg).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	PC Period: Placebo

Reporting group description:

Subjects received BIIB054-matching placebo, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

Reporting group title	PC Period: BIIB054 250 mg (Early Start)

Reporting group description:

Subjects received BIIB054, 250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

Reporting group title	PC Period: BIIB054 1250 mg (Early Start)

Reporting group description:

Subjects received BIIB054, 1250 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

Reporting group title	PC Period: BIIB054 3500 mg (Early Start)

Reporting group description:

Subjects received BIIB054, 3500 mg, IV infusion, on Day 1 and then every 4 weeks for Year 1 in the PC Period.

Reporting group title	DBE Period: Placebo to BIIB054 250 mg (Delayed Start)

Reporting group description:

Subjects received BIIB054 250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.

Reporting group title	DBE Period: BIIB054 250 mg (Early Start)

Reporting group description:

Subjects received BIIB054 250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 250 mg in the PC period were included in this arm.

Reporting group title	DBE Period: Placebo to BIIB054 1250 mg (Delayed Start)

Reporting group description:

Subjects received BIIB054 1250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.

Reporting group title	DBE Period: Placebo to BIIB054 3500 mg (Delayed Start)

Reporting group description:

Subjects received BIIB054 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received placebo in the PC period were included in this arm.

Reporting group title	DBE Period: BIIB054 1250 mg (Early Start)

Reporting group description:

Subjects received BIIB054 1250 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 1250 mg in the PC period were included in this arm.

Reporting group title	DBE Period: BIIB054 3500 mg (Early Start)

Reporting group description:

Subjects received BIIB054 3500 mg, IV infusion from Year 2 up to EOS (approximately 3 years) in the DBE Period. Subjects who received BIIB054 3500 mg in the PC period were included in this arm.

Serious adverse events	PC Period: Placebo	PC Period: BIIB054 250 mg (Early Start)	PC Period: BIIB054 1250 mg (Early Start)
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 100 (7.00%)	4 / 55 (7.27%)	4 / 102 (3.92%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 100 (0.00%)	1 / 55 (1.82%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			

subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 100 (1.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 100 (1.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			

subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle strain			
subjects affected / exposed	1 / 100 (1.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post lumbar puncture syndrome			
subjects affected / exposed	1 / 100 (1.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Palpitations			

subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 55 (1.82%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Intracranial mass			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	1 / 100 (1.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			

Monoclonal B-cell lymphocytosis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	1 / 100 (1.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis toxic			
subjects affected / exposed	1 / 100 (1.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 55 (1.82%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			

subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	1 / 102 (0.98%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 55 (1.82%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Perirectal abscess			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			

subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 100 (1.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	PC Period: BIIB054 3500 mg (Early Start)	DBE Period: Placebo to BIIB054 250 mg (Delayed Start)	DBE Period: BIIB054 250 mg (Early Start)
Total subjects affected by serious adverse events			
subjects affected / exposed	6 / 100 (6.00%)	2 / 20 (10.00%)	3 / 52 (5.77%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma			
subjects affected / exposed	1 / 100 (1.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			

subjects affected / exposed	1 / 100 (1.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	1 / 100 (1.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	1 / 100 (1.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			

Arthropod sting			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 100 (1.00%)	0 / 20 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 100 (1.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle strain			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			

subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 100 (1.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Intracranial mass			
subjects affected / exposed	1 / 100 (1.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			

subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 100 (1.00%)	1 / 20 (5.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	1 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Monoclonal B-cell lymphocytosis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis toxic			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			

subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	1 / 52 (1.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Perirectal abscess			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			

subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DBE Period: Placebo to BIIB054 1250 mg (Delayed Start)	DBE Period: Placebo to BIIB054 3500 mg (Delayed Start)	DBE Period: BIIB054 1250 mg (Early Start)
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 37 (8.11%)	3 / 39 (7.69%)	5 / 100 (5.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glioblastoma			

subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive lobular breast carcinoma			
subjects affected / exposed	1 / 37 (2.70%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 37 (2.70%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			

subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Arthropod sting			
subjects affected / exposed	1 / 37 (2.70%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaw fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscle strain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post lumbar puncture syndrome			

subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ulna fracture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Palpitations			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus bradycardia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			

subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Intracranial mass			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Monoclonal B-cell lymphocytosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis toxic			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Nephrolithiasis			

subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar spinal stenosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rotator cuff syndrome			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spondylolisthesis			

subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Perirectal abscess			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19			
subjects affected / exposed	1 / 37 (2.70%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 39 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	1 / 100 (1.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	DBE Period: BIIB054 3500 mg (Early Start)		
Total subjects affected by serious adverse events			
subjects affected / exposed	7 / 94 (7.45%)		
number of deaths (all causes)	1		
number of deaths resulting from	1		

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Glioblastoma			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Impaired healing			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			

Acute respiratory failure				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Depression				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Arthropod sting				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Jaw fracture				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscle strain				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Pelvic fracture				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post lumbar puncture syndrome				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ulna fracture				
subjects affected / exposed	1 / 94 (1.06%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Palpitations				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus bradycardia				
subjects affected / exposed	0 / 94 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bradycardia				

subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	1 / 1		
Nervous system disorders			
Intracranial mass			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sciatica			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Monoclonal B-cell lymphocytosis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Small intestinal obstruction			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatitis toxic			

subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lumbar spinal stenosis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rotator cuff syndrome			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Spinal stenosis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spondylolisthesis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Perirectal abscess			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral infection			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
COVID-19			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
COVID-19 pneumonia			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	PC Period: Placebo	PC Period: BIIB054 250 mg (Early Start)	PC Period: BIIB054 1250 mg (Early Start)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	58 / 100 (58.00%)	32 / 55 (58.18%)	61 / 102 (59.80%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of skin			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	5 / 100 (5.00%)	2 / 55 (3.64%)	3 / 102 (2.94%)
occurrences (all)	5	3	4
Asthenia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Atelectasis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Diaphragmatic paralysis			

subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 100 (4.00%)	0 / 55 (0.00%)	9 / 102 (8.82%)
occurrences (all)	4	0	9
Depression			
subjects affected / exposed	1 / 100 (1.00%)	3 / 55 (5.45%)	3 / 102 (2.94%)
occurrences (all)	1	3	3
Insomnia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Investigations			
Blood cholesterol increased			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Transaminases increased			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	5 / 100 (5.00%)	5 / 55 (9.09%)	6 / 102 (5.88%)
occurrences (all)	7	13	6
Skin laceration			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Ligament rupture			

subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Ventricular extrasystoles			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	3 / 100 (3.00%)	4 / 55 (7.27%)	9 / 102 (8.82%)
occurrences (all)	3	4	10
Headache			
subjects affected / exposed	18 / 100 (18.00%)	6 / 55 (10.91%)	19 / 102 (18.63%)
occurrences (all)	37	8	43
Parkinson's disease			
subjects affected / exposed	1 / 100 (1.00%)	4 / 55 (7.27%)	9 / 102 (8.82%)
occurrences (all)	1	4	9
Paraesthesia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Restless legs syndrome			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Transient ischaemic attack			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Coagulopathy			

subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Paraesthesia ear			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	5 / 100 (5.00%)	3 / 55 (5.45%)	5 / 102 (4.90%)
occurrences (all)	5	3	5
Diarrhoea			
subjects affected / exposed	4 / 100 (4.00%)	5 / 55 (9.09%)	5 / 102 (4.90%)
occurrences (all)	4	7	6
Nausea			
subjects affected / exposed	6 / 100 (6.00%)	1 / 55 (1.82%)	6 / 102 (5.88%)
occurrences (all)	10	1	9
Dysphagia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Haemorrhoids			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	3 / 100 (3.00%)	1 / 55 (1.82%)	0 / 102 (0.00%)
occurrences (all)	4	1	0
Skin irritation			

subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	7 / 100 (7.00%)	5 / 55 (9.09%)	9 / 102 (8.82%)
occurrences (all)	10	8	12
Back pain			
subjects affected / exposed	8 / 100 (8.00%)	3 / 55 (5.45%)	8 / 102 (7.84%)
occurrences (all)	11	4	15
Musculoskeletal stiffness			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	2 / 100 (2.00%)	4 / 55 (7.27%)	5 / 102 (4.90%)
occurrences (all)	2	4	6
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	3 / 100 (3.00%)	1 / 55 (1.82%)	7 / 102 (6.86%)
occurrences (all)	3	1	9
Nasopharyngitis			
subjects affected / exposed	12 / 100 (12.00%)	10 / 55 (18.18%)	10 / 102 (9.80%)
occurrences (all)	13	13	12
Upper respiratory tract infection			
subjects affected / exposed	3 / 100 (3.00%)	2 / 55 (3.64%)	6 / 102 (5.88%)
occurrences (all)	5	2	7
Urinary tract infection			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Bronchitis			

subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Calcium deficiency			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	0 / 100 (0.00%)	0 / 55 (0.00%)	0 / 102 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	PC Period: BIIB054 3500 mg (Early Start)	DBE Period: Placebo to BIIB054 250 mg (Delayed Start)	DBE Period: BIIB054 250 mg (Early Start)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	63 / 100 (63.00%)	16 / 20 (80.00%)	25 / 52 (48.08%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of skin			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	1 / 52 (1.92%)
occurrences (all)	0	1	1
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	9 / 100 (9.00%)	1 / 20 (5.00%)	1 / 52 (1.92%)
occurrences (all)	25	1	1
Asthenia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	2	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal			

disorders			
Cough			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Oropharyngeal pain			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Atelectasis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Diaphragmatic paralysis			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Hypoxia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	5 / 100 (5.00%)	1 / 20 (5.00%)	1 / 52 (1.92%)
occurrences (all)	6	1	1
Depression			
subjects affected / exposed	3 / 100 (3.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	3	1	0
Insomnia			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	3 / 52 (5.77%)
occurrences (all)	0	0	3
Investigations			
Blood cholesterol increased			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Blood glucose increased			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Transaminases increased			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Weight decreased			

subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	14 / 100 (14.00%)	2 / 20 (10.00%)	10 / 52 (19.23%)
occurrences (all)	16	3	12
Skin laceration			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	3 / 52 (5.77%)
occurrences (all)	0	1	5
Ligament rupture			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Procedural pain			
subjects affected / exposed	0 / 100 (0.00%)	2 / 20 (10.00%)	0 / 52 (0.00%)
occurrences (all)	0	2	0
Cardiac disorders			
Ventricular extrasystoles			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	6 / 100 (6.00%)	0 / 20 (0.00%)	1 / 52 (1.92%)
occurrences (all)	7	0	1
Headache			
subjects affected / exposed	21 / 100 (21.00%)	3 / 20 (15.00%)	1 / 52 (1.92%)
occurrences (all)	25	3	2
Parkinson's disease			
subjects affected / exposed	8 / 100 (8.00%)	1 / 20 (5.00%)	1 / 52 (1.92%)
occurrences (all)	9	1	2
Paraesthesia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Restless legs syndrome			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Somnolence			

subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Transient ischaemic attack			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	2	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Coagulopathy			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Paraesthesia ear			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Vertigo			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	2	0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	6 / 100 (6.00%)	1 / 20 (5.00%)	1 / 52 (1.92%)
occurrences (all)	6	2	1
Diarrhoea			
subjects affected / exposed	6 / 100 (6.00%)	1 / 20 (5.00%)	1 / 52 (1.92%)
occurrences (all)	9	1	1
Nausea			
subjects affected / exposed	6 / 100 (6.00%)	1 / 20 (5.00%)	2 / 52 (3.85%)
occurrences (all)	7	1	4
Dysphagia			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Haemorrhoids			

subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Toothache			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	1 / 52 (1.92%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	5 / 100 (5.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences (all)	5	0	0
Skin irritation			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Skin ulcer			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 100 (11.00%)	1 / 20 (5.00%)	3 / 52 (5.77%)
occurrences (all)	11	1	3
Back pain			
subjects affected / exposed	13 / 100 (13.00%)	0 / 20 (0.00%)	5 / 52 (9.62%)
occurrences (all)	15	0	5
Musculoskeletal stiffness			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	1 / 100 (1.00%)	0 / 20 (0.00%)	2 / 52 (3.85%)
occurrences (all)	1	0	2
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	1 / 100 (1.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			

subjects affected / exposed	13 / 100 (13.00%)	2 / 20 (10.00%)	2 / 52 (3.85%)
occurrences (all)	14	2	2
Upper respiratory tract infection			
subjects affected / exposed	7 / 100 (7.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences (all)	11	0	0
Urinary tract infection			
subjects affected / exposed	0 / 100 (0.00%)	2 / 20 (10.00%)	3 / 52 (5.77%)
occurrences (all)	0	2	3
Bronchitis			
subjects affected / exposed	0 / 100 (0.00%)	0 / 20 (0.00%)	0 / 52 (0.00%)
occurrences (all)	0	0	0
Tooth infection			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	1 / 52 (1.92%)
occurrences (all)	0	1	1
Metabolism and nutrition disorders			
Calcium deficiency			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0
Decreased appetite			
subjects affected / exposed	0 / 100 (0.00%)	1 / 20 (5.00%)	0 / 52 (0.00%)
occurrences (all)	0	1	0

Non-serious adverse events	DBE Period: Placebo to BIIB054 1250 mg (Delayed Start)	DBE Period: Placebo to BIIB054 3500 mg (Delayed Start)	DBE Period: BIIB054 1250 mg (Early Start)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	22 / 37 (59.46%)	22 / 39 (56.41%)	51 / 100 (51.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Benign neoplasm of skin			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 37 (5.41%)	2 / 39 (5.13%)	5 / 100 (5.00%)
occurrences (all)	2	2	6
General disorders and administration site conditions			

Fatigue			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	4 / 100 (4.00%)
occurrences (all)	0	0	4
Asthenia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Erectile dysfunction			
subjects affected / exposed	0 / 37 (0.00%)	2 / 39 (5.13%)	1 / 100 (1.00%)
occurrences (all)	0	2	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	2 / 37 (5.41%)	1 / 39 (2.56%)	1 / 100 (1.00%)
occurrences (all)	2	1	2
Oropharyngeal pain			
subjects affected / exposed	1 / 37 (2.70%)	1 / 39 (2.56%)	2 / 100 (2.00%)
occurrences (all)	1	2	2
Atelectasis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Diaphragmatic paralysis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Hypoxia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 37 (2.70%)	2 / 39 (5.13%)	1 / 100 (1.00%)
occurrences (all)	1	2	1
Depression			
subjects affected / exposed	2 / 37 (5.41%)	0 / 39 (0.00%)	2 / 100 (2.00%)
occurrences (all)	2	0	2
Insomnia			
subjects affected / exposed	4 / 37 (10.81%)	2 / 39 (5.13%)	2 / 100 (2.00%)
occurrences (all)	4	2	2

Investigations			
Blood cholesterol increased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Blood glucose increased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Transaminases increased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	2 / 37 (5.41%)	3 / 39 (7.69%)	16 / 100 (16.00%)
occurrences (all)	4	4	21
Skin laceration			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Ligament rupture			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Ventricular extrasystoles			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	2 / 37 (5.41%)	2 / 39 (5.13%)	4 / 100 (4.00%)
occurrences (all)	2	2	4
Headache			

subjects affected / exposed	5 / 37 (13.51%)	5 / 39 (12.82%)	7 / 100 (7.00%)
occurrences (all)	9	15	14
Parkinson's disease			
subjects affected / exposed	1 / 37 (2.70%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Paraesthesia			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Restless legs syndrome			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Somnolence			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	1 / 100 (1.00%)
occurrences (all)	0	1	1
Transient ischaemic attack			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	2	0	0
Coagulopathy			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Paraesthesia ear			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Vertigo			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	2 / 37 (5.41%)	1 / 39 (2.56%)	4 / 100 (4.00%)
occurrences (all)	2	1	4
Diarrhoea			

subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	2 / 100 (2.00%)
occurrences (all)	0	0	3
Nausea			
subjects affected / exposed	2 / 37 (5.41%)	4 / 39 (10.26%)	4 / 100 (4.00%)
occurrences (all)	4	5	5
Dysphagia			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	0 / 100 (0.00%)
occurrences (all)	0	1	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 37 (0.00%)	1 / 39 (2.56%)	2 / 100 (2.00%)
occurrences (all)	0	1	2
Haemorrhoids			
subjects affected / exposed	1 / 37 (2.70%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Toothache			
subjects affected / exposed	0 / 37 (0.00%)	2 / 39 (5.13%)	0 / 100 (0.00%)
occurrences (all)	0	2	0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 37 (0.00%)	3 / 39 (7.69%)	0 / 100 (0.00%)
occurrences (all)	0	3	0
Skin irritation			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Skin ulcer			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	4 / 37 (10.81%)	3 / 39 (7.69%)	7 / 100 (7.00%)
occurrences (all)	5	4	8
Back pain			
subjects affected / exposed	4 / 37 (10.81%)	6 / 39 (15.38%)	5 / 100 (5.00%)
occurrences (all)	4	6	12
Musculoskeletal stiffness			

subjects affected / exposed	1 / 37 (2.70%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	1 / 37 (2.70%)	2 / 39 (5.13%)	2 / 100 (2.00%)
occurrences (all)	1	2	3
Infections and infestations			
Covid-19			
subjects affected / exposed	2 / 37 (5.41%)	2 / 39 (5.13%)	6 / 100 (6.00%)
occurrences (all)	2	2	6
Influenza			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	4 / 100 (4.00%)
occurrences (all)	0	0	4
Upper respiratory tract infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	2 / 37 (5.41%)	1 / 39 (2.56%)	2 / 100 (2.00%)
occurrences (all)	3	1	2
Bronchitis			
subjects affected / exposed	2 / 37 (5.41%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	2	0	0
Tooth infection			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	1 / 100 (1.00%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Calcium deficiency			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0
Decreased appetite			
subjects affected / exposed	0 / 37 (0.00%)	0 / 39 (0.00%)	0 / 100 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	DBE Period: BIIB054 3500 mg (Early Start)		

Total subjects affected by non-serious adverse events subjects affected / exposed	56 / 94 (59.57%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Benign neoplasm of skin subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 3		
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	2 / 94 (2.13%) 2		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) Asthenia subjects affected / exposed occurrences (all)	5 / 94 (5.32%) 14 1 / 94 (1.06%) 1		
Reproductive system and breast disorders Erectile dysfunction subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Oropharyngeal pain subjects affected / exposed occurrences (all) Atelectasis subjects affected / exposed occurrences (all) Diaphragmatic paralysis subjects affected / exposed occurrences (all) Hypoxia	2 / 94 (2.13%) 2 1 / 94 (1.06%) 1 0 / 94 (0.00%) 0 0 / 94 (0.00%) 0		

subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	5		
Depression			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	5		
Insomnia			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Investigations			
Blood cholesterol increased			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Blood glucose increased			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Transaminases increased			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	16 / 94 (17.02%)		
occurrences (all)	19		
Skin laceration			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Ligament rupture			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Procedural pain			

subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Cardiac disorders			
Ventricular extrasystoles			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 94 (4.26%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	12 / 94 (12.77%)		
occurrences (all)	13		
Parkinson's disease			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Paraesthesia			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Restless legs syndrome			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Somnolence			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Transient ischaemic attack			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Coagulopathy			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			

Paraesthesia ear subjects affected / exposed occurrences (all)	0 / 94 (0.00%) 0		
Vertigo subjects affected / exposed occurrences (all)	0 / 94 (0.00%) 0		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	7 / 94 (7.45%) 7		
Diarrhoea subjects affected / exposed occurrences (all)	3 / 94 (3.19%) 3		
Nausea subjects affected / exposed occurrences (all)	7 / 94 (7.45%) 11		
Dysphagia subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	0 / 94 (0.00%) 0		
Haemorrhoids subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Toothache subjects affected / exposed occurrences (all)	3 / 94 (3.19%) 4		
Skin and subcutaneous tissue disorders Rash subjects affected / exposed occurrences (all)	2 / 94 (2.13%) 2		
Skin irritation subjects affected / exposed occurrences (all)	0 / 94 (0.00%) 0		
Skin ulcer			

subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Back pain			
subjects affected / exposed	8 / 94 (8.51%)		
occurrences (all)	10		
Musculoskeletal stiffness			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	2		
Infections and infestations			
Covid-19			
subjects affected / exposed	3 / 94 (3.19%)		
occurrences (all)	3		
Influenza			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	5 / 94 (5.32%)		
occurrences (all)	5		
Upper respiratory tract infection			
subjects affected / exposed	0 / 94 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	2 / 94 (2.13%)		
occurrences (all)	4		
Bronchitis			
subjects affected / exposed	1 / 94 (1.06%)		
occurrences (all)	1		
Tooth infection			

subjects affected / exposed occurrences (all)	1 / 94 (1.06%) 1		
Metabolism and nutrition disorders Calcium deficiency subjects affected / exposed occurrences (all) Decreased appetite subjects affected / exposed occurrences (all)	 0 / 94 (0.00%) 0 0 / 94 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 August 2017	- Reduced the length of the treatment period and total duration of subject participation in the study. - Increased the number of subjects in the study and updated the sample size considerations supporting that change. - Modified inclusion criteria to reduce the time from past diagnosis with PD, to clarify clinical presentation details, and to indicate that subjects with Lewy body dementia would not be included in the study. - Modified inclusion criteria to lengthen the washout duration for levodopa treatment before entry into the study from 4 weeks to 12 weeks, to describe PD medications excluded, and to shorten the maximum duration of allowed prior PD treatment regimens from 3 months to 30 days. - Changed the dose levels from 3 mg/kg, 15 mg/kg, and 45 mg/kg (dosing based on body weight) to 250 mg, 1250 mg, and 3500 mg (fixed dosing) for both cohorts.
22 October 2017	Added a 1-year active-treatment dose-blinded period, extending the total study treatment period to 2 years.
15 August 2018	Added retesting and rescreening flexibility for subjects with nonclinically significant out-of-range laboratory results as well as those who cannot complete the Day 1 visit within the designated screening period.
12 February 2019	Extended the screening period by 1 week (7 days).
11 July 2019	Extended the active treatment dose-blinded period from Year 2 into Years 3 and 4. Dosing would end when the last subject has received the last dose in Year 2 (at Week 96), and the study would end when the last subject has had the Final Visit in Year 2 (12 weeks after the last dose [Week 108 visit]).
03 February 2020	Specified the timing of DaT/SPECT scans for certain subjects, as requested by the German Radiology Authority.
11 August 2020	This amendment was for 2 primary reasons: the addition of remote visits to ease the conduct of the study during any public health emergency and changes to the study objectives and endpoints to increase the scientific value of the study as detailed below. 1. Added the use of remote visits 2. Modified the study objectives and endpoints as follows: - Primary objective and endpoints: - Upgraded the evaluation of clinical efficacy of BIIB054 via MDS-UPDRS Total Score from an exploratory to primary objective along with its associated endpoints - Updated the objective to clearly state that the clinical efficacy of BIIB054 will be assessed via dose response using the change from baseline in MDS-UPDRS Total Score - Added the change from baseline to Week 72 evaluation to the primary endpoint - Moved the current primary objective and endpoint related to safety from primary to secondary objective and endpoint. - Added the following objects and/or endpoints and/or evaluation timepoints: - Added the secondary objective and endpoint: To evaluate the clinical efficacy of BIIB054 via MDS-UPDRS Total Score as measured by the change from baseline in MDS-UPDRS Total Score (Sum of Parts I, II, and III) at end of study - Added the secondary endpoint: Change from baseline to Week 52, Week 72, and end of study in MDS-UPDRS of Subparts I, II, and III (each part separately) -Removed the delineation between Year 1 (Placebo-Controlled Portion of the Study)

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study did not meet its primary endpoint for year 1 and failed to meet secondary endpoints resulting in the development of BIIB054 for Parkinson's disease to be discontinued and SPARK study was closed.

Notes: