



Clinical trial results:

Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Assess the Safety, Tolerability, and Efficacy of BIIB092 in Subjects with Mild Cognitive Impairment due to Alzheimer's Disease or with Mild Alzheimer's Disease

Summary

EudraCT number	2017-002901-37
Trial protocol	DE SE ES IT PL FR
Global end of trial date	30 August 2021

Results information

Result version number	v1 (current)
This version publication date	11 September 2022
First version publication date	11 September 2022

Trial information

Trial identification

Sponsor protocol code	251AD201
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03352557
WHO universal trial number (UTN)	-

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 August 2021
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	30 August 2021
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the placebo-controlled (PC) period was to evaluate the safety and tolerability of BIIB092 in subjects with mild cognitive impairment (MCI) due to Alzheimer's disease (AD) or with mild AD.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 May 2018
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 355
Country: Number of subjects enrolled	Australia: 19
Country: Number of subjects enrolled	Germany: 62
Country: Number of subjects enrolled	Spain: 58
Country: Number of subjects enrolled	France: 54
Country: Number of subjects enrolled	Italy: 27
Country: Number of subjects enrolled	Japan: 19
Country: Number of subjects enrolled	Poland: 41
Country: Number of subjects enrolled	Sweden: 19
Worldwide total number of subjects	654
EEA total number of subjects	261

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
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)	146
From 65 to 84 years	508
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 100 investigational sites in United States, Australia, Germany, Spain, France, Italy, Japan, Poland and Sweden from 03 May 2018 to 30 August 2021. WBS=Withdrawal by Subject; WBP/G=Withdrawal by Parent/Guardian; SV=Study Visit; PR=Perceived Risks; CIT=Change in Treatment; EP=Enable

Pre-assignment

Screening details:

A total of 654 subjects with Alzheimer's Disease (AD) were enrolled and randomised to receive placebo or BIIB092 125/375/600/2000 milligrams (mg) in PC period. Following PC period, 521 subjects entered and 516 were dosed in Long-term Extension (LTE) period, and no subjects completed the study due to early termination of the study.

Period 1

Period 1 title	PC Period: Day 1 to Week 78
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

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

Arm description:

Subjects received BIIB092-matching placebo, intravenous (IV) infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.

Arm type	Placebo
Investigational medicinal product name	BIIB092-matching placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB092-matching placebo administered via IV infusion, on Day 1 and then every 4 weeks for 76 weeks.

Arm title	PC Period: BIIB092 125 mg/4 week
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Arm description:

Subjects received BIIB092, 125 milligrams (mg), IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.

Arm type	Experimental
Investigational medicinal product name	BIIB092
Investigational medicinal product code	
Other name	Formally known as BMS 986168
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB092 125 mg administered via IV infusion, on Day 1 and then every 4 weeks for 76 weeks.

Arm title	PC Period: BIIB092 375 mg/12 week
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Arm description:

Subjects received BIIB092, 375 mg, IV infusion, on Day 1 and then once every 12 weeks for 76 weeks during the PC period.

Arm type	Experimental
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Investigational medicinal product name	BIIB092
Investigational medicinal product code	
Other name	Formally known as BMS 986168
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
BIIB092 375 mg administered via IV infusion, on Day 1 and then every 12 weeks for 76 weeks.	
Arm title	PC Period: BIIB092 600 mg/4 week

Arm description:

Subjects received BIIB092, 600 mg, IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.

Arm type	Experimental
Investigational medicinal product name	BIIB092
Investigational medicinal product code	
Other name	Formally known as BMS 986168
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
BIIB092 600 mg administered via IV infusion, on Day 1 and then every 4 weeks for 76 weeks.	
Arm title	PC Period: BIIB092 2000 mg/4 week

Arm description:

Subjects received BIIB092, 2000 mg, IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.

Arm type	Experimental
Investigational medicinal product name	BIIB092
Investigational medicinal product code	
Other name	Formally known as BMS 986168
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use
Dosage and administration details:	
BIIB092 2000 mg administered via IV infusion, on Day 1 and then every 4 weeks for 76 weeks.	

Number of subjects in period 1	PC Period: Placebo	PC Period: BIIB092 125 mg/4 week	PC Period: BIIB092 375 mg/12 week
Started	214	58	58
Safety Analysis Set	214	58	58
Full Analysis Set (FAS)	214	58	58
Antidrug antibody (ADA) Evaluable Set	211	57	57
Completed	172	48	50
Not completed	42	10	8
WBS-Relocation (Moving or has Moved)	1	1	-
WBP/G-Other	-	2	-
WBP/G-SV Burden/Scheduling Conflicts	-	-	-
WBP/G-Desire for CIT (Unrelated to Safety)	1	-	-
Physician Decision-Unrelated to Safety	2	-	-

Adverse Event	10	1	1
Protocol Deviation	1	-	-
WBS-SV Burden/Scheduling Conflicts	7	1	1
WBS-Desire for CIT (Unrelated to Safety)	-	-	1
WBP/G-Unable to Continue to EP due to I/H/D	-	-	-
Site Terminated by Sponsor	2	1	1
WBS-Other	6	2	2
WBS-Concern About Study Procedures/PR	1	-	-
Noncompliance with Study Drug	1	-	-
Death	1	1	-
Progressive Disease	-	-	-
Not Specified	5	1	-
Randomised by Mistake	2	-	-
WBP/G-Concern About Study Procedures/PR	1	-	1
Not Dosed	-	-	-
Lost to follow-up	1	-	1

Number of subjects in period 1	PC Period: BIIB092 600 mg/4 week	PC Period: BIIB092 2000 mg/4 week
Started	106	218
Safety Analysis Set	106	214
Full Analysis Set (FAS)	106	214
Antidrug antibody (ADA) Evaluable Set	105	212
Completed	91	175
Not completed	15	43
WBS-Relocation (Moving or has Moved)	1	1
WBP/G-Other	-	3
WBP/G-SV Burden/Scheduling Conflicts	1	3
WBP/G-Desire for CIT (Unrelated to Safety)	-	1
Physician Decision-Unrelated to Safety	-	1
Adverse Event	-	5
Protocol Deviation	1	2
WBS-SV Burden/Scheduling Conflicts	-	5
WBS-Desire for CIT (Unrelated to Safety)	-	1
WBP/G-Unable to Continue to EP due to I/H/D	-	1
Site Terminated by Sponsor	1	2
WBS-Other	5	7

WBS-Concern About Study Procedures/PR	1	2
Noncompliance with Study Drug	-	-
Death	-	1
Progressive Disease	-	1
Not Specified	3	-
Randomised by Mistake	1	-
WBP/G-Concern About Study Procedures/PR	1	1
Not Dosed	-	4
Lost to follow-up	-	2

Period 2

Period 2 title	LTE Period: Week 80 to Week 173
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	LTE Period: BIIB092 125 mg/4 week

Arm description:

Subjects who received BIIB092, 125 mg, IV infusion during the PC period, continued to receive BIIB092, 125 mg, IV infusion once every 4 weeks from Week 80 to Week 155 during the LTE period.

Arm type	Experimental
Investigational medicinal product name	BIIB092
Investigational medicinal product code	
Other name	Formally known as BMS 986168
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB092 125 mg administered via IV infusion, once every 4 weeks from Week 80 to Week 155.

Arm title	LTE Period: BIIB092 375 mg/12 week
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Arm description:

Subjects who received BIIB092, 375 mg, IV infusion during the PC period, continued to receive BIIB092, 375 mg, IV infusion once every 12 weeks from Week 80 to Week 155 during the LTE period.

Arm type	Experimental
Investigational medicinal product name	BIIB092
Investigational medicinal product code	
Other name	Formally known as BMS 986168
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB092 375 mg administered via IV infusion, once every 12 weeks from Week 80 to Week 155.

Arm title	LTE Period: BIIB092 600 mg/4 week
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Arm description:

Subjects who received BIIB092, 600 mg, IV infusion during the PC period, continued to receive BIIB092, 600 mg, IV infusion once every 4 weeks from Week 80 to Week 155 during the LTE period.

Arm type	Experimental
Investigational medicinal product name	BIIB092
Investigational medicinal product code	
Other name	Formally known as BMS 986168
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB092 600 mg administered via IV infusion, once every 4 weeks from Week 80 to Week 155.

Arm title	LTE Period: BIIB092 2000 mg/4 week – Early Start
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Arm description:

Subjects who received BIIB092, 2000 mg, IV infusion during the PC period, continued to receive BIIB092, 2000 mg, IV infusion once every 4 weeks from Week 80 to Week 155 during the LTE period.

Arm type	Experimental
Investigational medicinal product name	BIIB092
Investigational medicinal product code	
Other name	Formally known as BMS 986168
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB092 2000 mg administered via IV infusion, once every 4 weeks from Week 80 to Week 155.

Arm title	LTE Period: BIIB092 2000 mg/4 week – Late Start
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Arm description:

Subjects who received BIIB092-matching placebo, IV infusion during the PC period, received BIIB092, 2000 mg, IV infusion once every 4 weeks from Week 80 to Week 155 during the LTE period.

Arm type	Experimental
Investigational medicinal product name	BIIB092
Investigational medicinal product code	
Other name	Formally known as BMS 986168
Pharmaceutical forms	Solution for injection/infusion
Routes of administration	Intravenous use

Dosage and administration details:

BIIB092 2000 mg administered via IV infusion, once every 4 weeks from Week 80 to Week 155.

Number of subjects in period 2^[1]	LTE Period: BIIB092 125 mg/4 week	LTE Period: BIIB092 375 mg/12 week	LTE Period: BIIB092 600 mg/4 week
Started	46	49	90
Safety Analysis Set	45	49	89
Completed	0	0	0
Not completed	46	49	90
WBS-Relocation (Moving or has Moved)	1	-	1
WBP/G-Other	1	-	-
WBP/G-SV Burden/Scheduling Conflicts	-	-	-
Adverse Event	3	-	-

Physician Decision	-	-	-
WBS-SV Burden/Scheduling Conflicts	1	-	5
WBP/G-Unable to Continue to EP due to I/H/D	-	-	2
WBS-Other	1	-	1
Site Terminated by Sponsor	-	-	-
Study Terminated by Sponsor	38	49	75
Death	1	-	1
Progressive Disease	-	-	1
Not Specified	-	-	1
WBP/G-Concern About Study Procedures/PR	-	-	1
WBP/G-Relocation (Moving or has Moved)	-	-	2
Lost to follow-up	-	-	-

Number of subjects in period 2^[1]	LTE Period: BIIB092 2000 mg/4 week – Early Start	LTE Period: BIIB092 2000 mg/4 week – Late Start
Started	169	167
Safety Analysis Set	168	165
Completed	0	0
Not completed	169	167
WBS-Relocation (Moving or has Moved)	1	-
WBP/G-Other	2	-
WBP/G-SV Burden/Scheduling Conflicts	2	1
Adverse Event	-	-
Physician Decision	-	3
WBS-SV Burden/Scheduling Conflicts	3	3
WBP/G-Unable to Continue to EP due to I/H/D	1	-
WBS-Other	1	4
Site Terminated by Sponsor	2	-
Study Terminated by Sponsor	151	154
Death	1	1
Progressive Disease	2	-
Not Specified	-	-
WBP/G-Concern About Study Procedures/PR	-	-
WBP/G-Relocation (Moving or has Moved)	-	-
Lost to follow-up	3	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: 536 subjects completed the PC period, out of which only 521 subjects entered in LTE period. 15 subjects from PC period did not enter LTE period.

Baseline characteristics

Reporting groups

Reporting group title	PC Period: Placebo
Reporting group description:	
Subjects received BIIB092-matching placebo, intravenous (IV) infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.	
Reporting group title	PC Period: BIIB092 125 mg/4 week
Reporting group description:	
Subjects received BIIB092, 125 milligrams (mg), IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.	
Reporting group title	PC Period: BIIB092 375 mg/12 week
Reporting group description:	
Subjects received BIIB092, 375 mg, IV infusion, on Day 1 and then once every 12 weeks for 76 weeks during the PC period.	
Reporting group title	PC Period: BIIB092 600 mg/4 week
Reporting group description:	
Subjects received BIIB092, 600 mg, IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.	
Reporting group title	PC Period: BIIB092 2000 mg/4 week
Reporting group description:	
Subjects received BIIB092, 2000 mg, IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.	

Reporting group values	PC Period: Placebo	PC Period: BIIB092 125 mg/4 week	PC Period: BIIB092 375 mg/12 week
Number of subjects	214	58	58
Age Categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	69.8	70.4	70.3
standard deviation	± 6.63	± 6.80	± 6.79
Gender Categorical Units: subjects			
Female	106	28	26
Male	108	30	32
Race Units: Subjects			
American Indian or Alaska Native	1	0	0
Asian	5	3	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	4	0	1
White	201	53	53
More than one race	0	0	0
Unknown or Not Reported	3	2	2
Ethnicity Units: Subjects			
Hispanic or Latino	3	2	2

Not Hispanic or Latino	208	53	55
Unknown or Not Reported	3	3	1

Reporting group values	PC Period: BIIB092 600 mg/4 week	PC Period: BIIB092 2000 mg/4 week	Total
Number of subjects	106	218	654
Age Categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	69.7 ± 6.66	69.4 ± 7.11	-
Gender Categorical Units: subjects			
Female	55	114	329
Male	51	104	325
Race Units: Subjects			
American Indian or Alaska Native	0	0	1
Asian	6	7	23
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	1	1	7
White	98	206	611
More than one race	0	0	0
Unknown or Not Reported	1	4	12
Ethnicity Units: Subjects			
Hispanic or Latino	1	9	17
Not Hispanic or Latino	103	208	627
Unknown or Not Reported	2	1	10

End points

End points reporting groups

Reporting group title	PC Period: Placebo
Reporting group description: Subjects received BIIB092-matching placebo, intravenous (IV) infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.	
Reporting group title	PC Period: BIIB092 125 mg/4 week
Reporting group description: Subjects received BIIB092, 125 milligrams (mg), IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.	
Reporting group title	PC Period: BIIB092 375 mg/12 week
Reporting group description: Subjects received BIIB092, 375 mg, IV infusion, on Day 1 and then once every 12 weeks for 76 weeks during the PC period.	
Reporting group title	PC Period: BIIB092 600 mg/4 week
Reporting group description: Subjects received BIIB092, 600 mg, IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.	
Reporting group title	PC Period: BIIB092 2000 mg/4 week
Reporting group description: Subjects received BIIB092, 2000 mg, IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.	
Reporting group title	LTE Period: BIIB092 125 mg/4 week
Reporting group description: Subjects who received BIIB092, 125 mg, IV infusion during the PC period, continued to receive BIIB092, 125 mg, IV infusion once every 4 weeks from Week 80 to Week 155 during the LTE period.	
Reporting group title	LTE Period: BIIB092 375 mg/12 week
Reporting group description: Subjects who received BIIB092, 375 mg, IV infusion during the PC period, continued to receive BIIB092, 375 mg, IV infusion once every 12 weeks from Week 80 to Week 155 during the LTE period.	
Reporting group title	LTE Period: BIIB092 600 mg/4 week
Reporting group description: Subjects who received BIIB092, 600 mg, IV infusion during the PC period, continued to receive BIIB092, 600 mg, IV infusion once every 4 weeks from Week 80 to Week 155 during the LTE period.	
Reporting group title	LTE Period: BIIB092 2000 mg/4 week – Early Start
Reporting group description: Subjects who received BIIB092, 2000 mg, IV infusion during the PC period, continued to receive BIIB092, 2000 mg, IV infusion once every 4 weeks from Week 80 to Week 155 during the LTE period.	
Reporting group title	LTE Period: BIIB092 2000 mg/4 week – Late Start
Reporting group description: Subjects who received BIIB092-matching placebo, IV infusion during the PC period, received BIIB092, 2000 mg, IV infusion once every 4 weeks from Week 80 to Week 155 during the LTE period.	
Subject analysis set title	PC Period: Placebo
Subject analysis set type	Full analysis
Subject analysis set description: Subjects received BIIB092-matching placebo, IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.	
Subject analysis set title	PC Period: BIIB092 Low Dose
Subject analysis set type	Full analysis
Subject analysis set description: Subjects received BIIB092, 125 mg, IV infusion, on Day 1 and then once every 4 weeks or BIIB092, 375 mg, IV infusion, on Day 1 and then once every 12 weeks for 76 weeks during the PC period.	
Subject analysis set title	PC Period: BIIB092 600 mg/4 week

Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received BIIB092, 600 mg, IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.	
Subject analysis set title	PC Period: BIIB092 2000 mg/4 week
Subject analysis set type	Full analysis
Subject analysis set description:	
Subjects received BIIB092, 2000 mg, IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.	

Primary: PC Period: Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs)

End point title	PC Period: Percentage of Subjects With Adverse Events (AEs) and Serious Adverse Events (SAEs) ^[1]
End point description:	
An AE is any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. An SAE is any untoward medical occurrence that at any dose, results in death; in the view of the investigator places the subject at immediate risk of death; requires inpatient hospitalisation or prolongation of existing hospitalisation; results in persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; is a medically important event. The safety analysis set included all randomised subjects who received at least one dose of study treatment (BIIB092 or placebo).	
End point type	Primary
End point timeframe:	
From Day 1 to Week 90	

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 for this endpoint.

End point values	PC Period: Placebo	PC Period: BIIB092 125 mg/4 week	PC Period: BIIB092 375 mg/12 week	PC Period: BIIB092 600 mg/4 week
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	214	58	58	106
Units: percentage of subjects				
number (not applicable)				
AEs	84.6	86.2	82.8	88.7
SAEs	12.1	10.3	10.3	12.3

End point values	PC Period: BIIB092 2000 mg/4 week			
Subject group type	Reporting group			
Number of subjects analysed	214			
Units: percentage of subjects				
number (not applicable)				
AEs	88.3			
SAEs	11.7			

Statistical analyses

No statistical analyses for this end point

Primary: LTE Period: Percentage of Subjects With AEs and SAEs

End point title	LTE Period: Percentage of Subjects With AEs and SAEs ^[2]
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End point description:

An AE is any untoward medical occurrence in a subject or clinical investigation subject administered a pharmaceutical product and that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. An SAE is any untoward medical occurrence that at any dose, results in death; in the view of the investigator places the subject at immediate risk of death; requires inpatient hospitalisation or prolongation of existing hospitalisation; results in persistent or significant disability/incapacity; results in a congenital anomaly/birth defect; is a medically important event. The safety analysis set included all randomised subjects who received at least one dose of study treatment (BIIB092 or placebo).

End point type	Primary
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End point timeframe:

From Week 80 to Week 173

Notes:

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

Justification: No statistical analysis was planned for this endpoint.

End point values	LTE Period: BIIB092 125 mg/4 week	LTE Period: BIIB092 375 mg/12 week	LTE Period: BIIB092 600 mg/4 week	LTE Period: BIIB092 2000 mg/4 week – Early Start
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	45	49	89	168
Units: percentage of subjects				
number (not applicable)				
AEs	68.9	55.1	58.4	61.3
SAEs	11.1	2.0	10.1	6.0

End point values	LTE Period: BIIB092 2000 mg/4 week – Late Start			
Subject group type	Reporting group			
Number of subjects analysed	165			
Units: percentage of subjects				
number (not applicable)				
AEs	60.0			
SAEs	7.9			

Statistical analyses

No statistical analyses for this end point

Secondary: PC Period: Change From Baseline Over Time at Week 78 on the Clinical Dementia Rating Scale - Sum of Boxes (CDR-SB) Score

End point title	PC Period: Change From Baseline Over Time at Week 78 on the Clinical Dementia Rating Scale - Sum of Boxes (CDR-SB) Score
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End point description:

The CDR-SB is a validated clinical assessment of global function in subjects with AD. The CDR is comprised of 6 domains: Memory, Orientation, Judgment and Problem Solving, Community Affairs, Home and Hobbies, and Personal Care. CDR-SB is the sum of the scores for these 6 domains. Impairment is scored in each of 6 cognitive categories on a scale in which none = 0, questionable = 0.5, mild = 1, moderate = 2, and severe = 3. The 6 individual category ratings, or "box scores", can be added together to give the CDR-SB score which ranges from 0 (none) to 18 (severe impairment). FAS included all randomised subjects who received study treatment (BIIB092 or placebo). The 'n' signifies number of subjects analysed at the specified time point.

End point type	Secondary
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End point timeframe:

Baseline, Week 78

End point values	PC Period: Placebo	PC Period: BIIB092 Low Dose	PC Period: BIIB092 600 mg/4 week	PC Period: BIIB092 2000 mg/4 week
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	214	116	106	214
Units: score on a scale				
arithmetic mean (standard deviation)				
Baseline (n=214,116,106,214)	3.07 (± 1.467)	2.92 (± 1.620)	3.24 (± 1.557)	3.04 (± 1.378)
Change at Week 78 (n=170,98,91,174)	1.71 (± 2.376)	2.10 (± 2.375)	2.23 (± 2.987)	1.76 (± 2.038)

Statistical analyses

No statistical analyses for this end point

Secondary: PC Period: Percentage of Subjects With Anti-BIIB092 Antibodies in Serum

End point title	PC Period: Percentage of Subjects With Anti-BIIB092 Antibodies in Serum
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End point description:

The ADA evaluable set is defined as subjects in the FAS who have an evaluable postbaseline ADA sample.

End point type	Secondary
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End point timeframe:
Baseline up to Week 76

End point values	PC Period: Placebo	PC Period: BIIB092 125 mg/4 week	PC Period: BIIB092 375 mg/12 week	PC Period: BIIB092 600 mg/4 week
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	211	57	57	105
Units: percentage of subjects				
number (not applicable)	1.9	0	0	1.0

End point values	PC Period: BIIB092 2000 mg/4 week			
Subject group type	Reporting group			
Number of subjects analysed	212			
Units: percentage of subjects				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first dose through 14 weeks after last dose of study drug (Up to approximately 173 weeks)

Adverse event reporting additional description:

The safety analysis set included all randomised subjects who received at least one dose of study treatment (BIIB092 or placebo). The total number of deaths (all causes) data and adverse events are reported for 'safety analysis set'.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.1
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Reporting groups

Reporting group title	PC Period: Placebo
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Reporting group description:

Subjects received BIIB092-matching placebo, IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.

Reporting group title	PC Period: BIIB092 125 mg/4 week
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Reporting group description:

Subjects received BIIB092, 125 mg, IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.

Reporting group title	PC Period: BIIB092 375 mg/12 week
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Reporting group description:

Subjects received BIIB092, 375 mg, IV infusion, on Day 1 and then once every 12 weeks for 76 weeks during the PC period.

Reporting group title	PC Period: BIIB092 600 mg/4 week
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Reporting group description:

Subjects received BIIB092, 600 mg, IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.

Reporting group title	PC Period: BIIB092 2000 mg/4 week
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Reporting group description:

Subjects received BIIB092, 2000 mg, IV infusion, on Day 1 and then once every 4 weeks for 76 weeks during the PC period.

Reporting group title	LTE Period: BIIB092 600 mg/4 week
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Reporting group description:

Subjects who received BIIB092, 600 mg, IV infusion during the PC period, continued to receive BIIB092, 600 mg, IV infusion once every 4 weeks from Week 80 to Week 155 during the LTE period.

Reporting group title	LTE Period: BIIB092 125 mg/4 week
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Reporting group description:

Subjects who received BIIB092, 125 mg, IV infusion during the PC period, continued to receive BIIB092, 125 mg, IV infusion once every 4 weeks from Week 80 to Week 155 during the LTE period.

Reporting group title	LTE Period: BIIB092 375 mg/12 week
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Reporting group description:

Subjects who received BIIB092, 375 mg, IV infusion during the PC period, continued to receive BIIB092, 375 mg, IV infusion once every 12 weeks from Week 80 to Week 155 during the LTE period.

Reporting group title	LTE Period: BIIB092 2000 mg/4 week – Early Start
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Reporting group description:

Subjects who received BIIB092, 2000 mg, IV infusion during the PC period, continued to receive BIIB092, 2000 mg, IV infusion once every 4 weeks from Week 80 to Week 155 during the LTE period.

Reporting group title	LTE Period: BIIB092 2000 mg/4 week – Late Start
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Reporting group description:

Subjects who received BIIB092-matching placebo, IV infusion during the PC period, received BIIB092, 2000 mg, IV infusion once every 4 weeks from Week 80 to Week 155 during the LTE period.

Serious adverse events	PC Period: Placebo	PC Period: BIIB092 125 mg/4 week	PC Period: BIIB092 375 mg/12 week
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 214 (12.15%)	6 / 58 (10.34%)	6 / 58 (10.34%)
number of deaths (all causes)	1	1	0
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer recurrent			
subjects affected / exposed	0 / 214 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Breast cancer stage II			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive breast carcinoma			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Malignant melanoma			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal carcinoma			
subjects affected / exposed	0 / 214 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Ovarian cancer			

subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Pancreatic carcinoma stage III			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Papillary thyroid cancer			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Penile squamous cell carcinoma			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 214 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Hepatocellular carcinoma			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Transitional cell carcinoma			

subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 214 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Deep vein thrombosis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Hypertensive crisis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Female genital tract fistula			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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			
Organising pneumonia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 214 (0.47%)	1 / 58 (1.72%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Pneumonitis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Pneumothorax			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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

Mental status changes			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Delusion			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Hallucination			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contusion			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol poisoning			

subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Ligament sprain			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Rib fracture			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Subdural haematoma			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ankle fracture			

subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Craniocerebral injury			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	2 / 214 (0.93%)	1 / 58 (1.72%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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			
Acute myocardial infarction			
subjects affected / exposed	0 / 214 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Angina pectoris			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Coronary artery disease			

subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Coronary artery stenosis			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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			
Ataxia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic encephalopathy			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	1 / 214 (0.47%)	1 / 58 (1.72%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			

subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Haemorrhagic stroke			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Dementia Alzheimer's type			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 214 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Eye disorders			

Cataract			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Idiopathic orbital inflammation			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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			
Constipation			
subjects affected / exposed	0 / 214 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Dysphagia			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Enterovesical fistula			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Faecaloma			
subjects affected / exposed	0 / 214 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Gastritis erosive			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hiatus hernia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Inguinal hernia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal stenosis			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			
subjects affected / exposed	0 / 214 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Colitis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Oesophageal ulcer haemorrhage			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Rectal prolapse			

subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis acute			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 214 (0.00%)	1 / 58 (1.72%)	0 / 58 (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
Nephrolithiasis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Arthritis			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Pain in extremity			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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 Appendicitis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 214 (0.47%) 0 / 1 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0
Atypical pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 214 (0.47%) 0 / 1 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0
COVID-19 pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 214 (0.47%) 0 / 1 0 / 1	0 / 58 (0.00%) 0 / 0 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0
Escherichia sepsis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 214 (0.00%) 0 / 0 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0
Escherichia urinary tract infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 214 (0.47%) 0 / 1 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0
Infection subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	1 / 214 (0.47%) 0 / 1 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0
Pelvic abscess subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 214 (0.00%) 0 / 0 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0
Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all	0 / 214 (0.00%) 0 / 0 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0	0 / 58 (0.00%) 0 / 0 0 / 0
Sepsis			

subjects affected / exposed	1 / 214 (0.47%)	0 / 58 (0.00%)	0 / 58 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Urinary tract infection			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	1 / 58 (1.72%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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 tract infection			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Retroperitoneal abscess			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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
Hypoglycaemia			
subjects affected / exposed	0 / 214 (0.00%)	0 / 58 (0.00%)	0 / 58 (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	PC Period: BIIB092	PC Period: BIIB092	LTE Period: BIIB092
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	600 mg/4 week	2000 mg/4 week	600 mg/4 week
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 106 (12.26%)	25 / 214 (11.68%)	9 / 89 (10.11%)
number of deaths (all causes)	0	1	1
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Bladder cancer recurrent			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Breast cancer stage II			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive breast carcinoma			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Malignant melanoma			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Oesophageal carcinoma			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Ovarian cancer			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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

Colon cancer			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Pancreatic carcinoma stage III			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Papillary thyroid cancer			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Penile squamous cell carcinoma			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Hepatocellular carcinoma			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Transitional cell carcinoma			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Pancreatic carcinoma metastatic			

subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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			
Aortic aneurysm			
subjects affected / exposed	1 / 106 (0.94%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Orthostatic hypotension			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Hypertensive crisis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Female genital tract fistula			
subjects affected / exposed	1 / 106 (0.94%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Organising pneumonia			

subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Pneumonia aspiration			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Pneumonitis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Pneumothorax			
subjects affected / exposed	0 / 106 (0.00%)	2 / 214 (0.93%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Mental status changes			

subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Delusion			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Hallucination			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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			
Concussion			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Contusion			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Alcohol poisoning			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Femur fracture			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Hip fracture			
subjects affected / exposed	1 / 106 (0.94%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament sprain			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post lumbar puncture syndrome			
subjects affected / exposed	1 / 106 (0.94%)	1 / 214 (0.47%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Subdural haematoma			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Ankle fracture			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Craniocerebral injury			

subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 106 (0.94%)	1 / 214 (0.47%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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			
Acute myocardial infarction			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Angina pectoris			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Atrial fibrillation			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Coronary artery disease			
subjects affected / exposed	2 / 106 (1.89%)	1 / 214 (0.47%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			

subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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 failure congestive			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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			
Ataxia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Toxic encephalopathy			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Syncope			
subjects affected / exposed	1 / 106 (0.94%)	2 / 214 (0.93%)	0 / 89 (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
Epilepsy			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 106 (0.94%)	1 / 214 (0.47%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			

subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Haemorrhagic stroke			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Dizziness			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Dementia Alzheimer's type			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Transient ischaemic attack			
subjects affected / exposed	1 / 106 (0.94%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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

Idiopathic orbital inflammation subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Enterovesical fistula			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Faecaloma			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Gastritis erosive			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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 haemorrhage			
subjects affected / exposed	1 / 106 (0.94%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Hiatus hernia			

subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Inguinal hernia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large intestinal stenosis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Umbilical hernia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Colitis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Oesophageal ulcer haemorrhage			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Small intestinal obstruction			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Rectal prolapse			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis acute			

subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Nephrolithiasis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	2 / 106 (1.89%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Arthritis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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			
Appendicitis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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

Atypical pneumonia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
COVID-19 pneumonia			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Escherichia sepsis			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Escherichia urinary tract infection			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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
Infection			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic abscess			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Pneumonia			
subjects affected / exposed	1 / 106 (0.94%)	0 / 214 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			

subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Urinary tract infection			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonsillar abscess			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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 tract infection			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	1 / 89 (1.12%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Retroperitoneal abscess			
subjects affected / exposed	0 / 106 (0.00%)	0 / 214 (0.00%)	0 / 89 (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 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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
Hypoglycaemia			
subjects affected / exposed	0 / 106 (0.00%)	1 / 214 (0.47%)	0 / 89 (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

Serious adverse events	LTE Period: BIIB092 125 mg/4 week	LTE Period: BIIB092 375 mg/12 week	LTE Period: BIIB092 2000 mg/4 week – Early Start
Total subjects affected by serious adverse events			
subjects affected / exposed	5 / 45 (11.11%)	1 / 49 (2.04%)	10 / 168 (5.95%)
number of deaths (all causes)	2	0	1
number of deaths resulting from			

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	1 / 168 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer recurrent			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Breast cancer stage II			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive breast carcinoma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Malignant melanoma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Oesophageal carcinoma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Ovarian cancer			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Colon cancer			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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

Pancreatic carcinoma stage III subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Papillary thyroid cancer subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Penile squamous cell carcinoma subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Squamous cell carcinoma of lung subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Hepatocellular carcinoma subjects affected / exposed	1 / 45 (2.22%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transitional cell carcinoma subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Pancreatic carcinoma metastatic subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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			

Aortic aneurysm			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Deep vein thrombosis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orthostatic hypotension			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Hypertensive crisis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Female genital tract fistula			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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			
Organising pneumonia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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 / 45 (0.00%)	0 / 49 (0.00%)	1 / 168 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Pulmonary embolism			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Pneumonitis			
subjects affected / exposed	1 / 45 (2.22%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Mental status changes			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	1 / 168 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delusion			

subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Hallucination			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Product issues			
Device dislocation			
subjects affected / exposed	0 / 45 (0.00%)	1 / 49 (2.04%)	0 / 168 (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
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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			
Concussion			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Contusion			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Alcohol poisoning			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	1 / 168 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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

Hip fracture			
subjects affected / exposed	1 / 45 (2.22%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ligament sprain			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post lumbar puncture syndrome			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Rib fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Subdural haematoma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Thoracic vertebral fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Ankle fracture			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Craniocerebral injury			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	1 / 168 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			

subjects affected / exposed	0 / 45 (0.00%)	1 / 49 (2.04%)	3 / 168 (1.79%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 45 (0.00%)	1 / 49 (2.04%)	1 / 168 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Angina pectoris			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Atrial fibrillation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Coronary artery disease			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Coronary artery stenosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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 failure congestive			

subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	1 / 168 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 45 (2.22%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic encephalopathy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Syncope			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	1 / 168 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Seizure			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	1 / 168 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Haemorrhagic stroke			

subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Dizziness			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Dementia Alzheimer's type			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	1 / 45 (2.22%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Idiopathic orbital inflammation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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			
Constipation			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Enterovesical fistula			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Faecaloma			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Gastritis erosive			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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 haemorrhage			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Hiatus hernia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Inguinal hernia			

subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Large intestinal stenosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Umbilical hernia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Colitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Oesophageal ulcer haemorrhage			
subjects affected / exposed	1 / 45 (2.22%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Rectal prolapse			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatitis acute			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Nephrolithiasis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal stenosis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Arthritis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Pain in extremity			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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			
Appendicitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Atypical pneumonia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

COVID-19 pneumonia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Escherichia sepsis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Escherichia urinary tract infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic abscess			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	1 / 168 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Upper respiratory tract infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Urinary tract infection			

subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Peritonsillar abscess			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	1 / 168 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory tract infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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
Retroperitoneal abscess			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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 / 45 (0.00%)	0 / 49 (0.00%)	1 / 168 (0.60%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (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	LTE Period: BIIB092 2000 mg/4 week – Late Start		
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 165 (7.88%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			

subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bladder cancer recurrent				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Breast cancer stage II				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Invasive breast carcinoma				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal carcinoma				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian cancer				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colon cancer				
subjects affected / exposed	1 / 165 (0.61%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pancreatic carcinoma stage III				

subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Papillary thyroid cancer			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Penile squamous cell carcinoma			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate cancer			
subjects affected / exposed	1 / 165 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatocellular carcinoma			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transitional cell carcinoma			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic aneurysm			

subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Deep vein thrombosis			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Orthostatic hypotension			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertensive crisis			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Female genital tract fistula			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Organising pneumonia			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonia aspiration			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Acute respiratory failure			
subjects affected / exposed	1 / 165 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory failure			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumonitis			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Mental status changes			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Delusion			
subjects affected / exposed	1 / 165 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hallucination			

subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Product issues			
Device dislocation			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Electrocardiogram QT prolonged			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Concussion			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Contusion			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Alcohol poisoning			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Femur fracture			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hip fracture			
subjects affected / exposed	1 / 165 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Ligament sprain				
subjects affected / exposed	1 / 165 (0.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post lumbar puncture syndrome				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thoracic vertebral fracture				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ankle fracture				
subjects affected / exposed	1 / 165 (0.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Craniocerebral injury				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	3 / 165 (1.82%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Femoral neck fracture				

subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Angina pectoris			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial fibrillation			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bradycardia			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery disease			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary artery stenosis			
subjects affected / exposed	1 / 165 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac failure congestive			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Myocardial infarction			

subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Ataxia			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Toxic encephalopathy			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Syncope			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Seizure			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Presyncope			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haemorrhagic stroke			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dizziness			

subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dementia Alzheimer's type			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	1 / 165 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	1 / 165 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Cataract			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Idiopathic orbital inflammation			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Constipation			

subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterovesical fistula				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Faecaloma				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis erosive				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hiatus hernia				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				

subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Large intestinal stenosis			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Umbilical hernia			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	1 / 165 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Oesophageal ulcer haemorrhage			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 165 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal prolapse			
subjects affected / exposed	1 / 165 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatitis acute			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

Acute kidney injury			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Spinal stenosis			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Arthritis			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pain in extremity			
subjects affected / exposed	1 / 165 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 165 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atypical pneumonia			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

COVID-19 pneumonia				
subjects affected / exposed	1 / 165 (0.61%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Escherichia sepsis				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia urinary tract infection				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic abscess				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 165 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				

subjects affected / exposed	1 / 165 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peritonsillar abscess			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory tract infection			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Retroperitoneal abscess			
subjects affected / exposed	1 / 165 (0.61%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	PC Period: Placebo	PC Period: BIIB092 125 mg/4 week	PC Period: BIIB092 375 mg/12 week
Total subjects affected by non-serious adverse events			
subjects affected / exposed	121 / 214 (56.54%)	39 / 58 (67.24%)	38 / 58 (65.52%)
Investigations			
Weight decreased			
subjects affected / exposed	4 / 214 (1.87%)	2 / 58 (3.45%)	3 / 58 (5.17%)
occurrences (all)	4	2	3

Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	6 / 214 (2.80%)	0 / 58 (0.00%)	1 / 58 (1.72%)
occurrences (all)	8	0	2
Fall			
subjects affected / exposed	23 / 214 (10.75%)	6 / 58 (10.34%)	11 / 58 (18.97%)
occurrences (all)	26	7	13
Limb injury			
subjects affected / exposed	0 / 214 (0.00%)	1 / 58 (1.72%)	3 / 58 (5.17%)
occurrences (all)	0	1	3
Vascular disorders			
Hypertension			
subjects affected / exposed	14 / 214 (6.54%)	5 / 58 (8.62%)	3 / 58 (5.17%)
occurrences (all)	18	6	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	13 / 214 (6.07%)	5 / 58 (8.62%)	2 / 58 (3.45%)
occurrences (all)	15	8	2
Headache			
subjects affected / exposed	20 / 214 (9.35%)	1 / 58 (1.72%)	6 / 58 (10.34%)
occurrences (all)	27	1	11
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	7 / 214 (3.27%)	1 / 58 (1.72%)	4 / 58 (6.90%)
occurrences (all)	9	1	5
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	8 / 214 (3.74%)	5 / 58 (8.62%)	1 / 58 (1.72%)
occurrences (all)	8	5	1
Diarrhoea			
subjects affected / exposed	12 / 214 (5.61%)	11 / 58 (18.97%)	3 / 58 (5.17%)
occurrences (all)	15	14	4
Nausea			
subjects affected / exposed	13 / 214 (6.07%)	4 / 58 (6.90%)	2 / 58 (3.45%)
occurrences (all)	16	4	2
Respiratory, thoracic and mediastinal disorders			

Cough subjects affected / exposed occurrences (all)	5 / 214 (2.34%) 5	1 / 58 (1.72%) 1	3 / 58 (5.17%) 3
Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 214 (0.47%) 1	1 / 58 (1.72%) 1	3 / 58 (5.17%) 3
Psychiatric disorders			
Anxiety subjects affected / exposed occurrences (all)	11 / 214 (5.14%) 12	4 / 58 (6.90%) 5	2 / 58 (3.45%) 2
Confusional state subjects affected / exposed occurrences (all)	5 / 214 (2.34%) 5	4 / 58 (6.90%) 5	0 / 58 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	13 / 214 (6.07%) 13	4 / 58 (6.90%) 4	2 / 58 (3.45%) 2
Disorientation subjects affected / exposed occurrences (all)	2 / 214 (0.93%) 3	3 / 58 (5.17%) 3	1 / 58 (1.72%) 1
Irritability subjects affected / exposed occurrences (all)	2 / 214 (0.93%) 2	3 / 58 (5.17%) 4	2 / 58 (3.45%) 3
Renal and urinary disorders			
Pollakiuria subjects affected / exposed occurrences (all)	0 / 214 (0.00%) 0	3 / 58 (5.17%) 4	1 / 58 (1.72%) 1
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	14 / 214 (6.54%) 16	6 / 58 (10.34%) 7	7 / 58 (12.07%) 7
Back pain subjects affected / exposed occurrences (all)	16 / 214 (7.48%) 18	5 / 58 (8.62%) 5	3 / 58 (5.17%) 4
Muscle spasms subjects affected / exposed occurrences (all)	3 / 214 (1.40%) 3	3 / 58 (5.17%) 3	0 / 58 (0.00%) 0

Neck pain subjects affected / exposed occurrences (all)	2 / 214 (0.93%) 2	3 / 58 (5.17%) 3	0 / 58 (0.00%) 0
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	22 / 214 (10.28%) 26	4 / 58 (6.90%) 5	6 / 58 (10.34%) 7
Sinusitis subjects affected / exposed occurrences (all)	2 / 214 (0.93%) 3	3 / 58 (5.17%) 3	0 / 58 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	15 / 214 (7.01%) 19	5 / 58 (8.62%) 6	3 / 58 (5.17%) 3
Urinary tract infection subjects affected / exposed occurrences (all)	13 / 214 (6.07%) 17	5 / 58 (8.62%) 6	3 / 58 (5.17%) 5
COVID-19 subjects affected / exposed occurrences (all)	0 / 214 (0.00%) 0	0 / 58 (0.00%) 0	0 / 58 (0.00%) 0
Metabolism and nutrition disorders			
Decreased appetite subjects affected / exposed occurrences (all)	2 / 214 (0.93%) 2	3 / 58 (5.17%) 3	0 / 58 (0.00%) 0

Non-serious adverse events	PC Period: BIIB092 600 mg/4 week	PC Period: BIIB092 2000 mg/4 week	LTE Period: BIIB092 600 mg/4 week
Total subjects affected by non-serious adverse events subjects affected / exposed	68 / 106 (64.15%)	139 / 214 (64.95%)	19 / 89 (21.35%)
Investigations			
Weight decreased subjects affected / exposed occurrences (all)	3 / 106 (2.83%) 3	5 / 214 (2.34%) 5	0 / 89 (0.00%) 0
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	8 / 106 (7.55%) 8	5 / 214 (2.34%) 8	0 / 89 (0.00%) 0
Fall			

subjects affected / exposed occurrences (all)	19 / 106 (17.92%) 20	30 / 214 (14.02%) 35	6 / 89 (6.74%) 6
Limb injury subjects affected / exposed occurrences (all)	1 / 106 (0.94%) 1	1 / 214 (0.47%) 1	0 / 89 (0.00%) 0
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	6 / 106 (5.66%) 6	13 / 214 (6.07%) 18	0 / 89 (0.00%) 0
Nervous system disorders Dizziness subjects affected / exposed occurrences (all)	9 / 106 (8.49%) 11	11 / 214 (5.14%) 13	0 / 89 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	11 / 106 (10.38%) 19	22 / 214 (10.28%) 31	4 / 89 (4.49%) 4
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	8 / 106 (7.55%) 9	12 / 214 (5.61%) 13	0 / 89 (0.00%) 0
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all)	2 / 106 (1.89%) 2	6 / 214 (2.80%) 6	0 / 89 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	6 / 106 (5.66%) 9	11 / 214 (5.14%) 11	0 / 89 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	6 / 106 (5.66%) 9	11 / 214 (5.14%) 14	0 / 89 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	7 / 106 (6.60%) 7	16 / 214 (7.48%) 20	0 / 89 (0.00%) 0
Rhinorrhoea			

subjects affected / exposed occurrences (all)	1 / 106 (0.94%) 1	2 / 214 (0.93%) 2	0 / 89 (0.00%) 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	3 / 106 (2.83%)	15 / 214 (7.01%)	0 / 89 (0.00%)
occurrences (all)	3	17	0
Confusional state			
subjects affected / exposed	4 / 106 (3.77%)	2 / 214 (0.93%)	0 / 89 (0.00%)
occurrences (all)	6	3	0
Depression			
subjects affected / exposed	4 / 106 (3.77%)	11 / 214 (5.14%)	0 / 89 (0.00%)
occurrences (all)	4	11	0
Disorientation			
subjects affected / exposed	1 / 106 (0.94%)	1 / 214 (0.47%)	0 / 89 (0.00%)
occurrences (all)	1	1	0
Irritability			
subjects affected / exposed	3 / 106 (2.83%)	3 / 214 (1.40%)	0 / 89 (0.00%)
occurrences (all)	3	3	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 106 (0.00%)	3 / 214 (1.40%)	0 / 89 (0.00%)
occurrences (all)	0	3	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 106 (8.49%)	19 / 214 (8.88%)	4 / 89 (4.49%)
occurrences (all)	11	23	4
Back pain			
subjects affected / exposed	9 / 106 (8.49%)	13 / 214 (6.07%)	2 / 89 (2.25%)
occurrences (all)	10	16	2
Muscle spasms			
subjects affected / exposed	3 / 106 (2.83%)	7 / 214 (3.27%)	0 / 89 (0.00%)
occurrences (all)	3	8	0
Neck pain			
subjects affected / exposed	2 / 106 (1.89%)	5 / 214 (2.34%)	0 / 89 (0.00%)
occurrences (all)	2	5	0
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	9 / 106 (8.49%) 12	24 / 214 (11.21%) 29	0 / 89 (0.00%) 0
Sinusitis subjects affected / exposed occurrences (all)	1 / 106 (0.94%) 1	7 / 214 (3.27%) 8	0 / 89 (0.00%) 0
Upper respiratory tract infection subjects affected / exposed occurrences (all)	6 / 106 (5.66%) 7	15 / 214 (7.01%) 18	0 / 89 (0.00%) 0
Urinary tract infection subjects affected / exposed occurrences (all)	8 / 106 (7.55%) 11	20 / 214 (9.35%) 26	0 / 89 (0.00%) 0
COVID-19 subjects affected / exposed occurrences (all)	0 / 106 (0.00%) 0	0 / 214 (0.00%) 0	9 / 89 (10.11%) 9
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	0 / 106 (0.00%) 0	2 / 214 (0.93%) 2	0 / 89 (0.00%) 0

Non-serious adverse events	LTE Period: BIIB092 125 mg/4 week	LTE Period: BIIB092 375 mg/12 week	LTE Period: BIIB092 2000 mg/4 week – Early Start
Total subjects affected by non-serious adverse events subjects affected / exposed	10 / 45 (22.22%)	11 / 49 (22.45%)	28 / 168 (16.67%)
Investigations Weight decreased subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 49 (0.00%) 0	0 / 168 (0.00%) 0
Injury, poisoning and procedural complications Contusion subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 49 (0.00%) 0	0 / 168 (0.00%) 0
Fall subjects affected / exposed occurrences (all)	5 / 45 (11.11%) 8	7 / 49 (14.29%) 7	14 / 168 (8.33%) 17
Limb injury			

subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 49 (0.00%) 0	0 / 168 (0.00%) 0
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 49 (0.00%) 0	0 / 168 (0.00%) 0
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0 1 / 45 (2.22%) 2	0 / 49 (0.00%) 0 3 / 49 (6.12%) 3	0 / 168 (0.00%) 0 3 / 168 (1.79%) 4
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 49 (0.00%) 0	0 / 168 (0.00%) 0
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0 0 / 45 (0.00%) 0 0 / 45 (0.00%) 0	0 / 49 (0.00%) 0 0 / 49 (0.00%) 0 0 / 49 (0.00%) 0	0 / 168 (0.00%) 0 0 / 168 (0.00%) 0 0 / 168 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0 0 / 45 (0.00%) 0	0 / 49 (0.00%) 0 0 / 49 (0.00%) 0	0 / 168 (0.00%) 0 0 / 168 (0.00%) 0
Psychiatric disorders			

Anxiety subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 49 (0.00%) 0	0 / 168 (0.00%) 0
Confusional state subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 49 (0.00%) 0	0 / 168 (0.00%) 0
Depression subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 49 (0.00%) 0	0 / 168 (0.00%) 0
Disorientation subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 49 (0.00%) 0	0 / 168 (0.00%) 0
Irritability subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 49 (0.00%) 0	0 / 168 (0.00%) 0
Renal and urinary disorders Pollakiuria subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 49 (0.00%) 0	0 / 168 (0.00%) 0
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	3 / 49 (6.12%) 4	6 / 168 (3.57%) 9
Back pain subjects affected / exposed occurrences (all)	3 / 45 (6.67%) 3	0 / 49 (0.00%) 0	5 / 168 (2.98%) 5
Muscle spasms subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 49 (0.00%) 0	0 / 168 (0.00%) 0
Neck pain subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 49 (0.00%) 0	0 / 168 (0.00%) 0
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	0 / 45 (0.00%) 0	0 / 49 (0.00%) 0	0 / 168 (0.00%) 0

Sinusitis			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences (all)	0	0	0
COVID-19			
subjects affected / exposed	2 / 45 (4.44%)	1 / 49 (2.04%)	2 / 168 (1.19%)
occurrences (all)	2	1	3
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 45 (0.00%)	0 / 49 (0.00%)	0 / 168 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	LTE Period: BIIB092 2000 mg/4 week – Late Start		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 165 (17.58%)		
Investigations			
Weight decreased			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		
Fall			
subjects affected / exposed	15 / 165 (9.09%)		
occurrences (all)	18		
Limb injury			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		
Vascular disorders			

Hypertension subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0		
Nervous system disorders Dizziness subjects affected / exposed occurrences (all) Headache subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0 6 / 165 (3.64%) 8		
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0		
Gastrointestinal disorders Constipation subjects affected / exposed occurrences (all) Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0 0 / 165 (0.00%) 0 0 / 165 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all) Rhinorrhoea subjects affected / exposed occurrences (all)	0 / 165 (0.00%) 0 0 / 165 (0.00%) 0		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Confusional state	0 / 165 (0.00%) 0		

subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		
Depression			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		
Disorientation			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		
Irritability			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 165 (1.82%)		
occurrences (all)	3		
Back pain			
subjects affected / exposed	5 / 165 (3.03%)		
occurrences (all)	12		
Muscle spasms			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		
Neck pain			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		
Sinusitis			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			

subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		
Urinary tract infection			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		
COVID-19			
subjects affected / exposed	3 / 165 (1.82%)		
occurrences (all)	3		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 165 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 September 2018	Updated the list of allowed concomitant medications for subjects enrolled in this study, washout period of Alzheimer's disease (AD) medications, added the requirement for stable doses of key concomitant medications prior to and during Screening and for the duration of the study.
29 March 2019	Added a dose-blinded long-term extension (LTE) period of approximately 3 years. The primary purpose of the LTE was to obtain long-term safety and tolerability information on BIIB092 and further explore its effects on immunogenicity, disease progression, and additional clinical and health outcomes.
13 January 2020	Updated the number of randomised subjects from 528 to 654.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was terminated based on lack of efficacy following the placebo-controlled period readout.

Notes: