Clinical trial results:
Effect of Passive Immunization on the Progression of Mild Alzheimer's Disease: Solanezumab (LY2062430) versus Placebo

Summary

EudraCT number	2013-001119-54
Trial protocol	GB DE IT SE ES
Global end of trial date	17 February 2017

Results information

Result version number	v1 (current)
This version publication date	04 March 2018
First version publication date	04 March 2018

Trial information

Trial identification

Sponsor protocol code	H8A-MC-LZAX

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01900665
WHO universal trial number (UTN)	-
Other trial identifiers	Trial Number: 15136

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:

The primary objective of this study was to test the idea that solanezumab will slow the cognitive decline of Alzheimer's Disease (AD) as compared with placebo in participants with mild AD.

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	12 August 2013
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Canada: 127
Country: Number of subjects enrolled	Sweden: 52
Country: Number of subjects enrolled	United States: 1078
Country: Number of subjects enrolled	Japan: 132
Country: Number of subjects enrolled	Poland: 102
Country: Number of subjects enrolled	Italy: 98
Country: Number of subjects enrolled	United Kingdom: 89
Country: Number of subjects enrolled	Australia: 68
Country: Number of subjects enrolled	France: 173
Country: Number of subjects enrolled	Germany: 96
Country: Number of subjects enrolled	Spain: 114
Worldwide total number of subjects	2129
EEA total number of subjects	724

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37	0

wk	
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	370
From 65 to 84 years	1636
85 years and over	123

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants were excluded after study enrollment,if PET imaging or CSF results did not show evidence of brain amyloid pathology,a screening MRI with results >4 ARIA-H(amyloid-related imaging abnormality-hemorrhage/hemosiderin deposition) or presence of ARIA-E(amyloid-related imaging abnormality-edema/effusions) and abnormal lab results were found.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Solanezumab

Arm description:

Participants received Solanezumab 400 milligrams (mg)Intravenously (IV) every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks.

Arm type	Experimental
Investigational medicinal product name	Solanezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Solanezumab 400 mg IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks.

Arm title	Placebo

Arm description:

Participants received Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks.

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

Dosage and administration details:

Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks

Number of subjects in period 1	Solanezumab	Placebo
Started	1057	1072
Received at Least 1 Dose of Study Drug	1054	1067
Completed	914	908
Not completed	143	164
Adverse event, serious fatal	9	16
Consent withdrawn by subject	33	45
Physician decision	11	7
Adverse event, non-fatal	48	39
Caregiver Decision	33	41
Lost to follow-up	3	-
Entry Criteria Not Met	5	9
Protocol deviation	1	7

Period 2

Period 2 title	Open Label Period
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Solanezumab

Arm description:

Participants received Solanezumab 400 milligrams (mg)Intravenously (IV) every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks.

Arm type	Experimental
Investigational medicinal product name	Solanezumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Solanezumab 400 mg IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks.

Arm title	Placebo

Arm description:

Participants received Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks.

Arm type	Placebo

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Infusion
Routes of administration	Intravenous use

Dosage and administration details:

Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks ofassessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks.

Number of subjects in period 2[1]	Solanezumab	Placebo
Started	881	859
Completed	0	0
Not completed	881	859
Adverse event, serious fatal	5	6
Parent/Caregiver Decision	33	34
Physician decision	4	4
Consent withdrawn by subject	20	28
Adverse event, non-fatal	16	20
Sponsor Decision	802	765
Lost to follow-up	1	1
Protocol deviation	-	1

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.
Justification: Subjects from Placebo Controlled Period were not required to enter into Open Label Period.

Baseline characteristics

Reporting groups	
Reporting group title	Solanezumab
Reporting group description:	
Participants received Solanezumab 400 milligrams (mg)Intravenously (IV) every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks.	

Reporting group values	Solanezumab	Placebo	Total
Number of subjects	1057	1072	2129
Age categorical Units: Subjects			
Age Continuous Units: years			
arithmetic mean	72.69	73.26	
standard deviation	± 7.814	± 7.966	-
Gender categorical Units: Subjects			
Female	600	631	1231
Male	457	441	898
Sex: Female, Male Units: Subjects			
Female	600	631	1231
Male	457	441	898
Ethnicity (NIH/OMB)			
All randomized participants who had baseline ethnicity data.			
Units: Subjects			
Hispanic or Latino	49	49	98
Not Hispanic or Latino	921	937	1858
Unknown or Not Reported	87	86	173
Race (NIH/OMB)			
All randomized participants who had baseline race data.			
Units: Subjects			
American Indian or Alaska Native	0	0	0
Asian	75	71	146
Native Hawaiian or Other Pacific Islander	1	0	1
Black or African American	14	19	33
White	878	894	1772
More than one race	2	2	4
Unknown or Not Reported	87	86	173
Region of Enrollment Units: Subjects			

Canada	61	66	127
Sweden	26	26	52
United States	537	541	1078
Japan	67	65	132
Poland	52	50	102
Italy	46	52	98
United Kingdom	45	44	89
Australia	32	36	68
France	87	86	173
Germany	48	48	96
Spain	56	58	114

End points

End points reporting groups

Reporting group title	Solanezumab
Reporting group description:	
Participants received Solanezumab 400 milligrams (mg)Intravenously (IV) every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks.	
Reporting group title	Solanezumab
Reporting group description:	
Participants received Solanezumab 400 milligrams (mg)Intravenously (IV) every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks.	
Reporting group title	Placebo
Reporting group description:	
Participants received Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks.	

Primary: Change from Baseline in Alzheimer's Disease Assessment Scale-Cognitive 14 Item Subscore (ADAS-Cog14)

End point title	Change from Baseline in Alzheimer's Disease Assessment Scale-Cognitive 14 Item Subscore (ADAS-Cog14)
End point description:	
The ADAS is a rater administered instrument that was designed to assess the severity of the dysfunction in the cognitive and noncognitive behaviors characteristic of persons with AD. The cognitive subscale of the ADAS that was used as the primary efficacy measure consists of 14 items assessing areas of cognitive function most typically impaired in AD: orientation, verbal memory, language, praxis, delayed free recall, digit cancellation, and maze completion measures. The ADAS-Cog14 scale ranges from 0 to 90. Higher scores indicate greater disease severity. Least Squares (LS) Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.	
End point type	Primary
End point timeframe:	
Baseline, Week 80	

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1053	1067		
Units: Units on a scale				
least squares mean (standard error)	6.65 (± 0.355)	7.44 (± 0.356)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.095 [1]
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.73
upper limit	0.14

Notes:

[1] - The Kenward-Roger approximation was used to estimate the denominator degrees of freedom.

Secondary: Change from Baseline in Alzheimer's Disease Cooperative Study-Instrumental Activities of Daily Living (ADCS-iADL)

End point title	Change from Baseline in Alzheimer's Disease Cooperative Study- Instrumental Activities of Daily Living (ADCS-iADL)

End point description:

The ADCS-ADL is a 23-item inventory developed as a rater-administered questionnaire answered by the participant's caregiver. The ADCS-ADL measures both 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 value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	908	896		
Units: Units on a scale				
least squares mean (standard error)	-6.17 (± 0.318)	-7.17 (± 0.320)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Solanezumab v Placebo

Number of subjects included in analysis	1804
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.019
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.17
upper limit	1.83

Secondary: Change from Baseline in Alzheimer's Disease Assessment Scale-Cognitive 11 Item Subscore (ADAS-Cog11)

End point title	Change from Baseline in Alzheimer's Disease Assessment Scale-Cognitive 11 Item Subscore (ADAS-Cog11)

End point description:

The cognitive subscale of ADAS (ADAS Cog11) consists of 11 items assessing areas of function most typically impaired in Alzheimer’s disease (AD): orientation, verbal memory, language, and praxis. The scale ranges from 0 to 70, with higher scores indicating greater disease severity. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1053	1067		
Units: Units on a scale				
least squares mean (standard error)	5.22 (± 0.284)	5.90 (± 0.285)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2120
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.068
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.68

Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.41
upper limit	0.05

Secondary: Change from Baseline in Mini-Mental State Examination (MMSE)

End point title	Change from Baseline in Mini-Mental State Examination (MMSE)

End point description:

MMSE is a brief screening instrument used to assess cognitive function (orientation, memory, attention, ability to name objects, follow verbal/written commands, write a sentence, and copy figures) in elderly participants. Total score ranges from 0 to 30; lower score indicates greater disease severity. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	893	876		
Units: Units on a scale				
least squares mean (standard error)	-3.17 (± 0.154)	-3.66 (± 0.156)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	1769
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.49
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.1
upper limit	0.88

Secondary: Change from Baseline in Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory (ADCS-ADL)

End point title	Change from Baseline in Alzheimer's Disease Cooperative Study Activities of Daily Living Inventory (ADCS-ADL)

End point description:

The ADCS-ADL is a 23-item inventory developed as a rater-administered questionnaire answered by the participant’s caregiver. The ADCS-ADL measures both 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 value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	908	897		
Units: Units on a scale				
least squares mean (standard error)	-7.42 (± 0.386)	-8.77 (± 0.387)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	1805
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.009
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.33
upper limit	2.37

Secondary: Change from Baseline in Functional Activities Questionnaire (FAQ)

End point title	Change from Baseline in Functional Activities Questionnaire (FAQ)

End point description:

FAQ is a 10-item, caregiver-based questionnaire and was administered to the study partner who was asked to rate the participant's ability to perform a variety of activities ranging from financial management, shopping, playing games, food preparation, traveling, keeping appointments, keeping track of current events, and understanding media. FAQ total score was calculated by adding the scores from each of the 10 items. A negative change indicated an improvement from baseline. FAQ Total Score is the sum of 10 items, ranging from 0 (best possible outcome) to 100 (worst possible outcome). LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	907	892		
Units: Units on a scale				
least squares mean (standard error)	5.17 (± 0.212)	5.57 (± 0.213)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	1799
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.14
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.4
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.93
upper limit	0.13

Secondary: Change from Baseline in Clinical Dementia Rating-Sum of Boxes (CDR-SB)

End point title	Change from Baseline 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 value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and

post baseline data.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	903	895		
Units: Units on a scale				
arithmetic mean (standard deviation)	1.91 (± 2.442)	2.23 (± 2.692)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	1798
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004
Method	ANCOVA
Parameter estimate	Mean difference (net)

Secondary: Change from Baseline in Neuropsychiatric Inventory (NPI)

End point title	Change from Baseline in Neuropsychiatric Inventory (NPI)

End point description:

NPI assesses psychopathology in participants with dementia and other neurologic disorders. Information is obtained from a caregiver familiar with the participant’s behavior. Total score ranges from 12 to 144; Higher scores indicate greater disease severity. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	909	891		
Units: Units on a scale				
least squares mean (standard error)	2.26 (± 3.11)	0.382 (± 0.387)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	1800
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.082
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	-1.82
upper limit	0.11

Secondary: Change from Baseline in Resource Utilization in Dementia-Lite (RUD-Lite)

End point title	Change from Baseline in Resource Utilization in Dementia-Lite (RUD-Lite)

End point description:

Assesses healthcare resource utilization (formal and informal care). Information gathered on both caregivers (care-giving time, work status) and participants (accommodation and healthcare resource utilization) was gathered from baseline and follow-up interviews. Reported number of hospitalizations per participant up to 76 weeks. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	909	891		
Units: Number of hospitalizations				
least squares mean (standard error)				
Basic ADL	0.34 (± 0.058)	0.35 (± 0.058)		
Instrumental ADL	0.55 (± 0.099)	0.50 (± 0.100)		
Sum of Basic and Instrumental ADL	0.91 (± 0.132)	0.86 (± 0.134)		
Supervision	0.72 (± 0.125)	0.88 (± 0.127)		

Statistical analyses

Statistical analysis title	Statistical analysis 1: Basic ADL
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	1800
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.97
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.15
upper limit	0.14

Statistical analysis title	Statistical analysis 2: Instrumental ADL
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	1800
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.69
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.2
upper limit	0.3

Statistical analysis title	Statistical analysis 3: Basic and Instrumental ADL
Comparison groups	Solanezumab v Placebo

Number of subjects included in analysis	1800
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.786
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.05
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.29
upper limit	0.38

Statistical analysis title	Statistical analysis 4: Supervision
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	1800
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.329
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	-0.16
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.48
upper limit	0.16

Secondary: Change from Baseline in Quality of Life in Alzheimer's Disease (QoL-AD)

End point title	Change from Baseline in Quality of Life in Alzheimer's Disease (QoL-AD)

End point description:

Assesses QoL for AD: participant rates mood, relationships, memory, finances, physical condition, and overall QoL assessment. Each of 13 items, rated on a 4-point scale. Sum of items=total score (range: 13 to 52). Higher scores indicate greater QoL. Participant’s primary caregiver asked to complete same measure. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data. QoL-AD self- report score was reported.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	853	812		
Units: Units on a scale				
least squares mean (standard error)	-0.55 (± 0.158)	-0.72 (± 0.161)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	1665
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.381
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	0.17
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.21
upper limit	0.56

Secondary: Change from Baseline in 5-Dimensional EuroQol Quality of Life Scale Proxy Version (EQ-5D Proxy)

End point title	Change from Baseline in 5-Dimensional EuroQol Quality of Life Scale Proxy Version (EQ-5D Proxy)

End point description:

EQ-5D (proxy version) measures mobility, self-care, usual activities, pain/discomfort, anxiety/depression. 3 severity levels: no, some, severe problems. Visual analog scale (VAS) assesses caregiver's impression of participant's health state; score ranges: 0 to 100 millimeter (mm). Lower scores=greater disease severity LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	904	892		
Units: mm				
least squares mean (standard error)	-1.10 (± 0.556)	-2.61 (± 0.562)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	1796
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.031
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1.5
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.13
upper limit	2.87

Secondary: Change from Baseline in Integrated Alzheimer's Disease Rating Scale (iADRS)

End point title	Change from Baseline in Integrated Alzheimer's Disease Rating Scale (iADRS)

End point description:

Integrated Alzheimer's Disease Rating Scale is used to assess that solanezumab slows down the cognitive and functional decline associated with AD compared with placebo. iADRS is a simple linear combination of ADAS-Cog 13 or 14 and the ADCS-iADL. The scale ranges from 0 to 146, where lower scores indicate worse performance. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	903	883		
Units: units on a scale				
least squares mean (standard error)	-12.92 (± 0.533)	-14.59 (± 0.537)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	1786
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.017
Method	Mixed models analysis
Parameter estimate	Mean difference (net)
Point estimate	1.68
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	3.06

Secondary: Percentage of Participants of Cognitive and Functional Responders

End point title	Percentage of Participants of Cognitive and Functional Responders

End point description:

Assess the proportion of participants who reach certain levels of cognitive and functional decline. Decline in cognition was defined as worsening from baseline by at least 6 or 9 points on the ADAS Cog14. If there is a cognitive decline of a specified cut-off or more at any time then the participant is considered a nonresponder. Functional nonresponders are participants who have not had any of the following at any time point: Clinically evident decline in ability to perform one or more basic ADL present at baseline; A clinically evident decline in ability to perform 20% or more of the instrumental ADL present at baseline; An increase in global CDR score of 1 point or more compared with baseline.A decline from no impairment to mild impairment (bADL, iADL is not considered clinically significant, but other declines of 1 or more points and any participant discontinuation within the first 6 months will be considered a non-responder.Analysis population included all randomized participants.

End point type	Secondary

End point timeframe:

Baseline through Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1057	1072		
Units: percentage of participants				
number (not applicable)				
Cognitive Responders: Cut-off 6	35.7	35.3		
Cognitive Responders: Cut-off 9	55.2	52.3		
Functional Responders	38.0	36.8		

Statistical analyses

Statistical analysis title	Statistical analysis 1:Cognitive: Cut-off 6
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.891
Method	Fisher exact
Parameter estimate	Fishers exact test

Statistical analysis title	Statistical analysis 2:Cognitive: Cut-off 9
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.203
Method	Fisher exact
Parameter estimate	Fishers exact test

Statistical analysis title	Statistical analysis 3:Functional Responders
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.588
Method	Fisher exact
Parameter estimate	Fishers exact test

Secondary: Change from Baseline in Plasma Amyloid-Beta (Aβ) Species	
End point title	Change from Baseline in Plasma Amyloid-Beta (Aβ) Species

End point description:

Concentration of amino acid peptide known as Aβ 1-42 in plasma. The change in plasma Aβ analytes after treatment were assessed separately for each plasma Aβ parameter. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1057	1072		
Units: Picogram/milliliter				
least squares mean (standard error)				
Modified amyloid beta 1-40	172754.36 (± 1613.534)	262.98 (± 1609.006)		
Modified amyloid beta1-42	18485.26 (± 104.913)	15.75 (± 105.237)		

Statistical analyses

Statistical analysis title	Statistical analysis 1: Modified amyloid beta 1-40
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	172491.38
Confidence interval	
level	95 %
sides	2-sided
lower limit	168131.33
upper limit	176851.43

Statistical analysis title	Statistical analysis 2: Modified amyloid beta 1-42
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	Mixed models analysis
Parameter estimate	Mean difference (final values)
Point estimate	18469.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	18187.59
upper limit	18751.44

Secondary: Change from Baseline in volumetric Magnetic Resonance Imaging (vMRI)

End point title	Change from Baseline in volumetric Magnetic Resonance

	Imaging (vMRI)

End point description:

The vMRI assessment of right and left hippocampal atrophy, is reported. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1057	1072		
Units: Cubic millimeter (mm^3)				
arithmetic mean (standard deviation)				
Right hippocampal atrophy	-145.7 (± 75.42)	-154.1 (± 81.06)		
Left hippocampal atrophy	-142.3 (± 74.27)	-146.3 (± 78.04)		
Right hippocampal atrophy+Left hippocampal atrophy	-288.0 (± 135.19)	-300.4 (± 138.52)		
Right entorhinal cortex atrophy	-77.3 (± 45.18)	-80.8 (± 45.16)		
Left entorhinal cortex atrophy	-91.6 (± 47.60)	-95.2 (± 53.46)		
Right+Left entorhinal cortex atrophy	-169.0 (± 79.65)	-176.0 (± 86.11)		
Atrophy of whole brain volume	-22725.6 (± 11920.78)	-23500.5 (± 12000.09)		
Enlargement of Ventricular volume	7055.4 (± 4580.36)	7226.6 (± 4545.73)		

Statistical analyses

Statistical analysis title	Statistical analysis 1: Right hippocampal atrophy
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.032
Method	ANCOVA
Parameter estimate	Mean difference (net)

Statistical analysis title	Statistical analysis 2: Left hippocampal atrophy
Comparison groups	Solanezumab v Placebo

Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.32
Method	ANCOVA
Parameter estimate	Mean difference (net)

Statistical analysis title	SA 3: Right + Left hippocampal atrophy
Statistical analysis description: Statistical Analysis 3 (SA 3)	
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.077
Method	ANCOVA
Parameter estimate	Mean difference (net)

Statistical analysis title	SA 4: Right entorhinal cortex atrophy
Statistical analysis description: Statistical analysis 4 (SA 4)	
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.186
Method	ANCOVA
Parameter estimate	Mean difference (net)

Statistical analysis title	SA 5: Left entorhinal cortex atrophy
Statistical analysis description: Statistical analysis 5 (SA 5)	
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.126
Method	ANCOVA
Parameter estimate	Mean difference (net)

Statistical analysis title	SA 6: Right + Left entorhinal cortex atrophy

Statistical analysis description:	
Statistical analysis 6 (SA 6)	
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.099
Method	ANCOVA
Parameter estimate	Mean difference (net)

Statistical analysis title	SA 7: Atrophy of whole brain volume
Statistical analysis description:	
Statistical analysis 7 (SA 7)	
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.095
Method	ANCOVA
Parameter estimate	Mean difference (net)

Statistical analysis title	SA 8: Enlargement of Ventricular volume
Statistical analysis description:	
Statistical analysis 8 (SA 8)	
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.227
Method	ANCOVA
Parameter estimate	Mean difference (net)

Secondary: Pharmacokinetics (PK): Area Under the Concentration Time Curve (AUC) of Solanezumab (LY2062430)

End point title	Pharmacokinetics (PK): Area Under the Concentration Time Curve (AUC) of Solanezumab (LY2062430)[2]

End point description:

Area Under the Concentration versus Time Curve was evaluated for Solanezumab. Analysis population included all randomized participants who received at least 1 dose of study medication (Solanezumab) with evaluable Solanezumab PK data.

End point type	Secondary

End point timeframe:

Visit 2 (Post-dose), Visit 5, 9, 15 (Pre-dose, Post-dose) and Visit 22 (Pre-dose): Pre-dose before the infusion, Post-dose 30 minutes End of Infusion

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: No inferential statistics were planned or conducted for this endpoint.

End point values	Solanezumab			
Subject group type	Reporting group			
Number of subjects analysed	1044			
Units: milligram*hour per milliliter (mg*h/mL)				
geometric mean (geometric coefficient of variation)	43.2 (± 24.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Baseline in Florbetapir Positron Emission Tomography (PET) Scan

End point title	Change from Baseline in Florbetapir Positron Emission Tomography (PET) Scan

End point description:

Florbetapir PET imaging was used to confirm the presence of amyloid pathology consistent with AD. Change from baseline was done to test the hypothesis that amyloid burden was reduced in participants in the treatment group. The change from baseline to the postbaseline visit of the composite summary standard uptake value ratio of florbetapir F18 standardized to subject-specific white matter. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.

End point type	Secondary

End point timeframe:

Baseline, Week 80

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	915	924		
Units: Composite summary				
least squares mean (standard error)				
Subject specific white matter corrected Mean whole cerebellum	0.02 (± 0.002) -0.01 (± 0.005)	0.02 (± 0.002) 0.00 (± 0.005)		

Statistical analyses

Statistical analysis title	SA1: Subject specific white matter corrected

Statistical analysis description:

Statistical analysis 1 (SA1)

Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	1839
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.131
Method	ANCOVA
Parameter estimate	Mean difference (net)

Statistical analysis title	SA2: Mean whole cerebellum
Statistical analysis description: Statistical analysis 2 (SA2)	
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	1839
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.181
Method	ANCOVA
Parameter estimate	Median difference (net)

Secondary: Change from Baseline in Cerebrospinal Fluid (CSF) Aβ Levels

End point title	Change from Baseline in Cerebrospinal Fluid (CSF) Aβ Levels
End point description: Concentration of CSF parameters includes amino acid peptide known as Aβ 1-40 and Aβ 1-42. Analyses of these CSF biomarkers was conducted in a subset of participants (as an addendum to the protocol). The dependent variable for each CSF parameter was its change from baseline to endpoint. LS Mean value was controlled for baseline value, baseline age, pooled investigator, treatment and visit. Analysis population included all randomized participants who received at least 1 dose of study drug and had baseline and post baseline data.	
End point type	Secondary
End point timeframe: Baseline, Week 80	

End point values	Solanezumab	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	1057	1072		
Units: picogram/milliliter				
least squares mean (standard error)				
Free amyloid beta 1-40, CSF	-714.60 (± 177.828)	-319.97 (± 182.519)		
Free amyloid beta 1-42, CSF	-37.33 (± 7.507)	-9.27 (± 8.175)		
Modified amyloid beta 1-40, CSF	1093.81 (± 624.059)	-2336.68 (± 637.126)		
Modified amyloid beta 1-42, CSF	315.69 (± 42.620)	-107.91 (± 42.907)		

Statistical analyses

Statistical analysis title	SA 1: Free amyloid beta 1-40, CSF
Statistical analysis description: Statistical analysis 1 (SA 1)	
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.073
Method	ANCOVA
Parameter estimate	Mean difference (net)

Statistical analysis title	SA 2: Free amyloid beta 1-42, CSF
Statistical analysis description: Statistical analysis 2 (SA 2)	
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.005
Method	ANCOVA
Parameter estimate	Mean difference (net)

Statistical analysis title	SA 3: Modified amyloid beta 1-40, CSF
Statistical analysis description: Statistical analysis 3 (SA 3)	
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)

Statistical analysis title	SA 4: Modified amyloid beta 1-42, CSF

Statistical analysis description:	
Statistical analysis 4 (SA 4)	
Comparison groups	Solanezumab v Placebo
Number of subjects included in analysis	2129
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANCOVA
Parameter estimate	Mean difference (net)

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up To 80 Weeks

Adverse event reporting additional description:

All randomized participants who received at least 1 dose of study drug.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Solanezumab 400mg - Double-Blind Phase

Reporting group description:

Participants received Solanezumab 400 mg IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who completed the full 80 weeks of treatment/assessment and decide to continue will take this regimen for up to an additional 208 weeks.

Reporting group title	Placebo - Double-Blind Phase

Reporting group description:

Participants received Placebo IV every 4 weeks for 76 weeks with an additional 4 weeks of assessments. Participants who complete the full 80 weeks of treatment/assessment and decide to continue will switch to solanezumab 400 mg every 4 weeks for up to an additional 208 weeks.

Reporting group title	Solanezumab 400mg: Solanezumab 400mg Open Label

Reporting group description:

Participants who complete 80 weeks treatment/assessment of the double-blind period were entered into open-label period. Participants received Solanezumab 400 mg IV every 4 weeks for 180 weeks with an additional 4 weeks of assessments.

Reporting group title	Placebo: Solanezumab 400mg Open Label

Reporting group description:

Participants who complete 80 weeks treatment/assessment of the double-blind period were entered into open-label period. Participants received Placebo IV every 4 weeks for 180 weeks with an additional 4 weeks of assessments.

Serious adverse events	Solanezumab 400mg - Double-Blind Phase	Placebo - Double-Blind Phase	Solanezumab 400mg: Solanezumab 400mg Open Label
Total subjects affected by serious adverse events			
subjects affected / exposed	175 / 1054 (16.60%)	203 / 1067 (19.03%)	102 / 879 (11.60%)
number of deaths (all causes)	9	17	5
number of deaths resulting from adverse events	2	2	2
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
abdominal neoplasm			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
adenocarcinoma of colon			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
b-cell lymphoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
basal cell carcinoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
benign small intestinal neoplasm			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bladder cancer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bladder neoplasm			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

breast cancer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
breast cancer metastatic			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cardiac myxoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
clear cell renal cell carcinoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
colon adenoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
colon cancer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
endometrial adenocarcinoma			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed[1]	0 / 599 (0.00%)	1 / 627 (0.16%)	0 / 501 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
glioblastoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
glioblastoma multiforme			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hepatic neoplasm			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
intraductal proliferative breast lesion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
invasive ductal breast carcinoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lip squamous cell carcinoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

lung adenocarcinoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lung cancer metastatic			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lung neoplasm malignant			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
malignant melanoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
malignant melanoma in situ			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
metastases to central nervous system			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
metastatic neoplasm			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
oesophageal adenocarcinoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ovarian cancer stage iv			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed[2]	0 / 599 (0.00%)	1 / 627 (0.16%)	0 / 501 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatic neoplasm			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
parathyroid tumour benign			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
plasma cell myeloma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
prostate cancer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed[3]	2 / 455 (0.44%)	0 / 440 (0.00%)	2 / 378 (0.53%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

prostate cancer metastatic			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed[4]	1 / 455 (0.22%)	1 / 440 (0.23%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rectal adenocarcinoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal cell carcinoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
small cell lung cancer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
squamous cell carcinoma of the tongue			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
transitional cell cancer of renal pelvis and ureter metastatic			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
transitional cell carcinoma			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
uterine cancer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed[5]	1 / 599 (0.17%)	0 / 627 (0.00%)	0 / 501 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
aortic aneurysm			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 1054 (0.28%)	0 / 1067 (0.00%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
aortic stenosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
deep vein thrombosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypertension			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypertensive crisis			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypotension			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lymphoedema			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
orthostatic hypotension			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peripheral arterial occlusive disease			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
cephalhaematoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
asthenia			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	2 / 1067 (0.19%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
chest discomfort			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
chest pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 1054 (0.28%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
death			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 2	0 / 0
gait disturbance			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
general physical health deterioration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
generalised oedema			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

multiple organ dysfunction syndrome			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
non-cardiac chest pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	7 / 1054 (0.66%)	5 / 1067 (0.47%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	1 / 8	0 / 7	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyrexia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 1054 (0.28%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
stent-graft endoleak			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sudden death			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
systemic inflammatory response syndrome			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	2 / 1054 (0.19%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Social circumstances			
immobilisation prolonged			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
respite care			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
acute respiratory failure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
asthma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
benign prostatic hyperplasia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed[6]	1 / 455 (0.22%)	1 / 440 (0.23%)	3 / 378 (0.79%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
chronic obstructive pulmonary disease			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dyspnoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
epistaxis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
organising pneumonia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pharyngeal mass			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pleural effusion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pleurisy			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

pneumonia aspiration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumothorax			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
prostatitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed[7]	1 / 455 (0.22%)	0 / 440 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pulmonary embolism			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	4 / 1054 (0.38%)	2 / 1067 (0.19%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 4	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
respiratory arrest			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sleep apnoea syndrome			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vulvar dysplasia			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed[8]	0 / 599 (0.00%)	1 / 627 (0.16%)	0 / 501 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
abnormal behaviour			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
affective disorder			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
aggression			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	2 / 1067 (0.19%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
agitation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 1054 (0.28%)	2 / 1067 (0.19%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
anxiety			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
behavioural and psychiatric symptoms of dementia			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
confusional state			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 1054 (0.28%)	1 / 1067 (0.09%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	1 / 3	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
delirium			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	5 / 1067 (0.47%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
delusion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
depression			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	1 / 1067 (0.09%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
disorientation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hallucination			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

mental status changes			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	4 / 1067 (0.37%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	1 / 2	1 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
phobia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
psychotic disorder			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
suicide attempt			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
heart rate irregular			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
troponin t increased			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
weight decreased			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
alcohol poisoning			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
animal bite			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ankle fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
arthropod sting			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cervical vertebral fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	1 / 1067 (0.09%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
chest injury			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
clavicle fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
concussion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
contusion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
coronary vascular graft occlusion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
craniocerebral injury			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fall			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	24 / 1054 (2.28%)	24 / 1067 (2.25%)	5 / 879 (0.57%)
occurrences causally related to treatment / all	2 / 26	1 / 27	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

femoral neck fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
femur fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	6 / 1054 (0.57%)	5 / 1067 (0.47%)	3 / 879 (0.34%)
occurrences causally related to treatment / all	0 / 7	0 / 5	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fibula fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fracture displacement			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
fractured coccyx			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastrointestinal stoma complication			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gun shot wound			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
head injury			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hip fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	5 / 1054 (0.47%)	6 / 1067 (0.56%)	3 / 879 (0.34%)
occurrences causally related to treatment / all	1 / 5	1 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
humerus fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
joint dislocation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
laceration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ligament sprain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

lumbar vertebral fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pelvic fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	2 / 1067 (0.19%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
periprosthetic fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
postoperative ileus			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pubis fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
radius fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rib fracture			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 1054 (0.09%)	4 / 1067 (0.37%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
road traffic accident			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
skull fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
spinal compression fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	2 / 1067 (0.19%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
spinal fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sternal fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
subdural haematoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	4 / 1067 (0.37%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1

upper limb fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
wound			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
wrist fracture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	1 / 1067 (0.09%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
adams-stokes syndrome			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
angina pectoris			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 1054 (0.28%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
aortic valve stenosis			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
arrhythmia supraventricular			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrial fibrillation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	5 / 1054 (0.47%)	9 / 1067 (0.84%)	4 / 879 (0.46%)
occurrences causally related to treatment / all	2 / 5	2 / 9	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrioventricular block			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrioventricular block complete			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atrioventricular block second degree			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bradycardia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	2 / 1067 (0.19%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

cardiac arrest alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	3 / 1067 (0.28%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 3	0 / 0
cardiac failure alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	3 / 1067 (0.28%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cardiac failure congestive alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cardio-respiratory arrest alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	1 / 1	0 / 0
coronary artery disease alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
myocardial infarction alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	4 / 1067 (0.37%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 2	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 2	0 / 0
myocardial ischaemia alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sinus bradycardia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sinus node dysfunction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
altered state of consciousness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
basal ganglia infarction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
carotid artery stenosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cerebellar haemorrhage			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
cerebellar infarction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cerebral haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	1 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
cerebral infarction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	3 / 879 (0.34%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cerebrovascular accident			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	5 / 1067 (0.47%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
cognitive disorder			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
coma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

dementia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dementia alzheimer's type			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
dementia of the alzheimer's type, with delirium			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
dizziness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
embolic stroke			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
encephalopathy			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
epilepsy			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
generalised tonic-clonic seizure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemorrhage intracranial			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemorrhagic stroke			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
headache			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	3 / 1067 (0.28%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypertensive encephalopathy			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypoaesthesia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

ischaemic stroke alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lacunar infarction alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
loss of consciousness alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
metabolic encephalopathy alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
presyncope alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 1054 (0.28%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
seizure alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	4 / 1067 (0.37%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
somnolence alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
spinal cord compression			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
spinal epidural haematoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
subarachnoid haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
syncope			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	8 / 1054 (0.76%)	14 / 1067 (1.31%)	5 / 879 (0.57%)
occurrences causally related to treatment / all	3 / 11	4 / 14	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thalamic infarction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
thalamus haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

thrombotic cerebral infarction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
tonic convulsion			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
transient ischaemic attack			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
anaemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lymphadenitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
vertigo			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vertigo positional			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
cataract			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
glaucoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
open angle glaucoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
retinal detachment			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
abdominal pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 1054 (0.28%)	3 / 1067 (0.28%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
abdominal pain upper			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
colitis ulcerative			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diarrhoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
duodenal perforation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastric ulcer			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastrointestinal disorder			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	2 / 1067 (0.19%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

gastrooesophageal reflux disease			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemorrhoidal haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
haemorrhoids			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hernial eventration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hiatus hernia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
inguinal hernia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intestinal obstruction			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	2 / 1054 (0.19%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intestinal perforation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intestinal polyp			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
large intestine polyp			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lower gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
mallory-weiss syndrome			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nausea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

oesophageal rupture			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pancreatitis acute			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peptic ulcer haemorrhage			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rectal prolapse			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
retroperitoneal haematoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
small intestinal obstruction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	3 / 1067 (0.28%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
upper gastrointestinal haemorrhage			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	3 / 1067 (0.28%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
vomiting			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
bile duct stone			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholangitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholecystitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholecystitis acute			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
cholelithiasis			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	2 / 1054 (0.19%)	0 / 1067 (0.00%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gallbladder perforation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hepatotoxicity			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
jaundice cholestatic			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
portal vein thrombosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
angioedema			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Renal and urinary disorders			
acute kidney injury			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	2 / 1054 (0.19%)	3 / 1067 (0.28%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
nephrolithiasis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal colic			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary bladder polyp			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary incontinence			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary retention			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Endocrine disorders			
toxic nodular goitre			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
foot deformity			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
lumbar spinal stenosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
musculoskeletal chest pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteoarthritis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	3 / 1067 (0.28%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 2	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteonecrosis			

alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 1054 (0.28%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
rhabdomyolysis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
spinal osteoarthritis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
spondylolisthesis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
tenosynovitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
abdominal abscess			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
appendicitis perforated			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atypical mycobacterial pneumonia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
atypical pneumonia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bacteraemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bacterial infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bacterial sepsis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
bronchitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

cellulitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
chronic sinusitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
clostridium difficile infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
escherichia sepsis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
extradural abscess			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
furuncle			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastroenteritis			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
gastroenteritis viral			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hepatitis e			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
herpes zoster			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
influenza			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	1 / 1067 (0.09%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
intervertebral discitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
localised infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

lung abscess			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
meningoencephalitis herpetic			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
oesophageal candidiasis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
ophthalmic herpes zoster			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
orchitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed[9]	0 / 455 (0.00%)	0 / 440 (0.00%)	0 / 378 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
osteomyelitis bacterial			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
paraspinal abscess			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pelvic abscess			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
peritonitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pneumonia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	11 / 1054 (1.04%)	8 / 1067 (0.75%)	3 / 879 (0.34%)
occurrences causally related to treatment / all	0 / 11	0 / 8	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
pneumonia influenzal			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
pyelonephritis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	3 / 1067 (0.28%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
sepsis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	2 / 1067 (0.19%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 1	1 / 1

septic shock alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
tooth infection alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
upper respiratory tract infection alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urinary tract infection alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 1054 (0.19%)	8 / 1067 (0.75%)	2 / 879 (0.23%)
occurrences causally related to treatment / all	0 / 2	0 / 9	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
urosepsis alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 1054 (0.09%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
viral infection alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	3 / 879 (0.34%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
wound infection alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	1 / 879 (0.11%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
cachexia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
decreased appetite			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	2 / 1067 (0.19%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
dehydration			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	3 / 1054 (0.28%)	4 / 1067 (0.37%)	3 / 879 (0.34%)
occurrences causally related to treatment / all	0 / 3	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
diabetic ketoacidosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hyponatraemia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	1 / 1067 (0.09%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
hypovolaemia			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	1 / 1054 (0.09%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
metabolic acidosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 1054 (0.00%)	0 / 1067 (0.00%)	0 / 879 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Placebo: Solanezumab 400mg Open Label		
Total subjects affected by serious adverse events			
subjects affected / exposed	114 / 856 (13.32%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
abdominal neoplasm			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
adenocarcinoma of colon			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
b-cell lymphoma			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
basal cell carcinoma			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
benign small intestinal neoplasm				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
bladder cancer				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
bladder neoplasm				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
breast cancer				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 856 (0.23%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
breast cancer metastatic				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cardiac myxoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

clear cell renal cell carcinoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
colon adenoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
colon cancer				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
endometrial adenocarcinoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed[1]	0 / 508 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
glioblastoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
glioblastoma multiforme				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hepatic neoplasm				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
intraductal proliferative breast lesion				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
invasive ductal breast carcinoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lip squamous cell carcinoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lung adenocarcinoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
lung cancer metastatic				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lung neoplasm malignant				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

malignant melanoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
malignant melanoma in situ				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
metastases to central nervous system				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
metastatic neoplasm				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
oesophageal adenocarcinoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ovarian cancer stage iv				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed[2]	0 / 508 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pancreatic neoplasm				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
parathyroid tumour benign				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
plasma cell myeloma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
prostate cancer				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed[3]	0 / 348 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
prostate cancer metastatic				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed[4]	1 / 348 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
rectal adenocarcinoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
renal cell carcinoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

small cell lung cancer				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
squamous cell carcinoma of the tongue				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
transitional cell cancer of renal pelvis and ureter metastatic				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
transitional cell carcinoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
uterine cancer				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed[5]	0 / 508 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
aortic aneurysm				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
aortic stenosis				
alternative dictionary used:				

MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
deep vein thrombosis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hypertension				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hypertensive crisis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hypotension				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 856 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
lymphoedema				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
orthostatic hypotension				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
peripheral arterial occlusive disease				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pregnancy, puerperium and perinatal conditions				
cephalhaematoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
asthenia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
chest discomfort				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
chest pain				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
death				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gait disturbance				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
general physical health deterioration				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
generalised oedema				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
multiple organ dysfunction syndrome				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
non-cardiac chest pain				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
pain				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

pyrexia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 856 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
stent-graft endoleak				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
sudden death				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
systemic inflammatory response syndrome				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Social circumstances				
immobilisation prolonged				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
respite care				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				

acute respiratory failure				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
asthma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
benign prostatic hyperplasia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed[6]	0 / 348 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
chronic obstructive pulmonary disease				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
dyspnoea				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
epistaxis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
organising pneumonia				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pharyngeal mass				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pleural effusion				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
pleurisy				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pneumonia aspiration				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pneumothorax				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
prostatitis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed[7]	0 / 348 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

pulmonary embolism				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 856 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
respiratory arrest				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
sleep apnoea syndrome				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
vulvar dysplasia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed[8]	0 / 508 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
abnormal behaviour				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
affective disorder				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
aggression				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	2 / 856 (0.23%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
agitation				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
anxiety				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
behavioural and psychiatric symptoms of dementia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
confusional state				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
delirium				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
delusion				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
depression				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
disorientation				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
hallucination				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
mental status changes				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 856 (0.23%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
phobia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
psychotic disorder				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

suicide attempt				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
heart rate irregular				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
troponin t increased				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
weight decreased				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
alcohol poisoning				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
animal bite				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ankle fracture				

alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
arthropod sting				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cervical vertebral fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
chest injury				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
clavicle fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
concussion				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
contusion				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	2 / 856 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
coronary vascular graft occlusion				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
craniocerebral injury				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
fall				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	12 / 856 (1.40%)			
occurrences causally related to treatment / all	0 / 12			
deaths causally related to treatment / all	0 / 0			
femoral neck fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 856 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
femur fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
fibula fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

fracture displacement				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
fractured coccyx				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gastrointestinal stoma complication				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gun shot wound				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
head injury				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hip fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	3 / 856 (0.35%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
humerus fracture				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
joint dislocation				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
laceration				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ligament sprain				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lumbar vertebral fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pelvic fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 856 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
periprosthetic fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

postoperative ileus				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pubis fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
radius fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
rib fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
road traffic accident				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
skull fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
spinal compression fracture				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	3 / 856 (0.35%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
spinal fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
sternal fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
subdural haematoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
upper limb fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
wound				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
wrist fracture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Cardiac disorders			
acute myocardial infarction			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
adams-stokes syndrome			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
angina pectoris			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 856 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
aortic valve stenosis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
arrhythmia supraventricular			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
atrial fibrillation			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	5 / 856 (0.58%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
atrioventricular block			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
atrioventricular block complete				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
atrioventricular block second degree				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
bradycardia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	3 / 856 (0.35%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
cardiac arrest				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
cardiac failure				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
cardiac failure congestive				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 856 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			

cardio-respiratory arrest				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
coronary artery disease				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
myocardial infarction				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
myocardial ischaemia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
sinus bradycardia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	3 / 856 (0.35%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
sinus node dysfunction				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
altered state of consciousness				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
basal ganglia infarction				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
carotid artery stenosis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cerebellar haemorrhage				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cerebellar infarction				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cerebral haemorrhage				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cerebral infarction				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

cerebrovascular accident				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	3 / 856 (0.35%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
cognitive disorder				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
coma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
dementia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 856 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
dementia alzheimer's type				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	4 / 856 (0.47%)			
occurrences causally related to treatment / all	2 / 5			
deaths causally related to treatment / all	0 / 1			
dementia of the alzheimer's type, with delirium				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
dizziness				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
embolic stroke			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
encephalopathy			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	1 / 856 (0.12%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
epilepsy			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	2 / 856 (0.23%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
generalised tonic-clonic seizure			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
haemorrhage intracranial			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
haemorrhagic stroke			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

headache				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hypertensive encephalopathy				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hypoaesthesia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
ischaemic stroke				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
lacunar infarction				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
loss of consciousness				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
metabolic encephalopathy				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
presyncope				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 856 (0.23%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
seizure				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
somnolence				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
spinal cord compression				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
spinal epidural haematoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
subarachnoid haemorrhage				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

syncope				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	7 / 856 (0.82%)			
occurrences causally related to treatment / all	0 / 7			
deaths causally related to treatment / all	0 / 0			
thalamic infarction				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
thalamus haemorrhage				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
thrombotic cerebral infarction				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
tonic convulsion				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
transient ischaemic attack				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
anaemia				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lymphadenitis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
vertigo				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
vertigo positional				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
cataract				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
glaucoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
open angle glaucoma				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
retinal detachment				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
abdominal pain				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
abdominal pain upper				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
colitis ulcerative				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
diarrhoea				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
duodenal perforation				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
gastric ulcer				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
gastrointestinal disorder				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gastrointestinal haemorrhage				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gastrooesophageal reflux disease				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
haemorrhoidal haemorrhage				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
haemorrhoids				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

hernial eventration				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hiatus hernia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
inguinal hernia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
intestinal obstruction				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
intestinal perforation				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
intestinal polyp				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
large intestine polyp				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lower gastrointestinal haemorrhage				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
mallory-weiss syndrome				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
nausea				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
oesophageal rupture				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pancreatitis acute				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
peptic ulcer haemorrhage				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

rectal prolapse				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
retroperitoneal haematoma				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
small intestinal obstruction				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
upper gastrointestinal haemorrhage				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
vomiting				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
bile duct stone				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
cholangitis				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cholecystitis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
cholecystitis acute				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
cholelithiasis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gallbladder perforation				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hepatotoxicity				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
jaundice cholestatic				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

portal vein thrombosis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
angioedema				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
acute kidney injury				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	3 / 856 (0.35%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
nephrolithiasis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
renal colic				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
renal failure				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
urinary bladder polyp				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
urinary incontinence			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
urinary retention			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
toxic nodular goitre			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
back pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
foot deformity			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	0 / 856 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
lumbar spinal stenosis			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
musculoskeletal chest pain				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
osteoarthritis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
osteonecrosis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
rhabdomyolysis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
spinal osteoarthritis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
spondylolisthesis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

tenosynovitis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
abdominal abscess				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
appendicitis perforated				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
atypical mycobacterial pneumonia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
atypical pneumonia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
bacteraemia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
bacterial infection				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
bacterial sepsis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
bronchitis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
cellulitis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
chronic sinusitis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
clostridium difficile infection				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
escherichia sepsis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

extradural abscess				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
furuncle				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gastroenteritis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
gastroenteritis viral				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
hepatitis e				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
herpes zoster				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
influenza				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
intervertebral discitis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
localised infection				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lung abscess				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
meningoencephalitis herpetic				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
oesophageal candidiasis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
ophthalmic herpes zoster				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

orchitis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed[9]	1 / 348 (0.29%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
osteomyelitis bacterial				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
paraspinal abscess				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pelvic abscess				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
peritonitis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pneumonia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	5 / 856 (0.58%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 1			
pneumonia influenzal				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
pyelonephritis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
sepsis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
septic shock				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
tooth infection				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
upper respiratory tract infection				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
urinary tract infection				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	3 / 856 (0.35%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			

urosepsis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
viral infection				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
wound infection				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
cachexia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
decreased appetite				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
dehydration				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	2 / 856 (0.23%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
diabetic ketoacidosis				
alternative dictionary used: MedDRA 19.0				

subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hyponatraemia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
hypovolaemia				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	0 / 856 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
metabolic acidosis				
alternative dictionary used: MedDRA 19.0				
subjects affected / exposed	1 / 856 (0.12%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	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.

[9] - 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	Solanezumab 400mg - Double-Blind Phase	Placebo - Double-Blind Phase	Solanezumab 400mg: Solanezumab 400mg Open Label
Total subjects affected by non-serious adverse events			
subjects affected / exposed	536 / 1054 (50.85%)	530 / 1067 (49.67%)	255 / 879 (29.01%)
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	146 / 1054 (13.85%)	144 / 1067 (13.50%)	67 / 879 (7.62%)
occurrences (all)	195	207	97
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	61 / 1054 (5.79%)	57 / 1067 (5.34%)	23 / 879 (2.62%)
occurrences (all)	66	65	24
headache			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	86 / 1054 (8.16%)	86 / 1067 (8.06%)	28 / 879 (3.19%)
occurrences (all)	96	151	34
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	76 / 1054 (7.21%)	87 / 1067 (8.15%)	23 / 879 (2.62%)
occurrences (all)	86	109	24
nausea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	54 / 1054 (5.12%)	46 / 1067 (4.31%)	23 / 879 (2.62%)
occurrences (all)	69	63	32
Respiratory, thoracic and mediastinal disorders			

cough			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	44 / 1054 (4.17%)	58 / 1067 (5.44%)	25 / 879 (2.84%)
occurrences (all)	53	69	27
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	54 / 1054 (5.12%)	58 / 1067 (5.44%)	15 / 879 (1.71%)
occurrences (all)	57	59	18
depression			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	60 / 1054 (5.69%)	57 / 1067 (5.34%)	18 / 879 (2.05%)
occurrences (all)	62	57	18
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	44 / 1054 (4.17%)	56 / 1067 (5.25%)	21 / 879 (2.39%)
occurrences (all)	51	62	23
back pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	63 / 1054 (5.98%)	60 / 1067 (5.62%)	26 / 879 (2.96%)
occurrences (all)	70	67	26
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	89 / 1054 (8.44%)	80 / 1067 (7.50%)	29 / 879 (3.30%)
occurrences (all)	114	99	31
upper respiratory tract infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	64 / 1054 (6.07%)	54 / 1067 (5.06%)	23 / 879 (2.62%)
occurrences (all)	74	61	25
urinary tract infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	58 / 1054 (5.50%)	72 / 1067 (6.75%)	38 / 879 (4.32%)
occurrences (all)	79	103	47

Non-serious adverse events	Placebo: Solanezumab 400mg Open Label		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	260 / 856 (30.37%)		
Injury, poisoning and procedural complications			
fall			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	80 / 856 (9.35%)		
occurrences (all)	109		
Nervous system disorders			
dizziness			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	29 / 856 (3.39%)		
occurrences (all)	31		
headache			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	29 / 856 (3.39%)		
occurrences (all)	42		
Gastrointestinal disorders			
diarrhoea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	17 / 856 (1.99%)		
occurrences (all)	18		
nausea			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	15 / 856 (1.75%)		
occurrences (all)	18		
Respiratory, thoracic and mediastinal disorders			
cough			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	18 / 856 (2.10%)		
occurrences (all)	22		
Psychiatric disorders			
anxiety			
alternative dictionary used: MedDRA 19.0			

subjects affected / exposed	17 / 856 (1.99%)		
occurrences (all)	17		
depression			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	20 / 856 (2.34%)		
occurrences (all)	20		
Musculoskeletal and connective tissue disorders			
arthralgia			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	22 / 856 (2.57%)		
occurrences (all)	22		
back pain			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	23 / 856 (2.69%)		
occurrences (all)	23		
Infections and infestations			
nasopharyngitis			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	32 / 856 (3.74%)		
occurrences (all)	36		
upper respiratory tract infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	21 / 856 (2.45%)		
occurrences (all)	23		
urinary tract infection			
alternative dictionary used: MedDRA 19.0			
subjects affected / exposed	36 / 856 (4.21%)		
occurrences (all)	46		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 September 2014	The duration of the protocol was extended to include a 24-month open-label period, which followed the initial 18-month treatment period. Added secondary objectives and corresponding statistical analyses for the open-label period including the delayed-start-analyses.
29 January 2016	Changed from cognitive and functional coprimary endpoints (ADAS-Cog14 and ADCS-iADL) to a single primary cognitive endpoint (ADAS-Cog14) with function (ADCS-iADL) as a key secondary endpoint. Added a secondary objective and corresponding analysis for the iADRS to incorporate an additional measure of both cognition and function.
03 August 2016	The open-label extension period was extended to include a second 24-month open-label period.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported