Clinical trial results:
Continued Efficacy and Safety Monitoring of Solanezumab, an Anti-Amyloid Antibody in Patients with Alzheimer's Disease

Summary

EudraCT number	2010-021155-11
Trial protocol	DE ES IT SE GB
Global end of trial date	17 February 2017

Results information

Result version number	v1
This version publication date	28 February 2018
First version publication date	28 February 2018

Trial information

Trial identification

Sponsor protocol code	H8A-MC-LZAO

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01127633
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 11935

Notes:

Sponsors

Sponsor organisation name	Eli Lilly and Company
Sponsor organisation address	Lilly Corporate Center, Indianapolis, IN, United States, 46285
Public contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 877CTLilly,
Scientific contact	Available Mon Fri 9 AM 5 PM EST, Eli Lilly and Company, 1 8772854559,

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	17 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	17 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

This study is an open-label extension study in Alzheimer's patients who have completed participation in either solanezumab Clinical Trial H8A-MC-LZAM or H8A-MC-LZAN (2008-007926-21).

Protection of trial subjects:

This study was conducted in accordance with International Conference on Harmonization (ICH) Good Clinical Practice, and the principles of the Declaration of Helsinki, in addition to following the laws and regulations of the country or countries in which a study is conducted.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	28 December 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	24 Months
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 81
Country: Number of subjects enrolled	Australia: 60
Country: Number of subjects enrolled	Brazil: 72
Country: Number of subjects enrolled	Canada: 78
Country: Number of subjects enrolled	France: 45
Country: Number of subjects enrolled	Germany: 79
Country: Number of subjects enrolled	Italy: 86
Country: Number of subjects enrolled	Japan: 156
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 65
Country: Number of subjects enrolled	Poland: 43
Country: Number of subjects enrolled	Russian Federation: 28
Country: Number of subjects enrolled	Spain: 37
Country: Number of subjects enrolled	Sweden: 36
Country: Number of subjects enrolled	Taiwan: 49
Country: Number of subjects enrolled	United Kingdom: 35
Country: Number of subjects enrolled	United States: 507
Worldwide total number of subjects	1457
EEA total number of subjects	361

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)	196
From 65 to 84 years	1123
85 years and over	138

Subject disposition

Recruitment

Recruitment details:

Participants who completed one of the feeder studies (Study H8A-MC-LZAM or H8A-MC-LZAN) were enrolled in this study.

Pre-assignment

Screening details:

No text entered

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Placebo administered intravenously every 4 weeks through Week 80.

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

Dosage and administration details:

Placebo administered intravenously every 4 weeks through Week 80.

Arm title	Solanezumab

Arm description:

400 mg administered once every 4 weeks by intravenous infusion (IV) for up to 8 years.

Arm type	Experimental
Investigational medicinal product name	Solanezumab
Investigational medicinal product code	
Other name	LY2062430
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

400 mg of Solanezumab administered once every 4 weeks by intravenous infusion (IV) for up to 8 years.

Number of subjects in period 1	Placebo	Solanezumab
Started	723	734
Received at Least 1 Dose of Study Drug	723	734
Completed	70	61
Not completed	653	673
Adverse event, serious fatal	40	43
Parent/Caregiver Decision	246	228
Physician decision	60	45
Consent withdrawn by subject	57	72
Adverse event, non-fatal	74	73
Sponsor Decision	163	195
Lost to follow-up	4	-
Abnormal Lab/ECG Result	-	1
Protocol deviation	8	16
Not treated	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
Placebo administered intravenously every 4 weeks through Week 80.	
Reporting group title	Solanezumab
Reporting group description:	
400 mg administered once every 4 weeks by intravenous infusion (IV) for up to 8 years.	

Reporting group values	Placebo	Solanezumab	Total
Number of subjects	723	734	1457
Age categorical Units: Subjects			
Age Continuous Units: Years			
arithmetic mean	73.10	72.96	
standard deviation	± 8.004	± 7.766	-
Gender categorical Units: Subjects			
Female	406	415	821
Male	317	319	636
Sex: Female, Male Units: Subjects			
Female	406	415	821
Male	317	319	636
Race (NIH/OMB) Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	137	149	286
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	13	16	29
White	571	566	1137
More than one race	2	3	5
Unknown or Not Reported	0	0	0
Region of Enrollment Units: Subjects			
Argentina	41	40	81
United States	264	243	507
Japan	69	87	156
United Kingdom	17	18	35
Spain	15	22	37
Russia	13	15	28
Canada	38	40	78
South Korea	33	32	65
Sweden	21	15	36
Taiwan	26	23	49

Poland	18	25	43
Brazil	38	34	72
Italy	41	45	86
Australia	30	30	60
France	22	23	45
Germany	37	42	79

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Placebo administered intravenously every 4 weeks through Week 80.	
Reporting group title	Solanezumab
Reporting group description:	
400 mg administered once every 4 weeks by intravenous infusion (IV) for up to 8 years.	

Primary: Assess the Number of Participants with One or More Drug-Related Adverse Events (AEs) or any Serious AEs (SAEs)

End point title	Assess the Number of Participants with One or More Drug-Related Adverse Events (AEs) or any Serious AEs (SAEs)[1]

End point description:

The number of participants with 1 or more AEs assessed as related to the study drug and is summarized cumulatively. In addition, the number of participants with 1 or more serious AEs is summarized cumulatively. A serious AE is defined as an event that results in death, initial or prolonged hospitalization, is life-threatening, leads to persistent or significant disability/incapacity, is associated with congenital anomaly/birth defect, or is considered significant by the investigator for any other reason. A summary of serious and other non-serious adverse events regardless of causality is located in the Reported Adverse Events module.
Analysis Population Description: All randomized participants who received at least one dose of study drug.

End point type	Primary

End point timeframe:

Baseline through Week 104

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No arm comparison analyses were planned or conducted.

End point values	Placebo	Solanezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	723	734		
Units: participants				
number (not applicable)				
SAE	308	299		
Other AE	485	514		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to 104-week endpoint in Alzheimer's Disease Assessment Scale - Cognitive 14-Item Scale (ADAS-Cog14)

End point title	Change from baseline to 104-week endpoint in Alzheimer's Disease Assessment Scale - Cognitive 14-Item Scale (ADAS-Cog14)

End point description:

ADAS-Cog14 is ADAS-Cog11 augmented with delayed free recall, digit cancellation, and maze completion measures. A score of 0 to 10 for delayed free recall and a conversion code of 0 to 5 for digit cancellation and maze completion provide total score ranges for this extended ADAS-Cog14 of 0 to 90. Higher scores indicate greater disease severity. Least Squares (LS) Mean was determined by mixed model repeated measures (MMRM) methodology with baseline, pooled investigator, treatment, visit, feeder visit 1 Mini-Mental State Examination (MMSE) status (mild/moderate), concomitant acetylcholinesterase inhibitors (AChEI)/Memantine use at baseline (yes/no), baseline age and treatment*visit.
Analysis Population Description: Feeder Intent-to-Treat Population: All randomized participants from feeder studies, who received at least one dose of study drug and had baseline & at least one post baseline observation for ADAS-Cog14.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Placebo	Solanezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	409	451		
Units: Units on a scale				
least squares mean (standard error)	17.58 (± 0.532)	17.56 (± 0.517)		

Statistical analyses

Statistical analysis title	STATISTICAL_ANALYSIS_TITLE
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	860
Analysis specification	Pre-specified
Analysis type	non-inferiority[2]
P-value	= 0.974
Method	Mixed models analysis
Parameter estimate	Median difference (net)
Point estimate	-0.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.14
upper limit	1.11

Notes:

[2] - The noninferiority margin for this hypothesis was specified as 50% of the treatment difference observed at the end of the feeder study. If the lower limit of the confidence interval (CI) was greater than 0, the noninferiority criterion was met, indicating that at least 50% of the treatment difference observed at the end of the feeder studies was maintained at specified time points in the delayed-start period.

Secondary: Change from baseline to 104-week endpoint in Alzheimer's Disease Cooperative Study - Activities of Daily Living Inventory (ADCS-ADL)

End point title	Change from baseline to 104-week endpoint in Alzheimer's Disease Cooperative Study - Activities of Daily Living Inventory (ADCS-ADL)

End point description:

ADCS-ADL is a 23-item inventory developed as a Rater-administered questionnaire answered by the participant's caregiver. It measures performance of basic and instrumental activities of daily living by participants. The total score ranges from 0 to 78, with lower scores indicating greater disease severity. LS Mean was determined by MMRM methodology with baseline, pooled investigator, treatment, visit, feeder visit 1 MMSE status (mild/moderate), concomitant AChEI/Memantine use at baseline (yes/no), baseline age and treatment*visit.
Analysis Population Description: Feeder Intent-to-Treat Population: All randomized participants from feeder studies, who received at least one dose of study drug and had baseline & at least one post baseline observation for ADCS-ADL.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Placebo	Solanezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	420	456		
Units: Units on a scale				
least squares mean (standard error)	-26.77 (± 0.888)	-24.77 (± 0.871)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to 104-week endpoint in Clinical Dementia Rating - Sum of Boxes (CDR-SB)

End point title	Change from baseline to 104-week endpoint in Clinical Dementia Rating - Sum of Boxes (CDR-SB)

End point description:

CDR-SB is a semi-structured interview of participants and their caregivers. Participant's cognitive status is rated across 6 domains of functioning, including memory, orientation, judgment/problem solving, community affairs, home/hobbies, and personal care. Severity score assigned for each of 6 domains; Total score (SB) ranges from 0 to 18. Higher scores indicate greater disease severity. LS Mean was determined by MMRM methodology with baseline, pooled investigator, treatment, visit, feeder visit 1 MMSE status (mild/moderate), concomitant AChEI/Memantine use at baseline (yes/no), baseline age and treatment*visit.
Analysis Population Description: Feeder Intent-to-Treat Population: All randomized participants from feeder studies, who received at least one dose of study drug and had baseline & at least one post baseline observation for CDR-SB.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Placebo	Solanezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	416	452		
Units: Units on a scale				
least squares mean (standard error)	5.59 (± 0.174)	5.27 (± 0.169)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to 104-week endpoint in Neuropsychiatric Inventory (NPI)

End point title	Change from baseline to 104-week endpoint in Neuropsychiatric Inventory (NPI)

End point description:

The NPI is a questionnaire administered to caregivers that quantifies behavioral changes in dementia. Each of the 12 behavioral domains the caregiver reports as present are scored for Frequency, scale: 1 (Occasionally) to 4 (Very Frequently), and Severity, scale: 1 (Mild) to 3 (Severe). If the domain is reported by the caregiver as 'Not Affected,' that domain is scored as 0. The individual domain scores are calculated by multiplying the frequency times the severity for each domain. NPI Total Score is calculated by adding the individual domain scores together for all 12 domains, with a scores range from 0 to 144. Lower scores indicated less severity and higher scores indicated a greater severity of neuropsychiatric disturbance. LS Mean was determined by MMRM methodology.
APD: All randomized participants from feeder studies, who received at least one dose of study drug and had baseline & at least one post baseline observation for NPI.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Placebo	Solanezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	414	457		
Units: Units on a scale				
least squares mean (standard error)				
Mild Alzheimer’s Disease	4.49 (± 0.788)	5.41 (± 0.773)		
Moderate Alzheimer’s Disease	11.90 (± 1.517)	8.10 (± 1.427)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to 104-week endpoint in Resource Utilization in Dementia - Lite (RUD-Lite) Caregiver Hours

End point title	Change from baseline to 104-week endpoint in Resource Utilization in Dementia - Lite (RUD-Lite) Caregiver Hours

End point description:

The RUD-Lite is a caregiver-completed assessment designed to assess the amount of formal and informal resources used by participants and the primary caregiver. It is completed by the caregiver and compiles data on the following resources: length of time the caregiver spends giving care, assisting participants with basic activities of daily living (BADL: eating dressing, grooming, bathing); assisting participants with instrumental activities of daily living (IADLs: shopping, cooking, housekeeping, laundry, transportation, taking medication, managing finances), and providing supervision. Scores range from 0 to 24 hours. Higher values indicate greater resource use. LS Mean was determined by MMRM methodology with baseline, pooled investigator, treatment, visit, concomitant AChEI/Memantine use at baseline (yes/no), baseline age and treatment*visit.
APD: All randomized participants from feeder studies, who received at least one dose of study drug and had baseline observation for RUD-Lite.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Placebo	Solanezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	415	451		
Units: hours per day (hr/day)				
least squares mean (standard error)				
Mild Alzheimer’s Disease-Basic ADL	1.96 (± 0.184)	1.21 (± 0.182)		
Mild Alzheimer’s Disease-Instrumental ADL	1.65 (± 0.207)	1.05 (± 0.205)		
Mild Alzheimer’s Disease-Supervision	2.84 (± 0.368)	2.59 (± 0.361)		
Moderate Alzheimer’s Disease-Basic ADL	3.19 (± 0.461)	3.54 (± 0.436)		
Moderate Alzheimer’s Disease-Instrumental ADL	1.75 (± 0.461)	1.72 (± 0.433)		
Moderate Alzheimer’s Disease-Supervision	5.03 (± 0.693)	4.47 (± 0.654)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to 104-week endpoint in EuroQol 5-Dimensional Health-Related Quality of Life Scale Proxy version (EQ-5D Proxy)

End point title	Change from baseline to 104-week endpoint in EuroQol 5-Dimensional Health-Related Quality of Life Scale Proxy version (EQ-5D Proxy)

End point description:

EQ-5D is a generic, multidimensional, health-related, quality-of-life instrument assessing caregiver's impression of participants overall health state. Profile allows caregivers to rate participant's health state in 5 health domains: mobility, self-care, usual activities, pain/discomfort, and mood using a 3-level scale: 1 (no problem), 2 (some problems), and 3 (major problems). These attribute combinations are converted into a weighted Health-State Index Score according to the United States (US) population-based algorithm. EQ-5D US Population-Based Index Scores range from -0.11 to 1.0. A score of 1.0 indicated perfect health. The Overall Health State Index Score is caregiver-reported using a visual analogue scale marked 0 (worst imaginable health) to 100 (best imaginable health state). LS Mean was determined by MMRM methodology.
APD: All randomized participants from feeder studies, who received at least one dose of study drug and had baseline & at least one post baseline observation.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Placebo	Solanezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	414	453		
Units: Units on a scale				
least squares mean (standard error)				
Mild Alzheimer’s Disease	-0.07 (± 0.010)	-0.06 (± 0.009)		
Moderate Alzheimer’s Disease	-0.16 (± 0.020)	-0.16 (± 0.019)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to 104-week endpoint in Quality of Life in Alzheimer's Disease (QoL-AD)

End point title	Change from baseline to 104-week endpoint in Quality of Life in Alzheimer's Disease (QoL-AD)

End point description:

The QoL-AD (Caregiver Total Score) is a disease-specific measure of quality of life for an Alzheimer's Disease (AD) population administered to the participant's primary caregiver, who answers on behalf of the participant. The assessment consists of 13 items covering physical health, energy, mood, living situations, memory, family, marriage, friends, chores, fun, money, self and life as a whole. The assessment is scored on a 4-point Likert scale with scores ranging from 1 (poor) to 4 (excellent). QoL-AD Total Score is defined as the sum of the 13 items with a scores range from 13 to 52. Higher scores denote a better quality of life. LS Mean was determined by MMRM methodology with baseline, pooled investigator, treatment, visit, concomitant AChEI/Memantine use at baseline (yes/no), baseline age and treatment*visit.
APD: All randomized participants from feeder studies, who received at least one dose of study drug and had baseline & at least one post baseline observation for QoL-AD.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Placebo	Solanezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	387	413		
Units: Units on a scale				
least squares mean (standard error)				
QLAD Self-Report Total Score-Mild Alzheimer’s	-1.37 (± 0.331)	-0.98 (± 0.327)		
QLAD Caregiver Total Score-Mild Alzheimer’s	-3.28 (± 0.350)	-3.63 (± 0.345)		
QLAD Self-Report Total Score-Moderate Alzheimer’s	-2.52 (± 0.605)	-2.34 (± 0.585)		

QLAD Caregiver Total Score-Moderate Alzheimer's	-4.26 (± 0.573)	-3.14 (± 0.552)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to 104-week endpoint in Mini-Mental State Examination (MMSE)

End point title	Change from baseline to 104-week endpoint in Mini-Mental State Examination (MMSE)

End point description:

The MMSE is an instrument used to assess a participant's cognitive function. The instrument is divided into 2 sections. The first section measures orientation, memory, and attention with scores ranging from 0 to 21 (lower scores indicate greater impairment). The second section tests the ability of the participant to name objects, follow verbal and written commands, write a sentence, and copy figures with scores ranging from 0 to 9 (lower scores indicate greater impairment). The range for MMSE Total Score is 0 to 30. Lower scores indicate more impairment. LS Mean was determined by MMRM methodology with baseline, pooled investigator, treatment, visit, concomitant AChEI/Memantine use at baseline (yes/no), baseline age and treatment*visit.
APD: Feeder Intent-to-Treat Population: All randomized participants from feeder studies, who received at least one dose of study drug and had baseline & at least one post baseline observation for MMSE.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Placebo	Solanezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	412	446		
Units: Units on a scale				
least squares mean (standard error)	-8.08 (± 0.270)	-7.60 (± 0.263)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to 52-week endpoint in Plasma Amyloid Beta (Aβ) Levels

End point title	Change from baseline to 52-week endpoint in Plasma Amyloid Beta (Aβ) Levels

End point description:

Concentration of the peptide Aβ 1-40 and Aβ 1-42 in plasma measured by immunoassay. The immunoassays for plasma Aβ 1-40 and Aβ 1-42 peptides were modified to render them tolerant to the presence of Solanezumab which would otherwise interfere with non-modified assays. LS Mean was determined by MMRM methodology with baseline, pooled investigator, treatment, visit, feeder visit 1 MMSE status (mild/moderate), concomitant AChEI/Memantine use at baseline (yes/no), baseline age and treatment*visit.

APD: All Feeder Intent-to-Treat Population: All randomized participants from feeder studies, who received at least one dose of study drug and had baseline & at least one post baseline observation for plasma Aβ 1-40 and Aβ 1-42.

End point type	Secondary

End point timeframe:

Baseline, Week 52

End point values	Placebo	Solanezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	515	532		
Units: picograms per milliliter (pg/mL)				
least squares mean (standard error)				
Aβ 1-40-Mild Alzheimer's Disease	176412.04 (± 3718.292)	173064.99 (± 3717.695)		
Aβ 1-42-Mild Alzheimer's Disease	19854.92 (± 366.392)	19723.48 (± 368.644)		
Aβ 1-40-Moderate Alzheimer's Disease	169356 (± 4627.8)	169087 (± 4511.6)		
Aβ 1-42-Moderate Alzheimer's Disease	19237 (± 556.3)	19552 (± 528.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to 104-week endpoint in volumetric Magnetic Resonance Imaging (vMRI)

End point title	Change from baseline to 104-week endpoint in volumetric Magnetic Resonance Imaging (vMRI)

End point description:

The vMRI assessment of right and left hippocampal volume is reported. LS Mean was determined by MMRM methodology with baseline, pooled investigator, treatment, visit, feeder visit 1 MMSE status (mild/moderate), concomitant AChEI/Memantine use at baseline (yes/no), baseline age and treatment*visit.
APD: Feeder Intent-to-Treat Population: All randomized participants from feeder studies, who received at least one dose of study drug and had baseline & at least one post baseline observation for vMRI.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Placebo	Solanezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	310	325		
Units: Cubic millimeter (mm^3)				
least squares mean (standard error)				
Right hippocampal volume-Mild Alzheimer's Disease	-230.23 (± 8.232)	-230.07 (± 8.195)		

Left hippocampal volume-Mild Alzheimer’s Disease	-257.15 (± 8.153)	-244.00 (± 8.115)		
Right hippocampal volume-Moderate Alzheimer’s	-261.39 (± 11.796)	-256.52 (± 11.246)		
Left hippocampal volume-Moderate Alzheimer’s	-255.16 (± 11.466)	-253.29 (± 10.858)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to 104-week endpoint in Alzheimer's Disease Assessment Scale - Cognitive Subscore 11-Item Scale (ADAS-Cog11)

End point title	Change from baseline to 104-week endpoint in Alzheimer's Disease Assessment Scale - Cognitive Subscore 11-Item Scale (ADAS-Cog11)

End point description:

The cognitive subscale of the ADAS (ADAS Cog11) was used as a primary efficacy measure and consists of 11 items assessing areas of function most typically impaired in Alzheimer’s disease: orientation, verbal memory, language, and praxis. The scale ranges from 0 to 70, with higher scores indicating greater disease severity. LS Mean was determined by MMRM methodology with baseline, pooled investigator, treatment, visit, feeder visit 1 MMSE status (mild/moderate), concomitant AChEI/Memantine use at baseline (yes/no), baseline age and treatment*visit.
APD: Feeder Intent-to-Treat Population: All randomized participants from feeder studies, who received at least one dose of study drug and had baseline & at least one post baseline observation for ADAS-Cog11.

End point type	Secondary

End point timeframe:

Baseline, Week 104

End point values	Placebo	Solanezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	375	409		
Units: units on a scale				
least squares mean (standard error)	17.78 (± 0.595)	17.38 (± 0.580)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline to 80-week endpoint in Amyloid Plaque Burden in the Brain using Positron Emission Tomography (PET) Imaging

End point title	Change from baseline to 80-week endpoint in Amyloid Plaque Burden in the Brain using Positron Emission Tomography (PET) Imaging

End point description:

Amyloid plaques are dense, mostly insoluble clumps of protein fragments. They leave a highly damaging substance outside and around the brain’s nerve cells. People with Alzheimer's Disease have a buildup of

these plaques in their hippocampus. changes in amyloid plaque burden will be determined using positron emission tomography (PET) imaging.
APD: Feeder Intent-to-Treat Population: All randomized participants with mild Alzheimer's Disease from feeder studies, who received at least one dose of study drug and had baseline & at least one post baseline observation for Amyloid Plaque Burden.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Placebo	Solanezumab		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	48		
Units: units on a scale				
arithmetic mean (standard deviation)	0.00 (± 0.131)	-0.01 (± 0.222)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Entire Study	
Adverse event reporting additional description:	
H8A-MC-LZAO	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups	
Reporting group title	Placebo: Solanezumab 400mg Open Label
Reporting group description: -	
Reporting group title	Solanezumab 400mg: Solanezumab 400mg Open Label
Reporting group description: -	

Serious adverse events	Placebo: Solanezumab 400mg Open Label	Solanezumab 400mg: Solanezumab 400mg Open Label	
Total subjects affected by serious adverse events			
subjects affected / exposed	308 / 723 (42.60%)	299 / 734 (40.74%)	
number of deaths (all causes)	39	43	
number of deaths resulting from adverse events	4	3	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
adenocarcinoma of colon			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
basal cell carcinoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
benign soft tissue neoplasm			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
bladder cancer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
bladder cancer recurrent			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
bladder transitional cell carcinoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
brain neoplasm			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
breast cancer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	3 / 734 (0.41%)	
occurrences causally related to treatment / all	0 / 0	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
breast cancer metastatic			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

chronic myeloid leukaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
colon cancer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
colon cancer metastatic			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
essential thrombocythaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastric cancer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
granular cell tumour			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
invasive ductal breast carcinoma			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
lung cancer metastatic			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
lung carcinoma cell type unspecified stage iv			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
lung neoplasm malignant			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lymphoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
malignant melanoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
malignant neoplasm of unknown primary site			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
malignant neoplasm progression			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
metastases to liver			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
metastatic malignant melanoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
neoplasm			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
non-small cell lung cancer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
oesophageal adenocarcinoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

pancreatic carcinoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)		
occurrences causally related to treatment / all	1 / 1	0 / 0		
deaths causally related to treatment / all	1 / 1	0 / 0		
pancreatic carcinoma metastatic				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
pancreatic neoplasm				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
papillary thyroid cancer				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)		
occurrences causally related to treatment / all	0 / 0	1 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
plasma cell myeloma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)		
occurrences causally related to treatment / all	0 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 1		
plasmacytoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)		
occurrences causally related to treatment / all	0 / 3	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
prostate cancer metastatic				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed[1]	0 / 317 (0.00%)	1 / 319 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
rectal cancer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
renal cell carcinoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal neoplasm			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
salivary gland neoplasm			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
squamous cell carcinoma of skin			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
uterine cancer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed[2]	1 / 406 (0.25%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	

Vascular disorders			
aortic aneurysm			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
aortic stenosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
arterial thrombosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
arteriosclerosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
deep vein thrombosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	6 / 734 (0.82%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
haematoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypertensive crisis			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypotension			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
peripheral artery thrombosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
peripheral ischaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
shock			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
thromboangiitis obliterans			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
thrombophlebitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

venous thrombosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
cataract operation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
abasia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
adverse drug reaction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
asthenia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	5 / 723 (0.69%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
catheter site haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
chest pain			

alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
complication associated with device			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
death			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	4 / 723 (0.55%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 4	0 / 1	
drowning			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
gait disturbance			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
general physical health deterioration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
non-cardiac chest pain			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	2 / 723 (0.28%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
oedema peripheral			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pyrexia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	3 / 734 (0.41%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
sudden death			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 3	0 / 1	
Social circumstances			
activities of daily living impaired			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
acquired hydrocele			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed[3]	0 / 317 (0.00%)	1 / 319 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
acute pulmonary oedema			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
acute respiratory failure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
aspiration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
benign prostatic hyperplasia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed[4]	2 / 317 (0.63%)	1 / 319 (0.31%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bronchospasm			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	2 / 723 (0.28%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cystocele			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed[5]	1 / 406 (0.25%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dyspnoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoxia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
interstitial lung disease			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
lung disorder			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
nasal polyps			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

organising pneumonia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pharyngeal oedema			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pleural effusion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	4 / 723 (0.55%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia aspiration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	5 / 723 (0.69%)	5 / 734 (0.68%)	
occurrences causally related to treatment / all	0 / 5	2 / 6	
deaths causally related to treatment / all	0 / 1	0 / 1	
pneumothorax			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumothorax spontaneous			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
prostatomegaly			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed[6]	0 / 317 (0.00%)	1 / 319 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary embolism			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	6 / 734 (0.82%)	
occurrences causally related to treatment / all	0 / 1	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
respiratory distress			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory failure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	3 / 734 (0.41%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	1 / 1	0 / 2	
uterine prolapse			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed[7]	1 / 406 (0.25%)	0 / 415 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
abnormal behaviour			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
affective disorder			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
aggression			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	1 / 2	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
agitation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	11 / 723 (1.52%)	7 / 734 (0.95%)	
occurrences causally related to treatment / all	1 / 11	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
alcohol abuse			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
behavioural and psychiatric symptoms of dementia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	7 / 723 (0.97%)	3 / 734 (0.41%)	
occurrences causally related to treatment / all	0 / 10	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
bipolar disorder			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
completed suicide			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
confusional state			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	6 / 734 (0.82%)	
occurrences causally related to treatment / all	0 / 1	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
delirium			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	5 / 723 (0.69%)	5 / 734 (0.68%)	
occurrences causally related to treatment / all	0 / 5	1 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
delirium febrile			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
delusion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
delusional perception			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
disorientation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

insomnia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
irritability			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
major depression			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
mental status changes			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	5 / 723 (0.69%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	1 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
restlessness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
suicidal behaviour			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
suicidal ideation			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
suicide attempt			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
blood pressure increased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hepatic enzyme increased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
acetabulum fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
ankle fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
bone contusion			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cervical vertebral fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
clavicle fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
concussion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
contusion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
craniocerebral injury			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
facial bones fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

fall			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	27 / 723 (3.73%)	23 / 734 (3.13%)	
occurrences causally related to treatment / all	0 / 27	0 / 25	
deaths causally related to treatment / all	0 / 0	0 / 0	
femoral neck fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	4 / 723 (0.55%)	13 / 734 (1.77%)	
occurrences causally related to treatment / all	0 / 4	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
femur fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	11 / 723 (1.52%)	3 / 734 (0.41%)	
occurrences causally related to treatment / all	1 / 11	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
fibula fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
flail chest			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
foot fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
forearm fracture			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
fractured ischium			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
head injury			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
hip fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	8 / 723 (1.11%)	11 / 734 (1.50%)	
occurrences causally related to treatment / all	0 / 8	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
humerus fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	4 / 723 (0.55%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
incisional hernia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
injury			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

joint dislocation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
joint injury			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
laceration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ligament sprain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lumbar vertebral fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
patella fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pelvic fracture			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 723 (0.00%)	4 / 734 (0.54%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
periprosthetic fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pubis fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary contusion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
radius fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
rib fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
road traffic accident			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

skull fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
spinal column injury				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
spinal compression fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	2 / 734 (0.27%)		
occurrences causally related to treatment / all	0 / 1	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
spinal fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)		
occurrences causally related to treatment / all	0 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
subdural haematoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	4 / 723 (0.55%)	5 / 734 (0.68%)		
occurrences causally related to treatment / all	0 / 4	1 / 5		
deaths causally related to treatment / all	0 / 0	0 / 0		
subdural haemorrhage				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)		
occurrences causally related to treatment / all	0 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
tibia fracture				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
traumatic haematoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
traumatic intracranial haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
upper limb fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
wound			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
wound dehiscence			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
wrist fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	4 / 723 (0.55%)	4 / 734 (0.54%)	
occurrences causally related to treatment / all	2 / 4	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
angina pectoris			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	4 / 734 (0.54%)	
occurrences causally related to treatment / all	2 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
arrhythmia supraventricular			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
atrial fibrillation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	5 / 723 (0.69%)	9 / 734 (1.23%)	
occurrences causally related to treatment / all	1 / 5	6 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
atrial flutter			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
atrioventricular block			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	1 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
atrioventricular block second degree			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bradycardia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	3 / 3	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
cardiac arrest			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	5 / 723 (0.69%)	5 / 734 (0.68%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 5	0 / 4	
cardiac failure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	3 / 734 (0.41%)	
occurrences causally related to treatment / all	0 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	1 / 1	
cardiac failure acute			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
cardiac failure congestive			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	6 / 723 (0.83%)	5 / 734 (0.68%)	
occurrences causally related to treatment / all	1 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
cardiac perforation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

cardio-respiratory arrest			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 2	0 / 2	
cardiogenic shock			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
cardiomyopathy			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
cardiopulmonary failure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
cardiovascular disorder			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
coronary artery stenosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
myocardial infarction			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	5 / 723 (0.69%)	4 / 734 (0.54%)	
occurrences causally related to treatment / all	2 / 5	1 / 4	
deaths causally related to treatment / all	1 / 1	1 / 3	
palpitations			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pericardial effusion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
sinus bradycardia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
sinus node dysfunction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	4 / 723 (0.55%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
tachycardia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ventricular extrasystoles			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Nervous system disorders			
altered state of consciousness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
brain stem haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
brain stem infarction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cerebral haematoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cerebral haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
cerebral infarction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	4 / 734 (0.54%)	
occurrences causally related to treatment / all	3 / 3	3 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
cerebral microhaemorrhage			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cerebrospinal fluid leakage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cerebrovascular accident			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	3 / 734 (0.41%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	1 / 1	0 / 1	
circadian rhythm sleep disorder			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cognitive disorder			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	3 / 734 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
coma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
complex partial seizures			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

dementia alzheimer's type			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	8 / 723 (1.11%)	5 / 734 (0.68%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 3	
dementia with lewy bodies			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
depressed level of consciousness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
dizziness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
encephalopathy			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
epilepsy			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
generalised tonic-clonic seizure			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	2 / 723 (0.28%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemorrhage intracranial			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemorrhagic cerebral infarction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemorrhagic stroke			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
headache			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hemiparesis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypoxic-ischaemic encephalopathy			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

intracranial aneurysm			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
intraventricular haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
ischaemic cerebral infarction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
ischaemic stroke			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	6 / 723 (0.83%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 6	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
lethargy			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
loss of consciousness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
metabolic encephalopathy			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
myoclonus			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
normal pressure hydrocephalus			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
presyncope			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
seizure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	11 / 734 (1.50%)	
occurrences causally related to treatment / all	0 / 3	3 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
somnolence			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
subarachnoid haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

syncope			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	10 / 723 (1.38%)	15 / 734 (2.04%)	
occurrences causally related to treatment / all	1 / 10	1 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
transient ischaemic attack			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
tremor			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
vasogenic cerebral oedema			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
anaemia folate deficiency			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
coagulopathy			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
normochromic normocytic anaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
cataract			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
glaucoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
retinal detachment			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
strabismus			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
vitreous haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
abdominal hernia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
abdominal pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
abdominal pain upper			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
colitis ischaemic			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
colonic fistula			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
colonic pseudo-obstruction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
constipation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diarrhoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	4 / 723 (0.55%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	2 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diarrhoea haemorrhagic			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diverticular fistula			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diverticulum			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

duodenal ulcer				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 723 (0.00%)	2 / 734 (0.27%)		
occurrences causally related to treatment / all	0 / 0	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
dyspepsia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
dysphagia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
erosive oesophagitis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
faecaloma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	3 / 734 (0.41%)		
occurrences causally related to treatment / all	0 / 1	0 / 3		
deaths causally related to treatment / all	0 / 0	0 / 0		
gastric ulcer				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
gastric ulcer haemorrhage				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastritis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
haematochezia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
haemorrhoids			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hiatus hernia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

ileus				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
ileus paralytic				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 723 (0.28%)	0 / 734 (0.00%)		
occurrences causally related to treatment / all	0 / 2	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
inguinal hernia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 723 (0.28%)	4 / 734 (0.54%)		
occurrences causally related to treatment / all	0 / 2	0 / 4		
deaths causally related to treatment / all	0 / 0	0 / 0		
intestinal obstruction				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	3 / 734 (0.41%)		
occurrences causally related to treatment / all	0 / 1	0 / 3		
deaths causally related to treatment / all	0 / 0	0 / 0		
jejunal perforation				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
large intestine polyp				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
lower gastrointestinal haemorrhage				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
oesophageal perforation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
oesophageal ulcer haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pancreatitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	5 / 723 (0.69%)	3 / 734 (0.41%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
pancreatitis acute			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
peptic ulcer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
rectal prolapse			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

rectal ulcer haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
small intestinal obstruction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
small intestinal perforation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
subileus			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
upper gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	3 / 734 (0.41%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
vomiting			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
bile duct obstruction			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
bile duct stone			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholangitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholecystitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholecystitis acute			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
cholelithiasis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
drug-induced liver injury			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

gallbladder polyp			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hepatic steatosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
dermatitis contact			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diabetic foot			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
drug eruption			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypersensitivity vasculitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
sebaceous gland disorder			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
urticaria			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	6 / 723 (0.83%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
acute prerenal failure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bladder tamponade			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
calculus bladder			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
haematuria			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
hydronephrosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
nephrolithiasis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
renal failure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary bladder haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary retention			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	3 / 734 (0.41%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
myxoedema			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
arthritis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
arthropathy			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
back pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
cervical spinal stenosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
dupuytren's contracture			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
foot deformity			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gouty arthritis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
intervertebral disc protrusion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
joint effusion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
joint swelling			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
lumbar spinal stenosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

muscle spasms			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
muscular weakness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
osteoarthritis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	7 / 723 (0.97%)	13 / 734 (1.77%)	
occurrences causally related to treatment / all	0 / 7	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
osteolysis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
rhabdomyolysis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
rotator cuff syndrome			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
spinal column stenosis			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
spondylolisthesis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
abdominal abscess			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
appendicitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
arthritis bacterial			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bacteraemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
bacterial infection			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
bronchitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	5 / 734 (0.68%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
campylobacter gastroenteritis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
cellulitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	7 / 734 (0.95%)	
occurrences causally related to treatment / all	0 / 1	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
clostridium difficile colitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
clostridium difficile infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
colostomy infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

cystitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
device related infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
diverticulitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	4 / 723 (0.55%)	3 / 734 (0.41%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
erysipelas			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
escherichia sepsis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
escherichia urinary tract infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
extradural abscess			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastroenteritis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
gastroenteritis viral			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	3 / 734 (0.41%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
groin abscess			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
herpes simplex encephalitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
herpes zoster			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
infected skin ulcer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

influenza				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 723 (0.28%)	4 / 734 (0.54%)		
occurrences causally related to treatment / all	0 / 2	0 / 4		
deaths causally related to treatment / all	0 / 0	0 / 0		
labyrinthitis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
lower respiratory tract infection				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)		
occurrences causally related to treatment / all	0 / 1	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
lung infection				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
mediastinitis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 1		
meningitis bacterial				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 0	0 / 0		
orchitis				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed[8]	0 / 317 (0.00%)	1 / 319 (0.31%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pericarditis tuberculous			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pharyngitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	27 / 723 (3.73%)	27 / 734 (3.68%)	
occurrences causally related to treatment / all	1 / 31	1 / 31	
deaths causally related to treatment / all	0 / 3	0 / 1	
pneumonia bacterial			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
pneumonia pneumococcal			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
post procedural infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

postoperative wound infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
pulmonary sepsis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
pulmonary tuberculosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
respiratory tract infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
sepsis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	6 / 734 (0.82%)	
occurrences causally related to treatment / all	0 / 4	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
septic shock			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 723 (0.28%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
sinusitis			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
tooth abscess			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
upper respiratory tract infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary tract infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	16 / 723 (2.21%)	17 / 734 (2.32%)	
occurrences causally related to treatment / all	1 / 21	1 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary tract infection bacterial			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
urinary tract infection staphylococcal			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
urosepsis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	5 / 734 (0.68%)	
occurrences causally related to treatment / all	0 / 4	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	

viral infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
wound infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
adult failure to thrive			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
decreased appetite			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 723 (0.41%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	3 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
dehydration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	7 / 723 (0.97%)	13 / 734 (1.77%)	
occurrences causally related to treatment / all	0 / 7	1 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
diabetes mellitus			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
failure to thrive			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
gout			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyperammonaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyperglycaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyperkalaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypernatraemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyperosmolar hyperglycaemic state			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

hypoglycaemia alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	4 / 723 (0.55%)	0 / 734 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
hyponatraemia alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
hypophagia alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
malnutrition alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 723 (0.14%)	2 / 734 (0.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
type 2 diabetes mellitus alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 723 (0.00%)	1 / 734 (0.14%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Notes:

[1] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.
[2] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.
[3] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

[4] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.
[5] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.
[6] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.
[7] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.
[8] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed to this adverse event. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

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

Non-serious adverse events	Placebo: Solanezumab 400mg Open Label	Solanezumab 400mg: Solanezumab 400mg Open Label	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	485 / 723 (67.08%)	514 / 734 (70.03%)	
Investigations			
weight decreased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	48 / 723 (6.64%)	38 / 734 (5.18%)	
occurrences (all)	51	40	
Injury, poisoning and procedural complications			
contusion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	45 / 723 (6.22%)	58 / 734 (7.90%)	
occurrences (all)	62	84	
fall			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	145 / 723 (20.06%)	136 / 734 (18.53%)	
occurrences (all)	222	245	
Vascular disorders			
hypertension			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	42 / 723 (5.81%)	36 / 734 (4.90%)	
occurrences (all)	43	38	
Nervous system disorders			

cerebral microhaemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	42 / 723 (5.81%)	56 / 734 (7.63%)	
occurrences (all)	47	61	
dizziness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	39 / 723 (5.39%)	43 / 734 (5.86%)	
occurrences (all)	43	53	
headache			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	49 / 723 (6.78%)	46 / 734 (6.27%)	
occurrences (all)	65	64	
General disorders and administration site conditions			
oedema peripheral			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	31 / 723 (4.29%)	37 / 734 (5.04%)	
occurrences (all)	33	38	
Gastrointestinal disorders			
constipation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	51 / 723 (7.05%)	64 / 734 (8.72%)	
occurrences (all)	56	71	
diarrhoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	58 / 723 (8.02%)	76 / 734 (10.35%)	
occurrences (all)	72	105	
vomiting			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	41 / 723 (5.67%)	51 / 734 (6.95%)	
occurrences (all)	51	70	
Respiratory, thoracic and mediastinal disorders			
benign prostatic hyperplasia			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed[9]	17 / 317 (5.36%)	9 / 319 (2.82%)	
occurrences (all)	17	10	
cough			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	50 / 723 (6.92%)	66 / 734 (8.99%)	
occurrences (all)	61	74	
Psychiatric disorders			
agitation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	75 / 723 (10.37%)	64 / 734 (8.72%)	
occurrences (all)	83	72	
anxiety			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	56 / 723 (7.75%)	86 / 734 (11.72%)	
occurrences (all)	78	114	
insomnia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	67 / 723 (9.27%)	74 / 734 (10.08%)	
occurrences (all)	70	80	
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	42 / 723 (5.81%)	33 / 734 (4.50%)	
occurrences (all)	51	40	
back pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	49 / 723 (6.78%)	67 / 734 (9.13%)	
occurrences (all)	54	75	
Infections and infestations			
bronchitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	32 / 723 (4.43%)	43 / 734 (5.86%)	
occurrences (all)	47	56	
nasopharyngitis			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	78 / 723 (10.79%)	88 / 734 (11.99%)	
occurrences (all)	129	145	
upper respiratory tract infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	59 / 723 (8.16%)	47 / 734 (6.40%)	
occurrences (all)	73	61	
urinary tract infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	98 / 723 (13.55%)	84 / 734 (11.44%)	
occurrences (all)	153	161	
Metabolism and nutrition disorders			
decreased appetite			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	35 / 723 (4.84%)	37 / 734 (5.04%)	
occurrences (all)	39	44	

Notes:

[9] - The number of subjects exposed to this adverse event is less than the total number of subjects exposed for the reporting group. These numbers are expected to be equal.
Justification: This event is gender specific, only occurring in male or female participants. The number of participants exposed has been adjusted accordingly.

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
19 November 2012	Amendment (c): Amended to specify the mild AD population as the primary population. In addition, all analyses were to be conducted in the moderate and overall (mild to moderate) populations. Finally, the duration of Study LZAO was extended for up to an additional 24 months or until solanezumab becomes commercially available in the host country, whichever occurs first.
16 September 2014	Amendment (d): Amended to extend the study for up to an additional 24 months or until solanezumab becomes commercially available in the host country, whichever occurs first. Additional secondary objectives and text were added to describe additional analyses to be performed with data from Study Periods 2 and 3.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported