

**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
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**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, clintrriage.rdg@boehringer-ingelheim.com
Scientific contact	QRPE Processes and Systems Coordination, Clinical Trial Information Disclosure, Boehringer Ingelheim, 001 8002430127, clintrriage.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:

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### 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
<b>Arm title</b>	Dabigatran etexilate 110 or 150 milligram (mg)

Arm description:

Participants were orally administered one 110 mg (for participants aged  $\geq 75$  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  $\geq 50$  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  $\geq 75$  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  $\geq 50$  mL/minute) Dabigatran etexilate (DE) capsule twice daily.

<b>Arm title</b>	Acetylsalicylic acid, Aspirin (ASA) 100 mg
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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.

<b>Number of subjects in period 1<sup>[1]</sup></b>	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

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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 $\geq 75$ 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 $\geq 50$ 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	$\pm 11.44$	$\pm 11.39$	-
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)
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Reporting group description:

Participants were orally administered one 110 mg (for participants aged  $\geq 75$  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  $\geq 50$  mL/minute) Dabigatran etexilate (DE) capsule twice daily.

Reporting group title	Acetylsalicylic acid, Aspirin (ASA) 100 mg
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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
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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
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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 <sup>[1]</sup>	2695 <sup>[2]</sup>		
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
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Statistical analysis description:

Covariates in model are age ( $< \text{or} \geq 75$  years), creatinine clearance  $< \text{or} \geq 50$  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
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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)
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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  $\geq 2$ units of blood or packed cells (equivalent to  $\geq 4.5$ units 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
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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 <sup>[3]</sup>	2674 <sup>[4]</sup>		
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
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Statistical analysis description:

Covariates in model are age ( $< \text{or} \geq 75$  years), creatinine clearance  $< \text{or} \geq 50$  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
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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 <sup>[5]</sup>	2695 <sup>[6]</sup>		
Units: Annualised event rate (%/ year)				
number (not applicable)	3.97	4.71		

Notes:

[5] - RS

[6] - RS

### Statistical analyses

<b>Statistical analysis title</b>	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
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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
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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 <sup>[7]</sup>	2695 <sup>[8]</sup>		
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
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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
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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 <sup>[9]</sup>	2695 <sup>[10]</sup>		
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 <sup>[11]</sup>	2695 <sup>[12]</sup>		
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 <sup>[13]</sup>	2674 <sup>[14]</sup>		
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:	
<p>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.</p>	
End point type	Secondary
End point timeframe:	
<p>Between the first trial medication intake up to 6 days after the last trial medication intake, approximately 42 months.</p>	

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 <sup>[15]</sup>	2674 <sup>[16]</sup>		
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:	
<p>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.</p>	

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.	

<b>End point values</b>	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 <sup>[17]</sup>	2674 <sup>[18]</sup>		
Units: Annualised event rate (%/ year)				
number (not applicable)	0.76	0.91		

Notes:

[17] - TS

[18] - TS

### Statistical analyses

<b>Statistical analysis title</b>	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.	

<b>End point values</b>	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 <sup>[19]</sup>	2674 <sup>[20]</sup>		
Units: Annualised event rate (%/ year)				
number (not applicable)	15.21	11.64		

Notes:

[19] - TS

[20] - TS

### Statistical analyses

<b>Statistical analysis title</b>	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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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### Reporting groups

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

Participants were orally administered one 110 mg (for participants aged  $\geq 75$  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  $\geq 50$  mL/minute) Dabigatran etexilate (DE) capsule twice daily.

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

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

<b>Serious adverse events</b>	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
<b>Basal cell carcinoma</b>		
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
<b>Bladder cancer</b>		
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
<b>Bladder cancer recurrent</b>		
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
<b>Bladder neoplasm</b>		
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
<b>Bladder transitional cell carcinoma</b>		
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
<b>Bowen's disease</b>		
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
<b>Brain neoplasm</b>		
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
<b>Brain neoplasm malignant</b>		

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>Breast cancer</b>		
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
<b>Breast cancer recurrent</b>		
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>Carcinoid tumour</b>		
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
<b>Cerebellar haemangioma</b>		
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>Cholangiocarcinoma</b>		
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
<b>Clear cell renal cell carcinoma</b>		
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>Colon adenoma</b>		
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
<b>Colon cancer</b>		

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
<b>Metastases to lymph nodes</b>		
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>Metastatic bronchial carcinoma</b>		
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
<b>Metastatic malignant melanoma</b>		
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
<b>Myelodysplastic syndrome</b>		
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
<b>Myelofibrosis</b>		
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
<b>Myeloproliferative neoplasm</b>		
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>Non-Hodgkin's lymphoma</b>		
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
<b>Oesophageal squamous cell carcinoma</b>		

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
<b>Arteritis</b>		
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
<b>Blue toe syndrome</b>		
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
<b>Circulatory collapse</b>		
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
<b>Deep vein thrombosis</b>		
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
<b>Embolism</b>		
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
<b>Extremity necrosis</b>		
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
<b>Hypertension</b>		
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
<b>Hypertensive crisis</b>		

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	
<b>General disorders and administration site conditions</b>			
<b>Asthenia</b>			
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	
<b>Chest discomfort</b>			
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	
<b>Chest pain</b>			
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	
<b>Death</b>			
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	
<b>Fatigue</b>			
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	
<b>Feeling cold</b>			
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>Gait disturbance</b>			
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	
<b>General physical health deterioration</b>			

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	
<b>Sudden death</b>			
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	
<b>Vascular stent stenosis</b>			
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>Immune system disorders</b>			
<b>Anaphylactic reaction</b>			
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	
<b>Hypersensitivity</b>			
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	
<b>Social circumstances</b>			
<b>Tanning</b>			
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	
<b>Reproductive system and breast disorders</b>			
<b>Acquired hydrocele</b>			
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	
<b>Balanoposthitis</b>			
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
<b>Dyspnoea</b>		
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
<b>Dyspnoea exertional</b>		
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
<b>Emphysema</b>		
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>Hypoxia</b>		
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>Interstitial lung disease</b>		
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
<b>Laryngeal oedema</b>		
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
<b>Nasal polyps</b>		
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>Pleural effusion</b>		

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	
<b>Panic attack</b>			
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	
<b>Post stroke depression</b>			
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>Schizophrenia</b>			
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>Somatic symptom disorder</b>			
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>Suicidal ideation</b>			
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	
<b>Product issues</b>			
<b>Device dislocation</b>			
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	
<b>Hepatobiliary disorders</b>			
<b>Acute hepatic failure</b>			
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	
<b>Bile duct obstruction</b>			

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	
<b>Injury, poisoning and procedural complications</b>			
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
<b>Atrial fibrillation</b>		
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
<b>Atrial flutter</b>		
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
<b>Atrial fibrillation or atrial flutter</b>		
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
<b>Atrioventricular block second degree</b>		
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
<b>Atrial tachycardia</b>		
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
<b>Bradycardia</b>		
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
<b>Cardiac arrest</b>		
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
<b>Cardiac disorder</b>		

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	
<b>Sinoatrial block</b>			
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	
<b>Sinus arrest</b>			
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>Sinus bradycardia</b>			
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	
<b>Sinus node dysfunction</b>			
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	
<b>Ventricular extrasystoles</b>			
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>Ventricular tachycardia</b>			
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	
<b>Nervous system disorders</b>			
<b>Aphasia</b>			
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	
<b>Ataxia</b>			

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
<b>Brain injury</b>		
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
<b>Brain stem infarction</b>		
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
<b>Brain stem stroke</b>		
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
<b>Carotid arteriosclerosis</b>		
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
<b>Carotid artery aneurysm</b>		
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
<b>Carotid artery stenosis</b>		
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
<b>Carpal tunnel syndrome</b>		
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>Central pain syndrome</b>		

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
<b>Cervicobrachial syndrome</b>		
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
<b>Cervicogenic headache</b>		
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>Cubital tunnel syndrome</b>		
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>Dementia</b>		
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
<b>Diabetic neuropathy</b>		
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
<b>Diplegia</b>		
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>Dizziness</b>		
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
<b>Dizziness postural</b>		

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
Embolitic 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
Embolitic 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
<b>Muscle spasticity</b>		
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>Neuralgia</b>		
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
<b>Neuralgic amyotrophy</b>		
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
<b>Neurodegenerative disorder</b>		
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>Neuroglycopenia</b>		
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
<b>Neurological symptom</b>		
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
<b>Neuropathy peripheral</b>		
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
<b>Paraesthesia</b>		

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
<b>Seizure</b>		
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
<b>Sensory disturbance</b>		
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>Sensory loss</b>		
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
<b>Status epilepticus</b>		
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
<b>Syncope</b>		
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
<b>Temporal lobe epilepsy</b>		
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>Thrombotic cerebral infarction</b>		
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>Tonic convulsion</b>		

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	
<b>Hypochromic anaemia</b>			
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	
<b>Iron deficiency anaemia</b>			
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	
<b>Pancytopenia</b>			
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	
<b>Ear and labyrinth disorders</b>			
<b>Deafness</b>			
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	
<b>Deafness neurosensory</b>			
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	
<b>Sudden hearing loss</b>			
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	
<b>Vertigo</b>			
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	
<b>Vertigo positional</b>			

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	
<b>Eye disorders</b>			
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
<b>Gastrointestinal haemorrhage</b>		
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
<b>Gastrointestinal necrosis</b>		
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>Gastrointestinal ulcer haemorrhage</b>		
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
<b>Gastrooesophageal reflux disease</b>		
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
<b>Haematochezia</b>		
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
<b>Haemorrhoidal haemorrhage</b>		
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
<b>Haemorrhoids</b>		
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>Hiatus hernia</b>		

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
<b>Irritable bowel syndrome</b>		
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
<b>Ischaemic enteritis</b>		
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>Large intestine perforation</b>		
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
<b>Large intestine polyp</b>		
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
<b>Lower gastrointestinal haemorrhage</b>		
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
<b>Melaena</b>		
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>Nausea</b>		
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
<b>Pancreatitis acute</b>		

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	
<b>Purpura</b>			
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	
<b>Skin ulcer</b>			
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	
<b>Renal and urinary disorders</b>			
<b>Acute kidney injury</b>			
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	
<b>Anuria</b>			
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>Calculus bladder</b>			
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	
<b>Calculus urinary</b>			
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	
<b>Chronic kidney disease</b>			
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>Diabetic nephropathy</b>			

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
<b>Limb discomfort</b>		
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>Lumbar spinal stenosis</b>		
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
<b>Meniscal degeneration</b>		
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
<b>Mobility decreased</b>		
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>Muscle haemorrhage</b>		
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
<b>Muscular weakness</b>		
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>Musculoskeletal chest pain</b>		
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
<b>Musculoskeletal pain</b>		

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	
<b>Rhabdomyolysis</b>			
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	
<b>Rotator cuff syndrome</b>			
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	
<b>Spinal osteoarthritis</b>			
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>Synovial cyst</b>			
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	
<b>Systemic lupus erythematosus</b>			
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>Systemic scleroderma</b>			
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	
<b>Infections and infestations</b>			
<b>Appendiceal abscess</b>			
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	
<b>Appendicitis</b>			

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
<b>Gastroenteritis</b>		
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
<b>Gastroenteritis norovirus</b>		
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
<b>Haematoma infection</b>		
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
<b>Herpes zoster</b>		
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
<b>Infection</b>		
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
<b>Infectious pleural effusion</b>		
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>Influenza</b>		
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
<b>Leptospirosis</b>		

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>Meningitis bacterial</b>		
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
<b>Mycotoxycosis</b>		
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>Neuroborreliosis</b>		
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
<b>Neurosyphilis</b>		
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
<b>Orchitis</b>		
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
<b>Osteomyelitis</b>		
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
<b>Otitis media acute</b>		
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
<b>Parotitis</b>		

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	
<b>Metabolism and nutrition disorders</b>			
<b>Dehydration</b>			
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	
<b>Diabetes mellitus</b>			
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	
<b>Diabetes mellitus inadequate control</b>			
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	
<b>Gout</b>			
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>Hyperglycaemia</b>			
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	
<b>Hypokalaemia</b>			
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	
<b>Hypoglycaemia</b>			
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>Hyponatraemia</b>			

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	
<b>Hypovolaemia</b>			
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	
<b>Lactic acidosis</b>			
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	
<b>Metabolic acidosis</b>			
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	
<b>Obesity</b>			
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>Type 2 diabetes mellitus</b>			
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 %

<b>Non-serious adverse events</b>	<b>Dabigatran etexilate 110 or 150 milligram (mg)</b>	<b>Acetylsalicylic acid, Aspirin (ASA) 100 mg</b>	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	306 / 2676 (11.43%)	295 / 2674 (11.03%)	
<b>Cardiac disorders</b>			
<b>Atrial fibrillation</b>			
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	
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## 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 $\geq 50$ to $\geq 18$ 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 were 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 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: