Clinical trial results:
A Study to Evaluate the Efficacy, Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of BIIB067 Administered to Adult Subjects with Amyotrophic Lateral Sclerosis and Confirmed Superoxide Dismutase 1 Mutation

Summary

EudraCT number	2015-004098-33
Trial protocol	SE DE GB BE DK PL IT
Global end of trial date	16 July 2021

Results information

Result version number	v2 (current)
This version publication date	24 August 2023
First version publication date	31 July 2022
Version creation reason	• Correction of full data set Updated '99999' explanations and added number of subjects analysed for Day 85 for endpoints: Cmax and Tmax.

Trial information

Trial identification

Sponsor protocol code	233AS101

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02623699
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Biogen
Sponsor organisation address	225 Binney Street, Cambridge, United States, 02142
Public contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com
Scientific contact	Biogen Study Medical Director, Biogen, clinicaltrials@biogen.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	16 July 2021
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	16 July 2021
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objectives of Parts A and B of this study are to evaluate the safety, tolerability, and pharmacokinetics (PK) of ascending doses of BIIB067 (tofersen) in adults with ALS and a documented superoxide dismutase 1 (SOD1) mutation. The secondary objective of Parts A and B of this study is to evaluate the effects of BIIB067 on levels of total SOD1 protein in the cerebrospinal fluid (CSF). The primary objective of Part C of this study is to evaluate the clinical efficacy of BIIB067 administered to adults with ALS and a confirmed SOD1 mutation. The secondary objectives of Part C are to evaluate the safety, tolerability, pharmacodynamic (PD), and biomarker effects of BIIB067.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	20 January 2016
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	France: 8
Country: Number of subjects enrolled	Canada: 27
Country: Number of subjects enrolled	Japan: 7
Country: Number of subjects enrolled	United States: 93
Country: Number of subjects enrolled	Germany: 11
Country: Number of subjects enrolled	Italy: 5
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	Denmark: 1
Country: Number of subjects enrolled	United Kingdom: 12
Worldwide total number of subjects	178
EEA total number of subjects	39

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)	156
From 65 to 84 years	22
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at the investigative sites in the Belgium, Canada, Denmark, France, Germany, Italy, Japan, United Kingdom, and the United States from 20 January 2016 to 16 July 2021.

Pre-assignment

Screening details:

Study included SAD (Part A), MAD (Part B) and pivotal portions (Part C). Total 176 subjects were enrolled 20 into Part A, 50 into Part B including 2 subjects who completed Part A, were re-enrolled in Part B after 12-week washout period, hence 2 subjects were analysed in both Parts A, B (for total of 68 in Parts A, B), Part C enrolled 108 subjects.

Period 1

Period 1 title	Parts A, B, and C (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer

Arms

Are arms mutually exclusive?	Yes
Arm title	Part A-SAD: Combined Placebo

Arm description:

Subjects were administered BIIB067-matching placebo once by intrathecal bolus injection on Day 1 of Cohorts 1, 2, 3, and 4 respectively.

Arm type	Placebo
Investigational medicinal product name	BIIB067-matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Subjects were administered BIIB067-matching placebo as specified in treatment arm.

Arm title	Part A-SAD: Cohort 1: BIIB067 10 mg

Arm description:

Subjects were administered BIIB067 10 mg once by intrathecal bolus injection on Day 1.

Arm type	Experimental
Investigational medicinal product name	BIIB067
Investigational medicinal product code	ISIS666853
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Subjects were administered BIIB067 10 mg as specified in the treatment arm.

Arm title	Part A-SAD: Cohort 2: BIIB067 20 mg

Arm description:

Subjects were administered BIIB067 20 mg once by intrathecal bolus injection on Day 1 of Cohort 2 after the safety review of Cohort 1.

Arm type	Experimental

Investigational medicinal product name	BIIB067
Investigational medicinal product code	ISIS666853
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Subjects were administered BIIB067 20 mg as specified in the treatment arm.

Arm title	Part A-SAD: Cohort 3: BIIB067 40 mg

Arm description:

Subjects were administered BIIB067 40 mg once by intrathecal bolus injection on Day 1 of Cohort 3 after the safety review of Cohort 2.

Arm type	Experimental
Investigational medicinal product name	BIIB067
Investigational medicinal product code	ISIS666853
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Subjects were administered BIIB067 40 mg as specified in the treatment arm.

Arm title	Part A-SAD: Cohort 4: BIIB067 60 mg

Arm description:

Subjects were administered BIIB067 60 mg once by intrathecal bolus injection on Day 1 of Cohort 4 after the safety review of Cohort 3.

Arm type	Experimental
Investigational medicinal product name	BIIB067
Investigational medicinal product code	ISIS666853
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Subjects were administered BIIB067 60 mg as specified in the treatment arm.

Arm title	Part B-MAD: Combined Placebo

Arm description:

Subjects were administered BIIB067-matching placebo, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection.

Arm type	Placebo
Investigational medicinal product name	BIIB067-matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Subjects were administered BIIB067-matching placebo as specified in treatment arm.

Arm title	Part B-MAD: Cohort 5: BIIB067 20 mg

Arm description:

Subjects were administered BIIB067 20 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection.

Arm type	Experimental

Investigational medicinal product name	BIIB067
Investigational medicinal product code	ISIS666853
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Subjects were administered BIIB067 20 mg as specified in the treatment arm.

Arm title	Part B-MAD: Cohort 6: BIIB067 40 mg

Arm description:

Subjects were administered BIIB067 40 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection after the safety and PK review of Cohort 5.

Arm type	Experimental
Investigational medicinal product name	BIIB067
Investigational medicinal product code	ISIS666853
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Subjects were administered BIIB067 40 mg as specified in the treatment arm.

Arm title	Part B-MAD: Cohort 7: BIIB067 60 mg

Arm description:

Subjects were administered BIIB067 60 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection after the safety, PK review and superoxide dismutase 1 (SOD1) PD review of Cohort 6.

Arm type	Experimental
Investigational medicinal product name	BIIB067
Investigational medicinal product code	ISIS666853
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Subjects were administered BIIB067 60 mg as specified in the treatment arm.

Arm title	Part B-MAD: Cohort 8: BIIB067 100 mg

Arm description:

Subjects were administered BIIB067 100 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection after the safety, PK review and SOD1 PD review of Cohort 7.

Arm type	Experimental
Investigational medicinal product name	BIIB067
Investigational medicinal product code	ISIS666853
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Subjects were administered BIIB067 100 mg as specified in the treatment arm.

Arm title	Part C-Pivotal: Placebo

Arm description:

Subjects were administered BIIB067-matching placebo, 3 loading doses administered once every 2 weeks on Days 1, 15, 29 followed by 5 maintenance doses administered once every 4 weeks on Days 57, 85, 113, 141, 169 up to 24 weeks by intrathecal bolus injection.

Arm type	Placebo

Investigational medicinal product name	BIIB067-matching Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Subjects were administered BIIB067-matching placebo as specified in treatment arm.

Arm title	Part C-Pivotal: BIIB067 100 mg

Arm description:

Subjects were administered BIIB067 100 mg, 3 loading doses administered once every 2 weeks on Days 1, 15, 29 followed by 5 maintenance doses administered once every 4 weeks on Days 57, 85, 113, 141, 169 up to 24 weeks by intrathecal bolus injection.

Arm type	Experimental
Investigational medicinal product name	BIIB067
Investigational medicinal product code	ISIS666853
Other name	
Pharmaceutical forms	Solution for injection
Routes of administration	Intrathecal use

Dosage and administration details:

Subjects were administered BIIB067 100 mg as specified in the treatment arm.

Number of subjects in period 1	Part A-SAD: Combined Placebo	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg
Started	5	3	3
Completed	5	2	3
Not completed	0	1	0
Disease progression	-	-	-
Death	-	-	-
Adverse event	-	-	-
Lost to follow-up	-	-	-
Consent Withdrawn	-	1	-

Number of subjects in period 1	Part A-SAD: Cohort 3: BIIB067 40 mg	Part A-SAD: Cohort 4: BIIB067 60 mg	Part B-MAD: Combined Placebo
Started	3	6	12
Completed	3	6	10
Not completed	0	0	2
Disease progression	-	-	-
Death	-	-	1
Adverse event	-	-	-
Lost to follow-up	-	-	-
Consent Withdrawn	-	-	1

Number of subjects in period 1	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg	Part B-MAD: Cohort 7: BIIB067 60 mg
Started	10	9	9

Completed	8	9	8
Not completed	2	0	1
Disease progression	-	-	-
Death	1	-	1
Adverse event	-	-	-
Lost to follow-up	1	-	-
Consent Withdrawn	-	-	-

Number of subjects in period 1	Part B-MAD: Cohort 8: BIIB067 100 mg	Part C-Pivotal: Placebo	Part C-Pivotal: BIIB067 100 mg
Started	10	36	72
Completed	10	33	64
Not completed	0	3	8
Disease progression	-	2	3
Death	-	-	1
Adverse event	-	-	2
Lost to follow-up	-	-	-
Consent Withdrawn	-	1	2

Baseline characteristics

Reporting groups

Reporting group title	Part A-SAD: Combined Placebo
Reporting group description:	
Subjects were administered BIIB067-matching placebo once by intrathecal bolus injection on Day 1 of Cohorts 1, 2, 3, and 4 respectively.	
Reporting group title	Part A-SAD: Cohort 1: BIIB067 10 mg
Reporting group description:	
Subjects were administered BIIB067 10 mg once by intrathecal bolus injection on Day 1.	
Reporting group title	Part A-SAD: Cohort 2: BIIB067 20 mg
Reporting group description:	
Subjects were administered BIIB067 20 mg once by intrathecal bolus injection on Day 1 of Cohort 2 after the safety review of Cohort 1.	
Reporting group title	Part A-SAD: Cohort 3: BIIB067 40 mg
Reporting group description:	
Subjects were administered BIIB067 40 mg once by intrathecal bolus injection on Day 1 of Cohort 3 after the safety review of Cohort 2.	
Reporting group title	Part A-SAD: Cohort 4: BIIB067 60 mg
Reporting group description:	
Subjects were administered BIIB067 60 mg once by intrathecal bolus injection on Day 1 of Cohort 4 after the safety review of Cohort 3.	
Reporting group title	Part B-MAD: Combined Placebo
Reporting group description:	
Subjects were administered BIIB067-matching placebo, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection.	
Reporting group title	Part B-MAD: Cohort 5: BIIB067 20 mg
Reporting group description:	
Subjects were administered BIIB067 20 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection.	
Reporting group title	Part B-MAD: Cohort 6: BIIB067 40 mg
Reporting group description:	
Subjects were administered BIIB067 40 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection after the safety and PK review of Cohort 5.	
Reporting group title	Part B-MAD: Cohort 7: BIIB067 60 mg
Reporting group description:	
Subjects were administered BIIB067 60 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection after the safety, PK review and superoxide dismutase 1 (SOD1) PD review of Cohort 6.	
Reporting group title	Part B-MAD: Cohort 8: BIIB067 100 mg
Reporting group description:	
Subjects were administered BIIB067 100 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection after the safety, PK review and SOD1 PD review of Cohort 7.	
Reporting group title	Part C-Pivotal: Placebo
Reporting group description:	
Subjects were administered BIIB067-matching placebo, 3 loading doses administered once every 2 weeks on Days 1, 15, 29 followed by 5 maintenance doses administered once every 4 weeks on Days 57, 85, 113, 141, 169 up to 24 weeks by intrathecal bolus injection.	
Reporting group title	Part C-Pivotal: BIIB067 100 mg
Reporting group description:	
Subjects were administered BIIB067 100 mg, 3 loading doses administered once every 2 weeks on Days 1, 15, 29 followed by 5 maintenance doses administered once every 4 weeks on Days 57, 85, 113, 141, 169 up to 24 weeks by intrathecal bolus injection.	

Reporting group values	Part A-SAD: Combined Placebo	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg
Number of subjects	5	3	3
Age Categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	58.4	50.3	55.3
standard deviation	± 9.29	± 7.64	± 17.62
Gender Categorical Units: Subjects			
Female	2	3	0
Male	3	0	3
Ethnicity			
Not reported indicates that ethnicity data was not reported due to confidentiality regulations.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	4	3	3
Not reported	1	0	0
Race Units: Subjects			
Asian	0	0	0
Black or African American	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	4	3	3
Not reported	1	0	0
Other	0	0	0
Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R)			
ALSFRS-R measures respiratory, bulbar function, gross, and fine motor skills. 12 questions, each scored from 0-4 (no-full function), for a total score of 48. Scores decline with disease progression. Higher scores represent better function. Modified ITT (mITT) population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: score on a scale			
arithmetic mean	99999	99999	99999
standard deviation	± 99999	± 99999	± 99999
CSF Levels of Total SOD1 Protein Concentration			
PD population is the subset of the ITT population with at least 1 post-dose PD measurement in Part B. mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N= 0, 0, 0, 0, 0, 4, 1, 1, 1, 4, 21, and 38 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part B and C arms groups.			
Units: nanograms per milliliter (ng/mL)			
geometric mean	99999	99999	99999
full range (min-max)	99999 to 99999	99999 to 99999	99999 to 99999
Percentage (%) Predicted Slow Vital Capacity (SVC)			
mITT population included all subjects who met the prognostic enrichment criteria for rapid disease			

progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: percent predicted			
arithmetic mean	99999	99999	99999
standard deviation	± 99999	± 99999	± 99999
Handheld Dynamometry (HHD) Megascore as Measured by the HHD Device			
16 muscle groups were evaluated in upper, lower extremities. Strength determinations were converted to Z scores, averaged for an HHD megascore. Muscle strength values normalized to Z scores as (post-baseline measurements – mean)/SD, averaged to provide HHD overall megascore.mITT population=all subjects who met prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, 39 for arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: score on a scale			
arithmetic mean	99999	99999	99999
standard deviation	± 99999	± 99999	± 99999
Neurofilament Light Chain (NfL) Concentration in Plasma			
mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: picograms per mL (pg/mL)			
geometric mean	99999	99999	99999
full range (min-max)	99999 to 99999	99999 to 99999	99999 to 99999

Reporting group values	Part A-SAD: Cohort 3: BIIB067 40 mg	Part A-SAD: Cohort 4: BIIB067 60 mg	Part B-MAD: Combined Placebo
Number of subjects	3	6	12
Age Categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	49.0	45.0	49.2
standard deviation	± 3.61	± 12.82	± 11.04
Gender Categorical			
Units: Subjects			
Female	1	4	5
Male	2	2	7
Ethnicity			
Not reported indicates that ethnicity data was not reported due to confidentiality regulations.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	1	5	9
Not reported	2	1	3
Race			
Units: Subjects			
Asian	0	0	0
Black or African American	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	1
White	1	5	7

Not reported	2	1	3
Other	0	0	1

Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R)			
ALSFRS-R measures respiratory, bulbar function, gross, and fine motor skills. 12 questions, each scored from 0-4 (no-full function), for a total score of 48. Scores decline with disease progression. Higher scores represent better function. Modified ITT (mITT) population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: score on a scale			
arithmetic mean	99999	99999	99999
standard deviation	± 99999	± 99999	± 99999
CSF Levels of Total SOD1 Protein Concentration			
PD population is the subset of the ITT population with at least 1 post-dose PD measurement in Part B. mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N= 0, 0, 0, 0, 0, 4, 1, 1, 1, 4, 21, and 38 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part B and C arms groups.			
Units: nanograms per milliliter (ng/mL)			
geometric mean	99999	99999	70.40
full range (min-max)	99999 to 99999	99999 to 99999	57.2 to 87.9
Percentage (%) Predicted Slow Vital Capacity (SVC)			
mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: percent predicted			
arithmetic mean	99999	99999	99999
standard deviation	± 99999	± 99999	± 99999
Handheld Dynamometry (HHD) Megascore as Measured by the HHD Device			
16 muscle groups were evaluated in upper, lower extremities. Strength determinations were converted to Z scores, averaged for an HHD megascore. Muscle strength values normalized to Z scores as (post-baseline measurements – mean)/SD, averaged to provide HHD overall megascore.mITT population=all subjects who met prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, 39 for arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: score on a scale			
arithmetic mean	99999	99999	99999
standard deviation	± 99999	± 99999	± 99999
Neurofilament Light Chain (NfL) Concentration in Plasma			
mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: picograms per mL (pg/mL)			
geometric mean	99999	99999	99999
full range (min-max)	99999 to 99999	99999 to 99999	99999 to 99999

Reporting group values	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg	Part B-MAD: Cohort 7: BIIB067 60 mg
Number of subjects	10	9	9

Age Categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	41.5	58.0	45.6
standard deviation	± 10.72	± 11.09	± 10.71
Gender Categorical Units: Subjects			
Female	3	5	3
Male	7	4	6
Ethnicity			
Not reported indicates that ethnicity data was not reported due to confidentiality regulations.			
Units: Subjects			
Hispanic or Latino	0	0	0
Not Hispanic or Latino	5	6	4
Not reported	5	3	5
Race Units: Subjects			
Asian	0	1	0
Black or African American	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0
White	5	5	4
Not reported	5	3	5
Other	0	0	0
Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R)			
ALSFRS-R measures respiratory, bulbar function, gross, and fine motor skills. 12 questions, each scored from 0-4 (no-full function), for a total score of 48. Scores decline with disease progression. Higher scores represent better function. Modified ITT (mITT) population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: score on a scale			
arithmetic mean	99999	99999	99999
standard deviation	± 99999	± 99999	± 99999
CSF Levels of Total SOD1 Protein Concentration			
PD population is the subset of the ITT population with at least 1 post-dose PD measurement in Part B. mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N= 0, 0, 0, 0, 0, 4, 1, 1, 1, 4, 21, and 38 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part B and C arms groups.			
Units: nanograms per milliliter (ng/mL)			
geometric mean	102.00	125.00	82.80
full range (min-max)	102.00 to 102.00	125.00 to 125.00	82.8 to 82.8
Percentage (%) Predicted Slow Vital Capacity (SVC)			
mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: percent predicted			
arithmetic mean	99999	99999	99999
standard deviation	± 99999	± 99999	± 99999

Handheld Dynamometry (HHD) Megascore as Measured by the HHD Device			
16 muscle groups were evaluated in upper, lower extremities. Strength determinations were converted to Z scores, averaged for an HHD megascore. Muscle strength values normalized to Z scores as (post-baseline measurements – mean)/SD, averaged to provide HHD overall megascore.mITT population=all subjects who met prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, 39 for arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: score on a scale			
arithmetic mean	99999	99999	99999
standard deviation	± 99999	± 99999	± 99999
Neurofilament Light Chain (NfL) Concentration in Plasma			
mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: picograms per mL (pg/mL)			
geometric mean	99999	99999	99999
full range (min-max)	99999 to 99999	99999 to 99999	99999 to 99999

Reporting group values	Part B-MAD: Cohort 8: BIIB067 100 mg	Part C-Pivotal: Placebo	Part C-Pivotal: BIIB067 100 mg
Number of subjects	10	36	72
Age Categorical			
Units: Subjects			
Age Continuous			
Units: years			
arithmetic mean	48.9	51.2	48.1
standard deviation	± 10.80	± 11.57	± 12.64
Gender Categorical			
Units: Subjects			
Female	6	17	29
Male	4	19	43
Ethnicity			
Not reported indicates that ethnicity data was not reported due to confidentiality regulations.			
Units: Subjects			
Hispanic or Latino	0	1	4
Not Hispanic or Latino	7	28	47
Not reported	3	7	21
Race			
Units: Subjects			
Asian	0	4	5
Black or African American	0	0	1
Native Hawaiian or Other Pacific Islander	0	0	0
White	7	25	44
Not reported	3	7	21
Other	0	0	1
Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R)			
ALSFRS-R measures respiratory, bulbar function, gross, and fine motor skills. 12 questions, each scored from 0-4 (no-full function), for a total score of 48. Scores decline with disease progression. Higher scores represent better function. Modified ITT (mITT) population included all subjects who met the			

prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: score on a scale			
arithmetic mean	99999	35.4	36.0
standard deviation	± 99999	± 5.66	± 6.40
CSF Levels of Total SOD1 Protein Concentration			
PD population is the subset of the ITT population with at least 1 post-dose PD measurement in Part B. mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N= 0, 0, 0, 0, 0, 4, 1, 1, 1, 4, 21, and 38 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part B and C arms groups.			
Units: nanograms per milliliter (ng/mL)			
geometric mean	135.86	107.07	103.32
full range (min-max)	92.5 to 199.0	60.0 to 322.0	38.8 to 282.0
Percentage (%) Predicted Slow Vital Capacity (SVC)			
mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: percent predicted			
arithmetic mean	99999	83.7	80.3
standard deviation	± 99999	± 17.87	± 14.22
Handheld Dynamometry (HHD) Megascore as Measured by the HHD Device			
16 muscle groups were evaluated in upper, lower extremities. Strength determinations were converted to Z scores, averaged for an HHD megascore. Muscle strength values normalized to Z scores as (post-baseline measurements – mean)/SD, averaged to provide HHD overall megascore.mITT population=all subjects who met prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, 39 for arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: score on a scale			
arithmetic mean	99999	0.0	0.0
standard deviation	± 99999	± 0.60	± 0.67
Neurofilament Light Chain (NfL) Concentration in Plasma			
mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: picograms per mL (pg/mL)			
geometric mean	99999	92.7	121.8
full range (min-max)	99999 to 99999	9 to 370	12 to 329

Reporting group values	Total		
Number of subjects	178		
Age Categorical			
Units: Subjects			

Age Continuous			
Units: years			
arithmetic mean			
standard deviation	-		

Gender Categorical Units: Subjects			
Female	78		
Male	100		
Ethnicity			
Not reported indicates that ethnicity data was not reported due to confidentiality regulations.			
Units: Subjects			
Hispanic or Latino	5		
Not Hispanic or Latino	122		
Not reported	51		
Race Units: Subjects			
Asian	10		
Black or African American	1		
Native Hawaiian or Other Pacific Islander	1		
White	113		
Not reported	51		
Other	2		
Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R)			
ALSFRS-R measures respiratory, bulbar function, gross, and fine motor skills. 12 questions, each scored from 0-4 (no-full function), for a total score of 48. Scores decline with disease progression. Higher scores represent better function. Modified ITT (mITT) population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: score on a scale arithmetic mean standard deviation	- -		
CSF Levels of Total SOD1 Protein Concentration			
PD population is the subset of the ITT population with at least 1 post-dose PD measurement in Part B. mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N= 0, 0, 0, 0, 0, 4, 1, 1, 1, 4, 21, and 38 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part B and C arms groups.			
Units: nanograms per milliliter (ng/mL) geometric mean full range (min-max)	 -		
Percentage (%) Predicted Slow Vital Capacity (SVC)			
mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: percent predicted arithmetic mean standard deviation	 -		
Handheld Dynamometry (HHD) Megascore as Measured by the HHD Device			
16 muscle groups were evaluated in upper, lower extremities. Strength determinations were converted to Z scores, averaged for an HHD megascore. Muscle strength values normalized to Z scores as (post-baseline measurements – mean)/SD, averaged to provide HHD overall megascore.mITT population=all subjects who met prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, 39 for arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms			

groups.			
Units: score on a scale arithmetic mean standard deviation	- -		
Neurofilament Light Chain (NfL) Concentration in Plasma			
mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. N=0, 0, 0, 0, 0, 0, 0, 0, 0, 0, 21, and 39 for the arms mentioned respectively. 99999=this study specific measure was only analyzed for Part C arms groups.			
Units: picograms per mL (pg/mL) geometric mean full range (min-max)	 -		

End points

End points reporting groups

Reporting group title	Part A-SAD: Combined Placebo
Reporting group description:	
Subjects were administered BIIB067-matching placebo once by intrathecal bolus injection on Day 1 of Cohorts 1, 2, 3, and 4 respectively.	
Reporting group title	Part A-SAD: Cohort 1: BIIB067 10 mg
Reporting group description:	
Subjects were administered BIIB067 10 mg once by intrathecal bolus injection on Day 1.	
Reporting group title	Part A-SAD: Cohort 2: BIIB067 20 mg
Reporting group description:	
Subjects were administered BIIB067 20 mg once by intrathecal bolus injection on Day 1 of Cohort 2 after the safety review of Cohort 1.	
Reporting group title	Part A-SAD: Cohort 3: BIIB067 40 mg
Reporting group description:	
Subjects were administered BIIB067 40 mg once by intrathecal bolus injection on Day 1 of Cohort 3 after the safety review of Cohort 2.	
Reporting group title	Part A-SAD: Cohort 4: BIIB067 60 mg
Reporting group description:	
Subjects were administered BIIB067 60 mg once by intrathecal bolus injection on Day 1 of Cohort 4 after the safety review of Cohort 3.	
Reporting group title	Part B-MAD: Combined Placebo
Reporting group description:	
Subjects were administered BIIB067-matching placebo, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection.	
Reporting group title	Part B-MAD: Cohort 5: BIIB067 20 mg
Reporting group description:	
Subjects were administered BIIB067 20 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection.	
Reporting group title	Part B-MAD: Cohort 6: BIIB067 40 mg
Reporting group description:	
Subjects were administered BIIB067 40 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection after the safety and PK review of Cohort 5.	
Reporting group title	Part B-MAD: Cohort 7: BIIB067 60 mg
Reporting group description:	
Subjects were administered BIIB067 60 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection after the safety, PK review and superoxide dismutase 1 (SOD1) PD review of Cohort 6.	
Reporting group title	Part B-MAD: Cohort 8: BIIB067 100 mg
Reporting group description:	
Subjects were administered BIIB067 100 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection after the safety, PK review and SOD1 PD review of Cohort 7.	
Reporting group title	Part C-Pivotal: Placebo
Reporting group description:	
Subjects were administered BIIB067-matching placebo, 3 loading doses administered once every 2 weeks on Days 1, 15, 29 followed by 5 maintenance doses administered once every 4 weeks on Days 57, 85, 113, 141, 169 up to 24 weeks by intrathecal bolus injection.	
Reporting group title	Part C-Pivotal: BIIB067 100 mg
Reporting group description:	
Subjects were administered BIIB067 100 mg, 3 loading doses administered once every 2 weeks on Days 1, 15, 29 followed by 5 maintenance doses administered once every 4 weeks on Days 57, 85, 113, 141, 169 up to 24 weeks by intrathecal bolus injection.	

Primary: Parts A and B: Number of Subjects Experiencing Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Parts A and B: Number of Subjects Experiencing Adverse Events (AEs) and Serious Adverse Events (SAEs)[1][2]

End point description:

An AE is any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. A SAE is any untoward medical occurrence that at any dose results in death, life-threatening event, requires inpatient hospitalization, significant disability/incapacity or congenital anomaly. Safety population included all randomized subjects who received at least 1 dose or a part of 1 dose of study treatment (BIIB067 or placebo) in Part A or B.

End point type	Primary

End point timeframe:

Part A: First dose up to Day 63; Part B: First dose up to Day 289

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: No statistical analysis was planned or performed for this endpoint.

[2] - 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: This endpoint was analysed only for the Part A and B arms of the study, so data was reported only for the Part A and B arm groups.

End point values	Part A-SAD: Combined Placebo	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	3
Units: subjects				
AEs	2	2	3	3
SAEs	0	0	0	0

End point values	Part A-SAD: Cohort 4: BIIB067 60 mg	Part B-MAD: Combined Placebo	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	12	10	9
Units: subjects				
AEs	6	12	10	9
SAEs	0	2	2	1

End point values	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg		

Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: subjects				
AEs	9	10		
SAEs	2	0		

Statistical analyses

No statistical analyses for this end point

Primary: Parts A and B: Number of Subjects With Clinically Significant Laboratory Abnormalities

End point title	Parts A and B: Number of Subjects With Clinically Significant Laboratory Abnormalities[3][4]

End point description:

Clinical laboratory assessments included hematology, chemistry, and urinalysis. Safety population included all randomized subjects who received at least 1 dose or a part of 1 dose of study treatment (BIIB067 or placebo) in Part A or B.

End point type	Primary

End point timeframe:

Part A: Up to Day 57; Part B: Up to Day 169

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned or performed for this endpoint.

[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: This endpoint was analysed only for the Part A and B arms of the study, so data was reported only for the Part A and B arm groups.

End point values	Part A-SAD: Combined Placebo	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	3
Units: subjects				
Pleocytosis	0	0	0	0
Eosinophilia	0	0	0	0
Blood Phosphorus Decreased	0	0	0	0
CSF Protein Increased	0	0	0	0
CSF White Blood Cell Count Increased	0	0	0	0
CSF White Blood Cell Count Positive	0	0	0	0
Gamma-Glutamyltransferase Increased	0	0	0	0
Urine Output Decreased	0	0	0	0

End point values	Part A-SAD: Cohort 4: BIIB067 60 mg	Part B-MAD: Combined Placebo	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	12	10	9

Units: subjects				
Pleocytosis	0	0	2	1
Eosinophilia	0	0	0	0
Blood Phosphorus Decreased	0	0	0	0
CSF Protein Increased	0	1	0	0
CSF White Blood Cell Count Increased	0	0	0	1
CSF White Blood Cell Count Positive	0	0	0	0
Gamma-Glutamyltransferase Increased	0	0	1	0
Urine Output Decreased	0	1	0	0

End point values	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: subjects				
Pleocytosis	0	0		
Eosinophilia	0	1		
Blood Phosphorus Decreased	1	0		
CSF Protein Increased	4	1		
CSF White Blood Cell Count Increased	3	0		
CSF White Blood Cell Count Positive	0	1		
Gamma-Glutamyltransferase Increased	0	0		
Urine Output Decreased	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Parts A and B: Number of Subjects With Clinically Significant Vital Sign Abnormalities

End point title	Parts A and B: Number of Subjects With Clinically Significant Vital Sign Abnormalities[5][6]

End point description:

Safety population included all randomized subjects who received at least 1 dose or a part of 1 dose of study treatment (BIIB067 or placebo) in Part A or B.

End point type	Primary

End point timeframe:

Part A: Up to Day 57; Part B: Up to Day 169

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was planned or performed for this endpoint.

[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: This endpoint was analysed only for the Part A and B arms of the study, so data was reported only for the Part A and B arm groups.

End point values	Part A-SAD: Combined Placebo	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	3
Units: subjects	0	0	0	0

End point values	Part A-SAD: Cohort 4: BIIB067 60 mg	Part B-MAD: Combined Placebo	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	12	10	9
Units: subjects	0	0	0	0

End point values	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: subjects	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Parts A and B: Number of Subjects With Clinically Significant Physical Examination Abnormalities

End point title	Parts A and B: Number of Subjects With Clinically Significant Physical Examination Abnormalities[7][8]

End point description:

Safety population included all randomized subjects who received at least 1 dose or a part of 1 dose of study treatment (BIIB067 or placebo) in Part A or B.

End point type	Primary

End point timeframe:

Part A: Up to Day 57; Part B: Up to Day 169

Notes:

[7] - 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: No statistical analysis was planned or performed for this endpoint.

[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: This endpoint was analysed only for the Part A and B arms of the study, so data was reported only for the Part A and B arm groups.

End point values	Part A-SAD: Combined Placebo	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	3
Units: subjects				
Weight Decreased	0	0	0	0

End point values	Part A-SAD: Cohort 4: BIIB067 60 mg	Part B-MAD: Combined Placebo	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	12	10	9
Units: subjects				
Weight Decreased	0	1	0	0

End point values	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: subjects				
Weight Decreased	0	1		

Statistical analyses

No statistical analyses for this end point

Primary: Parts A and B: Number of Subjects With Clinically Significant Neurological Examination Abnormalities

End point title	Parts A and B: Number of Subjects With Clinically Significant Neurological Examination Abnormalities[9][10]

End point description:

Safety population included all randomized subjects who received at least 1 dose or a part of 1 dose of study treatment (BIIB067 or placebo) in Part A or B.

End point type	Primary

End point timeframe:

Part A: Up to Day 57; Part B: Up to Day 169

Notes:

[9] - 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: No statistical analysis was planned or performed for this endpoint.

[10] - 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: This endpoint was analysed only for the Part A and B arms of the study, so data was reported only for the Part A and B arm groups.

End point values	Part A-SAD: Combined Placebo	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	3
Units: subjects				
Hyporeflexia	0	0	0	0

End point values	Part A-SAD: Cohort 4: BIIB067 60 mg	Part B-MAD: Combined Placebo	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	12	10	9
Units: subjects				
Hyporeflexia	1	0	0	0

End point values	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: subjects				
Hyporeflexia	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Parts A and B: Number of Subjects With Clinically Significant 12-lead Electrocardiograms (ECGs) Abnormalities

End point title	Parts A and B: Number of Subjects With Clinically Significant 12-lead Electrocardiograms (ECGs) Abnormalities[11][12]

End point description:

Safety population included all randomized subjects who received at least 1 dose or a part of 1 dose of study treatment (BIIB067 or placebo) in Part A or B. ms=milliseconds.

End point type	Primary

End point timeframe:

Part A: Up to Day 57; Part B: Up to Day 169

Notes:

[11] - 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: No statistical analysis was planned or performed for this endpoint.

[12] - 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: This endpoint was analysed only for the Part A and B arms of the study, so data was reported only for the Part A and B arm groups.

End point values	Part A-SAD: Combined Placebo	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	3	3	3
Units: subjects				
Maximum Increase From Baseline QTcF > 30 to 60 ms	0	0	0	0
Maximum Post-baseline QTcF > 480 to 500 ms	0	0	0	0

End point values	Part A-SAD: Cohort 4: BIIB067 60 mg	Part B-MAD: Combined Placebo	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	6	12	10	9
Units: subjects				
Maximum Increase From Baseline QTcF > 30 to 60 ms	0	3	1	2
Maximum Post-baseline QTcF > 480 to 500 ms	0	1	0	0

End point values	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	9	10		
Units: subjects				
Maximum Increase From Baseline QTcF > 30 to 60 ms	2	3		
Maximum Post-baseline QTcF > 480 to 500 ms	0	0		

Statistical analyses

No statistical analyses for this end point

Primary: Parts A and B: PK Parameter of BIIB067 in Plasma: Maximum Observed Concentration (Cmax)

End point title	Parts A and B: PK Parameter of BIIB067 in Plasma: Maximum Observed Concentration (Cmax)[13][14]

End point description:

PK population is the subset of the ITT population (all randomized subjects who received at least 1 dose or a part of 1 dose of study treatment) of subjects with at least 1 post-dose PK measurement in Part A or B. 99999=Data was not collected for subjects on Day 85 for Part A of the study.

End point type	Primary

End point timeframe:

Part A: Pre-dose, 1, 2, 4, 6 hrs post-dose on Day 1; Part B: Pre-dose, 1, 2, 4, 6 hrs post-dose on Day 1

and 1, 2, 4, 6 hrs post-dose on Day 85

Notes:

[13] - 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: No statistical analysis was planned or performed for this endpoint.

[14] - 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: This endpoint was analysed only for the Part A and B arms of the study, so data was reported only for the Part A and B arm groups.

End point values	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg	Part A-SAD: Cohort 4: BIIB067 60 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: ng/mL				
geometric mean (full range (min-max))				
Day 1	64.94 (38.8 to 159.0)	75.06 (43.0 to 144.0)	202.09 (174.0 to 236.0)	529.63 (148.0 to 1450.0)
Day 85 (n=0, 0, 0, 0, 10, 9, 9, 10)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)

End point values	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	9	10
Units: ng/mL				
geometric mean (full range (min-max))				
Day 1	80.75 (20.1 to 393.0)	229.41 (26.3 to 948.0)	437.28 (128.0 to 1930.0)	1031.74 (285.0 to 3530.0)
Day 85 (n=0, 0, 0, 0, 10, 9, 9, 10)	112.74 (29.7 to 203.0)	199.69 (93.6 to 537.0)	411.00 (74.1 to 1450.0)	1181.83 (170.0 to 3990.0)

Statistical analyses

No statistical analyses for this end point

Primary: Parts A and B: PK Parameter of BIIB067 in Plasma: Time to Reach Maximum Observed Concentration (Tmax)

End point title	Parts A and B: PK Parameter of BIIB067 in Plasma: Time to Reach Maximum Observed Concentration (Tmax)[15][16]

End point description:

PK population is the subset of the ITT population with at least 1 post-dose PK measurement in Part A or B. 99999=Data was not collected for subjects on Day 85 for Part A of the study.

End point type	Primary

End point timeframe:

Part A: Pre-dose, 1, 2, 4, 6 hrs post-dose on Day 1; Part B: Pre-dose, 1, 2, 4, 6 hrs post-dose on Day 1 and 1, 2, 4, 6 hrs post-dose on Day 85

Notes:

[15] - 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: No statistical analysis was planned or performed for this endpoint.

[16] - 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: This endpoint was analysed only for the Part A and B arms of the study, so data was reported only for the Part A and B arm groups.

End point values	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg	Part A-SAD: Cohort 4: BIIB067 60 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: hours				
geometric mean (full range (min-max))				
Day 1	4.58 (4.0 to 6.0)	4.16 (2.0 to 6.0)	6.00 (6.0 to 6.0)	2.70 (2.0 to 6.0)
Day 85 (n=0, 0, 0, 0, 10, 9, 9, 10)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)

End point values	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	9	10
Units: hours				
geometric mean (full range (min-max))				
Day 1	7.01 (2.0 to 24.0)	3.68 (1.0 to 6.0)	2.44 (1.0 to 6.0)	3.67 (1.0 to 24.0)
Day 85 (n=0, 0, 0, 0, 10, 9, 9, 10)	3.93 (2.0 to 6.0)	3.97 (1.0 to 6.0)	3.12 (1.0 to 6.0)	3.82 (1.0 to 6.0)

Statistical analyses

No statistical analyses for this end point

Primary: Parts A and B: PK Parameter of BIIB067 in Plasma: Area Under the Concentration-Time Curve From Time Zero to 24 hours (AUC0-24h)

End point title	Parts A and B: PK Parameter of BIIB067 in Plasma: Area Under the Concentration-Time Curve From Time Zero to 24 hours (AUC0-24h)[17][18]

End point description:

PK population is the subset of the ITT population with at least 1 post-dose PK measurement in Part A or B.

End point type	Primary

End point timeframe:

Parts A and B: Pre-dose, 1, 2, 4, 6 hrs post-dose on Day 1

Notes:

[17] - 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: No statistical analysis was planned or performed for this endpoint.

[18] - 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: This endpoint was analysed only for the Part A and B arms of the study, so data was reported only for the Part A and B arm groups.

End point values	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg	Part A-SAD: Cohort 4: BIIB067 60 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: hour*ng/mL				
geometric mean (full range (min-max))				
Day 1	879.86 (550.8 to 1989.5)	1027.18 (879.2 to 1263.2)	2873.77 (2347.2 to 3543.4)	5196.11 (2410.2 to 10977.3)

End point values	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	9	10
Units: hour*ng/mL				
geometric mean (full range (min-max))				
Day 1	1009.85 (372.8 to 2192.3)	2875.13 (541.1 to 6984.8)	4289.16 (1347.6 to 10637.1)	11344.47 (4025.5 to 26143.0)

Statistical analyses

No statistical analyses for this end point

Primary: Part A and B: PK Parameter of BIIB067 in Plasma: Area Under the Concentration-time Curve From Time Zero to Infinity (AUCinf)

End point title	Part A and B: PK Parameter of BIIB067 in Plasma: Area Under the Concentration-time Curve From Time Zero to Infinity (AUCinf)[19][20]

End point description:

PK population is the subset of the ITT population with at least 1 post-dose PK measurement in Part A or B. 99999=Data is not available as the concentration values were below the level of quantification and could not be quantified to estimate the AUC0-infinity values.

End point type	Primary

End point timeframe:

Part A: Pre-dose Day 1, Days 29 and 57; Part B: Pre-dose Days 1, 15, 29, 57 and 85; Day 106 and 169

Notes:

[19] - 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: No statistical analysis was planned or performed for this endpoint.

[20] - 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: This endpoint was analysed only for the Part A and B arms of the study, so data was reported only for the Part A and B arm groups.

End point values	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg	Part A-SAD: Cohort 4: BIIB067 60 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: hour*ng/mL				
arithmetic mean (standard deviation)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	9	10
Units: hour*ng/mL				
arithmetic mean (standard deviation)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Statistical analyses

No statistical analyses for this end point

Primary: Parts A and B: PK Parameter of BIIB067 in Plasma: Area Under the Concentration-time Curve From Time Zero to the Time of the Last Measurable Concentration (AUClast)

End point title	Parts A and B: PK Parameter of BIIB067 in Plasma: Area Under the Concentration-time Curve From Time Zero to the Time of the Last Measurable Concentration (AUClast)[21][22]

End point description:

PK population is the subset of the ITT population with at least 1 post-dose PK measurement in Part A or B. 99999=due to the large number of BLQ values at various times the last measurable concentration would have varied across individuals which makes this parameter not useful.

End point type	Primary

End point timeframe:

Part A: Pre-dose Day 1, Days 29 and 57; Part B: Pre-dose Days 1, 15, 29, 57 and 85; Day 106 and 169

Notes:

[21] - 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: No statistical analysis was planned or performed for this endpoint.

[22] - 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: This endpoint was analysed only for the Part A and B arms of the study, so data was reported only for the Part A and B arm groups.

End point values	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg	Part A-SAD: Cohort 4: BIIB067 60 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: hour*ng/mL				
arithmetic mean (standard deviation)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

End point values	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	9	10
Units: hour*ng/mL				
arithmetic mean (standard deviation)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)	99999 (± 99999)

Statistical analyses

No statistical analyses for this end point

Primary: Parts A and B: PK Parameter of BIIB067 in Plasma: Apparent Terminal Elimination Half-life (t1/2)

End point title	Parts A and B: PK Parameter of BIIB067 in Plasma: Apparent Terminal Elimination Half-life (t1/2)[23][24]

End point description:

PK population is the subset of the ITT population with at least 1 post-dose PK measurement in Part A or B. 99999=Data is not available as the concentration values were below the level of quantification and could not be quantified to estimate the apparent terminal t1/2 values.

End point type	Primary

End point timeframe:

Part A: Pre-dose Day 1, Days 29 and 57; Part B: Pre-dose Days 1, 15, 29, 57 and 85; Day 106 and 169

Notes:

[23] - 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: No statistical analysis was planned or performed for this endpoint.

[24] - 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: This endpoint was analysed only for the Part A and B arms of the study, so data was reported only for the Part A and B arm groups.

End point values	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg	Part A-SAD: Cohort 4: BIIB067 60 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: hours				
median (inter-quartile range (Q1-Q3))	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)

End point values	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	9	10
Units: hours				
median (inter-quartile range (Q1-Q3))	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)

Statistical analyses

No statistical analyses for this end point

Primary: Parts A and B: PK Parameters of BIIB067 in CSF Levels: Terminal Elimination Half-life (t1/2)

End point title	Parts A and B: PK Parameters of BIIB067 in CSF Levels: Terminal Elimination Half-life (t1/2)[25][26]

End point description:

PK population is the subset of the ITT population with at least 1 post-dose PK measurement in Part A or B. 99999= Data is not available as the concentration values were below the level of quantification and could not be quantified to estimate the terminal t1/2 values.

End point type	Primary

End point timeframe:

Part A: Pre-dose Day 1, Days 29 and 57; Part B: Pre-dose Days 1, 15, 29, 57 and 85; Day 106 and 169

Notes:

[25] - 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: No statistical analysis was planned or performed for this endpoint.

[26] - 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: This endpoint was analysed only for the Part A and B arms of the study, so data was reported only for the Part A and B arm groups.

End point values	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg	Part A-SAD: Cohort 4: BIIB067 60 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	3	3	3	6
Units: hours				
median (inter-quartile range (Q1-Q3))	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)

End point values	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	10	9	9	10
Units: hours				
median (inter-quartile range (Q1-Q3))	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)	99999 (99999 to 99999)

Statistical analyses

No statistical analyses for this end point

Primary: Part C: Change From Baseline in Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) Total Score at Week 28

End point title	Part C: Change From Baseline in Amyotrophic Lateral Sclerosis Functional Rating Scale-Revised (ALSFRS-R) Total Score at Week 28[27]

End point description:

The ALSFRS-R measures 4 functional domains, including respiratory, bulbar function, gross motor skills, and fine motor skills. There are 12 questions, each scored from 0 (no function) to 4 (full function), for a total possible score of 48. Scores decline with disease progression. ALSFRS-R scores calculated at diagnosis can be compared to scores throughout time to determine the speed of progression. Higher scores represent better function, negative change from baseline indicates disease progression. mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment.

End point type	Primary

End point timeframe:

Baseline, Week 28 (Day 197)

Notes:

[27] - 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: This endpoint was analysed only for the Part C arms of the study, so data was reported only for the Part C arm groups.

End point values	Part C-Pivotal: Placebo	Part C-Pivotal: BIIB067 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	39		
Units: score on scale				
least squares mean (standard error)	-8.1 (± 1.79)	-7.0 (± 1.42)		

Statistical analyses

Statistical analysis title	Part C-Pivotal: Placebo vs BIIB07 100 mg

Statistical analysis description:

ANCOVA model included treatment as a fixed effect, adjusts for the covariates: Baseline disease duration since symptom onset, baseline ALSFRS-R total score, and use of riluzole or edaravone. Multiple imputation was used to handle missing data for withdrawals. Joint rank test combining function and mortality were used for statistical inference and the estimates were from the ANCOVA model for change from baseline.

Comparison groups	Part C-Pivotal: BIIB067 100 mg v Part C-Pivotal: Placebo
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9689 [28]
Method	Joint rank
Parameter estimate	least square (LS) mean difference
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.19
upper limit	5.53
Variability estimate	Standard error of the mean
Dispersion value	2.22

Notes:

[28] - p-value was calculated from joint rank test.

Secondary: Part B: CSF Levels of Total SOD1 Protein Concentration Ratio to Baseline

End point title	Part B: CSF Levels of Total SOD1 Protein Concentration Ratio to Baseline[29]

End point description:

Total CSF SOD1 protein ratio to baseline was calculated. PD population is the subset of the ITT population with at least 1 post-dose PD measurement in Part B. 99999=Data is not estimable due to small sample size.

End point type	Secondary

End point timeframe:

Day 85

Notes:

[29] - 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: This endpoint was analysed only for the Part B arms of the study, so data was reported only for the Part B arm groups.

End point values	Part B-MAD: Combined Placebo	Part B-MAD: Cohort 5: BIIB067 20 mg	Part B-MAD: Cohort 6: BIIB067 40 mg	Part B-MAD: Cohort 7: BIIB067 60 mg
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	12	10	9	8
Units: ratio				
geometric mean (confidence interval 95%)				
Day 85	0.97 (0.83 to 1.13)	0.99 (0.83 to 1.18)	0.73 (0.61 to 0.87)	0.79 (0.66 to 0.94)

End point values	Part B-MAD: Cohort 8: BIIB067 100 mg			
Subject group type	Reporting group			
Number of subjects analysed	10			
Units: ratio				
geometric mean (confidence interval 95%)				
Day 85	0.64 (0.55 to 0.76)			

Statistical analyses

Statistical analysis title	Part B-MAD: Placebo vs Cohort 5 (BIIB067 20 mg)
Statistical analysis description:	
Day 85	
Comparison groups	Part B-MAD: Combined Placebo v Part B-MAD: Cohort 5: BIIB067 20 mg
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon rank sum test
Parameter estimate	diff in LS geometric mean ratio tof:pbo
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	0.84

Statistical analysis title	Part B-MAD: Placebo vs Cohort 6 (BIIB067 40 mg)
Statistical analysis description:	
Day 85	
Comparison groups	Part B-MAD: Combined Placebo v Part B-MAD: Cohort 6: BIIB067 40 mg
Number of subjects included in analysis	21
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0002
Method	Wilcoxon rank sum test
Parameter estimate	diff in LS geometric mean ratio tof:pbo
Point estimate	0.75

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.6
upper limit	0.95

Statistical analysis title	Part B-MAD: Placebo vs Cohort 7 (BIIB067 60 mg)
Statistical analysis description:	
Day 85	
Comparison groups	Part B-MAD: Combined Placebo v Part B-MAD: Cohort 7: BIIB067 60 mg
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0641
Method	Wilcoxon rank sum test
Parameter estimate	diff in LS geometric mean ratio tof:pbo
Point estimate	0.81
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.02

Statistical analysis title	Part B-MAD: Placebo vs Cohort 8 (BIIB067 100 mg)
Statistical analysis description:	
Day 85	
Comparison groups	Part B-MAD: Combined Placebo v Part B-MAD: Cohort 8: BIIB067 100 mg
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Wilcoxon rank sum test
Parameter estimate	diff in LS geometric mean ratio tof:pbo
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.53
upper limit	0.84

Secondary: Part C: CSF Levels of Total SOD1 Protein Concentration Ratio to Baseline

End point title	Part C: CSF Levels of Total SOD1 Protein Concentration Ratio to Baseline[30]

End point description:

Total CSF SOD1 protein ratio to baseline was calculated. mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. Data reported under LS mean refers to 'LS Geometric Mean Ratio to Baseline'.

End point type	Secondary

End point timeframe:

Week 28 (Day 197)

Notes:

[30] - 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: This endpoint was analysed only for the Part C arms of the study, so data was reported only for the Part C arm groups.

End point values	Part C-Pivotal: Placebo	Part C-Pivotal: BIIB067 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	39		
Units: ratio				
least squares mean (confidence interval 95%)	1.16 (0.96 to 1.40)	0.71 (0.62 to 0.83)		

Statistical analyses

Statistical analysis title	Part C-Pivotal: Placebo vs BIIB067 100 mg

Statistical analysis description:

The ANCOVA model included covariates for the corresponding baseline value i.e. log value, baseline disease duration since symptom onset, and use of riluzole or edaravone. Multiple imputation was used to handle missing data for withdrawals.

Comparison groups	Part C-Pivotal: Placebo v Part C-Pivotal: BIIB067 100 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [31]
Method	ANCOVA
Parameter estimate	diff in LS geometric mean ratio tof:pbo
Point estimate	0.62
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	0.78

Notes:

[31] - The analysis was based on ANCOVA model with natural log transformed data.

Secondary: Part C: Change From Baseline in Percent Predicted Slow Vital Capacity (SVC) at Week 28

End point title	Part C: Change From Baseline in Percent Predicted Slow Vital Capacity (SVC) at Week 28[32]

End point description:

Vital capacity was measured by means of an SVC test, administered in the upright position. mITT

population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Baseline, Week 28 (Day 197)

Notes:

[32] - 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: This endpoint was analysed only for the Part C arms of the study, so data was reported only for the Part C arm groups.

End point values	Part C-Pivotal: Placebo	Part C-Pivotal: BIIB067 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	39		
Units: percent predicted				
least squares mean (standard error)	-22.20 (± 4.771)	-14.31 (± 3.557)		

Statistical analyses

Statistical analysis title	Part C-Pivotal: Placebo vs BIIB067 100 mg

Statistical analysis description:

Multiple imputation was used to handle missing data for withdrawals. Joint rank test combining function and mortality were used for statistical inference and the estimates were from the ANCOVA for change from baseline.

Comparison groups	Part C-Pivotal: Placebo v Part C-Pivotal: BIIB067 100 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3233 [33]
Method	Joint rank
Parameter estimate	LS mean difference
Point estimate	7.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.528
upper limit	19.322
Variability estimate	Standard error of the mean
Dispersion value	5.829

Notes:

[33] - Joint rank p-value was calculated from ANCOVA model which included treatment as fixed effect, adjusts for covariates: Baseline disease duration since symptom onset, baseline ALSFRS-R total score, and use of riluzole or edaravone.

Secondary: Part C: Change From Baseline in Handheld Dynamometry (HHD) Megascore as Measured by the HHD Device at Week 28

End point title	Part C: Change From Baseline in Handheld Dynamometry (HHD) Megascore as Measured by the HHD Device at Week 28[34]

End point description:

Quantitative muscle strength was evaluated using HHD, which tests isometric strength of multiple muscles using standard subject positioning. Sixteen muscle groups were evaluated in both upper and lower extremities. Strength determinations were converted to Z scores and averaged to provide an HHD megascore. 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 all eight bilateral measurement Z scores, if no more than 10 (≤ 10) measures are missing. A negative change from baseline indicated decreased muscle strength. mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment.

End point type	Secondary

End point timeframe:

Baseline, Week 28 (Day 197)

Notes:

[34] - 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: This endpoint was analysed only for the Part C arms of the study, so data was reported only for the Part C arm groups.

End point values	Part C-Pivotal: Placebo	Part C-Pivotal: BIIB067 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	39		
Units: score on a scale				
least squares mean (standard error)	-0.37 (± 0.096)	-0.34 (± 0.073)		

Statistical analyses

Statistical analysis title	Part C-Pivotal: Placebo vs BIIB067 100 mg
Comparison groups	Part C-Pivotal: Placebo v Part C-Pivotal: BIIB067 100 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.839 [35]
Method	ANCOVA
Parameter estimate	LS mean difference
Point estimate	0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.207
upper limit	0.255
Variability estimate	Standard error of the mean
Dispersion value	0.118

Notes:

[35] - The ANCOVA model included treatment as a fixed effect and adjusts for the following covariates: baseline disease duration since symptom onset, baseline HHD overall megascore, and use of riluzole or edaravone.

Secondary: Part C: Time to Death or Permanent Ventilation

End point title	Part C: Time to Death or Permanent Ventilation[36]

End point description:

Time to Death or Permanent Ventilation is defined as the time to the earliest occurrence of one of the following events that were adjudicated by an independent committee: Death; Permanent ventilation (≥22 hours of mechanical ventilation [invasive or noninvasive] per day for ≥21 consecutive days). mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. 99999=not estimated due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

Baseline up to Week 28 (Day 197)

Notes:

[36] - 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: This endpoint was analysed only for the Part C arms of the study, so data was reported only for the Part C arm groups.

End point values	Part C-Pivotal: Placebo	Part C-Pivotal: BIIB067 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	39		
Units: days				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Time to Death

End point title	Part C: Time to Death[37]

End point description:

mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment. 99999=not estimated due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

Baseline up to Week 28 (Day 197)

Notes:

[37] - 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: This endpoint was analysed only for the Part C arms of the study, so data was reported only for the Part C arm groups.

End point values	Part C-Pivotal: Placebo	Part C-Pivotal: BIIB067 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	39		
Units: days				
median (confidence interval 95%)	99999 (99999 to 99999)	99999 (99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Part C: Number of Subjects Experiencing Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	Part C: Number of Subjects Experiencing Adverse Events (AEs) and Serious Adverse Events (SAEs)[38]

End point description:

An AE is any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. A SAE is any untoward medical occurrence that at any dose results in death, life-threatening event, requires inpatient hospitalization, significant disability/incapacity or congenital anomaly. Safety population included all subjects in Part C who were randomized and received at least one dose of study treatment.

End point type	Secondary

End point timeframe:

First dose up to Day 236

Notes:

[38] - 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: This endpoint was analysed only for the Part C arms of the study, so data was reported only for the Part C arm groups.

End point values	Part C-Pivotal: Placebo	Part C-Pivotal: BIIB067 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	36	72		
Units: subjects				
AEs	34	69		
SAEs	5	13		

Statistical analyses

No statistical analyses for this end point

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

End point title	Part C: Neurofilament Light Chain (NfL) Plasma Concentration Ratio to Baseline[39]

End point description:

NfL is a biomarker whose concentration was assessed in plasma. Plasma NfL ratio to baseline was calculated. mITT population included all subjects who met the prognostic enrichment criteria for rapid disease progression in Part C who were randomized and received at least 1 dose of study treatment.

Data reported under Geometric Mean refers to 'LS Geometric Mean'.

End point type	Secondary

End point timeframe:

Baseline, Day 197 (Week 28)

Notes:

[39] - 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: This endpoint was analysed only for the Part C arms of the study, so data was reported only for the Part C arm groups.

End point values	Part C-Pivotal: Placebo	Part C-Pivotal: BIIB067 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	21	39		
Units: ratio				
geometric mean (confidence interval 95%)				
Day 197	1.20 (0.94 to 1.52)	0.40 (0.33 to 0.48)		

Statistical analyses

Statistical analysis title	Part C-Pivotal: Placebo vs BIIB067 100 mg

Statistical analysis description:

Day 197 (Week 28)

Comparison groups	Part C-Pivotal: Placebo v Part C-Pivotal: BIIB067 100 mg
Number of subjects included in analysis	60
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [40]
Method	ANCOVA
Parameter estimate	diff in LS geometric mean ratio tof:pbo
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.25
upper limit	0.45

Notes:

[40] - The analysis was based on ANCOVA model with natural log transformed data. The model included covariates for the corresponding baseline value i.e. log value, baseline disease duration since symptom onset, and use of riluzole or edaravone.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Part A: First dose up to Day 63; Part B: First dose up to Day 289; Part C: First dose up to Day 236

Adverse event reporting additional description:

Safety population included all randomized subjects who received at least 1 dose or a part of 1 dose of study treatment (BIIB067 or placebo) in Part A or B. Safety population included all subjects in Part C who were randomized and received at least one dose of study treatment. MedDRA version for Parts A and B: 22.0, Part C: 24.0

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Part A-SAD: Cohort 1: BIIB067 10 mg

Reporting group description:

Subjects were administered BIIB067 10 mg once by intrathecal bolus injection on Day 1.

Reporting group title	Part A-SAD: Cohort 2: BIIB067 20 mg

Reporting group description:

Subjects were administered BIIB067 20 mg once by intrathecal bolus injection on Day 1 of Cohort 2 after the safety review of Cohort 1.

Reporting group title	Part A-SAD: Cohort 3: BIIB067 40 mg

Reporting group description:

Subjects were administered BIIB067 40 mg once by intrathecal bolus injection on Day 1 of Cohort 3 after the safety review of Cohort 2.

Reporting group title	Part A-SAD: Cohort 4: BIIB067 60 mg

Reporting group description:

Subjects were administered BIIB067 60 mg once by intrathecal bolus injection on Day 1 of Cohort 4 after the safety review of Cohort 3.

Reporting group title	Part A-SAD: Combined Placebo

Reporting group description:

Subjects were administered BIIB067-matching placebo once by intrathecal bolus injection on Day 1 of Cohorts 1, 2, 3, and 4 respectively.

Reporting group title	Part B-MAD: Cohort 5: BIIB067 20 mg

Reporting group description:

Subjects were administered BIIB067 20 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection.

Reporting group title	Part B-MAD: Cohort 6: BIIB067 40 mg

Reporting group description:

Subjects were administered BIIB067 40 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection after the safety and PK review of Cohort 5.

Reporting group title	Part B-MAD: Cohort 7: BIIB067 60 mg

Reporting group description:

Subjects were administered BIIB067 60 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection after the safety, PK review and SOD1 PD review of Cohort 6.

Reporting group title	Part B-MAD: Cohort 8: BIIB067 100 mg

Reporting group description:

Subjects were administered BIIB067 100 mg, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection after the safety, PK review and SOD1 PD review of Cohort 7.

Reporting group title	Part B-MAD: Combined Placebo

Reporting group description:

Subjects were administered BIIB067-matching placebo, 3 loading doses once every 2 weeks on Days 1, 15, 29 and 2 maintenance doses once every 4 weeks on Days 57 and 85 by intrathecal injection.

Reporting group title	Part C-Pivotal: BIIB067 100 mg

Reporting group description:

Subjects were administered BIIB067 100 mg, 3 loading doses administered once every 2 weeks on Days 1, 15, 29 followed by 5 maintenance doses administered once every 4 weeks on Days 57, 85, 113, 141, 169 up to 24 weeks by intrathecal bolus injection.

Reporting group title	Part C-Pivotal: Placebo

Reporting group description:

Subjects were administered BIIB067-matching placebo, 3 loading doses administered once every 2 weeks on Days 1, 15, 29 followed by 5 maintenance doses administered once every 4 weeks on Days 57, 85, 113, 141, 169 up to 24 weeks by intrathecal bolus injection.

Serious adverse events	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Csf protein increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Csf white blood cell count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Fibula fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Meningitis chemical			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Vascular disorders			
Deep vein thrombosis			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Loss of consciousness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar radiculopathy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Myelitis transverse			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Hypothermia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Impaired self-care			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 complication associated with device			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Faecaloma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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
Atelectasis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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			
Myelitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (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 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part A-SAD: Cohort 4: BIIB067 60 mg	Part A-SAD: Combined Placebo	Part B-MAD: Cohort 5: BIIB067 20 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
number of deaths (all causes)	0	0	1
number of deaths resulting from adverse events	0	0	0
Investigations			
Csf protein increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Csf white blood cell count increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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			
Fibula fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Meningitis chemical			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar radiculopathy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Myelitis transverse			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Hypothermia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Impaired self-care			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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 complication associated with device			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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			
Faecaloma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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
Atelectasis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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			
Myelitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (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 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part B-MAD: Cohort 6: BIIB067 40 mg	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 9 (11.11%)	2 / 9 (22.22%)	0 / 10 (0.00%)
number of deaths (all causes)	0	1	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Csf protein increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (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
Csf white blood cell count increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (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
Injury, poisoning and procedural complications			
Fibula fracture			

subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Meningitis chemical			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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			
Loss of consciousness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar radiculopathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Myelitis transverse			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Hypothermia			

subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Impaired self-care			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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 complication associated with device			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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			
Faecaloma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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
Atelectasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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 / 9 (11.11%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Infections and infestations			
Myelitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (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 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Part B-MAD: Combined Placebo	Part C-Pivotal: BIIB067 100 mg	Part C-Pivotal: Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 12 (16.67%)	13 / 72 (18.06%)	5 / 36 (13.89%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events	0	0	0
Investigations			
Csf protein increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (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
Csf white blood cell count increased			

subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (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			
Fibula fracture			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (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
Meningitis chemical			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (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
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (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
Cardiac disorders			
Cardiac failure congestive			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (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
Lumbar radiculopathy			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (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
Myelitis transverse			

subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (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
General disorders and administration site conditions			
Hypothermia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (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
Impaired self-care			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (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
Respiratory complication associated with device			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (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
Gastrointestinal disorders			
Faecaloma			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	1 / 12 (8.33%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (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
Atelectasis			

subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	2 / 36 (5.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	0 / 12 (0.00%)	2 / 72 (2.78%)	0 / 36 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	0 / 12 (0.00%)	3 / 72 (4.17%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 12 (8.33%)	1 / 72 (1.39%)	0 / 36 (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
Infections and infestations			
Myelitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	1 / 36 (2.78%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Part A-SAD: Cohort 1: BIIB067 10 mg	Part A-SAD: Cohort 2: BIIB067 20 mg	Part A-SAD: Cohort 3: BIIB067 40 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)	3 / 3 (100.00%)	3 / 3 (100.00%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Flushing			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Feeling abnormal			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion site bruising			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Infusion site swelling			

subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Oedema peripheral			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Immune system disorders			
Dust allergy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Choking			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Respiratory symptom			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sputum discoloured			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Investigations			
Csf protein increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Csf white blood cell count increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Csf white blood cell count positive			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Foot fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal procedural complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nasal injury			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Post procedural complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Post procedural contusion			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Post procedural discomfort			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Post-traumatic pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Procedural anxiety			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Procedural complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Procedural dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Procedural headache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Procedural nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Procedural pain			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	2	0
Skin abrasion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Subcutaneous haematoma			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sunburn			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tibia fracture			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Vaccination complication			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			

Balance disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 3 (0.00%)	2 / 3 (66.67%)	1 / 3 (33.33%)
occurrences (all)	0	2	1
Hypoaesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hyporeflexia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle contractions involuntary			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle spasticity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nerve compression			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Peroneal nerve palsy			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pleocytosis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinus headache			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Blood and lymphatic system disorders			
Eosinophilia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Constipation			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dysphagia			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Gastritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lip swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Salivary hypersecretion			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Toothache			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Cold sweat			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Eczema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Miliaria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Rash pruritic			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin disorder			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Skin plaque			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary retention			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Arthralgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Bursitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscle tightness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Neck pain			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	1 / 3 (33.33%)
occurrences (all)	0	0	1
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Fungal skin infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Gastric infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Labyrinthitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0

Nasopharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	1 / 3 (33.33%)	0 / 3 (0.00%)
occurrences (all)	0	1	0
Oral herpes			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	1 / 3 (33.33%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	1	0	0
Systemic viral infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 3 (0.00%)	0 / 3 (0.00%)	0 / 3 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part A-SAD: Cohort 4: BIIB067 60 mg	Part A-SAD: Combined Placebo	Part B-MAD: Cohort 5: BIIB067 20 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	6 / 6 (100.00%)	2 / 5 (40.00%)	10 / 10 (100.00%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Feeling abnormal			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Feeling hot			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infusion site bruising			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infusion site swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pyrexia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Immune system disorders			
Dust allergy			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Choking			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Dyspnoea			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oropharyngeal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	4
Respiratory symptom			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Rhinorrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Sputum discoloured			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Depression			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Investigations			
Csf protein increased			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood phosphorus decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Csf white blood cell count increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Csf white blood cell count positive			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Urine output decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Fall			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	3 / 10 (30.00%)
occurrences (all)	0	0	4
Foot fracture			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Joint injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ligament sprain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle strain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal procedural complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasal injury			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 6 (0.00%)	1 / 5 (20.00%)	4 / 10 (40.00%)
occurrences (all)	0	1	9
Post procedural complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Post procedural contusion			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
Post procedural discomfort			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Post-traumatic pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Procedural anxiety			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Procedural complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Procedural dizziness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Procedural headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Procedural nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Procedural pain			
subjects affected / exposed	3 / 6 (50.00%)	1 / 5 (20.00%)	4 / 10 (40.00%)
occurrences (all)	3	1	5
Skin abrasion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin laceration			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Subcutaneous haematoma			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sunburn			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tibia fracture			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Vaccination complication			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Tachycardia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dysaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	4 / 10 (40.00%)
occurrences (all)	1	0	4
Hypoaesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Hyporeflexia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Muscle contractions involuntary			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Migraine			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Muscle spasticity			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nerve compression			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peroneal nerve palsy			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pleocytosis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Sinus headache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Eosinophilia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Abdominal pain lower			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Constipation			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Faeces discoloured			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Gingival pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lip swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Salivary hypersecretion			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Toothache			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			

Cold sweat			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Eczema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Miliaria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rash pruritic			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin disorder			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Skin plaque			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 6 (33.33%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	2	0	1
Arthralgia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Bursitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Flank pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Joint swelling			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	2 / 6 (33.33%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Muscle tightness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscular weakness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			

subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Myalgia			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pain in extremity			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Ear infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 6 (16.67%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Gastric infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Hordeolum			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Labyrinthitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Lower respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	2 / 10 (20.00%)
occurrences (all)	0	0	2
Oral herpes			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Systemic viral infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Tooth abscess			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	4 / 10 (40.00%)
occurrences (all)	0	0	5
Urinary tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Viral upper respiratory tract infection			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 6 (0.00%)	0 / 5 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part B-MAD: Cohort 6: BIIB067 40 mg	Part B-MAD: Cohort 7: BIIB067 60 mg	Part B-MAD: Cohort 8: BIIB067 100 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	9 / 9 (100.00%)	9 / 9 (100.00%)	10 / 10 (100.00%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flushing			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Hypertension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Fatigue			

subjects affected / exposed	1 / 9 (11.11%)	2 / 9 (22.22%)	2 / 10 (20.00%)
occurrences (all)	1	2	2
Feeling abnormal			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Feeling hot			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Infusion site bruising			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Infusion site swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pyrexia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Immune system disorders			
Dust allergy			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Respiratory, thoracic and mediastinal disorders			

Choking			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	1 / 9 (11.11%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	1	1	0
Oropharyngeal pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Respiratory symptom			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Sleep apnoea syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Sputum discoloured			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Upper respiratory tract congestion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Upper-airway cough syndrome			
subjects affected / exposed	1 / 9 (11.11%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	2	1	0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	2	1
Depression			

subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Insomnia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Investigations			
Csf protein increased			
subjects affected / exposed	0 / 9 (0.00%)	3 / 9 (33.33%)	1 / 10 (10.00%)
occurrences (all)	0	3	1
Blood phosphorus decreased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Csf white blood cell count increased			
subjects affected / exposed	1 / 9 (11.11%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Csf white blood cell count positive			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Weight decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Arthropod bite			
subjects affected / exposed	1 / 9 (11.11%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	3	1	0
Contusion			

subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
Fall			
subjects affected / exposed	3 / 9 (33.33%)	2 / 9 (22.22%)	5 / 10 (50.00%)
occurrences (all)	3	3	11
Foot fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Head injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	3
Joint injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 9 (0.00%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Muscle strain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Musculoskeletal procedural complication			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasal injury			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Post lumbar puncture syndrome			
subjects affected / exposed	3 / 9 (33.33%)	3 / 9 (33.33%)	3 / 10 (30.00%)
occurrences (all)	9	5	7
Post procedural complication			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Post procedural contusion			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0

Post procedural discomfort			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Post-traumatic pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Procedural anxiety			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Procedural complication			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Procedural dizziness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Procedural headache			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	3
Procedural nausea			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Procedural pain			
subjects affected / exposed	1 / 9 (11.11%)	4 / 9 (44.44%)	7 / 10 (70.00%)
occurrences (all)	6	13	20
Skin abrasion			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Skin laceration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Subcutaneous haematoma			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Sunburn			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Tibia fracture			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Vaccination complication			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tachycardia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dizziness			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	3 / 10 (30.00%)
occurrences (all)	0	3	5
Dysaesthesia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	3
Headache			
subjects affected / exposed	2 / 9 (22.22%)	4 / 9 (44.44%)	6 / 10 (60.00%)
occurrences (all)	3	8	11
Hypoaesthesia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Hyporeflexia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Muscle contractions involuntary			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Migraine			

subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	3
Muscle spasticity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Nerve compression			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neuralgia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Paraesthesia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Peroneal nerve palsy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Pleocytosis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Sinus headache			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Eosinophilia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Abdominal pain			

subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Abdominal pain lower			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Dyspepsia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Dysphagia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Faeces discoloured			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorder			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Lip swelling			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	2 / 9 (22.22%)	1 / 9 (11.11%)	2 / 10 (20.00%)
occurrences (all)	2	1	2
Salivary hypersecretion			

subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	1 / 10 (10.00%)
occurrences (all)	0	1	1
Toothache			
subjects affected / exposed	2 / 9 (22.22%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Skin and subcutaneous tissue disorders			
Cold sweat			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Eczema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Erythema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Miliaria			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Night sweats			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Pruritus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Rash pruritic			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Skin disorder			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Skin plaque			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Urinary incontinence			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Urinary retention			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 9 (11.11%)	1 / 9 (11.11%)	5 / 10 (50.00%)
occurrences (all)	1	1	8
Arthralgia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 9 (11.11%)	2 / 10 (20.00%)
occurrences (all)	1	1	2
Bursitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Flank pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Joint swelling			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Muscle spasms			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Muscle tightness			

subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Muscular weakness			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	1	0	1
Musculoskeletal pain			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Neck pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Myalgia			
subjects affected / exposed	0 / 9 (0.00%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	0	7	0
Pain in extremity			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	3 / 10 (30.00%)
occurrences (all)	1	0	5
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Ear infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	2 / 9 (22.22%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	2	0	0
Gastroenteritis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Gastric infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Hordeolum			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Labyrinthitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 9 (11.11%)	3 / 9 (33.33%)	1 / 10 (10.00%)
occurrences (all)	1	3	1
Oral herpes			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	2
Pharyngitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	1	0	0
Pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	0	1	0
Sinusitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Systemic viral infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Upper respiratory tract infection			
subjects affected / exposed	0 / 9 (0.00%)	2 / 9 (22.22%)	0 / 10 (0.00%)
occurrences (all)	0	2	0
Urinary tract infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 9 (0.00%)	2 / 10 (20.00%)
occurrences (all)	1	0	2
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 9 (11.11%)	1 / 9 (11.11%)	0 / 10 (0.00%)
occurrences (all)	1	2	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	1 / 10 (10.00%)
occurrences (all)	0	0	1
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 9 (0.00%)	0 / 10 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Part B-MAD: Combined Placebo	Part C-Pivotal: BIIB067 100 mg	Part C-Pivotal: Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 12 (91.67%)	68 / 72 (94.44%)	34 / 36 (94.44%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Flushing			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Hypertension			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	2 / 36 (5.56%)
occurrences (all)	0	1	2
General disorders and administration site conditions			
Asthenia			

subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Chest pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Fatigue			
subjects affected / exposed	2 / 12 (16.67%)	12 / 72 (16.67%)	2 / 36 (5.56%)
occurrences (all)	2	22	2
Feeling abnormal			
subjects affected / exposed	1 / 12 (8.33%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Feeling hot			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Infusion site bruising			
subjects affected / exposed	1 / 12 (8.33%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Infusion site swelling			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	0 / 12 (0.00%)	2 / 72 (2.78%)	0 / 36 (0.00%)
occurrences (all)	0	2	0
Pain			
subjects affected / exposed	1 / 12 (8.33%)	7 / 72 (9.72%)	0 / 36 (0.00%)
occurrences (all)	1	13	0
Peripheral swelling			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	1 / 36 (2.78%)
occurrences (all)	0	1	2
Pyrexia			
subjects affected / exposed	0 / 12 (0.00%)	3 / 72 (4.17%)	1 / 36 (2.78%)
occurrences (all)	0	5	1
Immune system disorders			

Dust allergy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Choking			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Cough			
subjects affected / exposed	1 / 12 (8.33%)	5 / 72 (6.94%)	1 / 36 (2.78%)
occurrences (all)	1	5	1
Dyspnoea			
subjects affected / exposed	1 / 12 (8.33%)	4 / 72 (5.56%)	5 / 36 (13.89%)
occurrences (all)	1	4	5
Oropharyngeal pain			
subjects affected / exposed	0 / 12 (0.00%)	2 / 72 (2.78%)	2 / 36 (5.56%)
occurrences (all)	0	3	2
Respiratory symptom			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Rhinorrhoea			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Sleep apnoea syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Sputum discoloured			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract congestion			
subjects affected / exposed	1 / 12 (8.33%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Upper-airway cough syndrome			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			

Anxiety			
subjects affected / exposed	0 / 12 (0.00%)	4 / 72 (5.56%)	3 / 36 (8.33%)
occurrences (all)	0	5	3
Depression			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	3 / 36 (8.33%)
occurrences (all)	0	1	3
Insomnia			
subjects affected / exposed	0 / 12 (0.00%)	3 / 72 (4.17%)	3 / 36 (8.33%)
occurrences (all)	0	3	3
Investigations			
Csf protein increased			
subjects affected / exposed	1 / 12 (8.33%)	6 / 72 (8.33%)	1 / 36 (2.78%)
occurrences (all)	1	6	1
Blood phosphorus decreased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Csf white blood cell count increased			
subjects affected / exposed	0 / 12 (0.00%)	7 / 72 (9.72%)	0 / 36 (0.00%)
occurrences (all)	0	8	0
Csf white blood cell count positive			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Urine output decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Weight decreased			
subjects affected / exposed	1 / 12 (8.33%)	0 / 72 (0.00%)	2 / 36 (5.56%)
occurrences (all)	1	0	2
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Arthropod bite			

subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Contusion			
subjects affected / exposed	1 / 12 (8.33%)	3 / 72 (4.17%)	1 / 36 (2.78%)
occurrences (all)	1	3	1
Fall			
subjects affected / exposed	3 / 12 (25.00%)	17 / 72 (23.61%)	15 / 36 (41.67%)
occurrences (all)	7	38	38
Foot fracture			
subjects affected / exposed	1 / 12 (8.33%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Head injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	2
Joint injury			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	0	3	0
Ligament sprain			
subjects affected / exposed	0 / 12 (0.00%)	4 / 72 (5.56%)	2 / 36 (5.56%)
occurrences (all)	0	4	2
Muscle strain			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	1 / 36 (2.78%)
occurrences (all)	0	1	1
Musculoskeletal procedural complication			
subjects affected / exposed	0 / 12 (0.00%)	3 / 72 (4.17%)	3 / 36 (8.33%)
occurrences (all)	0	4	5
Nasal injury			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Post lumbar puncture syndrome			
subjects affected / exposed	3 / 12 (25.00%)	13 / 72 (18.06%)	11 / 36 (30.56%)
occurrences (all)	4	34	21
Post procedural complication			
subjects affected / exposed	1 / 12 (8.33%)	3 / 72 (4.17%)	4 / 36 (11.11%)
occurrences (all)	1	3	4

Post procedural contusion			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Post procedural discomfort			
subjects affected / exposed	1 / 12 (8.33%)	0 / 72 (0.00%)	1 / 36 (2.78%)
occurrences (all)	1	0	1
Post-traumatic pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Procedural anxiety			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Procedural complication			
subjects affected / exposed	0 / 12 (0.00%)	2 / 72 (2.78%)	1 / 36 (2.78%)
occurrences (all)	0	2	1
Procedural dizziness			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Procedural headache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Procedural nausea			
subjects affected / exposed	1 / 12 (8.33%)	2 / 72 (2.78%)	2 / 36 (5.56%)
occurrences (all)	1	2	2
Procedural pain			
subjects affected / exposed	5 / 12 (41.67%)	41 / 72 (56.94%)	21 / 36 (58.33%)
occurrences (all)	16	110	32
Skin abrasion			
subjects affected / exposed	0 / 12 (0.00%)	3 / 72 (4.17%)	3 / 36 (8.33%)
occurrences (all)	0	5	5
Skin laceration			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	3 / 36 (8.33%)
occurrences (all)	0	0	5
Subcutaneous haematoma			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0

Sunburn			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Tibia fracture			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Vaccination complication			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	2 / 36 (5.56%)
occurrences (all)	0	5	2
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	1 / 12 (8.33%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Tachycardia			
subjects affected / exposed	1 / 12 (8.33%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Nervous system disorders			
Balance disorder			
subjects affected / exposed	1 / 12 (8.33%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Dizziness			
subjects affected / exposed	0 / 12 (0.00%)	4 / 72 (5.56%)	3 / 36 (8.33%)
occurrences (all)	0	4	3
Dysaesthesia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	0	2	0
Headache			
subjects affected / exposed	7 / 12 (58.33%)	33 / 72 (45.83%)	16 / 36 (44.44%)
occurrences (all)	12	66	32
Hypoaesthesia			
subjects affected / exposed	0 / 12 (0.00%)	3 / 72 (4.17%)	1 / 36 (2.78%)
occurrences (all)	0	3	1
Hyporeflexia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Muscle contractions involuntary			

subjects affected / exposed	1 / 12 (8.33%)	4 / 72 (5.56%)	1 / 36 (2.78%)
occurrences (all)	1	4	1
Migraine			
subjects affected / exposed	0 / 12 (0.00%)	2 / 72 (2.78%)	1 / 36 (2.78%)
occurrences (all)	0	2	1
Muscle spasticity			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Nerve compression			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Neuralgia			
subjects affected / exposed	0 / 12 (0.00%)	4 / 72 (5.56%)	0 / 36 (0.00%)
occurrences (all)	0	4	0
Paraesthesia			
subjects affected / exposed	0 / 12 (0.00%)	6 / 72 (8.33%)	6 / 36 (16.67%)
occurrences (all)	0	6	10
Peroneal nerve palsy			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Pleocytosis			
subjects affected / exposed	0 / 12 (0.00%)	3 / 72 (4.17%)	0 / 36 (0.00%)
occurrences (all)	0	3	0
Sinus headache			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Blood and lymphatic system disorders			
Eosinophilia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 12 (8.33%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Gastrointestinal disorders			

Abdominal distension			
subjects affected / exposed	0 / 12 (0.00%)	2 / 72 (2.78%)	2 / 36 (5.56%)
occurrences (all)	0	2	2
Abdominal pain			
subjects affected / exposed	0 / 12 (0.00%)	2 / 72 (2.78%)	0 / 36 (0.00%)
occurrences (all)	0	2	0
Abdominal pain lower			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	1 / 12 (8.33%)	6 / 72 (8.33%)	4 / 36 (11.11%)
occurrences (all)	1	6	4
Diarrhoea			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	5 / 36 (13.89%)
occurrences (all)	0	1	6
Dyspepsia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Dysphagia			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Faeces discoloured			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Gastritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2
Gastrointestinal disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Gingival pain			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Lip swelling			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0

Nausea			
subjects affected / exposed	0 / 12 (0.00%)	9 / 72 (12.50%)	6 / 36 (16.67%)
occurrences (all)	0	24	9
Salivary hypersecretion			
subjects affected / exposed	0 / 12 (0.00%)	4 / 72 (5.56%)	1 / 36 (2.78%)
occurrences (all)	0	4	1
Toothache			
subjects affected / exposed	1 / 12 (8.33%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	1	1	0
Skin and subcutaneous tissue disorders			
Cold sweat			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Decubitus ulcer			
subjects affected / exposed	1 / 12 (8.33%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	2	0	0
Dermatitis allergic			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	0	2	0
Eczema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Erythema			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Miliaria			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Night sweats			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Pruritus			
subjects affected / exposed	0 / 12 (0.00%)	3 / 72 (4.17%)	1 / 36 (2.78%)
occurrences (all)	0	3	1
Rash			

subjects affected / exposed	1 / 12 (8.33%)	2 / 72 (2.78%)	0 / 36 (0.00%)
occurrences (all)	2	2	0
Rash pruritic			
subjects affected / exposed	1 / 12 (8.33%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Skin disorder			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Skin plaque			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	1 / 12 (8.33%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	1	0	0
Urinary incontinence			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Urinary retention			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 12 (0.00%)	15 / 72 (20.83%)	2 / 36 (5.56%)
occurrences (all)	0	25	3
Arthralgia			
subjects affected / exposed	1 / 12 (8.33%)	10 / 72 (13.89%)	2 / 36 (5.56%)
occurrences (all)	1	12	2
Bursitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Flank pain			
subjects affected / exposed	0 / 12 (0.00%)	2 / 72 (2.78%)	0 / 36 (0.00%)
occurrences (all)	0	2	0
Joint swelling			

subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	2 / 36 (5.56%)
occurrences (all)	0	2	2
Muscle spasms			
subjects affected / exposed	0 / 12 (0.00%)	5 / 72 (6.94%)	2 / 36 (5.56%)
occurrences (all)	0	5	3
Muscle tightness			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Muscular weakness			
subjects affected / exposed	1 / 12 (8.33%)	4 / 72 (5.56%)	4 / 36 (11.11%)
occurrences (all)	1	6	8
Musculoskeletal pain			
subjects affected / exposed	0 / 12 (0.00%)	4 / 72 (5.56%)	2 / 36 (5.56%)
occurrences (all)	0	4	2
Musculoskeletal stiffness			
subjects affected / exposed	0 / 12 (0.00%)	4 / 72 (5.56%)	0 / 36 (0.00%)
occurrences (all)	0	6	0
Neck pain			
subjects affected / exposed	3 / 12 (25.00%)	4 / 72 (5.56%)	4 / 36 (11.11%)
occurrences (all)	3	7	5
Myalgia			
subjects affected / exposed	0 / 12 (0.00%)	10 / 72 (13.89%)	2 / 36 (5.56%)
occurrences (all)	0	21	3
Pain in extremity			
subjects affected / exposed	2 / 12 (16.67%)	19 / 72 (26.39%)	6 / 36 (16.67%)
occurrences (all)	2	37	6
Infections and infestations			
Bronchitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Ear infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Fungal skin infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1

Gastroenteritis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	1 / 36 (2.78%)
occurrences (all)	0	0	1
Gastric infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Hordeolum			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	0 / 36 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	1 / 36 (2.78%)
occurrences (all)	0	1	1
Labyrinthitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Lower respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 12 (8.33%)	2 / 72 (2.78%)	7 / 36 (19.44%)
occurrences (all)	1	2	9
Oral herpes			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Pharyngitis			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 12 (0.00%)	1 / 72 (1.39%)	1 / 36 (2.78%)
occurrences (all)	0	2	2

Systemic viral infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Tooth abscess			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	5 / 72 (6.94%)	2 / 36 (5.56%)
occurrences (all)	0	5	2
Urinary tract infection			
subjects affected / exposed	1 / 12 (8.33%)	2 / 72 (2.78%)	2 / 36 (5.56%)
occurrences (all)	1	2	2
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 12 (0.00%)	3 / 72 (4.17%)	1 / 36 (2.78%)
occurrences (all)	0	3	1
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	0 / 36 (0.00%)
occurrences (all)	0	0	0
Type 2 diabetes mellitus			
subjects affected / exposed	0 / 12 (0.00%)	0 / 72 (0.00%)	2 / 36 (5.56%)
occurrences (all)	0	0	2

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
10 October 2016	Added the review of PK data and clarified the review of safety data prior to each dose escalation in Part B (MAD portion) of the study • Added the MMSE as part of the neurological examination • Other major changes were made to the study eligibility criteria for Part A (SAD) to allow only those subjects with ALS caused by a SOD1 mutation to enter the study.
17 November 2016	Corrected to reflect in the protocol that sampling for anti-BIIB067 antibodies was occurred during non-dosing clinical visits (except for predose on Day 1).
29 November 2017	Added an 8th treatment cohort to assess the safety and tolerability of up to 5 doses of BIB067 100 mg, and to include the option of an interim analysis during Part B (MAD portion) of the study. • Other major changes were made to the study stopping rules to clarify that SAEs or AEs determined to be unrelated to study treatment would not trigger dose suspension and to further specify situations that could trigger dose termination.
20 December 2018	Included a third part (Part C [Pivotal]) of approximately 60 subjects (2:1 randomization ratio of BIIB067:placebo) to assess the efficacy, safety, tolerability, PK, and PD of BIIB067 at 100 mg. Part C was to be conducted over a 4-week screening period, 24-week treatment period and 4-week follow-up period. Because the inclusion of Part C also warranted a change in the phase of development of the study, the title of the protocol was changed to accurately reflect study design and objectives and endpoints.
19 September 2019	Described the changes to the primary endpoint and statistical methodology, sample size considerations, and inclusion of an optional interim efficacy analysis for Part C (Pivotal) of the study. • The primary efficacy endpoint was revised from ALSFRS-R slope to total score (change from baseline to Week 28) and was analyzed via a joint-rank analysis that combines the ALSFRS-R score and survival time. This approach minimized the dependency on linearity assumptions (of the ALSFRS-R slope decline) and enabled a robust mechanism for accounting for missing data due to death. • The sample size for Part C of the study was increased to approximately 99 subjects (increased from up to 60 subjects) based on the following changes – Revised primary efficacy endpoint of change in ALSFRS-R total score from baseline to Day 197/Week 28 analyzed via the joint-rank methodology, two-sided alpha of 0.05 for the primary analysis, revised survival assumptions based on further review of natural history data and data from an interim analysis of Part B of this study (82% survival in the placebo control group and 90% survival in the tofersen group), • Under these assumptions, approximately 60 subjects (increased from 36) were needed in the mITT population (fast progressors) to achieve approximately 84% power. The target sample size for the non-fast progressor population was increased to approximately 39 subjects (increased from 24) to enable adequate power to detect a statistically significant reduction in CSF SOD1 concentrations. • Also, the assumptions for the sample size needed for the population outside the mITT were updated based on the current results from Part B of Study 2015-004098-33.
30 September 2019	Added a provision to collect subject's urine sample for future exploratory research, in all regions where not prohibited by regulatory authorities or ethics committee.
15 June 2021	Updated the final statistical analysis plan for Part C.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported