



## Clinical trial results:

### A Phase 1/2 Multiple-Ascending-Dose Study With a Long-Term Open-Label Extension to Assess the Safety, Tolerability, Pharmacokinetics, Pharmacodynamics, and Effect on Disease Progression of BII105 Administered Intrathecally to Adults With Amyotrophic Lateral Sclerosis With or Without Poly-CAG Expansion in the Ataxin-2 Gene

#### Summary

EudraCT number	2020-000207-36
Trial protocol	NL
Global end of trial date	13 August 2024

#### Results information

Result version number	v1
This version publication date	28 August 2025
First version publication date	28 August 2025

#### Trial information

##### Trial identification

Sponsor protocol code	275AS101
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04494256
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	225 Binney Street, Cambridge, Massachusetts, United States, 02142
Public contact	Study Medical Director, Biogen, clinicaltrials@biogen.com
Scientific contact	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	13 August 2024
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	13 August 2024
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

Part 1: The primary objective was to evaluate the safety and tolerability of BIIB105 in participants with amyotrophic lateral sclerosis (ALS) or poly-CAG expansion (polyQ)-ALS. Part 2: The primary objective was to evaluate the long-term safety and tolerability of BIIB105 in participants with ALS or polyQ-ALS. Integrated Parts 1 and 2: The primary objective was to evaluate the long-term safety and tolerability of BIIB105 in participants with ALS or polyQ-ALS.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 September 2020
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: 81
Country: Number of subjects enrolled	Netherlands: 10
Country: Number of subjects enrolled	Canada: 7
Country: Number of subjects enrolled	Italy: 1
Worldwide total number of subjects	99
EEA total number of subjects	11

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)	69
From 65 to 84 years	30
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details:

Participants diagnosed with amyotrophic lateral sclerosis (ALS) and ALS associated with ataxin-2 (ATXN2) polyCAG expansion (polyQALS) took part in the study at investigational sites in the United States, Netherlands, Canada and Italy from 28 September 2020 to 13 August 2024.

### Pre-assignment

Screening details:

A total of 99 participants were randomised in Part 1 (placebo-controlled) of study to receive BIIB105 or placebo, of which 80 participants completed Part 1. A total of 70 eligible participants who completed Part 1 were enrolled into Part 2 (open-label) of study to receive BIIB105. Part 2 of study was terminated early based on Sponsor's decision.

### Period 1

Period 1 title	Part 1: Double blinded Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

### Arms

Are arms mutually exclusive?	No
<b>Arm title</b>	Part 1: Pooled Placebo 1+2

Arm description:

Participants with ALS and polyQ-ALS from Cohorts A, B, C1 and C2 received 3 loading doses of BIIB105-matched placebo, administered every 2 weeks (on Days 1, 15 and 29), followed by 2 maintenance doses administered once every 4 weeks (on Days 57 and 85), for a total of 5 doses over approximately 13 weeks. Participants with ALS and polyQ-ALS from Cohorts D1 and D2 received 3 loading doses of BIIB105- matched placebo administered every 2 weeks (on Days 1, 15, and 29), followed by 5 maintenance doses administered once every 4 weeks (on Days 57, 85, 113, 141, and 169), for a total of 8 doses over approximately 25 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intrathecal use

Dosage and administration details:

Administered as specified in the treatment arm.

<b>Arm title</b>	Part 1: Cohort A: BIIB105 5 mg
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Arm description:

Participants with ALS received 3 loading doses of BIIB105 5 mg, IT, administered every 2 weeks (on Days 1, 15, and 29), followed by 2 maintenance doses administered once every 4 weeks (on Days 57 and 85), for a total of 5 doses over approximately 13 weeks.

Arm type	Experimental
Investigational medicinal product name	BIIB105
Investigational medicinal product code	BIIB105
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intrathecal use

Dosage and administration details:

Administered as specified in the treatment arm.

<b>Arm title</b>	Part 1: Cohort B: BIIB105 20 mg
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Arm description:

Participants with ALS received 3 loading doses of BIIB105 20 mg, IT, administered every 2 weeks (on Days 1, 15, and 29), followed by 2 maintenance doses administered once every 4 weeks (on Days 57 and 85), for a total of 5 doses over approximately 13 weeks.

Arm type	Experimental
Investigational medicinal product name	BIIB105
Investigational medicinal product code	BIIB105
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intrathecal use

Dosage and administration details:

Administered as specified in the treatment arm.

<b>Arm title</b>	Part 1: Cohorts C1+C2: BIIB105 60 mg
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Arm description:

Participants from cohorts A-C2, who received 5, 20 and 60 mg doses of BIIB105 and placebo in Part 1 and completed Week 25 (Day 175) visit in Part 1 received BIIB105 60 mg in Part 2.

Arm type	Experimental
Investigational medicinal product name	BIIB105
Investigational medicinal product code	BIIB105
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intrathecal use

Dosage and administration details:

Administered as specified in the treatment arm.

<b>Arm title</b>	Part 1: Cohorts D1 + D2: BIIB105 120 mg
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Arm description:

Participants from Cohorts D1 and D2 who received 120 mg dose of BIIB105 and placebo in Part 1 and completed Week 25 (Day 176) visit in Part 1 received BIIB105 120 mg in Part 2.

Arm type	Experimental
Investigational medicinal product name	BIIB105
Investigational medicinal product code	BIIB105
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intrathecal use

Dosage and administration details:

Administered as specified in the treatment arm.

<b>Number of subjects in period 1</b>	Part 1: Pooled Placebo 1+2	Part 1: Cohort A: BIIB105 5 mg	Part 1: Cohort B: BIIB105 20 mg
Started	28	6	6
Completed	26	6	5
Not completed	2	0	1
Subject Withdrawal- Visit Burden/Scheduling Conflict	-	-	-
Adverse event, non-fatal	1	-	-
Reason Not Specified	-	-	-
Withdrawal by Subject - Other	1	-	1
Disease Progression - As Defined by the Protocol	-	-	-

Protocol deviation	-	-	-
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Number of subjects in period 1	Part 1: Cohorts C1+C2: BIIB105 60 mg	Part 1: Cohorts D1 + D2: BIIB105 120 mg
Started	11	48
Completed	9	34
Not completed	2	14
Subject Withdrawal- Visit Burden/Scheduling Conflict	1	3
Adverse event, non-fatal	-	3
Reason Not Specified	-	1
Withdrawal by Subject - Other	1	1
Disease Progression - As Defined by the Protocol	-	5
Protocol deviation	-	1

## Period 2

Period 2 title	Part 2: Open Label Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

## Arms

Are arms mutually exclusive?	No
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<b>Arm title</b>	Part 2: BIIB105 60 mg
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### Arm description:

Participants from cohorts A-C2, who received 5, 20 and 60 mg doses of BIIB105 and placebo in Part 1 and completed Week 25 (Day 175) visit in Part 1 received BIIB105 60 mg in Part 2.

Arm type	Experimental
Investigational medicinal product name	BIIB105
Investigational medicinal product code	BIIB105
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intrathecal use

### Dosage and administration details:

Administered as specified in the treatment arm.

<b>Arm title</b>	Part 2: BIIB105 120 mg
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### Arm description:

Participants from Cohorts D1 and D2 who received 120 mg dose of BIIB105 and placebo in Part 1 and completed Week 25 (Day 176) visit in Part 1 received BIIB105 120 mg in Part 2.

Arm type	Experimental
Investigational medicinal product name	BIIB105
Investigational medicinal product code	BIIB105
Other name	
Pharmaceutical forms	Solution for injection in vial
Routes of administration	Intrathecal use

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Dosage and administration details:

Administered as specified in the treatment arm.

<b>Number of subjects in period 2</b>	Part 2: BIIB105 60 mg	Part 2: BIIB105 120 mg
Started	19	51
Completed	0	0
Not completed	19	51
Adverse event, serious fatal	4	2
SubjectWithdrawal- VisitBurden/SchedulingConflict	5	4
Lack of Efficacy - Based on Subject Perception	-	1
Adverse event, non-fatal	-	2
Study Terminated by Sponsor	4	35
Withdrawal by Subject - Other	1	1
Disease Progression - As Defined by the Protocol	5	6

## Baseline characteristics

### Reporting groups

Reporting group title	Part 1: Pooled Placebo 1+2
Reporting group description: Participants with ALS and polyQ-ALS from Cohorts A, B, C1 and C2 received 3 loading doses of BIIB105-matched placebo, administered every 2 weeks (on Days 1, 15 and 29), followed by 2 maintenance doses administered once every 4 weeks (on Days 57 and 85), for a total of 5 doses over approximately 13 weeks. Participants with ALS and polyQ-ALS from Cohorts D1 and D2 received 3 loading doses of BIIB105- matched placebo administered every 2 weeks (on Days 1, 15, and 29), followed by 5 maintenance doses administered once every 4 weeks (on Days 57, 85, 113, 141, and 169), for a total of 8 doses over approximately 25 weeks.	
Reporting group title	Part 1: Cohort A: BIIB105 5 mg
Reporting group description: Participants with ALS received 3 loading doses of BIIB105 5 mg, IT, administered every 2 weeks (on Days 1, 15, and 29), followed by 2 maintenance doses administered once every 4 weeks (on Days 57 and 85), for a total of 5 doses over approximately 13 weeks.	
Reporting group title	Part 1: Cohort B: BIIB105 20 mg
Reporting group description: Participants with ALS received 3 loading doses of BIIB105 20 mg, IT, administered every 2 weeks (on Days 1, 15, and 29), followed by 2 maintenance doses administered once every 4 weeks (on Days 57 and 85), for a total of 5 doses over approximately 13 weeks.	
Reporting group title	Part 1: Cohorts C1+C2: BIIB105 60 mg
Reporting group description: Participants from cohorts A-C2, who received 5, 20 and 60 mg doses of BIIB105 and placebo in Part 1 and completed Week 25 (Day 175) visit in Part 1 received BIIB105 60 mg in Part 2.	
Reporting group title	Part 1: Cohorts D1 + D2: BIIB105 120 mg
Reporting group description: Participants from Cohorts D1 and D2 who received 120 mg dose of BIIB105 and placebo in Part 1 and completed Week 25 (Day 176) visit in Part 1 received BIIB105 120 mg in Part 2.	

Reporting group values	Part 1: Pooled Placebo 1+2	Part 1: Cohort A: BIIB105 5 mg	Part 1: Cohort B: BIIB105 20 mg
Number of subjects	28	6	6
Age Categorical			
Units: Subjects			

Age continuous			
Units: years			
arithmetic mean	59.9	60.5	49.3
standard deviation	± 11.15	± 5.72	± 17.84
Gender categorical			
Units: Subjects			
Female	9	2	3
Male	19	4	3
Ethnicity (NIH/OMB)			
Units: Subjects			
Hispanic or Latino	4	0	2
Not Hispanic or Latino	23	6	4
Unknown or Not Reported	1	0	0
Race/Ethnicity, Customized			
Units: Subjects			
American Indian or Alaska Native	0	0	0



Asian	3	0	0
Black or African American	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	22	6	5
Multiple	0	0	0
Not reported due to confidentiality regulations	1	0	0
Other	2	0	1

<b>Reporting group values</b>	Part 1: Cohorts C1+C2: BIIB105 60 mg	Part 1: Cohorts D1 + D2: BIIB105 120 mg	Total
Number of subjects	11	48	99
Age Categorical Units: Subjects			

Age continuous Units: years arithmetic mean standard deviation	53.3 ± 12.77	57.7 ± 11.45	-
Gender categorical Units: Subjects			
Female	3	14	31
Male	8	34	68
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	1	3	10
Not Hispanic or Latino	10	45	88
Unknown or Not Reported	0	0	1
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	0	1	1
Asian	0	1	4
Black or African American	0	1	1
Native Hawaiian or Other Pacific Islander	0	1	1
White	10	40	83
Multiple	0	1	1
Not reported due to confidentiality regulations	0	0	1
Other	1	3	7

## End points

### End points reporting groups

Reporting group title	Part 1: Pooled Placebo 1+2
Reporting group description: Participants with ALS and polyQ-ALS from Cohorts A, B, C1 and C2 received 3 loading doses of BIIB105-matched placebo, administered every 2 weeks (on Days 1, 15 and 29), followed by 2 maintenance doses administered once every 4 weeks (on Days 57 and 85), for a total of 5 doses over approximately 13 weeks. Participants with ALS and polyQ-ALS from Cohorts D1 and D2 received 3 loading doses of BIIB105-matched placebo administered every 2 weeks (on Days 1, 15, and 29), followed by 5 maintenance doses administered once every 4 weeks (on Days 57, 85, 113, 141, and 169), for a total of 8 doses over approximately 25 weeks.	
Reporting group title	Part 1: Cohort A: BIIB105 5 mg
Reporting group description: Participants with ALS received 3 loading doses of BIIB105 5 mg, IT, administered every 2 weeks (on Days 1, 15, and 29), followed by 2 maintenance doses administered once every 4 weeks (on Days 57 and 85), for a total of 5 doses over approximately 13 weeks.	
Reporting group title	Part 1: Cohort B: BIIB105 20 mg
Reporting group description: Participants with ALS received 3 loading doses of BIIB105 20 mg, IT, administered every 2 weeks (on Days 1, 15, and 29), followed by 2 maintenance doses administered once every 4 weeks (on Days 57 and 85), for a total of 5 doses over approximately 13 weeks.	
Reporting group title	Part 1: Cohorts C1+C2: BIIB105 60 mg
Reporting group description: Participants from cohorts A-C2, who received 5, 20 and 60 mg doses of BIIB105 and placebo in Part 1 and completed Week 25 (Day 175) visit in Part 1 received BIIB105 60 mg in Part 2.	
Reporting group title	Part 1: Cohorts D1 + D2: BIIB105 120 mg
Reporting group description: Participants from Cohorts D1 and D2 who received 120 mg dose of BIIB105 and placebo in Part 1 and completed Week 25 (Day 176) visit in Part 1 received BIIB105 120 mg in Part 2.	
Reporting group title	Part 2: BIIB105 60 mg
Reporting group description: Participants from cohorts A-C2, who received 5, 20 and 60 mg doses of BIIB105 and placebo in Part 1 and completed Week 25 (Day 175) visit in Part 1 received BIIB105 60 mg in Part 2.	
Reporting group title	Part 2: BIIB105 120 mg
Reporting group description: Participants from Cohorts D1 and D2 who received 120 mg dose of BIIB105 and placebo in Part 1 and completed Week 25 (Day 176) visit in Part 1 received BIIB105 120 mg in Part 2.	
Subject analysis set title	Early-start BIIB105 120 mg
Subject analysis set type	Full analysis
Subject analysis set description: Participants from Cohorts D1 and D2 from the Part 1 FAS population who received BIIB105 120 mg in Part 1, who may or may not have continued their study treatment in Part 2 were included in this group.	
Subject analysis set title	Placebo/Delayed-start BIIB105 120 mg
Subject analysis set type	Full analysis
Subject analysis set description: Participants from Cohorts D1 and D2 from the Part 1 FAS population who received placebo in Part 1, who may or may not have rolled over to Part 2 and started active treatment with BIIB105 were included in this group.	

### Primary: Part 1: Number of Participants with Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs)

End point title	Part 1: Number of Participants with Treatment-Emergent Adverse Events (TEAEs) and Treatment-Emergent Serious Adverse Events (TESAEs) <sup>[1]</sup>
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**End point description:**

An AE was any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An SAE was any untoward medical occurrence that at any dose results in death, places the participant at immediate risk of death, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, results in a congenital anomaly/birth defect, or is a medically important event. A TEAE/TESAE was defined as any AE/SAE with an onset date that is on or after the first dose of study drug or any pre-existing condition that has worsened in severity after the first dose of study drug. Part 1 safety analysis population included all randomised participants who received at least 1 dose of study treatment in Part 1.

End point type	Primary
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**End point timeframe:**

From first dose of the study drug in Part 1 up to end of follow up period in Part 1 (up to Day 260)

**Notes:**

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: Only descriptive statistics were planned for this endpoint.

<b>End point values</b>	Part 1: Pooled Placebo 1+2	Part 1: Cohort A: BIIB105 5 mg	Part 1: Cohort B: BIIB105 20 mg	Part 1: Cohorts C1+C2: BIIB105 60 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	6	6	11
Units: participants				
TEAEs	28	6	6	11
TESAEs	5	0	0	1

<b>End point values</b>	Part 1: Cohorts D1 + D2: BIIB105 120 mg			
Subject group type	Reporting group			
Number of subjects analysed	48			
Units: participants				
TEAEs	48			
TESAEs	7			

**Statistical analyses**

No statistical analyses for this end point

**Primary: Part 2: Number of Participants with TEAEs and TESAEs**

End point title	Part 2: Number of Participants with TEAEs and TESAEs <sup>[2]</sup>
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**End point description:**

An AE was any untoward medical occurrence in a participant or clinical investigation participant administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An SAE was any untoward medical occurrence that at any dose results in death, places the participant at immediate risk of death, requires inpatient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity, results in a congenital anomaly/birth defect, or is a medically important event. A TEAE/TESAE was defined as any AE/SAE with an onset date that is on or after the first dose of study drug or any pre-existing condition that has worsened in severity after the first dose of study drug. Part 1 safety analysis population included all randomised participants who received at least 1 dose of study treatment in Part 1.

End point type	Primary
End point timeframe:	
From first dose of the study in Part 2 up to end of follow up period in Part 2 (up to Day 1184)	
Notes:	
[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.	
Justification: Only descriptive statistics were planned for this endpoint.	

End point values	Part 2: BIIB105 60 mg	Part 2: BIIB105 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	51		
Units: participants				
TEAEs	19	49		
TESAEs	7	14		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part 1: Serum Concentrations of BIIB105

End point title	Part 1: Serum Concentrations of BIIB105 <sup>[3]</sup>
End point description:	
The Part 1 pharmacokinetic (PK) analysis population included all randomised participants who received at least 1 dose of study treatment and had at least 1 postdose serum and/or cerebrospinal fluid (CSF) BIIB105 measurement in Part 1. '99999' signifies that since no participant was evaluable, geometric mean and coefficient of variation were not estimated. 'Number analysed (n)' signifies number of participants evaluable for this outcome measure at the specified timepoint.	
End point type	Secondary
End point timeframe:	
Pre-dose and 1, 2, 4, 6 hours post-dose on days 1, 15, 29, 57, 85, 113, 141, 169 and on days 2, 8, 92, and 176	
Notes:	
[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.	
Justification: Part 1 arms were planned to be analysed for this end point.	

End point values	Part 1: Cohort A: BIIB105 5 mg	Part 1: Cohort B: BIIB105 20 mg	Part 1: Cohorts C1+C2: BIIB105 60 mg	Part 1: Cohorts D1 + D2: BIIB105 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	11	48
Units: nanograms per milliliter (ng/mL)				
geometric mean (geometric coefficient of variation)				
Day 1: Pre-dose (n=6,6,11,47)	0.00 (± 0.00)	0.00 (± 0.00)	0.00 (± 0.00)	0.00 (± 0.00)
Day 1: 1 HR post (n=6,6,11,47)	7.21 (± 500.18)	57.70 (± 285.30)	34.98 (± 465.78)	187.14 (± 351.05)
Day 1: 2 HR post-dose (n=6,6,11,47)	32.20 (± 177.01)	135.71 (± 109.27)	250.28 (± 101.57)	620.38 (± 132.37)
Day 1: 4 HR post-dose (n=6,6,11,47)	41.38 (± 125.95)	211.34 (± 68.29)	488.11 (± 51.22)	798.21 (± 86.03)

Day 1: 6 HR post-dose (n=6,6,11,47)	39.27 (± 102.97)	165.05 (± 60.63)	528.45 (± 61.49)	774.73 (± 60.51)
Day 2 (n=6,6,11,48)	6.76 (± 65.90)	29.07 (± 76.82)	118.70 (± 103.89)	260.03 (± 67.59)
Day 8 (n=6,6,11,44)	0.46 (± 18.74)	0.47 (± 36.02)	1.38 (± 74.15)	2.97 (± 43.60)
Day 15: Pre-dose (n=6,6,11,44)	0.00 (± 0.00)	0.50 (± 20.12)	0.78 (± 52.94)	1.90 (± 43.15)
Day 15: 1 HR post-dose (n=6,6,11,41)	3.85 (± 172.70)	22.24 (± 226.26)	56.01 (± 489.04)	257.73 (± 290.21)
Day 15: 2 HR post-dose (n=6,6,11,41)	16.89 (± 111.49)	94.51 (± 140.45)	246.73 (± 142.61)	972.44 (± 110.25)
Day 15: 4 HR post-dose (n=6,6,11,41)	30.07 (± 74.48)	139.75 (± 137.49)	363.86 (± 77.37)	996.20 (± 83.48)
Day 15: 6 HR post-dose (n=6,6,11,41)	27.28 (± 106.96)	139.00 (± 98.33)	411.61 (± 49.33)	897.25 (± 78.56)
Day 29: Pre-dose (n=6,6,11,43)	0.45 (± 24.48)	0.48 (± 28.47)	1.23 (± 64.84)	2.59 (± 59.99)
Day 29: 1 HR post-dose (n=6,6,11,42)	5.80 (± 117.90)	16.45 (± 557.48)	114.69 (± 226.87)	248.00 (± 152.63)
Day 29: 2 HR post-dose (n=6,6,11,42)	16.53 (± 121.68)	51.58 (± 602.03)	420.39 (± 116.92)	773.11 (± 95.92)
Day 29: 4 HR post-dose (n=6,6,11,42)	31.29 (± 120.91)	102.80 (± 200.28)	566.43 (± 71.83)	953.50 (± 80.75)
Day 29: 6 HR post-dose (n=6,6,11,40)	33.28 (± 127.43)	151.47 (± 87.99)	555.65 (± 52.83)	942.06 (± 69.00)
Day 57: Pre-dose (n=6,6,11,41)	0.00 (± 0.00)	0.41 (± 21.53)	0.79 (± 80.26)	1.83 (± 69.80)
Day 57: 1 HR post-dose (n=6,6,11,41)	7.45 (± 275.61)	7.98 (± 159.54)	44.33 (± 615.14)	227.06 (± 214.59)
Day 57: 2 HR post-dose (n=6,6,11,40)	22.05 (± 153.51)	26.59 (± 107.62)	274.02 (± 128.39)	713.36 (± 122.48)
Day 57: 4 HR post-dose (n=6,6,11,41)	27.72 (± 123.67)	74.60 (± 85.53)	471.12 (± 95.76)	887.82 (± 105.32)
Day 57: 6 HR post-dose (n=6,6,11,40)	27.33 (± 105.30)	89.38 (± 74.82)	416.91 (± 94.12)	889.54 (± 89.20)
Day 85: Pre-dose (n=6,5,10,41)	0.50 (± 0.00)	0.40 (± 33.26)	0.74 (± 64.453)	1.91 (± 113.18)
Day 85: 1 HR post-dose (n=6,5,10,40)	7.02 (± 111.81)	18.91 (± 240.40)	77.63 (± 142.75)	231.31 (± 236.91)
Day 85: 2 HR post-dose (n=6,5,10,40)	20.60 (± 95.33)	69.04 (± 265.82)	248.33 (± 84.14)	651.00 (± 127.92)
Day 85: 4 HR post-dose (n=6,5,10,40)	27.69 (± 111.28)	140.04 (± 91.00)	416.74 (± 80.90)	799.70 (± 89.26)
Day 85: 6 HR post-dose (n=6,5,10,40)	29.83 (± 119.17)	140.74 (± 50.95)	453.58 (± 74.39)	837.50 (± 73.65)
Day 92 (n=6,5,10,6)	0.43 (± 23.54)	0.56 (± 47.98)	2.05 (± 92.02)	4.47 (± 64.10)
Day 113: Pre-dose (n=0,0,0,39)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	1.95 (± 59.79)
Day 113: 1 HR post-dose (n=0,0,0,39)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	193.04 (± 198.68)
Day 113: 2 HR post-dose (n=0,0,0,39)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	632.28 (± 91.07)
Day 113: 4 HR post-dose (n=0,0,0,39)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	802.46 (± 91.76)
Day 113: 6 HR post-dose (n=0,0,0,39)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	858.58 (± 86.76)
Day 141: Pre-dose (n=0,0,0,38)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	2.07 (± 80.82)
Day 141: 1 HR post-dose (n=0,0,0,37)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	457.25 (± 162.57)
Day 141: 2 HR post-dose (n=0,0,0,37)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	949.31 (± 120.40)
Day 141: 4 HR post-dose (n=0,0,0,37)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	1044.80 (± 101.09)

Day 141: 6 HR post-dose (n=0,0,0,36)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	996.44 (± 85.54)
Day 169: Pre-dose (n=0,0,0,36)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	2.95 (± 153.02)
Day 169: 1 HR post-dose (n=0,0,0,35)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	288.75 (± 217.19)
Day 169: 2 HR post-dose (n=0,0,0,35)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	702.24 (± 107.10)
Day 169: 4 HR post-dose (n=0,0,0,36)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	816.90 (± 86.61)
Day 169: 6 HR post-dose (n=0,0,0,37)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	683.89 (± 158.85)
Day 176 (n=0,0,0,33)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	6.97 (± 132.41)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part 1: CSF Concentrations of BIIB105

End point title	Part 1: CSF Concentrations of BIIB105 <sup>[4]</sup>
End point description:	
The Part 1 PK analysis population included all randomised participants who received at least 1 dose of study treatment and had at least 1 postdose serum and/or CSF BIIB105 measurement in Part 1. '99999' signifies that since no participant was evaluable, geometric mean and coefficient of variation were not estimated. 'Number analysed (n)' signifies number of participants evaluable for this outcome measure at the specified time point.	
End point type	Secondary
End point timeframe:	
Pre-dose on Days 1, 15, 29, 57, 85, 113, 141, 169, and on days 92, 130, 175, and 176	
Notes:	
[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Part 1 arms were planned to be analysed for this end point.	

End point values	Part 1: Cohort A: BIIB105 5 mg	Part 1: Cohort B: BIIB105 20 mg	Part 1: Cohorts C1+C2: BIIB105 60 mg	Part 1: Cohorts D1 + D2: BIIB105 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	11	48
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1 : Pre-dose (n=6,6,11,47)	0.00 (± 0.00)	0.00 (± 0.00)	0.00 (± 0.00)	0.00 (± 0.00)
Day 15 : Pre-dose (n=6,6,11,44)	1.93 (± 41.54)	2.71 (± 55.21)	5.75 (± 62.33)	14.54 (± 82.48)
Day 29 : Pre-dose (n=6,6,11,43)	3.53 (± 33.52)	4.32 (± 52.42)	11.53 (± 49.38)	17.53 (± 95.18)
Day 57 : Pre-dose (n=6,6,11,42)	2.32 (± 28.96)	2.65 (± 46.23)	4.82 (± 59.33)	10.29 (± 79.90)
Day 85 : Pre-dose (n=6,5,10,40)	2.37 (± 30.35)	3.18 (± 72.73)	6.50 (± 36.23)	14.06 (± 77.42)
Day 92 (n=6,5,10,0)	5.01 (± 30.62)	6.28 (± 74.45)	25.51 (± 66.26)	99999 (± 99999)

Day 113 (n=0,0,0,40)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	17.08 (± 86.41)
Day 130 (n=6,5,10,0)	2.09 (± 32.22)	2.45 (± 57.06)	5.42 (± 40.72)	99999 (± 99999)
Day 141 (n=0,0,0,38)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	17.91 (± 84.83)
Day 169 (n=0,0,0,37)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	18.88 (± 74.23)
Day 175 (n=6,6,11,0)	1.16 (± 54.77)	1.16 (± 36.06)	2.68 (± 46.05)	99999 (± 99999)
Day 176 (n=0,0,0,2)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	17.35 (± 0.04)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part 1: Area Under the Serum Concentration-Time Curve From Time Zero to Infinity (AUCinf)

End point title	Part 1: Area Under the Serum Concentration-Time Curve From Time Zero to Infinity (AUCinf) <sup>[5]</sup>
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End point description:

AUCinf is the area under the serum concentration-time profile from time 0 extrapolated to infinite time. AUCinf was reported following dose 1 as planned. Part 1 PK analysis population included all randomised participants who received at least 1 dose of study treatment and had at least 1 postdose serum and/or CSF BIIB105 measurement in Part 1. 'Overall number of participants analysed' signifies number of participants with data available for outcome measure analysis.

End point type	Secondary
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End point timeframe:

Day 1

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Part 1 arms were planned to be analysed for this end point.

End point values	Part 1: Cohort A: BIIB105 5 mg	Part 1: Cohort B: BIIB105 20 mg	Part 1: Cohorts C1+C2: BIIB105 60 mg	Part 1: Cohorts D1 + D2: BIIB105 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	5	10	42
Units: Hour*nanogram per milliliter (h*ng/mL)				
geometric mean (geometric coefficient of variation)	934.22 (± 52.89)	3546.89 (± 53.50)	11258.45 (± 14.57)	24466.44 (± 30.24)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part 1: Area Under the Serum Concentration-Time Curve From Time Zero to Time of the Last Measurable Concentration (AUClast)

End point title	Part 1: Area Under the Serum Concentration-Time Curve From Time Zero to Time of the Last Measurable Concentration (AUClast) <sup>[6]</sup>
End point description: AUClast was reported following dose 1 as planned. Part 1 PK analysis population included all randomised participants who received at least 1 dose of study treatment and had at least 1 postdose serum and/or CSF BIIB105 measurement in Part 1. 'Overall number of participants analysed' signifies number of participants with data available for outcome measure analysis.	
End point type	Secondary
End point timeframe: Day 1	

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Part 1 arms were planned to be analysed for this end point.

End point values	Part 1: Cohort A: BIIB105 5 mg	Part 1: Cohort B: BIIB105 20 mg	Part 1: Cohorts C1+C2: BIIB105 60 mg	Part 1: Cohorts D1 + D2: BIIB105 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	11	44
Units: h*ng/mL				
geometric mean (geometric coefficient of variation)	574.59 (± 79.16)	3239.40 (± 52.73)	11758.68 (± 21.12)	24289.70 (± 30.50)

## Statistical analyses

No statistical analyses for this end point

## Secondary: Part 1: Maximum Observed Serum Concentration (Cmax)

End point title	Part 1: Maximum Observed Serum Concentration (Cmax) <sup>[7]</sup>
End point description: Part 1 PK analysis population included all randomised participants who received at least 1 dose of study treatment and had at least 1 postdose serum and/or CSF BIIB105 measurement in Part 1. '99999' signifies that since no participant was evaluable, geometric mean and coefficient of variation were not estimated. 'Number analysed (n)' signifies number of participants evaluable for this outcome measure at the specified timepoint.	
End point type	Secondary
End point timeframe: Days 1, 15, 29, 57, 85, 113, 141 and 169	

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: Part 1 arms were planned to be analysed for this end point.

End point values	Part 1: Cohort A: BIIB105 5 mg	Part 1: Cohort B: BIIB105 20 mg	Part 1: Cohorts C1+C2: BIIB105 60 mg	Part 1: Cohorts D1 + D2: BIIB105 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	11	48
Units: ng/mL				
geometric mean (geometric coefficient of variation)				



Day 1 (n=6,6,11,47)	52.18 (± 123.13)	227.80 (± 73.20)	644.10 (± 55.31)	1019.11 (± 76.61)
Day 15 (n=6,6,11,41)	31.03 (± 78.23)	165.37 (± 118.45)	495.03 (± 76.73)	1312.42 (± 93.96)
Day 29 (n=6,6,11,40)	34.11 (± 119.62)	164.15 (± 101.46)	616.02 (± 61.54)	1173.71 (± 75.74)
Day 57 (n=6,6,11,40)	31.92 (± 136.57)	94.60 (± 75.30)	513.84 (± 98.01)	1052.70 (± 99.57)
Day 85 (n=6,5,10,40)	31.43 (± 117.43)	168.38 (± 59.96)	476.91 (± 75.87)	1009.44 (± 84.68)
Day 113 (n=0,0,0,39)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	949.58 (± 83.69)
Day 141 (n=0,0,0,36)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	1243.75 (± 91.13)
Day 169 (n=0,0,0,36)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	957.24 (± 86.51)

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part 1: Time to Reach Maximum Observed Serum Concentration (Tmax)

End point title	Part 1: Time to Reach Maximum Observed Serum Concentration (Tmax) <sup>[8]</sup>
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End point description:

Part 1 PK analysis population included all randomised participants who received at least 1 dose of study treatment and had at least 1 postdose serum and/or CSF BIIB105 measurement in Part 1. '99999' signifies that since no participant was evaluable, median and full range were not estimated. 'Number analysed (n)' signifies number of participants evaluable for this outcome measure at the specified timepoint.

End point type	Secondary
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End point timeframe:

Days 1, 15, 29, 57, 85, 113, 141 and 169

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Part 1 arms were planned to be analysed for this end point.

End point values	Part 1: Cohort A: BIIB105 5 mg	Part 1: Cohort B: BIIB105 20 mg	Part 1: Cohorts C1+C2: BIIB105 60 mg	Part 1: Cohorts D1 + D2: BIIB105 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	6	11	48
Units: hour				
median (full range (min-max))				
Day 1 (n=6,6,11,47)	4.2 (2 to 6)	4.2 (2 to 6)	5.8 (2 to 23)	4.3 (1 to 24)
Day 15 (n=6,6,11,41)	5.0 (4 to 6)	5.0 (2 to 6)	5.9 (2 to 6)	4.1 (1 to 6)
Day 29 (n=6,6,11,40)	5.8 (4 to 6)	5.8 (2 to 6)	4.2 (2 to 6)	4.1 (2 to 6)
Day 57 (n=6,6,11,40)	5.8 (2 to 6)	5.0 (4 to 6)	4.2 (1 to 6)	4.5 (1 to 6)
Day 85 (n=6,5,10,40)	5.1 (4 to 6)	4.3 (4 to 6)	5.8 (4 to 6)	5.8 (2 to 6)
Day 113 (n=0,0,0,39)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	5.3 (1 to 6)
Day 141 (n=0,0,0,36)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	4.0 (1 to 6)

Day 169 (n=0,0,0,36)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	4.1 (1 to 6)
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## Statistical analyses

No statistical analyses for this end point

### Secondary: Part 1: Elimination Half-Life (t1/2) in Serum

End point title	Part 1: Elimination Half-Life (t1/2) in Serum <sup>[9]</sup>
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End point description:

Elimination half-life (t1/2) was reported following dose 1 as planned. Part 1 PK analysis population included all randomised participants who received at least 1 dose of study treatment and had at least 1 postdose serum and/or CSF BIIB105 measurement in Part 1. 'Overall number of participants' signifies number of participants evaluable for this outcome measure.

End point type	Secondary
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End point timeframe:

Day 1

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: Part 1 arms were planned to be analysed for this end point.

End point values	Part 1: Cohort A: BIIB105 5 mg	Part 1: Cohort B: BIIB105 20 mg	Part 1: Cohorts C1+C2: BIIB105 60 mg	Part 1: Cohorts D1 + D2: BIIB105 120 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	2	5	10	42
Units: hour				
median (full range (min-max))	14.0 (5 to 23)	26.6 (17 to 62)	41.7 (33 to 62)	39.8 (22 to 82)

## Statistical analyses

No statistical analyses for this end point

### Secondary: Part 1: Neurofilament Light Chain (NfL) Plasma Concentration Ratio to Baseline

End point title	Part 1: Neurofilament Light Chain (NfL) Plasma Concentration Ratio to Baseline
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End point description:

Plasma NfL ratio to baseline was reported in terms of geometric mean ratio. The Part 1 pharmacodynamic (PD) population included participants who received at least 1 dose of study treatment and have at least 1 available postdose evaluation of the respective PD endpoint in the study in Part 1. '99999' signifies that since one or no participant was evaluable, geometric mean and coefficient of variation were not estimated. 'Number analysed (n)' indicates the number of participants evaluable for the outcome measure at the specified timepoint.

End point type	Secondary
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End point timeframe:

Days 29, 57, 85, 113, 130 (For cohorts A, B, C1 and C2)/141 (For cohorts D1 and D2), 169 (For cohorts A, B, C1 and C2)/175 (For cohorts D1 and D2) and 241

End point values	Part 1: Pooled Placebo 1+2	Part 1: Cohort A: BIIB105 5 mg	Part 1: Cohort B: BIIB105 20 mg	Part 1: Cohorts C1+C2: BIIB105 60 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	28	6	6	11
Units: ratio				
geometric mean (geometric coefficient of variation)				
Day 29 (n=28,6,6,11,45)	1.04 (± 20.32)	1.05 (± 8.47)	0.83 (± 47.1)	1.06 (± 11.23)
Day 57 (n=28,6,6,11,44)	1.08 (± 19.91)	0.95 (± 14.63)	0.97 (± 15.95)	1.08 (± 20.43)
Day 85 (n=27,6,5,10,41)	0.99 (± 17.27)	0.99 (± 15.7)	0.98 (± 26.4)	1.11 (± 19.85)
Day 113 (n=17,0,0,0,40)	1.06 (± 19.95)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)
Day130(A,B,C1,C2)/Day141(D1,D2)n=25,6,5,10,39	1.09 (± 20.46)	1.10 (± 8.58)	0.92 (± 40.79)	0.99 (± 30.8)
Day 169 (A,B,C1,C2)/Day 175 (D1,D2)n=24,6,5,9,39	1.10 (± 23.67)	1.02 (± 22.58)	1.10 (± 24.55)	1.08 (± 29.73)
Day 214 (n=0,0,0,0,1)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Part 1: Cohorts D1 + D2: BIIB105 120 mg			
Subject group type	Reporting group			
Number of subjects analysed	47			
Units: ratio				
geometric mean (geometric coefficient of variation)				
Day 29 (n=28,6,6,11,45)	1.15 (± 72.72)			
Day 57 (n=28,6,6,11,44)	1.03 (± 21.7)			
Day 85 (n=27,6,5,10,41)	0.99 (± 19.62)			
Day 113 (n=17,0,0,0,40)	1.01 (± 21.77)			
Day130(A,B,C1,C2)/Day141(D1,D2)n=25,6,5,10,39	1.03 (± 41.35)			
Day 169 (A,B,C1,C2)/Day 175 (D1,D2)n=24,6,5,9,39	1.06 (± 24.92)			
Day 214 (n=0,0,0,0,1)	1.07 (± 99999)			

## Statistical analyses

No statistical analyses for this end point

## Secondary: Integrated Part 1 and Part 2: CSF PK Concentration of BIIB105

End point title	Integrated Part 1 and Part 2: CSF PK Concentration of BIIB105
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End point description:

Integrated data for Part 1 and Part 2 was analysed based on the PK population defined for Part 1. Part 1

PK analysis population included all randomised participants who received at least 1 dose of study treatment and had at least 1 postdose serum and/or CSF BIIB105 measurement in Part 1. '99999' signifies that since one or no participant was evaluable, geometric mean and coefficient of variation were not estimated. 'Overall number of participants analysed' signifies number of participants with data available for outcome measure analysis. 'Number analysed (n)': number of participants evaluable at the specified timepoint.

End point type	Secondary
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End point timeframe:

Predose on Days 1,15,29,57,85 and on Days

1,15,29,57,85,113,141,169,176,197,210,225,253,281,309,337,365,393,420,448,476,504,532,560,588,616,644,672,700,726,728

End point values	Early-start BIIB105 120 mg	Placebo/Delaye d-start BIIB105 120 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	17		
Units: ng/mL				
geometric mean (geometric coefficient of variation)				
Day 1 : Pre-dose (n=48,0)	0.13 (± 0.00)	99999 (± 99999)		
Day 1 (n=0,17)	99999 (± 99999)	0.15 (± 37.88)		
Day 15 : Pre-dose (n=44,0)	14.54 (± 82.48)	99999 (± 99999)		
Day 15 (n=1,17)	31.04 (± 99999)	12.93 (± 70.31)		
Day 29: Pre-dose (n=43,0)	17.53 (± 95.18)	99999 (± 99999)		
Day 29: (n=0,17)	99999 (± 99999)	18.62 (± 93.41)		
Day 57 : Pre-dose (n=42,0)	10.29 (± 79.90)	99999 (± 99999)		
Day 57 (n=0,14)	99999 (± 99999)	9.72 (± 49.08)		
Day 85 : Pre-dose (n=40,0)	14.06 (± 77.42)	99999 (± 99999)		
Day 85 (n=0,13)	99999 (± 99999)	14.54 (± 63.76)		
Day 113 (n=40,11)	17.08 (± 86.41)	20.70 (± 56.82)		
Day 141 (n=38,8)	17.91 (± 84.83)	24.50 (± 30.13)		
Day 169 (n=37,7)	18.88 (± 74.23)	19.32 (± 36.08)		
Day 176 (n=2,0)	17.35 (± 0.04)	99999 (± 99999)		
Day 197 (n=32,5)	24.88 (± 57.69)	24.99 (± 71.18)		
Day 210 (n=31,0)	49.04 (± 67.88)	99999 (± 99999)		
Day 225 (n=33,5)	24.14 (± 63.21)	30.52 (± 13.97)		
Day 253 (n=33,5)	23.54 (± 62.86)	21.68 (± 70.34)		
Day 281 (n=27,2)	26.51 (± 73.96)	23.79 (± 8.69)		

Day 309 (n=25,2)	27.14 (± 63.54)	30.47 (± 13.01)		
Day 337 (n=20,2)	31.34 (± 71.84)	22.11 (± 16.80)		
Day 365 (n=16,0)	30.16 (± 62.35)	99999 (± 99999)		
Day 393 (n=11,2)	23.56 (± 31.29)	15.36 (± 13.95)		
Day 420 (n=11,1)	25.84 (± 42.82)	21.91 (± 99999)		
Day 448 (n=9,1)	23.53 (± 40.75)	28.43 (± 99999)		
Day 476 (n=7,1)	30.87 (± 28.29)	25.95 (± 99999)		
Day 504 (n=6,0)	28.24 (± 38.06)	99999 (± 99999)		
Day 532 (n=5,0)	26.73 (± 44.19)	99999 (± 99999)		
Day 560 (n=4,0)	26.42 (± 36.82)	99999 (± 99999)		
Day 588 (n=3,0)	40.26 (± 68.00)	99999 (± 99999)		
Day 616 (n=3,0)	24.69 (± 109.22)	99999 (± 99999)		
Day 644 (n=4,0)	21.15 (± 39.95)	99999 (± 99999)		
Day 672 (n=3,0)	30.75 (± 48.18)	99999 (± 99999)		
Day 700 (n=2,0)	23.85 (± 1.63)	99999 (± 99999)		
Day 726 (n=1,0)	28.22 (± 99999)	99999 (± 99999)		
Day 728 (n=1,0)	26.28 (± 99999)	99999 (± 99999)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Integrated Part 1 and Part 2: Neurofilament Light Chain (NfL) Plasma Concentration Ratio to Baseline

End point title	Integrated Part 1 and Part 2: Neurofilament Light Chain (NfL) Plasma Concentration Ratio to Baseline
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End point description:

Plasma NfL ratio to baseline was reported in terms of geometric mean ratio. '99999' signifies that since one or no participant was evaluable, geometric mean and coefficient of variation were not estimated. 'Number analysed (n)' indicates the number of participants evaluable for the outcome measure at the specified timepoint.

End point type	Secondary
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End point timeframe:

Days 29, 57, 85, 113, 141, 169, 197, 225, 253, 281, 309, 337, 365, 393, 421, 449, 477, 505, 533, 561, 589, 617, 645, 673, 701

End point values	Early-start BIIB105 120 mg	Placebo/Delaye d-start BIIB105 120 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	47	19		
Units: ratio				
geometric mean (geometric coefficient of variation)				
Day 29 (n=45,19)	1.15 (± 72.72)	1.03 (± 22.35)		
Day 57 (n=44,19)	1.03 (± 21.7)	1.11 (± 18.9)		
Day 85 (n=41,18)	0.99 (± 19.62)	1.00 (± 18.00)		
Day 113 (n=40,17)	1.01 (± 21.77)	1.06 (± 19.95)		
Day 141 (n=39,16)	1.03 (± 41.35)	1.10 (± 20.84)		
Day 169 (n=39,16)	1.06 (± 24.92)	1.06 (± 20.33)		
Day 197 (n=31,13)	1.08 (± 28.28)	1.08 (± 23.6)		
Day 225 (n=31,13)	1.12 (± 38.42)	1.12 (± 31.12)		
Day 253 (n=26,12)	1.15 (± 28.4)	1.06 (± 27.71)		
Day 281 (n=22,10)	1.14 (± 26.57)	1.18 (± 21.26)		
Day 309 (n=17,9)	1.07 (± 31.81)	1.09 (± 24.46)		
Day 337 (n=12,6)	1.05 (± 38.67)	1.18 (± 23.3)		
Day 365 (n=11,4)	0.99 (± 32.42)	1.20 (± 29.59)		
Day 393 (n=9,4)	0.95 (± 48.05)	1.26 (± 24.88)		
Day 421 (n=9,3)	0.92 (± 36.61)	1.21 (± 58.82)		
Day 449 (n=7,3)	0.82 (± 28.9)	1.06 (± 32.94)		
Day 477 (n=5,2)	0.85 (± 23.15)	0.92 (± 32.52)		
Day 505 (n=3,2)	0.77 (± 25.18)	0.88 (± 46.94)		
Day 533 (n=4,2)	0.78 (± 14.58)	1.15 (± 32.24)		
Day 561 (n=3,0)	0.65 (± 14.63)	99999 (± 99999)		
Day 589 (n=3,2)	0.77 (± 39.28)	0.90 (± 23.38)		
Day 617 (n=3,1)	0.80 (± 38.48)	0.70 (± 99999)		
Day 645 (n=2,0)	0.76 (± 52.68)	99999 (± 99999)		
Day 673 (n=2,0)	0.66 (± 30.22)	99999 (± 99999)		
Day 701 (n=1,0)	0.54 (± 99999)	99999 (± 99999)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Integrated Part 1 and Part 2: Serum Concentration of BIIB105

End point title	Integrated Part 1 and Part 2: Serum Concentration of BIIB105
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End point description:

Serum concentration of BIIB105 was not analysed for Integrated Parts 1 and 2 as serum samples for BIIB105 concentration were not collected and analysed after completion of Part 1. Serum PK concentration for Part 1 is reported in another outcome measure.

End point type	Secondary
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End point timeframe:

Days 1, 2, 8, 15, 29, 57,85, 92, 113, 142, 169, 176, 337, 505, 673, 841 and 1009

End point values	Early-start BIIB105 120 mg	Placebo/Delaye d-start BIIB105 120 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	17		
Units: ng/mL				
geometric mean (geometric coefficient of variation)	99999 ( $\pm$ 99999)	99999 ( $\pm$ 99999)		

## Statistical analyses

No statistical analyses for this end point

## Secondary: Integrated Part 1 and Part 2: Change From Baseline in Percent Predicted Slow Vital Capacity (SVC)

End point title	Integrated Part 1 and Part 2: Change From Baseline in Percent Predicted Slow Vital Capacity (SVC)
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End point description:

Vital capacity was measured by means of the slow vital capacity (SVC) test using a facemask with the participant sitting upright. SVC was determined by performing at least 3 trials. If the difference between the two highest values of the three trials was  $\geq 10\%$ , then up to 5 trials were performed. The highest percent predicted SVC value at each visit was used for the analysis. Here, baseline is defined as Part 1 day 1 value prior to the study drug. As specified in SAP, change from baseline at Week 40 (Day 281) in least square means and corresponding standard errors was summarized using the analysis of covariance (ANCOVA) model. Negative change from baseline indicates decrease in lung function. Integrated data for Part 1 and Part 2 was analysed based on the clinical function population defined for Part 1. The Part 1 clinical function population included participants from the FAS population who have at least 1 postdose measurement in Part 1.

End point type	Secondary
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End point timeframe:

Baseline, Day 281

End point values	Early-start BIIB105 120 mg	Placebo/Delaye d-start BIIB105 120 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	19		
Units: percent predicted				
least squares mean (standard error)	-14.49 ( $\pm$ 4.093)	-14.41 ( $\pm$ 7.133)		

## Statistical analyses

Statistical analysis title	Early-start vs Placebo/Delayed-start BIIB105 120mg
Comparison groups	Placebo/Delayed-start BIIB105 120 mg v Early-start BIIB105

	120 mg
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9924 <sup>[10]</sup>
Method	ANCOVA
Parameter estimate	Least square (LS) mean difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-15.47
upper limit	15.32
Variability estimate	Standard error of the mean
Dispersion value	7.84

Notes:

[10] - ANCOVA model included: treatment as a fixed effect and adjusted for the following covariates: baseline disease duration since symptom onset, baseline percent predicted SVC, baseline plasma NfL, and use of riluzole or edaravone.

### Secondary: Integrated Part 1 and Part 2: Change From Baseline in Amyotrophic Lateral Sclerosis Functional Rating Scale - Revised (ALSFRS-R) Score

End point title	Integrated Part 1 and Part 2: Change From Baseline in Amyotrophic Lateral Sclerosis Functional Rating Scale - Revised (ALSFRS-R) Score
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End point description:

The ALSFRS-R is a questionnaire that measured degree of impairment in 4 functional domains: respiratory function, bulbar function, gross motor skills, and fine motor skills. Each domain consists of 3 items, each scored from 0 to 4, with higher scores representing better function. Each domain score can have maximum score of 12 calculated as the sum of scores of 3 items for that domain and the total possible score for ALSFRS-R is 48. The total score is the sum of the 4 functional domain scores or all individual item scores if no missing item scores are present. Here, baseline is defined as Part 1 day 1 value prior to the study drug. Negative change from baseline indicates disease progression. As specified in SAP change from baseline at Week 40 (Day 281) in least square means and corresponding standard errors was summarized using the ANCOVA model. Integrated data for Part 1 and 2 was analysed based on clinical function population defined for Part 1.

End point type	Secondary
End point timeframe:	
Baseline, Day 281	

End point values	Early-start BIIB105 120 mg	Placebo/Delayed-start BIIB105 120 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	19		
Units: score on a scale				
least squares mean (standard error)	-8.46 (± 1.105)	-8.26 (± 1.819)		

### Statistical analyses



<b>Statistical analysis title</b>	Early-start vs Placebo/Delayed-start BIIB105 120mg
Comparison groups	Early-start BIIB105 120 mg v Placebo/Delayed-start BIIB105 120 mg
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9203 <sup>[11]</sup>
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-4.14
upper limit	3.74
Variability estimate	Standard error of the mean
Dispersion value	2.01

Notes:

[11] - ANCOVA model included: treatment as a fixed effect and adjusted for the following covariates: baseline disease duration since symptom onset, baseline percent predicted SVC, baseline plasma NfL, and use of riluzole or edaravone.

### Secondary: Integrated Part 1 and Part 2: Change From Baseline in Muscle Strength as Measured by Handheld Dynamometry (HHD) Megascore

End point title	Integrated Part 1 and Part 2: Change From Baseline in Muscle Strength as Measured by Handheld Dynamometry (HHD) Megascore
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End point description:

Quantitative muscle strength was evaluated using HHD, which tested isometric strength of multiple muscles using standard participant positioning. Approximately 8 muscle groups were examined (per each side) in both upper and lower extremities. The muscle strength values were normalized to Z scores as (post-baseline measurements - mean)/SD and averaged to provide HHD overall megascore. The overall megascore was created by averaging Z scores, if no more than 14 ( $\leq 14$ ) measures are missing. Higher scores indicate greater strength. A negative change from baseline indicated decreased muscle strength. As specified in SAP, for the integrated analyses of Part 1 and 2, change from baseline at Week 40 (Day 281) in LS means and corresponding SE is reported at Week 40. Integrated data for Part 1 and 2 was analysed based on clinical function population defined for Part 1. Part 1 clinical function population: participants from FAS population who have at least 1 postdose measurement in Part 1.

End point type	Secondary
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End point timeframe:

Baseline, Day 281

End point values	Early-start BIIB105 120 mg	Placebo/Delayed-start BIIB105 120 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	19		
Units: score on a scale				
least squares mean (standard error)	-0.46 ( $\pm$ 0.066)	-0.28 ( $\pm$ 0.105)		

## Statistical analyses

<b>Statistical analysis title</b>	Early-start vs Placebo/Delayed-start BIIB105 120mg
Comparison groups	Early-start BIIB105 120 mg v Placebo/Delayed-start BIIB105 120 mg
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1069 <sup>[12]</sup>
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	-0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.41
upper limit	0.04
Variability estimate	Standard error of the mean
Dispersion value	0.12

Notes:

[12] - ANCOVA model included: treatment as a fixed effect and adjusted for the following covariates: baseline disease duration since symptom onset, baseline percent predicted SVC, baseline plasma NfL, and use of riluzole or edaravone.

## Secondary: Integrated Part 1 and Part 2: Time to Death or Permanent Ventilation

End point title	Integrated Part 1 and Part 2: Time to Death or Permanent Ventilation
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End point description:

Time to death or permanent ventilation is defined as the time from first dose to death or permanent ventilation ( ≥ 22 hours of mechanical ventilation [invasive or noninvasive] per day for ≥ 21 consecutive days), whichever comes first. Participants who did not meet the endpoint definition were censored on the date of participant's last contact in Part 1 or Part 2. Time to death or permanent ventilation data was summarized using Kaplan-Meier curves based on randomisation in Part 1. '99999' signifies median and 95% confidence interval (CI) were not estimable due to low number events of permanent ventilation or death. Integrated data for Part 1 and Part 2 was analysed based on the FAS population defined for Part 1. Part 1 FAS population included all randomised participants who received at least 1 dose of study treatment in Part 1 and 2.

End point type	Secondary
End point timeframe:	
Baseline up to Day 1184	

End point values	Early-start BIIB105 120 mg	Placebo/Delayed-start BIIB105 120 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	19		
Units: weeks				
median (confidence interval 95%)	99999 (72.7 to 99999)	99999 (99999 to 99999)		

## Statistical analyses

<b>Statistical analysis title</b>	Early-start vs Placebo/Delayed-start BIIB105 120mg
Comparison groups	Early-start BIIB105 120 mg v Placebo/Delayed-start BIIB105 120 mg
Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1003
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	4.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.433
upper limit	42.587

## Secondary: Integrated Parts 1 and 2: Time to Death

End point title	Integrated Parts 1 and 2: Time to Death
End point description:	
Time to death was defined as the time from first dose to death. Integrated data for Part 1 and Part 2 was analysed based on the FAS population defined for Part 1. Part 1 FAS population included all randomised participants who received at least 1 dose of study treatment in Part 1 and 2. '99999' signifies median and 95% confidence interval (CI) were not estimable due to low number events of death. Integrated data for Part 1 and Part 2 was analysed based on the FAS population defined for Part 1. Part 1 FAS population included all randomised participants who received at least 1 dose of study treatment in Part 1 and 2.	
End point type	Secondary
End point timeframe:	
Baseline up to Day 1184	

End point values	Early-start BIIB105 120 mg	Placebo/Delayed-start BIIB105 120 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	48	19		
Units: weeks				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

## Statistical analyses

<b>Statistical analysis title</b>	Early-start vs Placebo/Delayed-start BIIB105 120mg
Comparison groups	Early-start BIIB105 120 mg v Placebo/Delayed-start BIIB105 120 mg

Number of subjects included in analysis	67
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1143
Method	Kaplan-Meier product limit method
Parameter estimate	Hazard ratio (HR)
Point estimate	99999
Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	99999

### Secondary: Integrated Part 1 and Part 2: Time to Death, Incorporating Post-Study Withdrawal or Study Completion Vital Status Data

End point title	Integrated Part 1 and Part 2: Time to Death, Incorporating Post-Study Withdrawal or Study Completion Vital Status Data
End point description:	
End point type	Secondary
End point timeframe:	
Up to Day 1184	

End point values	Early-start BIIB105 120 mg	Placebo/Delayed-start BIIB105 120 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	0 <sup>[13]</sup>	0 <sup>[14]</sup>		
Units: hour				
median (full range (min-max))	( to )	( to )		

Notes:

[13] - Time to death analysis with post-study vital status was not done as data were unavailable.

[14] - Time to death analysis with post-study vital status was not done as data were unavailable.

### Statistical analyses

No statistical analyses for this end point

### Post-hoc: Part 2: Serum Concentration of BIIB105

End point title	Part 2: Serum Concentration of BIIB105
End point description:	
The PK analysis population is defined as all randomised participants who received at least 1 dose of study treatment and have at least 1 postdose serum and/or CSF BIIB105 measurement. '99999' signifies that since no participant was evaluable, geometric mean and coefficient of variation were not estimated. 'Number analysed' indicates the number of participants evaluable at the specified time point.	
End point type	Post-hoc
End point timeframe:	
Days 1, 169, 337, 505 and 673	

<b>End point values</b>	Part 2: BIIB105 60 mg	Part 2: BIIB105 120 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	19	51		
Units: ng/ml				
geometric mean (geometric coefficient of variation)				
Day 1 (n=19,50)	0.50 (± 0.00)	1.47 (± 139.00)		
Day 169 (n=11,18)	1.25 (± 186.75)	3.50 (± 151.48)		
Day 337 (n=9,7)	2.46 (± 333.20)	2.50 (± 95.95)		
Day 505(n=7,1)	3.53 (± 340.11)	8.54 (± 0.00)		
Day 673 (n=3,0)	18.89 (± 164.41)	99999 (± 99999)		

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From first dose of study drug up to end of study (up to 1416 days)

Adverse event reporting additional description:

The Part 1 safety analysis population included all randomised participants who received at least 1 dose of study treatment in Part 1. The Part 2 safety analysis population included all participants who received at least 1 dose of study treatment in Part 2.

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	27.0
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### Reporting groups

Reporting group title	Part 1: Pooled Placebo 1+2
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Reporting group description:

Participants with ALS and polyQ-ALS from Cohorts A, B, C1 and C2 received 3 loading doses of BIIB105-matched placebo, administered every 2 weeks (on Days 1, 15 and 29), followed by 2 maintenance doses administered once every 4 weeks (on Days 57 and 85), for a total of 5 doses over approximately 13 weeks. Participants with ALS and polyQ-ALS from Cohorts D1 and D2 received 3 loading doses of BIIB105-matched placebo administered every 2 weeks (on Days 1, 15, and 29), followed by 5 maintenance doses administered once every 4 weeks (on Days 57, 85, 113, 141, and 169), for a total of 8 doses over approximately 25 weeks.

Reporting group title	Part 1: Cohort A: BIIB105 5 mg
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Reporting group description:

Participants with ALS received 3 loading doses of BIIB105 5mg, IT, administered every 2 weeks (on Days 1, 15, and 29), followed by 2 maintenance doses administered once every 4 weeks (on Days 57 and 85), for a total of 5 doses over approximately 13 weeks.

Reporting group title	Part 1: Cohort B: BIIB105 20 mg
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Reporting group description:

Participants with ALS received 3 loading doses of BIIB105 20 mg, IT, administered every 2 weeks (on Days 1, 15, and 29), followed by 2 maintenance doses administered once every 4 weeks (on Days 57 and 85), for a total of 5 doses over approximately 13 weeks.

Reporting group title	Part 2: BIIB105 120 mg
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Reporting group description:

Participants from Cohorts D1 and D2 who received 120 mg dose of BIIB105 and placebo in Part 1 and completed Week 25 (Day 176) visit in Part 1 received BIIB105 120 mg in Part 2.

Reporting group title	Part 1: Cohorts D1 + D2: BIIB105 120 mg
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Reporting group description:

Participants with ALS (Cohort D1) and polyQ-ALS (Cohort D2) received BIIB105 120 mg, IT, as 3 loading doses administered every 2 weeks (on Days 1, 15, and 29), followed by 5 maintenance doses administered once every 4 weeks (on Days 57, 85, 113, 141, and 169), for a total of 8 doses over approximately 25 weeks.

Reporting group title	Part 2: BIIB105 60 mg
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Reporting group description:

Participants from cohorts A-C2, who received 5, 20 and 60 mg doses of BIIB105 and placebo in Part 1 and completed Week 25 (Day 175) visit in Part 1 received BIIB105 60 mg in Part 2.

Reporting group title	Part 1: Cohorts C1+C2: BIIB105 60 mg
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Reporting group description:

Participants with ALS (Cohort C1) and polyQ-ALS (Cohort C2) received 3 loading doses of BIIB105 60 mg, IT, administered every 2 weeks (on Days 1, 15, and 29), followed by 2 maintenance doses administered once every 4 weeks (on Days 57 and 85), for a total of 5 doses over approximately 13 weeks.

<b>Serious adverse events</b>	<b>Part 1: Pooled Placebo 1+2</b>	<b>Part 1: Cohort A: BIIB105 5 mg</b>	<b>Part 1: Cohort B: BIIB105 20 mg</b>
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 28 (17.86%)	0 / 6 (0.00%)	0 / 6 (0.00%)
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)			
Plasma cell myeloma			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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			
Craniofacial fracture			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (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	2 / 28 (7.14%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (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
Procedural pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Humerus fracture			

subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Tendon rupture			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (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
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Balance disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Cerebral venous sinus thrombosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Radiculopathy			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Toxic encephalopathy			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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			
Ileus			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Food poisoning			



subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Dysphagia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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			
Cholecystitis acute			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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			
Chronic respiratory failure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Aspiration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Acute respiratory failure			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Pulmonary embolism			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Dyspnoea			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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 failure			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (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
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Seronegative arthritis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (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
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Pneumonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Pneumonia aspiration			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (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
Pulmonary sepsis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Sepsis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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

Urosepsis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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
Malnutrition			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (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

<b>Serious adverse events</b>	Part 2: BIIB105 120 mg	Part 1: Cohorts D1 + D2: BIIB105 120 mg	Part 2: BIIB105 60 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	14 / 51 (27.45%)	7 / 48 (14.58%)	7 / 19 (36.84%)
number of deaths (all causes)	6	0	4
number of deaths resulting from adverse events	4	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma cell myeloma			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 19 (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
Injury, poisoning and procedural complications			
Craniofacial fracture			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (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	2 / 51 (3.92%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			

subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (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
Procedural pain			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (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	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (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
Humerus fracture			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (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
Tendon rupture			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (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			
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Balance disorder			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (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
Cerebral venous sinus thrombosis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 19 (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
Radiculopathy			

subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (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
Toxic encephalopathy			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (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
Gastrointestinal disorders			
Ileus			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (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
Food poisoning			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (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
Hepatobiliary disorders			
Cholecystitis acute			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (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			
Chronic respiratory failure			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (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
Aspiration			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Acute respiratory failure			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary embolism			
subjects affected / exposed	1 / 51 (1.96%)	1 / 48 (2.08%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	3 / 51 (5.88%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	2 / 51 (3.92%)	1 / 48 (2.08%)	2 / 19 (10.53%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 2
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seronegative arthritis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (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			
Covid-19			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pneumonia aspiration			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (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
Pulmonary sepsis			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 19 (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
Sepsis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 51 (1.96%)	1 / 48 (2.08%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	1 / 51 (1.96%)	1 / 48 (2.08%)	0 / 19 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0

<b>Serious adverse events</b>	Part 1: Cohorts C1+C2: BIIB105 60 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 11 (9.09%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Plasma cell myeloma			

subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Craniofacial fracture			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subdural haematoma			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Procedural pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Jaw fracture			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Humerus fracture			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tendon rupture			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			



Amyotrophic lateral sclerosis subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Balance disorder subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cerebral venous sinus thrombosis subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Radiculopathy subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Toxic encephalopathy subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders Ileus subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Food poisoning subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysphagia subjects affected / exposed	1 / 11 (9.09%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			

Cholecystitis acute			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Chronic respiratory failure			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspiration			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seronegative arthritis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Covid-19			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary sepsis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Urosepsis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			

Dehydration			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malnutrition			
subjects affected / exposed	0 / 11 (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 %

<b>Non-serious adverse events</b>	Part 1: Pooled Placebo 1+2	Part 1: Cohort A: BIIB105 5 mg	Part 1: Cohort B: BIIB105 20 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	27 / 28 (96.43%)	6 / 6 (100.00%)	6 / 6 (100.00%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Flushing			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypertension			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Asthenia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Chills			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Fatigue			

subjects affected / exposed	3 / 28 (10.71%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Medical device site burn			
subjects affected / exposed	0 / 28 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Pyrexia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	2 / 28 (7.14%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 28 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Oedema			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Swelling face			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Vaccination site pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 28 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Breast pain			

subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	4 / 28 (14.29%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	5	0	0
Dyspnoea			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Dyspnoea at rest			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Laryngospasm			
subjects affected / exposed	0 / 28 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Nasal congestion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasal polyps			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Respiratory failure			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Respiratory tract congestion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Affect lability			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Insomnia			

subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Depression			
subjects affected / exposed	0 / 28 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Confusional state			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sleep disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device dislocation			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood uric acid increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Breath sounds abnormal			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Csf protein increased			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Csf white blood cell count increased			

subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Weight decreased subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Bone contusion subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Concussion subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Fall subjects affected / exposed occurrences (all)	14 / 28 (50.00%) 32	1 / 6 (16.67%) 1	4 / 6 (66.67%) 9
Femur fracture subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Head injury subjects affected / exposed occurrences (all)	2 / 28 (7.14%) 2	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Immunisation reaction subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Post procedural inflammation			



subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Neurological procedural complication			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Post lumbar puncture syndrome			
subjects affected / exposed	7 / 28 (25.00%)	3 / 6 (50.00%)	1 / 6 (16.67%)
occurrences (all)	15	4	1
Post procedural contusion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Post procedural discomfort			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	3	0	1
Musculoskeletal procedural complication			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Post procedural swelling			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Procedural complication			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Procedural dizziness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Procedural nausea			
subjects affected / exposed	2 / 28 (7.14%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Procedural pain			
subjects affected / exposed	15 / 28 (53.57%)	5 / 6 (83.33%)	4 / 6 (66.67%)
occurrences (all)	34	19	10
Skin laceration			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1

Rib fracture			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Road traffic accident			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Shoulder fracture			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Skin abrasion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Procedural vomiting			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Stoma site discharge			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Stoma site pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Cluster headache			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Clonus			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Brain fog			
subjects affected / exposed	0 / 28 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Balance disorder			

subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Cognitive disorder			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	3 / 28 (10.71%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Dysgeusia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Head discomfort			
subjects affected / exposed	2 / 28 (7.14%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Muscle contractions involuntary			
subjects affected / exposed	2 / 28 (7.14%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Loss of consciousness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hypoaesthesia			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hemihypoaesthesia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	12 / 28 (42.86%)	3 / 6 (50.00%)	4 / 6 (66.67%)
occurrences (all)	19	4	15
Menstrual headache			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Neuropathy peripheral			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Syncope			

subjects affected / exposed	2 / 28 (7.14%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Speech disorder			
subjects affected / exposed	0 / 28 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Radicular pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Post-traumatic headache			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	1	0	1
Pleocytosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Parosmia			
subjects affected / exposed	0 / 28 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Paraesthesia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 28 (0.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	0	1	0
Hypoacusis			

subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Tinnitus subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Vertigo positional subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Eye disorders Conjunctival haemorrhage subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 6 (0.00%) 0	1 / 6 (16.67%) 1
Abdominal distension subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Constipation subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Dysphagia subjects affected / exposed occurrences (all)	1 / 28 (3.57%) 1	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Food poisoning subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Gastritis subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	0 / 6 (0.00%) 0	0 / 6 (0.00%) 0
Mouth ulceration subjects affected / exposed occurrences (all)	0 / 28 (0.00%) 0	1 / 6 (16.67%) 1	0 / 6 (0.00%) 0
Haematemesis			

subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Hiatus hernia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Nausea			
subjects affected / exposed	3 / 28 (10.71%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	3	0	2
Oesophagitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Oral dysaesthesia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	2 / 28 (7.14%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Hyperhidrosis			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0

Nodular rash			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	2 / 28 (7.14%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Rash			
subjects affected / exposed	1 / 28 (3.57%)	1 / 6 (16.67%)	1 / 6 (16.67%)
occurrences (all)	1	5	1
Skin lesion			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Ecchymosis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	2 / 28 (7.14%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Pollakiuria			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 28 (7.14%)	2 / 6 (33.33%)	3 / 6 (50.00%)
occurrences (all)	4	3	6
Muscle tightness			
subjects affected / exposed	2 / 28 (7.14%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Back pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	2 / 6 (33.33%)
occurrences (all)	1	0	3
Joint swelling			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Mobility decreased			

subjects affected / exposed	2 / 28 (7.14%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	4	0	0
Muscle spasms			
subjects affected / exposed	6 / 28 (21.43%)	1 / 6 (16.67%)	2 / 6 (33.33%)
occurrences (all)	9	3	2
Myalgia			
subjects affected / exposed	2 / 28 (7.14%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 28 (3.57%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	1	0	0
Muscular weakness			
subjects affected / exposed	3 / 28 (10.71%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Neck pain			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	1 / 6 (16.67%)
occurrences (all)	0	0	1
Pain in extremity			
subjects affected / exposed	7 / 28 (25.00%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	9	1	0
Infections and infestations			
Hordeolum			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Device related infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis viral			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0



Covid-19			
subjects affected / exposed	2 / 28 (7.14%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	2	0	0
Influenza			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	2 / 28 (7.14%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	3	0	0
Pneumonia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	2 / 28 (7.14%)	1 / 6 (16.67%)	0 / 6 (0.00%)
occurrences (all)	2	1	0
Urinary tract infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Stoma site infection			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperuricaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Hyperglycaemia			
subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0
Dehydration			

subjects affected / exposed	0 / 28 (0.00%)	0 / 6 (0.00%)	0 / 6 (0.00%)
occurrences (all)	0	0	0

<b>Non-serious adverse events</b>	Part 2: BIIB105 120 mg	Part 1: Cohorts D1 + D2: BIIB105 120 mg	Part 2: BIIB105 60 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	45 / 51 (88.24%)	47 / 48 (97.92%)	19 / 19 (100.00%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Flushing			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Hypertension			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 51 (3.92%)	1 / 48 (2.08%)	0 / 19 (0.00%)
occurrences (all)	3	1	0
Asthenia			
subjects affected / exposed	4 / 51 (7.84%)	5 / 48 (10.42%)	0 / 19 (0.00%)
occurrences (all)	7	7	0
Chills			
subjects affected / exposed	1 / 51 (1.96%)	4 / 48 (8.33%)	0 / 19 (0.00%)
occurrences (all)	2	6	0
Fatigue			
subjects affected / exposed	7 / 51 (13.73%)	8 / 48 (16.67%)	3 / 19 (15.79%)
occurrences (all)	10	9	5
Medical device site burn			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	5 / 51 (9.80%)	2 / 48 (4.17%)	1 / 19 (5.26%)
occurrences (all)	6	2	1
Oedema peripheral			

subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	2 / 48 (4.17%) 2	0 / 19 (0.00%) 0
Pain subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 3	0 / 48 (0.00%) 0	1 / 19 (5.26%) 1
Peripheral swelling subjects affected / exposed occurrences (all)	2 / 51 (3.92%) 2	3 / 48 (6.25%) 3	0 / 19 (0.00%) 0
Oedema subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 48 (2.08%) 1	1 / 19 (5.26%) 1
Swelling face subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 48 (2.08%) 1	0 / 19 (0.00%) 0
Vaccination site pain subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	0 / 19 (0.00%) 0
Immune system disorders Seasonal allergy subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 48 (0.00%) 0	0 / 19 (0.00%) 0
Reproductive system and breast disorders Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 48 (0.00%) 0	0 / 19 (0.00%) 0
Breast pain subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	0 / 19 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	4 / 51 (7.84%) 4	2 / 48 (4.17%) 3	1 / 19 (5.26%) 1
Dyspnoea subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 4	2 / 48 (4.17%) 2	0 / 19 (0.00%) 0
Dyspnoea at rest			

subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Laryngospasm			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Nasal congestion			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Nasal polyps			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Respiratory failure			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Respiratory tract congestion			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	2 / 51 (3.92%)	2 / 48 (4.17%)	0 / 19 (0.00%)
occurrences (all)	2	2	0
Affect lability			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Insomnia			
subjects affected / exposed	1 / 51 (1.96%)	1 / 48 (2.08%)	2 / 19 (10.53%)
occurrences (all)	1	1	2
Depression			
subjects affected / exposed	1 / 51 (1.96%)	1 / 48 (2.08%)	1 / 19 (5.26%)
occurrences (all)	1	1	1
Confusional state			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Anxiety			
subjects affected / exposed	1 / 51 (1.96%)	4 / 48 (8.33%)	1 / 19 (5.26%)
occurrences (all)	1	4	1

Sleep disorder subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 48 (0.00%) 0	0 / 19 (0.00%) 0
Product issues Device dislocation subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 48 (2.08%) 2	1 / 19 (5.26%) 1
Investigations Alanine aminotransferase increased subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	2 / 19 (10.53%) 2
Aspartate aminotransferase increased subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 48 (0.00%) 0	2 / 19 (10.53%) 2
Blood uric acid increased subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	1 / 19 (5.26%) 1
Breath sounds abnormal subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	1 / 19 (5.26%) 1
Csf protein increased subjects affected / exposed occurrences (all)	7 / 51 (13.73%) 7	11 / 48 (22.92%) 11	4 / 19 (21.05%) 4
Csf white blood cell count increased subjects affected / exposed occurrences (all)	7 / 51 (13.73%) 7	6 / 48 (12.50%) 7	3 / 19 (15.79%) 4
Gamma-glutamyltransferase increased subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	2 / 19 (10.53%) 2
Hepatic enzyme increased subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	2 / 48 (4.17%) 2	1 / 19 (5.26%) 1
Weight decreased subjects affected / exposed occurrences (all)	6 / 51 (11.76%) 6	1 / 48 (2.08%) 1	4 / 19 (21.05%) 4
Injury, poisoning and procedural			

complications			
Contusion			
subjects affected / exposed	2 / 51 (3.92%)	5 / 48 (10.42%)	2 / 19 (10.53%)
occurrences (all)	4	7	4
Bone contusion			
subjects affected / exposed	0 / 51 (0.00%)	3 / 48 (6.25%)	0 / 19 (0.00%)
occurrences (all)	0	3	0
Concussion			
subjects affected / exposed	2 / 51 (3.92%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	3	0	0
Fall			
subjects affected / exposed	19 / 51 (37.25%)	18 / 48 (37.50%)	9 / 19 (47.37%)
occurrences (all)	62	56	25
Femur fracture			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Head injury			
subjects affected / exposed	0 / 51 (0.00%)	2 / 48 (4.17%)	2 / 19 (10.53%)
occurrences (all)	0	2	3
Immunisation reaction			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Post procedural inflammation			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Neurological procedural complication			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Post lumbar puncture syndrome			
subjects affected / exposed	7 / 51 (13.73%)	15 / 48 (31.25%)	7 / 19 (36.84%)
occurrences (all)	18	23	20
Post procedural contusion			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Post procedural discomfort			

subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal procedural complication			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Post procedural swelling			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Procedural complication			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Procedural dizziness			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Procedural nausea			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	20 / 51 (39.22%)	25 / 48 (52.08%)	13 / 19 (68.42%)
occurrences (all)	46	50	45
Skin laceration			
subjects affected / exposed	3 / 51 (5.88%)	1 / 48 (2.08%)	1 / 19 (5.26%)
occurrences (all)	3	1	1
Rib fracture			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Road traffic accident			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Shoulder fracture			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Skin abrasion			
subjects affected / exposed	3 / 51 (5.88%)	2 / 48 (4.17%)	0 / 19 (0.00%)
occurrences (all)	5	2	0

Procedural vomiting subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	1 / 19 (5.26%) 1
Stoma site discharge subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	1 / 19 (5.26%) 1
Stoma site pain subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	2 / 48 (4.17%) 2	2 / 19 (10.53%) 2
Cardiac disorders Tachycardia subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	1 / 48 (2.08%) 1	1 / 19 (5.26%) 1
Nervous system disorders Cluster headache subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	1 / 19 (5.26%) 1
Clonus subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 48 (0.00%) 0	0 / 19 (0.00%) 0
Brain fog subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	1 / 19 (5.26%) 1
Balance disorder subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 4	6 / 48 (12.50%) 10	0 / 19 (0.00%) 0
Cognitive disorder subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	1 / 19 (5.26%) 1
Dizziness subjects affected / exposed occurrences (all)	5 / 51 (9.80%) 6	8 / 48 (16.67%) 11	0 / 19 (0.00%) 0
Dysgeusia subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	0 / 19 (0.00%) 0
Head discomfort			



subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Muscle contractions involuntary			
subjects affected / exposed	0 / 51 (0.00%)	2 / 48 (4.17%)	0 / 19 (0.00%)
occurrences (all)	0	2	0
Loss of consciousness			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hypoaesthesia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hemihypoaesthesia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	19 / 51 (37.25%)	28 / 48 (58.33%)	5 / 19 (26.32%)
occurrences (all)	26	45	6
Menstrual headache			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Neuropathy peripheral			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Syncope			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Speech disorder			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Sciatica			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	3
Radicular pain			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	2
Presyncope			

subjects affected / exposed	1 / 51 (1.96%)	2 / 48 (4.17%)	1 / 19 (5.26%)
occurrences (all)	1	2	1
Post-traumatic headache			
subjects affected / exposed	1 / 51 (1.96%)	1 / 48 (2.08%)	0 / 19 (0.00%)
occurrences (all)	2	1	0
Pleocytosis			
subjects affected / exposed	4 / 51 (7.84%)	6 / 48 (12.50%)	3 / 19 (15.79%)
occurrences (all)	6	7	3
Parosmia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 51 (0.00%)	4 / 48 (8.33%)	0 / 19 (0.00%)
occurrences (all)	0	8	0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 51 (1.96%)	1 / 48 (2.08%)	0 / 19 (0.00%)
occurrences (all)	1	1	0
Hypoacusis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Tinnitus			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Vertigo positional			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	1 / 19 (5.26%)
occurrences (all)	0	1	1
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Gastrointestinal disorders			

Diarrhoea			
subjects affected / exposed	4 / 51 (7.84%)	7 / 48 (14.58%)	4 / 19 (21.05%)
occurrences (all)	5	9	5
Abdominal distension			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	7 / 51 (13.73%)	2 / 48 (4.17%)	6 / 19 (31.58%)
occurrences (all)	8	2	11
Dysphagia			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Food poisoning			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	2
Gastritis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	2 / 19 (10.53%)
occurrences (all)	0	0	2
Mouth ulceration			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Haematemesis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	0	0	0
Hiatus hernia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gastrooesophageal reflux disease			
subjects affected / exposed	2 / 51 (3.92%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Nausea			
subjects affected / exposed	2 / 51 (3.92%)	5 / 48 (10.42%)	4 / 19 (21.05%)
occurrences (all)	2	7	4
Oesophagitis			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1

Oral dysaesthesia subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	1 / 19 (5.26%) 1
Vomiting subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	3 / 48 (6.25%) 5	1 / 19 (5.26%) 1
Salivary hypersecretion subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	2 / 48 (4.17%) 2	0 / 19 (0.00%) 0
Skin and subcutaneous tissue disorders			
Dermatitis allergic subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	0 / 19 (0.00%) 0
Decubitus ulcer subjects affected / exposed occurrences (all)	3 / 51 (5.88%) 3	1 / 48 (2.08%) 1	2 / 19 (10.53%) 2
Erythema subjects affected / exposed occurrences (all)	1 / 51 (1.96%) 1	0 / 48 (0.00%) 0	1 / 19 (5.26%) 1
Hyperhidrosis subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	1 / 19 (5.26%) 1
Nodular rash subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	1 / 19 (5.26%) 1
Pruritus subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	2 / 48 (4.17%) 2	0 / 19 (0.00%) 0
Rash subjects affected / exposed occurrences (all)	6 / 51 (11.76%) 7	1 / 48 (2.08%) 1	0 / 19 (0.00%) 0
Skin lesion subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	1 / 19 (5.26%) 1
Ecchymosis			

subjects affected / exposed occurrences (all)	0 / 51 (0.00%) 0	0 / 48 (0.00%) 0	0 / 19 (0.00%) 0
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	5 / 51 (9.80%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	6	0	1
Pollakiuria			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	3 / 19 (15.79%)
occurrences (all)	0	1	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 51 (21.57%)	6 / 48 (12.50%)	3 / 19 (15.79%)
occurrences (all)	16	9	7
Muscle tightness			
subjects affected / exposed	0 / 51 (0.00%)	1 / 48 (2.08%)	0 / 19 (0.00%)
occurrences (all)	0	1	0
Back pain			
subjects affected / exposed	2 / 51 (3.92%)	12 / 48 (25.00%)	1 / 19 (5.26%)
occurrences (all)	3	15	1
Joint swelling			
subjects affected / exposed	2 / 51 (3.92%)	1 / 48 (2.08%)	1 / 19 (5.26%)
occurrences (all)	2	1	1
Mobility decreased			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	2 / 51 (3.92%)	3 / 48 (6.25%)	2 / 19 (10.53%)
occurrences (all)	3	3	2
Myalgia			
subjects affected / exposed	7 / 51 (13.73%)	7 / 48 (14.58%)	2 / 19 (10.53%)
occurrences (all)	12	21	3
Musculoskeletal stiffness			
subjects affected / exposed	5 / 51 (9.80%)	2 / 48 (4.17%)	0 / 19 (0.00%)
occurrences (all)	5	3	0
Musculoskeletal pain			

subjects affected / exposed	2 / 51 (3.92%)	2 / 48 (4.17%)	1 / 19 (5.26%)
occurrences (all)	2	4	1
Musculoskeletal chest pain			
subjects affected / exposed	2 / 51 (3.92%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	2	0	0
Muscular weakness			
subjects affected / exposed	7 / 51 (13.73%)	9 / 48 (18.75%)	3 / 19 (15.79%)
occurrences (all)	10	10	6
Neck pain			
subjects affected / exposed	1 / 51 (1.96%)	2 / 48 (4.17%)	3 / 19 (15.79%)
occurrences (all)	1	2	3
Pain in extremity			
subjects affected / exposed	7 / 51 (13.73%)	11 / 48 (22.92%)	4 / 19 (21.05%)
occurrences (all)	12	25	8
Infections and infestations			
Hordeolum			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	1
Device related infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Gastroenteritis viral			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Covid-19			
subjects affected / exposed	6 / 51 (11.76%)	4 / 48 (8.33%)	4 / 19 (21.05%)
occurrences (all)	6	4	6
Influenza			
subjects affected / exposed	4 / 51 (7.84%)	1 / 48 (2.08%)	2 / 19 (10.53%)
occurrences (all)	4	1	4
Nasopharyngitis			
subjects affected / exposed	6 / 51 (11.76%)	3 / 48 (6.25%)	2 / 19 (10.53%)
occurrences (all)	9	4	3
Pneumonia			
subjects affected / exposed	0 / 51 (0.00%)	2 / 48 (4.17%)	1 / 19 (5.26%)
occurrences (all)	0	2	4

Sinusitis			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	1	0	2
Upper respiratory tract infection			
subjects affected / exposed	1 / 51 (1.96%)	0 / 48 (0.00%)	0 / 19 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	3 / 51 (5.88%)	2 / 48 (4.17%)	1 / 19 (5.26%)
occurrences (all)	5	5	2
Stoma site infection			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hyperuricaemia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Hyperglycaemia			
subjects affected / exposed	0 / 51 (0.00%)	0 / 48 (0.00%)	1 / 19 (5.26%)
occurrences (all)	0	0	1
Dehydration			
subjects affected / exposed	1 / 51 (1.96%)	2 / 48 (4.17%)	1 / 19 (5.26%)
occurrences (all)	1	3	1

<b>Non-serious adverse events</b>	Part 1: Cohorts C1+C2: BIIB105 60 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 11 (100.00%)		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Flushing			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		

Hypertension subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
General disorders and administration site conditions			
Chest pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Asthenia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Chills subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Fatigue subjects affected / exposed occurrences (all)	5 / 11 (45.45%) 8		
Medical device site burn subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Pyrexia subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Oedema peripheral subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Peripheral swelling subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Oedema subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Swelling face			



subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Vaccination site pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	3		
Immune system disorders			
Seasonal allergy			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Breast pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Dyspnoea			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Dyspnoea at rest			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Laryngospasm			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Nasal congestion			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Nasal polyps			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Respiratory failure			

subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Respiratory tract congestion			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Suicidal ideation			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Affect lability			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Confusional state			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Sleep disorder			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Product issues			
Device dislocation			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Aspartate aminotransferase increased			

subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Blood uric acid increased			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Breath sounds abnormal			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Csf protein increased			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Csf white blood cell count increased			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Hepatic enzyme increased			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Weight decreased			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Bone contusion			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Concussion			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Fall			

subjects affected / exposed	4 / 11 (36.36%)		
occurrences (all)	14		
Femur fracture			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Head injury			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Immunisation reaction			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Post procedural inflammation			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Neurological procedural complication			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Post lumbar puncture syndrome			
subjects affected / exposed	6 / 11 (54.55%)		
occurrences (all)	18		
Post procedural contusion			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Post procedural discomfort			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Musculoskeletal procedural complication			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Post procedural swelling			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	2		
Procedural complication			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		

Procedural dizziness subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Procedural nausea subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2		
Procedural pain subjects affected / exposed occurrences (all)	7 / 11 (63.64%) 21		
Skin laceration subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 3		
Rib fracture subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Road traffic accident subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Shoulder fracture subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Skin abrasion subjects affected / exposed occurrences (all)	3 / 11 (27.27%) 3		
Procedural vomiting subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1		
Stoma site discharge subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Stoma site pain subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Cardiac disorders Tachycardia			

subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Cluster headache			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Clonus			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Brain fog			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Balance disorder			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Cognitive disorder			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	3		
Dysgeusia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Head discomfort			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Muscle contractions involuntary			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Loss of consciousness			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Hypoaesthesia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		

Hemihypoaesthesia			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Headache			
subjects affected / exposed	5 / 11 (45.45%)		
occurrences (all)	11		
Menstrual headache			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Neuropathy peripheral			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Syncope			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Speech disorder			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Sciatica			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Radicular pain			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Presyncope			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Post-traumatic headache			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Pleocytosis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Parosmia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		

Paraesthesia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Blood and lymphatic system disorders Iron deficiency anaemia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Ear and labyrinth disorders Ear pain subjects affected / exposed occurrences (all)  Hypoacusis subjects affected / exposed occurrences (all)  Tinnitus subjects affected / exposed occurrences (all)  Vertigo positional subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0  0 / 11 (0.00%) 0  0 / 11 (0.00%) 0  0 / 11 (0.00%) 0		
Eye disorders Conjunctival haemorrhage subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all)  Abdominal distension subjects affected / exposed occurrences (all)  Constipation subjects affected / exposed occurrences (all)  Dysphagia subjects affected / exposed occurrences (all)	1 / 11 (9.09%) 1  1 / 11 (9.09%) 1  1 / 11 (9.09%) 2  1 / 11 (9.09%) 1		



Food poisoning			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Mouth ulceration			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Haematemesis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Hiatus hernia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	3		
Oesophagitis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Oral dysaesthesia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Salivary hypersecretion			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dermatitis allergic			

subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Decubitus ulcer			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Hyperhidrosis			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Nodular rash			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Pruritus			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Skin lesion			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Ecchymosis			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Renal and urinary disorders			
Urinary retention			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Pollakiuria			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	4 / 11 (36.36%)		
occurrences (all)	7		
Muscle tightness			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Back pain			
subjects affected / exposed	3 / 11 (27.27%)		
occurrences (all)	5		
Joint swelling			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Mobility decreased			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Muscle spasms			
subjects affected / exposed	4 / 11 (36.36%)		
occurrences (all)	5		
Myalgia			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	5		
Musculoskeletal stiffness			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	3		
Musculoskeletal chest pain			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Muscular weakness			
subjects affected / exposed	1 / 11 (9.09%)		
occurrences (all)	1		
Neck pain			
subjects affected / exposed	2 / 11 (18.18%)		
occurrences (all)	2		

Pain in extremity subjects affected / exposed occurrences (all)	2 / 11 (18.18%) 2		
Infections and infestations			
Hordeolum subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Device related infection subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Gastroenteritis viral subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Covid-19 subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Influenza subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Pneumonia subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Sinusitis subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Upper respiratory tract infection subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Urinary tract infection subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Stoma site infection			

subjects affected / exposed occurrences (all)	0 / 11 (0.00%) 0		
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Hyperuricaemia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		
Dehydration			
subjects affected / exposed	0 / 11 (0.00%)		
occurrences (all)	0		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2021	<ul style="list-style-type: none"><li>- Clarified the dosing of the sentinel pair in cohort C2 to avoid the possible unblinding of study participants' treatment assignment.</li><li>- Note associated with the Columbia Suicide Severity Rating Scale (C-SSRS) Questionnaire was corrected to indicate that the "since last visit" version of the C-SSRS should be used from Day 8 forward, as indicated in the corresponding row in the Schedule of Activities.</li><li>- The definition of the ALSFRS-R slope calculation was corrected.</li></ul>
17 November 2021	<ul style="list-style-type: none"><li>- Extended the treatment period for cohorts D1 and D2 from approximately 13 weeks to approximately 25 weeks, and added a second part to the study (Part 2, open-label long-term extension).</li><li>- New nonclinical study information was added.</li><li>- The natural history run-in period for Cohort D2 was removed from the protocol.</li><li>- Language was added allowing follow-up of health status after withdrawal from or end of study, if a participant consents to data collection after withdrawal or study completion.</li><li>- Safety surveillance team review criteria for Cohorts D1 and D2 was separated from the criteria for Cohorts A, B, C1, and C2.</li><li>- Cohort study stopping rules were updated to include additional information on the role of the SST.</li><li>- Study termination criteria were clarified.</li><li>- Part 1 inclusion criteria were updated.</li><li>- A rescreening option was added for screen failures.</li><li>- Text was updated to state that indwelling injection ports/catheters are prohibited only during Part 1 of the study.</li><li>- Information was updated to clearly reflect Part 1 and Part 2 assessment requirements.</li><li>- Text was added defining the analysis populations.</li><li>- Details were added to clarify the planned statistical analyses of AEs.</li><li>- Details for planned laboratory analyses were added.</li><li>- A section was added to account for the digital data collected by participants.</li></ul>

09 September 2022	<ul style="list-style-type: none"> <li>- Increased the sample size in Cohort D1 from n = 20 to n = 48.</li> <li>- Details about the study structure, objectives, and phase was added.</li> <li>- Information on a newly approved ALS therapy was added.</li> <li>- Newly available data from fertility and fetal toxicity studies were summarized.</li> <li>- References to new nonclinical reproductive and developmental toxicity data and emerging clinical data from the ongoing study were added to the Benefit-Risk Assessment, and a Sponsor position on the benefit-risk profile was added.</li> <li>- CSF PK and plasma NfL were elevated from exploratory to secondary endpoints. PD and biomarker objectives and endpoints were separated out by study part (Part 1, Part 2) and prospectively defined for the integrated analyses (Integrated Part 1 and Part 2).</li> <li>- Safety surveillance team review criteria for Cohorts D1 and D2 were updated.</li> <li>- ICF requirements were updated in the inclusion criteria.</li> <li>- The minimum prescreening ALFRS-R slope requirement was removed for Cohort D1 in the exclusion criteria (Part 1).</li> <li>- A new exclusion criterion (for Part 1) was added to restrict allowable ALS treatment for study participants.</li> <li>- Exclusion criterion of Part 2 was updated to permit participants who contracted HIV, HBV, or HCV during Part 1 to continue into Part 2 if appropriate in the exclusion criteria.</li> <li>- Screen failure section was updated to allow re-use of screening assessments that will not change over time.</li> <li>- Optional collection of vital status was permitted.</li> <li>- Clarified that separate analyses will be performed for separate Parts of the study and on integrated data study populations were defined</li> <li>- Method of analysis section was updated that included handling of data from different parts of the study.</li> <li>- Described early-termination scenarios and permit additional interim analyses.</li> </ul>
07 September 2023	<ul style="list-style-type: none"> <li>- Updated to reflect changes in the BIIB105 manufacturing process. The manufacturing changes affected the study drug product presentation (concentration and volume) but did not have any impact on the final formulation of BIIB105 administered to study participants</li> <li>- Extended the maintenance dosing portion of the treatment period of Part 2 by up to approximately 52 weeks.</li> <li>- Amended dose termination rules, including lifting them if SST review of Cohort D1 data supports continued dosing at the highest dose level.</li> <li>- Updated how data will be analysed and presented for safety, PK, clinical function and quality of life measures, time to death or permanent ventilation, and time to death.</li> </ul>

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.

Study terminated because of sponsor's decision.

Notes: