Clinical trial results:
A Phase 3 Multicenter, Randomized, Double-Blind, Placebo-Controlled, Parallel-Group Study to Evaluate the Efficacy and Safety of Aducanumab (BIIB037) in Subjects with Early Alzheimer's Disease

Summary

EudraCT number	2015-000967-15
Trial protocol	DE SE NL ES BE FR PL FI IT
Global end of trial date	05 August 2019

Results information

Result version number	v2 (current)
This version publication date	06 October 2021
First version publication date	20 November 2020
Version creation reason	

Trial information

Trial identification

Sponsor protocol code	221AD302

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02484547
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	05 August 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	05 August 2019
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to evaluate the efficacy of monthly doses of aducanumab in slowing cognitive and functional impairment as measured by changes in the Clinical Dementia Rating Sum of Boxes (CDR-SB) score as compared with placebo in participants with early Alzheimer's disease.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	15 September 2015
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	4 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 652
Country: Number of subjects enrolled	Poland: 193
Country: Number of subjects enrolled	Germany: 122
Country: Number of subjects enrolled	Japan: 121
Country: Number of subjects enrolled	Canada: 96
Country: Number of subjects enrolled	Italy: 82
Country: Number of subjects enrolled	France: 79
Country: Number of subjects enrolled	Spain: 78
Country: Number of subjects enrolled	Switzerland: 52
Country: Number of subjects enrolled	Belgium: 49
Country: Number of subjects enrolled	Netherlands: 49
Country: Number of subjects enrolled	Sweden: 37
Country: Number of subjects enrolled	Finland: 33
Worldwide total number of subjects	1643
EEA total number of subjects	722

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	324
From 65 to 84 years	1303
85 years and over	16

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at 181 investigative sites in the United States, Belgium, Canada, Finland, France, Germany, Italy, Japan, Netherlands, Poland, Spain, Sweden, and Switzerland from 15 September 2015 to 13 July 2018.

Pre-assignment

Screening details:

A total of 1643 subjects with Alzhiemer's disease were enrolled and randomised in the study. Of these, 1638 subjects received the study drug in placebo-controlled (PC) period. After completing PC period, 771 subjects entered and 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	Placebo-Controlled Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo (PC Period)

Arm description:

Subjects received a maximum of 20 infusions of BIIB037-matching placebo intravenously (IV) in PC period, administered approximately once every 4 weeks for up to approximately 1.5 years.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion, once every 4 weeks.

Arm title	BIIB037 Low Dose (PC Period)

Arm description:

Subjects received a maximum of 20 infusions of BIIB037 low dose IV in PC period, administered approximately once every 4 weeks for up to approximately 1.5 years.

Arm type	Experimental
Investigational medicinal product name	BIIB037
Investigational medicinal product code	
Other name	Aducanumab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion, once every 4 weeks.

Arm title	BIIB037 High Dose (PC Period)

Arm description:

Subjects received a maximum of 20 infusions of BIIB037 high dose IV in PC period, administered approximately once every 4 weeks for up to approximately 1.5 years.

Arm type	Experimental

Investigational medicinal product name	BIIB037
Investigational medicinal product code	
Other name	Aducanumab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion, once every 4 weeks.

Number of subjects in period 1[1]	Placebo (PC Period)	BIIB037 Low Dose (PC Period)	BIIB037 High Dose (PC Period)
Started	548	543	547
Completed	288	291	295
Not completed	260	252	252
Relocation	1	1	1
Adverse Event	10	13	20
Death	5	-	6
Withdrawal by Parent/Guardian	4	1	1
Investigator Decision	2	2	5
Lost to follow-up	3	1	3
Study Visit Burden	2	8	5
Disease Progression	2	-	1
Reason not Specified	216	194	183
Change of Treatment	-	-	1
Consent Withdrawn	15	32	26

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.

Justification: The number of subjects reported in the baseline period is for intent to treat population (548 subjects in placebo arm, 543 subjects in BIIB037 Low Dose arm, 547 subjects in BIIB037 High Dose arm).

Period 2

Period 2 title	Long-Term Extension Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes

Arm title	BIIB037 Late Start: Low Dose (LTE Period)

Arm description:

Following PC period, subjects randomised to placebo received BIIB037 low dose, IV infusion, approximately every 4 weeks for up to 2 years in LTE period.

Arm type	Experimental
Investigational medicinal product name	BIIB037
Investigational medicinal product code	
Other name	Aducanumab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion, once every 4 weeks.

Arm title	BIIB037 Late Start: High Dose (LTE Period)

Arm description:

Following PC period, subjects randomised to placebo received BIIB037 high dose, IV infusion, approximately every 4 weeks for up to 2 years in LTE period.

Arm type	Experimental
Investigational medicinal product name	BIIB037
Investigational medicinal product code	
Other name	Aducanumab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion, once every 4 weeks.

Arm title	BIIB037 Early Start: Low Dose (LTE Period)

Arm description:

Following PC period, subjects randomised to low dose BIIB037 continued to receive the same dose, IV infusion, approximately every 4 weeks for up to 2 years in LTE period.

Arm type	Experimental
Investigational medicinal product name	BIIB037
Investigational medicinal product code	
Other name	Aducanumab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion, once every 4 weeks.

Arm title	BIIB037 Early Start: High Dose (LTE Period)

Arm description:

Following PC period, subjects randomised to high dose BIIB037 continued to receive the same dose, IV infusion, approximately every 4 weeks for up to 2 years in LTE period.

Arm type	Experimental
Investigational medicinal product name	BIIB037
Investigational medicinal product code	
Other name	Aducanumab
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Intravenous infusion, once every 4 weeks.

Number of subjects in period 2[2]	BIIB037 Late Start: Low Dose (LTE Period)	BIIB037 Late Start: High Dose (LTE Period)	BIIB037 Early Start: Low Dose (LTE Period)
Started	131	132	251
Completed	0	0	0
Not completed	131	132	251
Relocation	1	1	-
Loss of Capacity	-	1	-
Adverse Event	-	1	3
Death	-	-	3
Withdrawal by Parent/Guardian	-	1	3
Investigator Decision	2	1	-
Lost to follow-up	1	1	2
Study Visit Burden	2	-	-
Reason not Specified	119	117	223
Disease Progression	-	2	4
Change of Treatment	-	-	-
Consent Withdrawn	6	7	13

Number of subjects in period 2[2]	BIIB037 Early Start: High Dose (LTE Period)
Started	257
Completed	0
Not completed	257
Relocation	-
Loss of Capacity	-
Adverse Event	2
Death	-
Withdrawal by Parent/Guardian	2
Investigator Decision	1
Lost to follow-up	-
Study Visit Burden	3
Reason not Specified	231
Disease Progression	-
Change of Treatment	1
Consent Withdrawn	17

Notes:

[2] - 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: 874 subjects completed the PC period, out of which only 771 subjects entered in LTE period. 103 subjects from PC period did not enter LTE period.

Baseline characteristics

Reporting groups	
Reporting group title	Placebo (PC Period)
Reporting group description:	
Subjects received a maximum of 20 infusions of BIIB037-matching placebo intravenously (IV) in PC period, administered approximately once every 4 weeks for up to approximately 1.5 years.	
Reporting group title	BIIB037 Low Dose (PC Period)
Reporting group description:	
Subjects received a maximum of 20 infusions of BIIB037 low dose IV in PC period, administered approximately once every 4 weeks for up to approximately 1.5 years.	
Reporting group title	BIIB037 High Dose (PC Period)
Reporting group description:	
Subjects received a maximum of 20 infusions of BIIB037 high dose IV in PC period, administered approximately once every 4 weeks for up to approximately 1.5 years.	

Reporting group values	Placebo (PC Period)	BIIB037 Low Dose (PC Period)	BIIB037 High Dose (PC Period)
Number of subjects	548	543	547
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	70.8	70.6	70.6
standard deviation	± 7.40	± 7.45	± 7.47
Sex: Female, Male Units: subjects			
Female	290	269	284
Male	258	274	263
Race Units: Subjects			
American Indian or Alaska Native	1	0	0
Asian	47	39	42
Black or African American	1	6	4
White	431	432	422
Not Reported due to Confidentiality Regulations	67	65	75
Other	1	1	3
Unknown	0	0	1
Ethnicity Units: Subjects			
Hispanic or Latino	22	22	23
Not Hispanic or Latino	470	470	461
Not reported due to confidentiality regulations	56	51	62
Unknown	0	0	1

Reporting group values	Total		
Number of subjects	1638		

Age categorical Units: Subjects			

Age Continuous Units: years arithmetic mean standard deviation	- -		
Sex: Female, Male Units: subjects			
Female	843		
Male	795		
Race Units: Subjects			
American Indian or Alaska Native	1		
Asian	128		
Black or African American	11		
White	1285		
Not Reported due to Confidentiality Regulations	207		
Other	5		
Unknown	1		
Ethnicity Units: Subjects			
Hispanic or Latino	67		
Not Hispanic or Latino	1401		
Not reported due to confidentiality regulations	169		
Unknown	1		

End points

End points reporting groups

Reporting group title	Placebo (PC Period)
Reporting group description:	
Subjects received a maximum of 20 infusions of BIIB037-matching placebo intravenously (IV) in PC period, administered approximately once every 4 weeks for up to approximately 1.5 years.	
Reporting group title	BIIB037 Low Dose (PC Period)
Reporting group description:	
Subjects received a maximum of 20 infusions of BIIB037 low dose IV in PC period, administered approximately once every 4 weeks for up to approximately 1.5 years.	
Reporting group title	BIIB037 High Dose (PC Period)
Reporting group description:	
Subjects received a maximum of 20 infusions of BIIB037 high dose IV in PC period, administered approximately once every 4 weeks for up to approximately 1.5 years.	
Reporting group title	BIIB037 Late Start: Low Dose (LTE Period)
Reporting group description:	
Following PC period, subjects randomised to placebo received BIIB037 low dose, IV infusion, approximately every 4 weeks for up to 2 years in LTE period.	
Reporting group title	BIIB037 Late Start: High Dose (LTE Period)
Reporting group description:	
Following PC period, subjects randomised to placebo received BIIB037 high dose, IV infusion, approximately every 4 weeks for up to 2 years in LTE period.	
Reporting group title	BIIB037 Early Start: Low Dose (LTE Period)
Reporting group description:	
Following PC period, subjects randomised to low dose BIIB037 continued to receive the same dose, IV infusion, approximately every 4 weeks for up to 2 years in LTE period.	
Reporting group title	BIIB037 Early Start: High Dose (LTE Period)
Reporting group description:	
Following PC period, subjects randomised to high dose BIIB037 continued to receive the same dose, IV infusion, approximately every 4 weeks for up to 2 years in LTE period.	

Primary: Change From Baseline in Clinical Dementia Rating Scale - Sum of Boxes (CDR-SB) Score at Week 78

End point title	Change From Baseline in Clinical Dementia Rating Scale - Sum of Boxes (CDR-SB) Score at Week 78
End point description:	
CDR-SB integrates assessments from 3 domains of cognition (memory, orientation, judgment/problem-solving) and 3 domains of function (community affairs, home/hobbies, personal care). Following caregiver interview and systematic patient examination, the rater assigns a score describing the subject's current performance level in each of these domains of life functioning. Prespecified severity anchors range from none = 0, questionable = 0.5, mild = 1, moderate = 2 to severe = 3 (the personal care domain omits the 0.5 score). "Sum of boxes" scoring methodology sums the score for each of the 6 domains and provides a value ranging from 0 to 18 that can change in increments of 0.5 or greater. Higher scores indicate greater disease severity. Mixed model for repeated measures (MMRM) analysis was used to analyse change from baseline in CDR-SB. A positive change from baseline indicates clinical decline. Intent-to-Treat (ITT) population. n=number of subjects analysed at specific timepoint.	
End point type	Primary
End point timeframe:	
Baseline, Week 78	

End point values	Placebo (PC Period)	BIIB037 Low Dose (PC Period)	BIIB037 High Dose (PC Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	548	543	547	
Units: score on a scale				
arithmetic mean (standard error)				
Change at Week 78 (n =288,290,299)	1.74 (± 0.115)	1.47 (± 0.116)	1.35 (± 0.115)	

Statistical analyses

Statistical analysis title	Placebo vs BIIB037 High Dose

Statistical analysis description:

Adjusted mean for each treatment group (Placebo, BIIB037 Low Dose, BIIB037 High Dose), difference with Placebo, 95% confidence interval and p-value at each time point were based on an MMRM model, with change from baseline in CDR-SB as dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline CDR-SB, baseline CDR-SB by visit

Comparison groups	Placebo (PC Period) v BIIB037 High Dose (PC Period)
Number of subjects included in analysis	1095
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.012
Method	MMRM
Parameter estimate	Difference
Point estimate	-0.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.694
upper limit	-0.086

Statistical analysis title	Placebo vs BIIB037 Low Dose

Statistical analysis description:

Adjusted mean for each treatment group (Placebo, BIIB037 Low Dose, BIIB037 High Dose), difference with Placebo, 95% confidence interval and p-value at each time point were based on an MMRM model, with change from baseline in CDR-SB as dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline CDR-SB, baseline CDR-SB by visit interaction, baseline MMSE, AD symptomatic medication use at baseline, region, and laboratory ApoE status.

Comparison groups	Placebo (PC Period) v BIIB037 Low Dose (PC Period)
Number of subjects included in analysis	1091
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0901
Method	mixed model for repeated measures (MMRM)
Parameter estimate	Difference
Point estimate	-0.26

Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.569
upper limit	0.041

Secondary: Change From Baseline in Mini Mental State Examination (MMSE) score at Week 78

End point title	Change From Baseline in Mini Mental State Examination (MMSE) score at Week 78

End point description:

The MMSE is a widely used performance-based test of global cognitive status. It consists of 11 tasks that assess orientation, word recall, attention and calculation, language abilities, and visuospatial functions. The scores from the 11 tests are combined to obtain the total score, which ranges from 0 to 30, with lower scores over time indicating increasing cognitive impairment. MMRM analysis was used to analyse change from baseline in MMSE. A negative change from baseline indicates clinical decline. ITT is defined as all randomised subjects who had received at least one dose of study treatment (Aducanumab or Placebo). Here, 'n' signifies number of subjects analysed at specific timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 78

End point values	Placebo (PC Period)	BIIB037 Low Dose (PC Period)	BIIB037 High Dose (PC Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	548	543	547	
Units: score on a scale				
arithmetic mean (standard error)				
Change at Week 78 (n =288, 293, 299)	-3.3 (± 0.22)	-3.3 (± 0.22)	-2.7 (± 0.21)	

Statistical analyses

Statistical analysis title	Placebo vs BIIB037 High Dose

Statistical analysis description:

Adjusted mean for each treatment group (Placebo, BIIB037 Low Dose, BIIB037 High Dose), difference from Placebo, 95% confidence interval and p-value at each time point were based on an MMRM model, with change from baseline in MMSE as dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline MMSE, baseline MMSE by visit interaction, AD symptomatic medication use at baseline, region, and laboratory ApoE status.

Comparison groups	Placebo (PC Period) v BIIB037 High Dose (PC Period)
Number of subjects included in analysis	1095
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0493
Method	MMRM
Parameter estimate	Difference
Point estimate	0.6

Confidence interval	
level	95 %
sides	2-sided
lower limit	0
upper limit	1.13

Statistical analysis title	Placebo vs BIIB037 Low Dose

Statistical analysis description:

Adjusted mean for each treatment group (Placebo, BIIB037 Low Dose, BIIB037 High Dose), difference from Placebo, 95% confidence interval and p-value at each time point were based on an MMRM model, with change from baseline in MMSE as dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline MMSE, baseline MMSE by visit interaction, AD symptomatic medication use at baseline, region, and laboratory ApoE status.

Comparison groups	Placebo (PC Period) v BIIB037 Low Dose (PC Period)
Number of subjects included in analysis	1091
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7578
Method	MMRM
Parameter estimate	Difference
Point estimate	-0.1
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.65
upper limit	0.48

Secondary: Change From Baseline in Alzheimer's Disease Assessment Scale-Cognitive Subscale (13 items) (ADAS-Cog 13) at Week 78

End point title	Change From Baseline in Alzheimer's Disease Assessment Scale-Cognitive Subscale (13 items) (ADAS-Cog 13) at Week 78

End point description:

ADAS-Cog13 comprises both cognitive tasks and clinical ratings of cognitive performance. The scale items capture word recall, ability to follow commands, the ability to correctly copy or draw an image, naming, the ability to interact with everyday objects, orientation, word recognition, memory, comprehension of spoken language, word-finding, and language ability, with a measure for delayed word recall and concentration/distractibility. The total score ranges from 0 to 85. An increase in score over time indicates increasing cognitive impairment. MMRM analysis was used to analyse change from baseline in ADAS-Cog 13. A positive change from baseline indicates clinical decline. ITT is defined as all randomised subjects who had received at least one dose of study treatment (Aducanumab or Placebo). Here, 'n' signifies number of subjects analysed at specific timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 78

End point values	Placebo (PC Period)	BIIB037 Low Dose (PC Period)	BIIB037 High Dose (PC Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	548	543	547	
Units: score on a scale				
arithmetic mean (standard error)				
Change at Week 78 (n =287, 289, 293)	5.162 (± 0.4049)	4.461 (± 0.4074)	3.763 (± 0.4036)	

Statistical analyses

Statistical analysis title	Placebo vs BIIB037 Low Dose

Statistical analysis description:

Adjusted mean for each treatment group(Placebo, BIIB037 Low Dose, BIIB037 High Dose),difference from Placebo, 95% confidence interval and p-value at each time point were based on an MMRM model, with change from baseline in ADASCog 13 as dependent variable and with fixed effects of treatment group,categorical visit,treatment-by-visit interaction,baseline ADAS-Cog 13,baseline ADAS-Cog 13 by visit interaction,baseline MMSE,AD symptomatic medication use at baseline,region,and laboratory ApoE status.

Comparison groups	Placebo (PC Period) v BIIB037 Low Dose (PC Period)
Number of subjects included in analysis	1091
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1962
Method	MMRM
Parameter estimate	Difference
Point estimate	-0.701
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.7649
upper limit	0.3627

Statistical analysis title	Placebo vs BIIB037 High Dose

Statistical analysis description:

Adjusted mean for each treatment group(Placebo, BIIB037 Low Dose, BIIB037 High Dose),difference from Placebo, 95% confidence interval and p-value at each time point were based on an MMRM model, with change from baseline in ADASCog 13 as dependent variable and with fixed effects of treatment group,categorical visit,treatment-by-visit interaction,baseline ADAS-Cog 13,baseline ADAS-Cog 13 by visit interaction,baseline MMSE,AD symptomatic medication use at baseline,region,and laboratory ApoE status.

Comparison groups	Placebo (PC Period) v BIIB037 High Dose (PC Period)
Number of subjects included in analysis	1095
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0097
Method	MMRM
Parameter estimate	Difference
Point estimate	-1.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	-2.4596
upper limit	-0.3396

Secondary: Change From Baseline in Alzheimer's Disease Cooperative Study-Activities of Daily Living Inventory (Mild Cognitive Impairment version) (ADCS-ADL-MCI) Score at Week 78

End point title	Change From Baseline in Alzheimer's Disease Cooperative Study-Activities of Daily Living Inventory (Mild Cognitive Impairment version) (ADCS-ADL-MCI) Score at Week 78

End point description:

The ADCS-ADL-MCI consists of 17 instrumental items (e.g., shopping, preparing meals, using household appliances) and 1 basic item (getting dressed). Ratings reflect caregiver observations about the patient's actual functioning over the previous month and provide an assessment of change in the functional state of the participant over time. The total score ranges from 0 to 53, with lower values over time reflecting functional deterioration. MMRM analysis was used to analyse change from baseline in ADAS-ADL-MCI. A negative change from baseline indicates clinical decline. ITT is defined as all randomised subjects who had received at least one dose of study treatment (Aducanumab or Placebo). Here, 'n' signifies number of subjects analysed at specific timepoint.

End point type	Secondary

End point timeframe:

Baseline, Week 78

End point values	Placebo (PC Period)	BIIB037 Low Dose (PC Period)	BIIB037 High Dose (PC Period)	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	548	543	547	
Units: score on a scale				
arithmetic mean (standard error)				
Change at Week 78 (n =283, 286, 295)	-4.3 (± 0.38)	-3.5 (± 0.38)	-2.5 (± 0.38)	

Statistical analyses

Statistical analysis title	Placebo vs BIIB037 High Dose

Statistical analysis description:

Adjusted mean for each treatment group (Placebo, BIIB037 Low dose and BIIB037 High Dose), difference from Placebo,95% CI and p-value at each time point were based on an MMRM model, with change from baseline in ADCSADL-MCI as dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline ADCS-ADL-MCI, baseline ADCS-ADL-MCI by visit interaction, baseline MMSE,AD symptomatic medication use at baseline, region, and laboratory ApoE status.

Comparison groups	Placebo (PC Period) v BIIB037 High Dose (PC Period)

Number of subjects included in analysis	1095
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0006
Method	MMRM
Parameter estimate	Difference
Point estimate	1.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	2.74

Statistical analysis title	Placebo vs BIIB037 Low Dose

Statistical analysis description:

Adjusted mean for each treatment group (Placebo, BIIB037 Low dose and BIIB037 High Dose), difference from Placebo,95% CI and p-value at each time point were based on an MMRM model, with change from baseline in ADCSADL-MCI as dependent variable and with fixed effects of treatment group, categorical visit, treatment-by-visit interaction, baseline ADCS-ADL-MCI, baseline ADCS-ADL-MCI by visit interaction, baseline MMSE,AD symptomatic medication use at baseline, region, and laboratory ApoE status.

Comparison groups	Placebo (PC Period) v BIIB037 Low Dose (PC Period)
Number of subjects included in analysis	1091
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1515
Method	MMRM
Parameter estimate	Difference
Point estimate	0.7
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	1.73

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From First Dose to End of Study (up to 4 years)

Adverse event reporting additional description:

Safety population was all randomised subjects who received at least one dose of study treatment. In PC period,1 subject randomised to placebo, inadvertently received 1 or more doses of active treatment (Low Dose) during the PC period. For subjects affected, a subject was counted only once within each system organ class/preferred term/study period.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	22.0

Reporting groups

Reporting group title	BIIB037 Low Dose (PC Period)

Reporting group description:

Subjects received a maximum of 20 infusions of BIIB037 low dose IV in PC period, administered approximately once every 4 weeks for up to approximately 1.5 years.

Reporting group title	Placebo (PC Period)

Reporting group description:

Subjects received a maximum of 20 infusions of BIIB037-matching placebo intravenously (IV) in PC period, administered approximately once every 4 weeks for up to approximately 1.5 years.

Reporting group title	BIIB037 Late Start: High Dose (LTE Period)

Reporting group description:

Following PC period, subjects randomised to placebo received BIIB037 high dose, IV infusion, approximately every 4 weeks for up to 2 years in LTE period.

Reporting group title	BIIB037 Early Start: Low Dose (LTE Period)

Reporting group description:

Following PC period, subjects randomised to low dose BIIB037 continued to receive the same dose, IV infusion, approximately every 4 weeks for up to 2 years in LTE period.

Reporting group title	BIIB037 Early Start: High Dose (LTE Period)

Reporting group description:

Following PC period, subjects randomised to high dose BIIB037 continued to receive the same dose, IV infusion, approximately every 4 weeks for up to 2 years in LTE period.

Reporting group title	BIIB037 High Dose (PC Period)

Reporting group description:

Subjects received a maximum of 20 infusions of BIIB037 high dose IV in PC period, administered approximately once every 4 weeks for up to approximately 1.5 years.

Reporting group title	BIIB037 Late Start: Low Dose (LTE period)

Reporting group description:

Following PC period, subjects randomised to placebo received BIIB037 low dose, IV infusion, approximately every 4 weeks for up to 2 years in LTE period.

Serious adverse events	BIIB037 Low Dose (PC Period)	Placebo (PC Period)	BIIB037 Late Start: High Dose (LTE Period)
Total subjects affected by serious adverse events			
subjects affected / exposed	72 / 544 (13.24%)	81 / 547 (14.81%)	9 / 132 (6.82%)
number of deaths (all causes)	0	5	0
number of deaths resulting from			

adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	2 / 544 (0.37%)	0 / 547 (0.00%)	0 / 132 (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
Bladder papilloma			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Breast cancer			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Cholangiocarcinoma			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholesteatoma			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Diffuse large b-cell lymphoma			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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

Endometrial adenocarcinoma			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Endometrial cancer			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	1 / 544 (0.18%)	1 / 547 (0.18%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal neoplasm			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 ductal breast carcinoma			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Invasive lobular breast carcinoma			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Lung adenocarcinoma stage iv			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Malignant melanoma			

subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 in situ			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medullary thyroid cancer			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Metastatic neoplasm			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Ovarian cancer			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural mesothelioma			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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	2 / 544 (0.37%)	1 / 547 (0.18%)	0 / 132 (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
Prostatic adenoma			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Salivary gland cancer			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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 cell lung cancer			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Squamous cell carcinoma			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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 the oral cavity			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
T-cell lymphoma			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Thymoma malignant			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Vascular disorders			
Aortic aneurysm rupture			

subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic stenosis			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 / 544 (0.18%)	1 / 547 (0.18%)	0 / 132 (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
Hypertension			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			
subjects affected / exposed	0 / 544 (0.00%)	2 / 547 (0.37%)	0 / 132 (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
Hypertensive urgency			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Hypotension			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			

subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Discomfort			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Gait disturbance			
subjects affected / exposed	1 / 544 (0.18%)	1 / 547 (0.18%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device site joint pain			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Non-cardiac chest pain			
subjects affected / exposed	1 / 544 (0.18%)	2 / 547 (0.37%)	0 / 132 (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
Pyrexia			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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			

Adnexa uteri cyst			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 544 (0.18%)	1 / 547 (0.18%)	0 / 132 (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
Cervical polyp			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gynaecomastia			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 cyst			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spermatic cord cyst			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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			
Asthma			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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

Laryngeal oedema			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Lung perforation			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Pneumothorax			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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			
Agitation			
subjects affected / exposed	0 / 544 (0.00%)	3 / 547 (0.55%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Behaviour disorder			

subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bipolar disorder			
subjects affected / exposed	1 / 544 (0.18%)	1 / 547 (0.18%)	0 / 132 (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
Confusional state			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Delirium			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Depression			
subjects affected / exposed	0 / 544 (0.00%)	2 / 547 (0.37%)	0 / 132 (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
Intentional self-injury			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Mania			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Mental status changes			

subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Neuropsychiatric symptoms			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Psychotic disorder			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Somatic symptom disorder			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Suicide attempt			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Investigations			
Weight decreased			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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

Accidental overdose			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Alcohol poisoning			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Animal attack			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Animal scratch			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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	1 / 544 (0.18%)	2 / 547 (0.37%)	0 / 132 (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
Bone contusion			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 contusion			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Concussion			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Craniocerebral injury			

subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Epiphyseal fracture			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Fall			
subjects affected / exposed	9 / 544 (1.65%)	12 / 547 (2.19%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 9	0 / 12	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	2 / 544 (0.37%)	3 / 547 (0.55%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal procedural complication			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Head injury			
subjects affected / exposed	1 / 544 (0.18%)	1 / 547 (0.18%)	0 / 132 (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
Hip fracture			

subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Joint dislocation			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Lumbar vertebral fracture			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Pelvic fracture			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Pubis fracture			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary contusion			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Radius fracture			

subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Rib fracture			
subjects affected / exposed	0 / 544 (0.00%)	5 / 547 (0.91%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	2 / 544 (0.37%)	1 / 547 (0.18%)	0 / 132 (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
Skin laceration			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Skull fracture			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 fracture			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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	3 / 544 (0.55%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 limb fracture			

subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Wrist fracture			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Acute left ventricular failure			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Acute myocardial infarction			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Angina unstable			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Aortic valve incompetence			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Atrial fibrillation			

subjects affected / exposed	0 / 544 (0.00%)	2 / 547 (0.37%)	0 / 132 (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
Atrial flutter			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block second degree			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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 arrest			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 / 544 (0.00%)	2 / 547 (0.37%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Coronary artery disease			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial infarction			

subjects affected / exposed	1 / 544 (0.18%)	2 / 547 (0.37%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Sinus bradycardia			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Sinus node dysfunction			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Sinus tachycardia			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Stress cardiomyopathy			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Supraventricular extrasystoles			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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			
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	4 / 544 (0.74%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	5 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	5 / 544 (0.92%)	1 / 547 (0.18%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	6 / 6	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Carpal tunnel syndrome			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebellar infarction			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haematoma			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	2 / 544 (0.37%)	2 / 547 (0.37%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	1 / 544 (0.18%)	1 / 547 (0.18%)	0 / 132 (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
Dementia alzheimer's type			
subjects affected / exposed	0 / 544 (0.00%)	2 / 547 (0.37%)	0 / 132 (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
Dizziness			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic cerebral infarction			

subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Encephalopathy			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Focal dyscognitive seizures			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Guillain-barre syndrome			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Intracranial venous sinus thrombosis			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			

subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Lacunar infarction			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Loss of consciousness			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Memory impairment			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Metabolic encephalopathy			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Quadriparesis			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Sensorimotor disorder			

subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Superficial siderosis of central nervous system			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	2 / 544 (0.37%)	3 / 547 (0.55%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic stroke			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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			
Deafness bilateral			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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

Meniere's disease			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Vertigo			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Eye disorders			
Age-related macular degeneration			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cataract nuclear			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Vitreous floaters			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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			
Abdominal pain			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Acquired oesophageal web			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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

Barrett's oesophagus			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Colitis			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Colitis ischaemic			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Diarrhoea			
subjects affected / exposed	0 / 544 (0.00%)	2 / 547 (0.37%)	0 / 132 (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
Diverticular perforation			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Duodenal ulcer perforation			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Dysphagia			

subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Femoral hernia strangulated			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 necrosis			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Haemorrhoidal haemorrhage			
subjects affected / exposed	2 / 544 (0.37%)	0 / 547 (0.00%)	0 / 132 (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
Haemorrhoids			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			

subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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	2 / 544 (0.37%)	0 / 547 (0.00%)	0 / 132 (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
Intestinal obstruction			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Intestinal perforation			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 intestine polyp			
subjects affected / exposed	0 / 544 (0.00%)	2 / 547 (0.37%)	0 / 132 (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
Nausea			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Obstructive pancreatitis			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	1 / 544 (0.18%)	1 / 547 (0.18%)	0 / 132 (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
Pancreatitis acute			

subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumoperitoneum			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Rectal prolapse			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Vomiting			
subjects affected / exposed	0 / 544 (0.00%)	2 / 547 (0.37%)	0 / 132 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 544 (0.00%)	2 / 547 (0.37%)	0 / 132 (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
Cholelithiasis			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis acute			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			

subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus bladder			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Nephrolithiasis			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Prerenal failure			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 failure			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral disorder			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Urethral stenosis			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 retention			

subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Bursitis			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Intervertebral disc protrusion			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Muscular weakness			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 pain			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 stiffness			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	3 / 544 (0.55%)	2 / 547 (0.37%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Rhabdomyolysis			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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 osteoarthritis			
subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Vertebral foraminal stenosis			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Bacterial infection			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Bronchitis			

subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Cellulitis			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Cystitis klebsiella			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Erysipelas			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Gastroenteritis			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Human anaplasmosis			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphangitis			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Otitis media			

subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 544 (0.37%)	2 / 547 (0.37%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	1 / 2	1 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 influenzal			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 respiratory syncytial viral			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary sepsis			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
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 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Urosepsis			

subjects affected / exposed	0 / 544 (0.00%)	1 / 547 (0.18%)	0 / 132 (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
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	0 / 544 (0.00%)	0 / 547 (0.00%)	0 / 132 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Hypoglycaemia			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	0 / 132 (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
Hyponatraemia			
subjects affected / exposed	1 / 544 (0.18%)	0 / 547 (0.00%)	1 / 132 (0.76%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	BIIB037 Early Start: Low Dose (LTE Period)	BIIB037 Early Start: High Dose (LTE Period)	BIIB037 High Dose (PC Period)
Total subjects affected by serious adverse events			
subjects affected / exposed	25 / 251 (9.96%)	25 / 257 (9.73%)	73 / 547 (13.35%)
number of deaths (all causes)	3	0	6
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma pancreas			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder papilloma			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangiocarcinoma			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Cholesteatoma			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diffuse large b-cell lymphoma			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial adenocarcinoma			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endometrial cancer			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 neoplasm			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive ductal breast carcinoma			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung adenocarcinoma stage iv			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung neoplasm malignant			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Malignant melanoma in situ			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medullary thyroid cancer			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic neoplasm			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural mesothelioma			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Prostate cancer			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostatic adenoma			

subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Salivary gland cancer			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 cell lung cancer			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 the oral cavity			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
T-cell lymphoma			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thymoma malignant			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 rupture			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic stenosis			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 urgency			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Chest pain			
subjects affected / exposed	1 / 251 (0.40%)	1 / 257 (0.39%)	0 / 547 (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
Death			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Discomfort			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gait disturbance			
subjects affected / exposed	0 / 251 (0.00%)	2 / 257 (0.78%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Medical device site joint pain			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	2 / 547 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Reproductive system and breast disorders			
Adnexa uteri cyst			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Benign prostatic hyperplasia			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical polyp			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gynaecomastia			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 cyst			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spermatic cord cyst			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
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, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (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
Laryngeal oedema			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Lung perforation			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (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
Pulmonary embolism			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	2 / 547 (0.37%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Respiratory failure			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Agitation			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (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
Behaviour disorder			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (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
Bipolar disorder			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delusion			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intentional self-injury			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mania			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neuropsychiatric symptoms			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychotic disorder			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somatic symptom disorder			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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			
Weight decreased			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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			
Accident			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (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
Accidental overdose			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
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 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Animal attack			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Animal scratch			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone contusion			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac contusion			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Concussion			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epiphyseal fracture			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.40%)	6 / 257 (2.33%)	4 / 547 (0.73%)
occurrences causally related to treatment / all	0 / 1	1 / 6	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot fracture			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 procedural complication			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hand fracture			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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	0 / 251 (0.00%)	2 / 257 (0.78%)	0 / 547 (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
Humerus fracture			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pelvic fracture			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis fracture			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary contusion			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rib fracture			

subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (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
Road traffic accident			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin laceration			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skull fracture			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 fracture			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	1 / 257 (0.39%)	2 / 547 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thoracic vertebral fracture			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
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 limb fracture			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wrist fracture			

subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 left ventricular failure			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 myocardial infarction			
subjects affected / exposed	1 / 251 (0.40%)	1 / 257 (0.39%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 unstable			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic valve incompetence			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Atrial flutter			

subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Atrioventricular block second degree			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 arrest			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	2 / 547 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Cardiac failure congestive			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Coronary artery disease			
subjects affected / exposed	0 / 251 (0.00%)	2 / 257 (0.78%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Sinus bradycardia			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus node dysfunction			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stress cardiomyopathy			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Supraventricular extrasystoles			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (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
Nervous system disorders			
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	2 / 547 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	8 / 547 (1.46%)
occurrences causally related to treatment / all	0 / 0	0 / 0	8 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Carpal tunnel syndrome			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cerebellar infarction			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 2
Cerebral haematoma			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral haemorrhage			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral infarction			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.40%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic cerebral infarction			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Embolic stroke			

subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (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
Encephalopathy			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Focal dyscognitive seizures			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Generalised tonic-clonic seizure			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Guillain-barre syndrome			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial venous sinus thrombosis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 251 (0.40%)	1 / 257 (0.39%)	0 / 547 (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
Lacunar infarction			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Loss of consciousness			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Memory impairment			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
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 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Quadriparesis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
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	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sensorimotor disorder			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Superficial siderosis of central nervous system			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	3 / 547 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	4 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	2 / 251 (0.80%)	2 / 257 (0.78%)	4 / 547 (0.73%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombotic stroke			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toxic encephalopathy			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	2 / 547 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Ear and labyrinth disorders			
Deafness bilateral			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniere's disease			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertigo			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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			
Age-related macular degeneration			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Cataract nuclear			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (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
Vitreous floaters			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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			
Abdominal pain			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acquired oesophageal web			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Barrett's oesophagus			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 ischaemic			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Constipation			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Duodenal ulcer perforation			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral hernia strangulated			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	2 / 547 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
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 necrosis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Haemorrhoids			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (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
Ileus			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	3 / 547 (0.55%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (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
Large intestine polyp			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive pancreatitis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumoperitoneum			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatitis acute			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus bladder			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Nephrolithiasis			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prerenal failure			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 failure			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Urethral disorder			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			

Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthritis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (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
Bursitis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal stiffness			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Osteoarthritis			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 osteoarthritis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vertebral foraminal stenosis			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacterial infection			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			

subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	2 / 547 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cystitis klebsiella			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	0 / 547 (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
Gastroenteritis viral			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Human anaplasmosis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymphangitis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Otitis media			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia bacterial			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 influenzal			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	0 / 547 (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 respiratory syncytial viral			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 sepsis			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 251 (0.00%)	1 / 257 (0.39%)	2 / 547 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	1 / 251 (0.40%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
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 / 251 (0.00%)	0 / 257 (0.00%)	0 / 547 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	1 / 547 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	BIIB037 Late Start: Low Dose (LTE period)		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 131 (11.45%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma pancreas			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bladder papilloma				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Breast cancer				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholangiocarcinoma				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholesteatoma				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diffuse large b-cell lymphoma				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endometrial adenocarcinoma				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endometrial cancer				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric cancer				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal neoplasm				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Invasive ductal breast carcinoma				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Invasive lobular breast carcinoma				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung adenocarcinoma stage iv				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung neoplasm malignant				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma in situ				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Medullary thyroid cancer				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastatic neoplasm				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal carcinoma				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian cancer				
subjects affected / exposed	0 / 131 (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 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural mesothelioma				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostatic adenoma				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Salivary gland cancer				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small cell lung cancer				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of the oral cavity				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
T-cell lymphoma				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thymoma malignant				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Aortic aneurysm rupture				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic stenosis				
subjects affected / exposed	0 / 131 (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 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive crisis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive urgency				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Discomfort				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gait disturbance				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Medical device site joint pain				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Hypersensitivity				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Adnexa uteri cyst				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Benign prostatic hyperplasia				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Cervical polyp				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gynaecomastia				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ovarian cyst				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spermatic cord cyst				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Asthma				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemothorax				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngeal oedema				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung perforation				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Pneumonia aspiration				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Agitation				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anxiety				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Behaviour disorder				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bipolar disorder				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Confusional state				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Delirium				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Delusion				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intentional self-injury				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mania				
subjects affected / exposed	0 / 131 (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 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuropsychiatric symptoms				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychotic disorder				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Somatic symptom disorder				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Weight decreased				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Accident				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Accidental overdose				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Alcohol poisoning				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Animal attack			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Animal scratch			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ankle fracture			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bone contusion			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac contusion			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Concussion			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Craniocerebral injury			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Epiphyseal fracture			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			

subjects affected / exposed	2 / 131 (1.53%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Femoral neck fracture				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foot fracture				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal procedural complication				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hand fracture				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Humerus fracture				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Joint dislocation				

subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lower limb fracture				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lumbar vertebral fracture				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pelvic fracture				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pubis fracture				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary contusion				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radius fracture				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road traffic accident				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin laceration				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skull fracture				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal fracture				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	0 / 131 (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 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper limb fracture				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute left ventricular failure				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aortic valve incompetence				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block second degree				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 131 (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 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic cardiomyopathy				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus bradycardia				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus node dysfunction				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus tachycardia				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stress cardiomyopathy				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Supraventricular extrasystoles				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Amyloid related imaging abnormality-oedema/effusion				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Carpal tunnel syndrome				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebellar infarction				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Cerebral haematoma				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral infarction				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dementia alzheimer's type				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Embolic cerebral infarction				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Embolic stroke				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Focal dyscognitive seizures				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Generalised tonic-clonic seizure				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Guillain-barre syndrome				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intracranial venous sinus thrombosis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lacunar infarction				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Memory impairment				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolic encephalopathy				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Quadriparesis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sensorimotor disorder				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Superficial siderosis of central nervous system				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				

subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Thrombotic stroke			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Toxic encephalopathy			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Iron deficiency anaemia			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Deafness bilateral			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Meniere's disease			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vertigo			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Eye disorders			

Age-related macular degeneration				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cataract nuclear				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retinal detachment				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vitreous floaters				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal pain				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acquired oesophageal web				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Barrett's oesophagus				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis ischaemic				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticular perforation				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulum intestinal haemorrhagic				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer perforation				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femoral hernia strangulated				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastritis				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal necrosis				
subjects affected / exposed	0 / 131 (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 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhoidal haemorrhage				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large intestine polyp				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Obstructive pancreatitis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumoperitoneum				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal prolapse				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatitis acute				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Jaundice				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
Acute kidney injury				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Calculus bladder				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prerenal failure				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urethral disorder				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urethral stenosis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Inappropriate antidiuretic hormone secretion				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				

Arthritis			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Back pain			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bursitis			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intervertebral disc protrusion			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Muscular weakness			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal pain			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal stiffness			
subjects affected / exposed	1 / 131 (0.76%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Osteonecrosis			

subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rhabdomyolysis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal osteoarthritis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vertebral foraminal stenosis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Appendicitis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial infection				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cystitis klebsiella				

subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Human anaplasmosis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphangitis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis media				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia bacterial				

subjects affected / exposed	1 / 131 (0.76%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia influenzal				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia respiratory syncytial viral				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary sepsis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	0 / 131 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				

subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 131 (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	BIIB037 Low Dose (PC Period)	Placebo (PC Period)	BIIB037 Late Start: High Dose (LTE Period)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	385 / 544 (70.77%)	353 / 547 (64.53%)	56 / 132 (42.42%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	59 / 544 (10.85%)	62 / 547 (11.33%)	7 / 132 (5.30%)
occurrences (all)	82	86	8
Nervous system disorders			
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	86 / 544 (15.81%)	37 / 547 (6.76%)	11 / 132 (8.33%)
occurrences (all)	114	42	17
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	138 / 544 (25.37%)	12 / 547 (2.19%)	31 / 132 (23.48%)
occurrences (all)	199	13	46
Dizziness			
subjects affected / exposed	42 / 544 (7.72%)	43 / 547 (7.86%)	0 / 132 (0.00%)
occurrences (all)	55	46	0
Headache			

subjects affected / exposed	109 / 544 (20.04%)	84 / 547 (15.36%)	13 / 132 (9.85%)
occurrences (all)	196	116	16
Superficial siderosis of central nervous system			
subjects affected / exposed	51 / 544 (9.38%)	14 / 547 (2.56%)	17 / 132 (12.88%)
occurrences (all)	64	18	23
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	27 / 544 (4.96%)	37 / 547 (6.76%)	0 / 132 (0.00%)
occurrences (all)	29	44	0
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	38 / 544 (6.99%)	29 / 547 (5.30%)	7 / 132 (5.30%)
occurrences (all)	47	31	8
Nausea			
subjects affected / exposed	29 / 544 (5.33%)	27 / 547 (4.94%)	0 / 132 (0.00%)
occurrences (all)	40	35	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	24 / 544 (4.41%)	28 / 547 (5.12%)	4 / 132 (3.03%)
occurrences (all)	28	31	4
Psychiatric disorders			
Anxiety			
subjects affected / exposed	30 / 544 (5.51%)	21 / 547 (3.84%)	0 / 132 (0.00%)
occurrences (all)	30	24	0
Confusional state			
subjects affected / exposed	16 / 544 (2.94%)	15 / 547 (2.74%)	0 / 132 (0.00%)
occurrences (all)	18	17	0
Depression			
subjects affected / exposed	29 / 544 (5.33%)	28 / 547 (5.12%)	0 / 132 (0.00%)
occurrences (all)	31	28	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	17 / 544 (3.13%)	31 / 547 (5.67%)	0 / 132 (0.00%)
occurrences (all)	20	35	0
Back pain			

subjects affected / exposed	38 / 544 (6.99%)	36 / 547 (6.58%)	3 / 132 (2.27%)
occurrences (all)	39	40	3
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	71 / 544 (13.05%)	91 / 547 (16.64%)	7 / 132 (5.30%)
occurrences (all)	87	124	12
Upper respiratory tract infection			
subjects affected / exposed	42 / 544 (7.72%)	41 / 547 (7.50%)	2 / 132 (1.52%)
occurrences (all)	55	52	2
Urinary tract infection			
subjects affected / exposed	39 / 544 (7.17%)	36 / 547 (6.58%)	0 / 132 (0.00%)
occurrences (all)	55	47	0

Non-serious adverse events	BIIB037 Early Start: Low Dose (LTE Period)	BIIB037 Early Start: High Dose (LTE Period)	BIIB037 High Dose (PC Period)
Total subjects affected by non-serious adverse events			
subjects affected / exposed	87 / 251 (34.66%)	107 / 257 (41.63%)	428 / 547 (78.24%)
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	15 / 251 (5.98%)	32 / 257 (12.45%)	73 / 547 (13.35%)
occurrences (all)	16	49	109
Nervous system disorders			
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	12 / 251 (4.78%)	21 / 257 (8.17%)	106 / 547 (19.38%)
occurrences (all)	15	24	160
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	11 / 251 (4.38%)	22 / 257 (8.56%)	183 / 547 (33.46%)
occurrences (all)	13	27	298
Dizziness			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	55 / 547 (10.05%)
occurrences (all)	0	0	78
Headache			
subjects affected / exposed	20 / 251 (7.97%)	19 / 257 (7.39%)	107 / 547 (19.56%)
occurrences (all)	35	25	167
Superficial siderosis of central nervous system			

subjects affected / exposed	4 / 251 (1.59%)	10 / 257 (3.89%)	71 / 547 (12.98%)
occurrences (all)	5	13	92
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	34 / 547 (6.22%)
occurrences (all)	0	0	43
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	9 / 251 (3.59%)	6 / 257 (2.33%)	42 / 547 (7.68%)
occurrences (all)	10	6	58
Nausea			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	31 / 547 (5.67%)
occurrences (all)	0	0	35
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	7 / 251 (2.79%)	14 / 257 (5.45%)	33 / 547 (6.03%)
occurrences (all)	7	15	36
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	19 / 547 (3.47%)
occurrences (all)	0	0	22
Confusional state			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	28 / 547 (5.12%)
occurrences (all)	0	0	35
Depression			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	23 / 547 (4.20%)
occurrences (all)	0	0	23
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	34 / 547 (6.22%)
occurrences (all)	0	0	40
Back pain			
subjects affected / exposed	9 / 251 (3.59%)	10 / 257 (3.89%)	42 / 547 (7.68%)
occurrences (all)	9	13	45
Infections and infestations			

Nasopharyngitis			
subjects affected / exposed	18 / 251 (7.17%)	19 / 257 (7.39%)	89 / 547 (16.27%)
occurrences (all)	24	24	129
Upper respiratory tract infection			
subjects affected / exposed	13 / 251 (5.18%)	11 / 257 (4.28%)	38 / 547 (6.95%)
occurrences (all)	13	11	42
Urinary tract infection			
subjects affected / exposed	0 / 251 (0.00%)	0 / 257 (0.00%)	29 / 547 (5.30%)
occurrences (all)	0	0	37

Non-serious adverse events	BIIB037 Late Start: Low Dose (LTE period)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	55 / 131 (41.98%)		
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	13 / 131 (9.92%)		
occurrences (all)	18		
Nervous system disorders			
Amyloid related imaging abnormality-microhaemorrhages and haemosiderin deposits			
subjects affected / exposed	18 / 131 (13.74%)		
occurrences (all)	22		
Amyloid related imaging abnormality-oedema/effusion			
subjects affected / exposed	23 / 131 (17.56%)		
occurrences (all)	29		
Dizziness			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	10 / 131 (7.63%)		
occurrences (all)	19		
Superficial siderosis of central nervous system			
subjects affected / exposed	13 / 131 (9.92%)		
occurrences (all)	14		
General disorders and administration site conditions			

Fatigue subjects affected / exposed occurrences (all)	0 / 131 (0.00%) 0		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Nausea subjects affected / exposed occurrences (all)	 3 / 131 (2.29%) 3 0 / 131 (0.00%) 0		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	 4 / 131 (3.05%) 4		
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all) Confusional state subjects affected / exposed occurrences (all) Depression subjects affected / exposed occurrences (all)	 0 / 131 (0.00%) 0 0 / 131 (0.00%) 0 0 / 131 (0.00%) 0		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all)	 0 / 131 (0.00%) 0 8 / 131 (6.11%) 9		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all) Upper respiratory tract infection	 6 / 131 (4.58%) 6		

subjects affected / exposed	8 / 131 (6.11%)		
occurrences (all)	8		
Urinary tract infection			
subjects affected / exposed	0 / 131 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
21 July 2016	(1) To allow participants who suspend dosing after a first observance of ARIA to (a) restart at the same dose (rather than the next lower dose per Version 1) after ARIA resolution and (b) titrate up to the originally assigned dose (rather than continue on the next lower dose for the duration of the study). (2) Removed requirement to permanently discontinue treatment after severe symptomatic ARIA or serious ARIA (other medically important" criteria only); instead, in such participants, dosing could be suspended and then resumed at the same dose after ARIA and symptoms resolved or stabilized. (3) Regarding the management of recurrent ARIA, the amendment (a) allowed participants who had suspended dosing after a second episode to restart dosing, after ARIA resolution, at the next lower dose and continue uptitration (rather than remaining on the restart dose as in Version 1) and (b) required treatment discontinuation after 3 ARIA episodes (rather than requiring a third dose reduction with Sponsor approval).
24 March 2017	To allow apolipoprotein E (ApoE) ε4 carrier subjects randomised to high-dose aducanumab to receive the same high-dose aducanumab regimen already received by ApoE ε4 non-carriers (i.e., per this amendment, the high dose for carriers was changed from 6 to 10 mg/kg, which was also the high dose for noncarriers).
18 September 2017	(1) Modified the percentage of primary endpoint data estimated to be available at the time of a potential blinded sample size re-estimation. (2) Provided additional details on the planned sample size re-estimation (including the maximum potential sample size). (3) Added information on an additional concentration and formulation for aducanumab used in the study.
28 June 2018	(1) To reflect the agreement of the DMC that the characteristics or outcomes of the first event and recurrent events of ARIA were similar, the management of recurrent ARIA was modified so that a third episode of ARIA that requires dose suspension will no longer require study treatment discontinuation, and after recurrent ARIA resolves or stabilizes, dosing will resume at the same dose. (2) To extend the study such that participants nearing study completion under Protocol Version 5 can continue in the study and receive treatment until either the participant's EOT Visit at Week 338 (an additional 3 years of treatment) or until the last participant has had his or her Week 182 Visit, whichever occurred first. (3) To adjust the sample size from 450 to 535 participants per treatment group following the blinded sample size re-estimation to ensure adequate power to detect a mean treatment effect of 0.5 for the primary endpoint, as prespecified in Protocol Version 1.

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 halted prematurely based on a prespecified futility analysis and not based on safety concerns. Subjects discontinued due to study termination are included in "Reason not Specified" category in subject disposition tables above.

Notes: