Clinical trial results:
Randomized, double-blind, Evaluation in secondary Stroke Prevention comparing the EfficaCy and safety of the oral Thrombin inhibitor dabigatran etexilate (110 milligram (mg) or 150 mg, oral b.i.d.) versus acetylsalicylic acid (100 mg oral q.d.) in patients with Embolic Stroke of Undetermined Source (RESPECT ESUS)

Summary

EudraCT number	2013-003444-24
Trial protocol	PT DE BE AT HU IT SE SI ES CZ SK PL HR GR EE
Global end of trial date	14 August 2018

Results information

Result version number	v1
This version publication date	29 August 2019
First version publication date	29 August 2019

Trial information

Trial identification

Sponsor protocol code	1160.189

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02239120
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Boehringer Ingelheim
Sponsor organisation address	Binger Strasse 173, Ingelheim am Rhein, Germany, 55216
Public contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim, 001 8002430127, clintriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim, 001 8002430127, clintriage.rdg@boehringer-ingelheim.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 September 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	14 August 2018
Global end of trial reached?	Yes
Global end of trial date	14 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this trial was to demonstrate that the efficacy of dabigatran etexilate (DE, dosed using either 110 mg twice daily or 150 mg twice daily according to age and renal function) is superior to 100 mg once daily acetylsalicylic acid (ASA) for the prevention of stroke recurrence in patients with embolic stroke of undetermined source (ESUS). The trial characterised also the safety of DE in this patient population.

Protection of trial subjects:

Only participants that met all the study inclusion and none of the exclusion criteria were to be entered in the study. All participants were free to withdraw from the clinical trial at any time for any reason given. Close monitoring of all participants was adhered to throughout the trial conduct. Rescue medication was allowed for all participants as required.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	03 December 2014
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	Argentina: 62
Country: Number of subjects enrolled	Australia: 177
Country: Number of subjects enrolled	Austria: 68
Country: Number of subjects enrolled	Belgium: 197
Country: Number of subjects enrolled	Brazil: 84
Country: Number of subjects enrolled	Canada: 157
Country: Number of subjects enrolled	Chile: 28
Country: Number of subjects enrolled	China: 124
Country: Number of subjects enrolled	Serbia: 52
Country: Number of subjects enrolled	Singapore: 29
Country: Number of subjects enrolled	Colombia: 35
Country: Number of subjects enrolled	Croatia: 31
Country: Number of subjects enrolled	Czech Republic: 124
Country: Number of subjects enrolled	Estonia: 22
Country: Number of subjects enrolled	France: 117
Country: Number of subjects enrolled	Germany: 1119
Country: Number of subjects enrolled	Greece: 75

Country: Number of subjects enrolled	Hong Kong: 11
Country: Number of subjects enrolled	Hungary: 51
Country: Number of subjects enrolled	India: 114
Country: Number of subjects enrolled	Israel: 17
Country: Number of subjects enrolled	Italy: 273
Country: Number of subjects enrolled	Japan: 634
Country: Number of subjects enrolled	Korea, Republic of: 194
Country: Number of subjects enrolled	Malaysia: 22
Country: Number of subjects enrolled	Mexico: 24
Country: Number of subjects enrolled	New Zealand: 16
Country: Number of subjects enrolled	Peru: 11
Country: Number of subjects enrolled	Portugal: 161
Country: Number of subjects enrolled	Russian Federation: 190
Country: Number of subjects enrolled	Slovakia: 11
Country: Number of subjects enrolled	Slovenia: 14
Country: Number of subjects enrolled	South Africa: 6
Country: Number of subjects enrolled	Spain: 447
Country: Number of subjects enrolled	Sweden: 59
Country: Number of subjects enrolled	Switzerland: 92
Country: Number of subjects enrolled	Taiwan: 103
Country: Number of subjects enrolled	Thailand: 72
Country: Number of subjects enrolled	Turkey: 60
Country: Number of subjects enrolled	Ukraine: 91
Country: Number of subjects enrolled	United States: 544
Country: Number of subjects enrolled	Poland: 112
Worldwide total number of subjects	5830
EEA total number of subjects	2881

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	2728
From 65 to 84 years	2997
85 years and over	105

Subject disposition

Recruitment

Recruitment details:

This was randomised, active comparator, double-blind, 2 arms (1:1 ratio) event-driven Phase III trial in participants with embolic stroke of undetermined source (ESUS). Study was conducted at multiple centers in 42 countries between 3 Dec 2014 (first participant enrollment) and 14 August 2018 (last participant visit).

Pre-assignment

Screening details:

All participants were screened for eligibility to participate in the trial. Participants attended specialist sites which would then ensure that all participants met all inclusion/exclusion criteria. Participants were not to be randomized to trial treatment if any one of the specific entry criteria were not met.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Investigator, Monitor, Subject, Carer, Data analyst, Assessor

Blinding implementation details:

This was a double-blind trial.

Arms

Are arms mutually exclusive?	Yes
Arm title	Dabigatran etexilate 110 or 150 milligram (mg)

Arm description:

Participants were orally administered one 110 mg (for participants aged ≥75 years or with a creatinine clearance (CrCl) of 30 to <50 millilitre/ minute (mL/min)) or one 150 mg (for participants aged <75 years and with a CrCl of ≥50 mL/minute) Dabigatran etexilate (DE) capsule twice daily.

Arm type	Experimental
Investigational medicinal product name	Dabigatran etexilate
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants were orally administered one 110 mg (for participants aged ≥75 years or with a creatinine clearance (CrCl) of 30 to <50 millilitre/ minute (mL/min)) or one 150 mg (for participants aged <75 years and with a CrCl of ≥50 mL/minute) Dabigatran etexilate (DE) capsule twice daily.

Arm title	Acetylsalicylic acid, Aspirin (ASA) 100 mg

Arm description:

Participants were orally administered one 100 mg ASA non-enteric coated tablet once daily.

Arm type	Active comparator
Investigational medicinal product name	Acetylsalicylic acid, Aspirin (ASA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Participants were orally administered one 100 mg ASA non-enteric coated tablet once daily.

Number of subjects in period 1[1]	Dabigatran etexilate 110 or 150 milligram (mg)	Acetylsalicylic acid, Aspirin (ASA) 100 mg
Started	2695	2695
Completed	2620	2623
Not completed	75	72
Adverse event, serious fatal	56	58
Lost to follow-up	19	14

Notes:

[1] - The number of subjects reported to be in the baseline period are not the same as the worldwide number enrolled in the trial. It is expected that these numbers will be the same.
Justification: Baseline characteristics are based on patients who were randomised after successfully completing the screening period and received at least one dose of the trial medication.

Baseline characteristics

Reporting groups	
Reporting group title	Dabigatran etexilate 110 or 150 milligram (mg)
Reporting group description:	
Participants were orally administered one 110 mg (for participants aged ≥75 years or with a creatinine clearance (CrCl) of 30 to <50 millilitre/ minute (mL/min)) or one 150 mg (for participants aged <75 years and with a CrCl of ≥50 mL/minute) Dabigatran etexilate (DE) capsule twice daily.	
Reporting group title	Acetylsalicylic acid, Aspirin (ASA) 100 mg
Reporting group description:	
Participants were orally administered one 100 mg ASA non-enteric coated tablet once daily.	

Reporting group values	Dabigatran etexilate 110 or 150 milligram (mg)	Acetylsalicylic acid, Aspirin (ASA) 100 mg	Total
Number of subjects	2695	2695	5390
Age categorical			
Units: Subjects			
Age Continuous			
Randomised set (RS): The RS consisted of all patients who were randomised, regardless of whether they took trial medication. The start date of the observation period for this population was the date of randomisation.			
Units: years			
arithmetic mean	64.5	63.9	
standard deviation	± 11.44	± 11.39	-
Sex: Female, Male			
RS			
Units: Subjects			
Female	1001	986	1987
Male	1694	1709	3403
Race (NIH/OMB)			
RS. Information on race was not collected for all patients in France.			
Units: Subjects			
American Indian or Alaska Native	11	20	31
Asian	631	597	1228
Native Hawaiian or Other Pacific Islander	2	4	6
Black or African American	54	40	94
White	1926	1966	3892
More than one race	10	12	22
Unknown or Not Reported	61	56	117
Ethnicity (NIH/OMB)			
RS. Information on ethnicity was not collected for all patients in France.			
Units: Subjects			
Hispanic or Latino	281	268	549
Not Hispanic or Latino	2354	2371	4725
Unknown or Not Reported	60	56	116

End points

End points reporting groups

Reporting group title	Dabigatran etexilate 110 or 150 milligram (mg)
Reporting group description:	
Participants were orally administered one 110 mg (for participants aged ≥75 years or with a creatinine clearance (CrCl) of 30 to <50 millilitre/ minute (mL/min)) or one 150 mg (for participants aged <75 years and with a CrCl of ≥50 mL/minute) Dabigatran etexilate (DE) capsule twice daily.	
Reporting group title	Acetylsalicylic acid, Aspirin (ASA) 100 mg
Reporting group description:	
Participants were orally administered one 100 mg ASA non-enteric coated tablet once daily.	

Primary: Adjudicated recurrent stroke

End point title	Adjudicated recurrent stroke
End point description:	
Adjudicated recurrent stroke (ischemic, hemorrhagic, or unspecified) is presented. The annualised event rate represents the average number of events per patient during a 1-year period. Randomised set (RS): RS consisted of all participants who were randomised, regardless of whether they took trial medication. The start date of the observation period for this population was the date of randomisation.	
End point type	Primary
End point timeframe:	
From randomisation until full follow up period, approximately 43 months.	

End point values	Dabigatran etexilate 110 or 150 milligram (mg)	Acetylsalicylic acid, Aspirin (ASA) 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2695[1]	2695[2]		
Units: Annualised event rate (%/ year)				
number (not applicable)	4.09	4.80		

Notes:

[1] - RS

[2] - RS

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Statistical analysis description:	
Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke.	
Comparison groups	Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg

Number of subjects included in analysis	5390
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1028
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	1.03

Primary: First major bleed (adjudicated)

End point title	First major bleed (adjudicated)

End point description:

First major bleed is primary safety endpoint. Major bleeds were defined according to International Society of Thrombosis and Haemostasis(ISTH) as: Symptomatic bleeding in a critical area or organ, such as intracranial, intraspinal, intraocular, retroperitoneal, intra-articular or pericardial, or intramuscular with compartment syndrome and/or, Bleeding (which should be overt) associated with a reduction in haemoglobin of at least 2grams/deciliter (g/dL)(1.24millimoles/Litre(mmol/L)), or leading to transfusion of ≥2units of blood or packed cells (equivalent to ≥4.5units in Japan); the haemoglobin drop should be considered to be due to and temporally related to the bleeding event and/or, Fatal bleed. The annualised event rate represents the average number of events per patient during 1-year period. Treated set (TS) consisted of all patients who were treated with at least 1 dose of trial medication. For TS date of first intake of trial medication was start date of the observation period.

End point type	Primary

End point timeframe:

Between the first trial medication intake up to 6 days after the last trial medication intake, approximately 42 months.

End point values	Dabigatran etexilate 110 or 150 milligram (mg)	Acetylsalicylic acid, Aspirin (ASA) 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2676[3]	2674[4]		
Units: Annualised event rate (%/ year)				
number (not applicable)	1.84	1.33		

Notes:

[3] - TS

[4] - TS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke.

Comparison groups	Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg

Number of subjects included in analysis	5350
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1076
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.36
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.94
upper limit	1.97

Secondary: Adjudicated ischaemic stroke

End point title	Adjudicated ischaemic stroke

End point description:

Adjudicated ischaemic stroke is a key secondary endpoint. The annualised event rate represents the average number of events per patient during a 1-year period.

End point type	Secondary

End point timeframe:

From randomisation until full follow up period, up to 43 months.

End point values	Dabigatran etexilate 110 or 150 milligram (mg)	Acetylsalicylic acid, Aspirin (ASA) 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2695[5]	2695[6]		
Units: Annualised event rate (%/ year)				
number (not applicable)	3.97	4.71		

Notes:

[5] - RS

[6] - RS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke.

Comparison groups	Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg

Number of subjects included in analysis	5390
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0892
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	1.03

Secondary: Adjudicated composite of non-fatal stroke, non-fatal myocardial infarction, or cardiovascular death

End point title	Adjudicated composite of non-fatal stroke, non-fatal myocardial infarction, or cardiovascular death

End point description:

Adjudicated composite of non-fatal stroke, non-fatal myocardial infarction (MI), or cardiovascular death is a key secondary endpoint. The annualised event rate represents the average number of events per patient during a 1-year period.

End point type	Secondary

End point timeframe:

From randomisation until full follow up period, up to 43 months.

End point values	Dabigatran etexilate 110 or 150 milligram (mg)	Acetylsalicylic acid, Aspirin (ASA) 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2695[7]	2695[8]		
Units: Annualised event rate (%/ year)				
number (not applicable)	4.80	5.40		

Notes:

[7] - RS

[8] - RS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke.

Comparison groups	Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg

Number of subjects included in analysis	5390
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1911
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.73
upper limit	1.06

Secondary: Disabling stroke

End point title	Disabling stroke

End point description:

Disabling stroke (modified Rankin Scale greater than or equal to 4, as determined 3 months after recurrent stroke) is presented. The annualised event rate represents the average number of events per patient during a 1-year period.

End point type	Secondary

End point timeframe:

From randomisation until full follow up period, up to 43 months.

End point values	Dabigatran etexilate 110 or 150 milligram (mg)	Acetylsalicylic acid, Aspirin (ASA) 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2695[9]	2695[10]		
Units: Annualised event rate (%/ year)				
number (not applicable)	0.55	0.93		

Notes:

[9] - RS

[10] - RS

Statistical analyses

Statistical analysis title	Statistical Analysis 1 for

Statistical analysis description:

Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke.

Comparison groups	Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg

Number of subjects included in analysis	5390
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0354
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.36
upper limit	0.96

Secondary: All-cause death

End point title	All-cause death

End point description:

All-cause death is presented. The annualised event rate represents the average number of events per patient during a 1-year period.

End point type	Secondary

End point timeframe:

From randomisation until full follow up period, up to 43 months.

End point values	Dabigatran etexilate 110 or 150 milligram (mg)	Acetylsalicylic acid, Aspirin (ASA) 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2695[11]	2695[12]		
Units: Annualised event rate (%/ year)				
number (not applicable)	1.24	1.28		

Notes:

[11] - RS

[12] - RS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke.

Comparison groups	Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg

Number of subjects included in analysis	5390
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8074
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.66
upper limit	1.38

Secondary: Adjudicated intracranial hemorrhage

End point title	Adjudicated intracranial hemorrhage

End point description:

Adjudicated intracranial haemorrhage comprised the subtypes of intracerebral bleeds, intraventricular bleeds, subdural bleeds, epidural bleeds, and subarachnoid bleeds. Microbleeds did not qualify as intracranial haemorrhage, except when they were symptomatic. The annualised event rate represents the average number of events per patient during a 1-year period.

End point type	Secondary

End point timeframe:

Between the first trial medication intake up to 6 days after the last trial medication intake, approximately 42 months.

End point values	Dabigatran etexilate 110 or 150 milligram (mg)	Acetylsalicylic acid, Aspirin (ASA) 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2676[13]	2674[14]		
Units: Annualised event rate (%/ year)				
number (not applicable)	0.67	0.63		

Notes:

[13] - TS

[14] - TS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke.

Comparison groups	Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg

Number of subjects included in analysis	5350
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9064
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.58
upper limit	1.83

Secondary: Adjudicated fatal bleed

End point title	Adjudicated fatal bleed

End point description:

Adjudicated fatal bleeding was defined as a bleeding event which the Independent Event Adjudication Committee (IAC) determined as the primary cause of death or contributed directly to death. The annualised event rate represents the average number of events per patient during a 1-year period. Because there were 0 events in one treatment group, the hazard ratio is unable to be calculated.

End point type	Secondary

End point timeframe:

Between the first trial medication intake up to 6 days after the last trial medication intake, approximately 42 months.

End point values	Dabigatran etexilate 110 or 150 milligram (mg)	Acetylsalicylic acid, Aspirin (ASA) 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2676[15]	2674[16]		
Units: Annualised event rate (%/ year)				
number (not applicable)	0.00	0.05		

Notes:

[15] - TS

[16] - TS

Statistical analyses

No statistical analyses for this end point

Secondary: Adjudicated life-threatening bleed

End point title	Adjudicated life-threatening bleed

End point description:

Major bleeds were to be classified as life-threatening if they met one or more of the following criteria: fatal bleed, symptomatic intracranial bleed, reduction in haemoglobin of at least 5 grams/ deciliter (g/dL), transfusion of at least 4 units of packed red blood cells (equivalent to 9 units in Japan), associated with hypotension requiring the use of intravenous inotropic agents, or necessitated surgical intervention. The annualised event rate represents the average number of events per patient during a 1-year period.

End point type	Secondary

End point timeframe:

Between the first trial medication intake up to 6 days after the last trial medication intake, approximately 42 months.

End point values	Dabigatran etexilate 110 or 150 milligram (mg)	Acetylsalicylic acid, Aspirin (ASA) 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2676[17]	2674[18]		
Units: Annualised event rate (%/ year)				
number (not applicable)	0.76	0.91		

Notes:

[17] - TS

[18] - TS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke.

Comparison groups	Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg
Number of subjects included in analysis	5350
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4352
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.82
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.49
upper limit	1.36

Secondary: Any bleed (investigator-reported)

End point title	Any bleed (investigator-reported)

End point description:

This was the sum of all major and minor bleeds (Minor bleeds were clinical bleeds that did not fulfil the criteria for major bleeds), regardless of severity. The annualised event rate represents the average number of events per patient during a 1-year period.

End point type	Secondary

End point timeframe:

Between the first trial medication intake up to 6 days after the last trial medication intake, approximately 42 months.

End point values	Dabigatran etexilate 110 or 150 milligram (mg)	Acetylsalicylic acid, Aspirin (ASA) 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	2676[19]	2674[20]		
Units: Annualised event rate (%/ year)				
number (not applicable)	15.21	11.64		

Notes:

[19] - TS

[20] - TS

Statistical analyses

Statistical analysis title	Statistical Analysis 1

Statistical analysis description:

Covariates in model are age (<or>= 75 years), creatinine clearance < or >= 50 mL/min and stroke or transient ischaemic attack (TIA) prior to index stroke.

Comparison groups	Dabigatran etexilate 110 or 150 milligram (mg) v Acetylsalicylic acid, Aspirin (ASA) 100 mg
Number of subjects included in analysis	5350
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.28
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.12
upper limit	1.47

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AdverseEvents(AE)and serious AE starting between first trial medication intake up to 6Days after the last trial medication intake,approximately 42months. Deaths (all causes) reported from randomisation until full follow up period,approximately 43months.

Adverse event reporting additional description:

Number of deaths resulting from AE were determined by counting the number of deaths resulting from related AE. Total number of deaths (all causes) are based on randomized set whereas Serious Adverse Events (SAE) and non-SAE are based on treated set.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Dabigatran etexilate 110 or 150 milligram (mg)

Reporting group description:

Participants were orally administered one 110 mg (for participants aged ≥75 years or with a creatinine clearance (CrCl) of 30 to <50 millilitre/ minute (mL/min)) or one 150 mg (for participants aged <75 years and with a CrCl of ≥50 mL/minute) Dabigatran etexilate (DE) capsule twice daily.

Reporting group title	Acetylsalicylic acid, Aspirin (ASA) 100 mg

Reporting group description:

Participants were orally administered one 100 mg ASA non-enteric coated tablet once daily.

Serious adverse events	Dabigatran etexilate 110 or 150 milligram (mg)	Acetylsalicylic acid, Aspirin (ASA) 100 mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	724 / 2676 (27.06%)	740 / 2674 (27.67%)	
number of deaths (all causes)	56	58	
number of deaths resulting from adverse events	1	2	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 2676 (0.04%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenoma benign			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	9 / 2676 (0.34%)	12 / 2674 (0.45%)	
occurrences causally related to treatment / all	0 / 11	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	1 / 2676 (0.04%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer recurrent			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bowen's disease			
subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm			
subjects affected / exposed	1 / 2676 (0.04%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	1 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Brain neoplasm malignant			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer recurrent			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carcinoid tumour			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar haemangioma			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Clear cell renal cell carcinoma			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon adenoma			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			

subjects affected / exposed	8 / 2676 (0.30%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 8	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer metastatic			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer stage IV			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon neoplasm			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal cancer			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal neoplasm			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial adenocarcinoma			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial cancer			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Essential thrombocythaemia			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric adenoma			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	3 / 2676 (0.11%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Glioblastoma multiforme			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatocellular carcinoma			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypopharyngeal cancer			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive breast carcinoma			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer stage 0			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lip and/or oral cavity cancer			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung neoplasm			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant melanoma			
subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma in situ			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lung			

subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lymph nodes			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic bronchial carcinoma			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastatic malignant melanoma			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelofibrosis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myeloproliferative neoplasm			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal squamous cell carcinoma			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian adenoma			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian epithelial cancer metastatic			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Papillary thyroid cancer			
subjects affected / exposed	3 / 2676 (0.11%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polycythaemia vera			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	7 / 2676 (0.26%)	6 / 2674 (0.22%)	
occurrences causally related to treatment / all	0 / 7	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer recurrent			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic adenoma			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma recurrent			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin cancer			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestine carcinoma			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			
subjects affected / exposed	3 / 2676 (0.11%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the vulva			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thymoma			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour obstruction			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine leiomyoma			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic occlusion			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteritis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blue toe syndrome			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Deep vein thrombosis			
subjects affected / exposed	4 / 2676 (0.15%)	9 / 2674 (0.34%)	
occurrences causally related to treatment / all	0 / 4	1 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	4 / 2676 (0.15%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			

subjects affected / exposed	11 / 2676 (0.41%)	4 / 2674 (0.15%)	
occurrences causally related to treatment / all	0 / 15	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery occlusion			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemia			
subjects affected / exposed	0 / 2676 (0.00%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 2676 (0.04%)	4 / 2674 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	1 / 2676 (0.04%)	5 / 2674 (0.19%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			

subjects affected / exposed	1 / 2676 (0.04%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasospasm			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Cardiac pacemaker insertion			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hysterectomy			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myomectomy			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth extraction			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	7 / 2676 (0.26%)	5 / 2674 (0.19%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 0	
Death			
subjects affected / exposed	3 / 2676 (0.11%)	6 / 2674 (0.22%)	
occurrences causally related to treatment / all	0 / 3	1 / 6	
deaths causally related to treatment / all	0 / 3	1 / 6	
Fatigue			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Feeling cold			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ill-defined disorder			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incarcerated hernia			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	0 / 2676 (0.00%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrosis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sudden death			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular stent stenosis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Tanning			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Acquired hydrocele			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balanoposthitis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Benign prostatic hyperplasia			
subjects affected / exposed	5 / 2676 (0.19%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast mass			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical dysplasia			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical polyp			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menorrhagia			
subjects affected / exposed	3 / 2676 (0.11%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spermatocele			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine polyp			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal haemorrhage			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vaginal polyp			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Alveolitis allergic			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atelectasis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis chronic			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumopathy			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic obstructive pulmonary disease			

subjects affected / exposed	6 / 2676 (0.22%)	6 / 2674 (0.22%)	
occurrences causally related to treatment / all	0 / 8	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 1	
Dyspnoea			
subjects affected / exposed	8 / 2676 (0.30%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 8	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea exertional			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal oedema			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal polyps			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			

subjects affected / exposed	1 / 2676 (0.04%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleurisy			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary alveolar haemorrhage			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary congestion			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	0 / 2676 (0.00%)	7 / 2674 (0.26%)	
occurrences causally related to treatment / all	0 / 0	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	0 / 2676 (0.00%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			

subjects affected / exposed	2 / 2676 (0.07%)	4 / 2674 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 2	
Sleep apnoea syndrome			
subjects affected / exposed	3 / 2676 (0.11%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 5	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachypnoea			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Adjustment disorder			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aggression			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol withdrawal syndrome			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	1 / 2676 (0.04%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar I disorder			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar disorder			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Confusional state			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	5 / 2676 (0.19%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	7 / 2676 (0.26%)	4 / 2674 (0.15%)	
occurrences causally related to treatment / all	0 / 9	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised anxiety disorder			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic attack			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post stroke depression			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somatic symptom disorder			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicidal ideation			
subjects affected / exposed	2 / 2676 (0.07%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct obstruction			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	0 / 2676 (0.00%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	3 / 2676 (0.11%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	4 / 2676 (0.15%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic failure			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct pressure increased			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose increased			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Computerised tomogram thorax abnormal			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Creatinine renal clearance decreased			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram Q waves			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza A virus test positive			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic specific antigen increased			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Acetabulum fracture			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Airway burns			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol poisoning			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	4 / 2676 (0.15%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial injury			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest injury			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Exposure during pregnancy			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	21 / 2676 (0.78%)	9 / 2674 (0.34%)	
occurrences causally related to treatment / all	0 / 22	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	3 / 2676 (0.11%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	3 / 2676 (0.11%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			

subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture displacement			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hand fracture			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw fracture			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint injury			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	1 / 2676 (0.04%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	1 / 2676 (0.04%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	0 / 2676 (0.00%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb traumatic amputation			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	4 / 2676 (0.15%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple fractures			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle strain			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Near drowning			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Overdose			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Poisoning deliberate			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative ileus			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pubis fracture			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary contusion			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	2 / 2676 (0.07%)	4 / 2674 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	4 / 2676 (0.15%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			

subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Scapula fracture			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skull fracture			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	3 / 2676 (0.11%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord injury			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal cord injury cervical			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	2 / 2676 (0.07%)	4 / 2674 (0.15%)	
occurrences causally related to treatment / all	1 / 2	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			

subjects affected / exposed	7 / 2676 (0.26%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	5 / 7	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haemorrhage			
subjects affected / exposed	3 / 2676 (0.11%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	2 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon rupture			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haemothorax			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ulna fracture			

subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 2676 (0.00%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	3 / 2676 (0.11%)	4 / 2674 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal dystrophy			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cryopyrin associated periodic syndrome			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Factor V Leiden mutation			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart disease congenital			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phimosis			
subjects affected / exposed	4 / 2676 (0.15%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular septal defect			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	11 / 2676 (0.41%)	8 / 2674 (0.30%)	
occurrences causally related to treatment / all	0 / 11	1 / 8	
deaths causally related to treatment / all	0 / 3	0 / 0	
Angina pectoris			
subjects affected / exposed	3 / 2676 (0.11%)	4 / 2674 (0.15%)	
occurrences causally related to treatment / all	1 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	4 / 2676 (0.15%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve incompetence			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			

subjects affected / exposed	1 / 2676 (0.04%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	24 / 2676 (0.90%)	20 / 2674 (0.75%)	
occurrences causally related to treatment / all	0 / 24	0 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	10 / 2676 (0.37%)	10 / 2674 (0.37%)	
occurrences causally related to treatment / all	0 / 10	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation or atrial flutter			
subjects affected / exposed	34 / 2676 (1.27%)	29 / 2674 (1.08%)	
occurrences causally related to treatment / all	0 / 34	0 / 30	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial tachycardia			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	3 / 2676 (0.11%)	5 / 2674 (0.19%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 3	
Cardiac disorder			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	5 / 2676 (0.19%)	10 / 2674 (0.37%)	
occurrences causally related to treatment / all	0 / 5	2 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure acute			
subjects affected / exposed	1 / 2676 (0.04%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac ventricular thrombosis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	4 / 2676 (0.15%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiomyopathy			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congestive cardiomyopathy			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	6 / 2676 (0.22%)	11 / 2674 (0.41%)	
occurrences causally related to treatment / all	0 / 6	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	0 / 2676 (0.00%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	8 / 2676 (0.30%)	8 / 2674 (0.30%)	
occurrences causally related to treatment / all	0 / 8	0 / 8	
deaths causally related to treatment / all	0 / 2	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prinzmetal angina			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinoatrial block			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrest			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 2676 (0.04%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Aphasia			
subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ataxia			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain injury			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem infarction			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem stroke			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid arteriosclerosis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery aneurysm			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	3 / 2676 (0.11%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central pain syndrome			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			
subjects affected / exposed	0 / 2676 (0.00%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar stroke			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral cyst			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	25 / 2676 (0.93%)	42 / 2674 (1.57%)	
occurrences causally related to treatment / all	7 / 26	3 / 44	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebral ischaemia			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral vasoconstriction			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			

subjects affected / exposed	95 / 2676 (3.55%)	97 / 2674 (3.63%)	
occurrences causally related to treatment / all	9 / 105	15 / 102	
deaths causally related to treatment / all	0 / 1	1 / 3	
Cervicobrachial syndrome			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervicogenic headache			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cubital tunnel syndrome			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia			
subjects affected / exposed	1 / 2676 (0.04%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplegia			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	8 / 2676 (0.30%)	4 / 2674 (0.15%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness postural			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic cerebral infarction			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolic stroke			
subjects affected / exposed	1 / 2676 (0.04%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	18 / 2676 (0.67%)	25 / 2674 (0.93%)	
occurrences causally related to treatment / all	0 / 20	0 / 28	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 2676 (0.00%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paresis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Focal dyscognitive seizures			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			

subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Haemorrhagic cerebral infarction			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic transformation stroke			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	3 / 2676 (0.11%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemianaesthesia			
subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			

subjects affected / exposed	5 / 2676 (0.19%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive encephalopathy			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	1 / 2676 (0.04%)	4 / 2674 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic coma			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxic-ischaemic encephalopathy			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction			
subjects affected / exposed	1 / 2676 (0.04%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	47 / 2676 (1.76%)	45 / 2674 (1.68%)	
occurrences causally related to treatment / all	9 / 48	5 / 47	
deaths causally related to treatment / all	0 / 1	0 / 1	
Lacunar infarction			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Memory impairment			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine with aura			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoparesis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoplegia			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle spasticity			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgic amyotrophy			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurodegenerative disorder			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroglycopenia			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological symptom			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropathy peripheral			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			

subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	5 / 2676 (0.19%)	5 / 2674 (0.19%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post stroke epilepsy			
subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	1 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post stroke seizure			
subjects affected / exposed	3 / 2676 (0.11%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudostroke			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radial nerve compression			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			

subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	17 / 2676 (0.64%)	16 / 2674 (0.60%)	
occurrences causally related to treatment / all	1 / 21	0 / 23	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sensory disturbance			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sensory loss			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	3 / 2676 (0.11%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	8 / 2676 (0.30%)	6 / 2674 (0.22%)	
occurrences causally related to treatment / all	0 / 8	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Temporal lobe epilepsy			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic cerebral infarction			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonic convulsion			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient global amnesia			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	46 / 2676 (1.72%)	41 / 2674 (1.53%)	
occurrences causally related to treatment / all	3 / 50	3 / 45	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			
subjects affected / exposed	1 / 2676 (0.04%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual field defect			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord paralysis			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	7 / 2676 (0.26%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	4 / 7	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Febrile neutropenia			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochromic anaemia			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deafness neurosensory			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden hearing loss			
subjects affected / exposed	6 / 2676 (0.22%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	7 / 2676 (0.26%)	8 / 2674 (0.30%)	
occurrences causally related to treatment / all	0 / 10	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			

subjects affected / exposed	3 / 2676 (0.11%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Age-related macular degeneration			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amaurosis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amaurosis fugax			
subjects affected / exposed	3 / 2676 (0.11%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angle closure glaucoma			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blepharitis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	4 / 2676 (0.15%)	7 / 2674 (0.26%)	
occurrences causally related to treatment / all	0 / 6	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract nuclear			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dacryostenosis acquired			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinopathy			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye haemorrhage			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	6 / 2676 (0.22%)	6 / 2674 (0.22%)	
occurrences causally related to treatment / all	1 / 6	1 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic orbital inflammation			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular degeneration			
subjects affected / exposed	3 / 2676 (0.11%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular fibrosis			
subjects affected / exposed	1 / 2676 (0.04%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular hole			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Narrow anterior chamber angle			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic atrophy			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic ischaemic neuropathy			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pterygium			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal artery occlusion			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal drusen			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal tear			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision blurred			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal hernia			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	3 / 2676 (0.11%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendix disorder			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ulcerative			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erosive oesophagitis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Faecaloma			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric polyps			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	1 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Gastritis			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	7 / 2676 (0.26%)	5 / 2674 (0.19%)	
occurrences causally related to treatment / all	6 / 7	2 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal necrosis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal ulcer haemorrhage			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematochezia			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			

subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileal perforation			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Inguinal hernia			
subjects affected / exposed	5 / 2676 (0.19%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	0 / 2676 (0.00%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal polyp			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intra-abdominal haemorrhage			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic enteritis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	3 / 2676 (0.11%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal haemorrhage			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal perforation			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retroperitoneal haemorrhage			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			

subjects affected / exposed	1 / 2676 (0.04%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	1 / 1	3 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis atopic			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage subcutaneous			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity vasculitis			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nail disorder			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Purpura			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	8 / 2676 (0.30%)	10 / 2674 (0.37%)	
occurrences causally related to treatment / all	0 / 8	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anuria			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus bladder			
subjects affected / exposed	3 / 2676 (0.11%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	3 / 2676 (0.11%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic nephropathy			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerulonephritis proliferative			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	6 / 2676 (0.22%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	6 / 6	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	6 / 2676 (0.22%)	5 / 2674 (0.19%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pollakiuria			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postrenal failure			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 2676 (0.04%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			

subjects affected / exposed	4 / 2676 (0.15%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal ischaemia			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal mass			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal tubular necrosis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureteric obstruction			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 2676 (0.00%)	4 / 2674 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urogenital haemorrhage			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Adrenal haematoma			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal mass			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Goitre			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperthyroidism			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypothyroidism			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inappropriate antidiuretic hormone secretion			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic nodular goitre			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 2676 (0.11%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	3 / 2676 (0.11%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical spinal stenosis			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diffuse idiopathic skeletal hyperostosis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot deformity			

subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture nonunion			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin pain			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemarthrosis			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	3 / 2676 (0.11%)	4 / 2674 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw cyst			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint stiffness			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb discomfort			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscal degeneration			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mobility decreased			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle haemorrhage			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			

subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrotising myositis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	12 / 2676 (0.45%)	19 / 2674 (0.71%)	
occurrences causally related to treatment / all	0 / 13	0 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporotic fracture			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyalgia rheumatica			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudarthrosis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriatic arthropathy			

subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	3 / 2676 (0.11%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic lupus erythematosus			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic scleroderma			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendiceal abscess			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			

subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	2 / 2676 (0.07%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis bacterial			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	3 / 2676 (0.11%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conjunctivitis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis intestinal haemorrhagic			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear infection			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			

subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	3 / 2676 (0.11%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis norovirus			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	5 / 2676 (0.19%)	4 / 2674 (0.15%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leptospirosis			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis bacterial			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mycotoxicosis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroborreliosis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurosyphilis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	0 / 2676 (0.00%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media acute			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal abscess			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periodontitis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perirectal abscess			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis bacterial			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonsillar abscess			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	18 / 2676 (0.67%)	14 / 2674 (0.52%)	
occurrences causally related to treatment / all	1 / 21	0 / 14	
deaths causally related to treatment / all	0 / 3	0 / 0	
Pneumonia bacterial			

subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia viral			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulpitis dental			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	3 / 2676 (0.11%)	4 / 2674 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	2 / 2676 (0.07%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sepsis			

subjects affected / exposed	5 / 2676 (0.19%)	6 / 2674 (0.22%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 2	
Septic embolus			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			
subjects affected / exposed	2 / 2676 (0.07%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sialoadenitis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis septic			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculous pleurisy			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	13 / 2676 (0.49%)	5 / 2674 (0.19%)	
occurrences causally related to treatment / all	2 / 14	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			

subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 2676 (0.04%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	3 / 2676 (0.11%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 2676 (0.04%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	2 / 2676 (0.07%)	3 / 2674 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			

subjects affected / exposed	2 / 2676 (0.07%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic acidosis			
subjects affected / exposed	1 / 2676 (0.04%)	0 / 2674 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	0 / 2676 (0.00%)	1 / 2674 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 2676 (0.04%)	2 / 2674 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Dabigatran etexilate 110 or 150 milligram (mg)	Acetylsalicylic acid, Aspirin (ASA) 100 mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	306 / 2676 (11.43%)	295 / 2674 (11.03%)	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	136 / 2676 (5.08%)	128 / 2674 (4.79%)	
occurrences (all)	161	149	

Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	173 / 2676 (6.46%) 213	170 / 2674 (6.36%) 221	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
06 August 2015	This amendment introduced several changes to facilitate patient recruitment and to operationally simplify trial procedures. The lower age limit was changed from ≥50 to ≥18 years to allow participation of younger patients with embolic stroke of undetermined source (ESUS). The planned analysis of brain imaging via computed tomography or magnetic resonance imaging (MRI) was moved from the main analysis into a separate substudy. To rule out AF prior to trial entry, the minimum number of hours of cardiac monitoring was reduced from 24 to 20 hour. The possibility of additional cardiac monitoring and the corresponding documentation were introduced. Broader time windows for sampling of several laboratory assessments for early randomisation and safety were introduced. The wording of several inclusion/exclusion criteria were clarified and definitions ere updated: the wording of inclusion criterion #3 was modified in line with the ESUS definition to allow inclusion of patients with full artery occlusion due to an embolus of unknown origin. Exclusion criterion #7 was modified to exclude patients at high risk for future intracranial haemorrhage. Exclusion criterion #8 was modified to allow exclusion of patients if they if they had a high propensity for falls and thus, increased bleeding risk. Exclusion criterion #21 was modified to provide a definition of lacunar stroke. The definition of cerebral microbleeds was added; it was clarified that asymptomatic microbleeds did not qualify as intracranial haemorrhage. The montreal cognitive assessment(MoCA) assessment times and analysis were clarified. The guidelines for transitioning to non-trial antithrombotic medications were added. Further information on concomitant medication were given: concomitant optional ASA was restricted to patients with coronary artery disease. The use of idarucizumab was added. Lastly, several editorial changes were made.
21 April 2016	This amendment introduced several changes to facilitate logistics and to operationally simplify trial procedures. The clinical trial protocol (CTP) specified that for all patients, the source documents at the sites had to include the detailed results of the required diagnostic imaging for the index stroke. As the central re-assessment of source data regarding the diagnosis of ESUS was omitted (in agreement with the Food and Drug Administration (FDA)), the corresponding sensitivity analysis was removed which included only those patients. This change related only to data collection and did neither affect patients' safety nor the integrity of the overall trial.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

One subject had a missing data for age-group and hence that subject is put under age-category " 85 years and over".

Notes: