Clinical trial results:
Multicenter, randomized, double-blind, double-dummy, active-comparator, event-driven, superiority phase III study of secondary prevention of stroke and prevention of systemic embolism in patients with a recent Embolic Stroke of Undetermined Source (ESUS), comparing rivaroxaban 15 mg once daily with aspirin 100 mg (NAVIGATE ESUS)

Summary

EudraCT number	2013-000768-27
Trial protocol	SE IE PT CZ BE ES IT HU FI DK GB AT GR
Global end of trial date	15 February 2018

Results information

Result version number	v2 (current)
This version publication date	03 February 2019
First version publication date	06 December 2018
Version creation reason	• Correction of full data set Update wording of the endpoints.

Trial information

Trial identification

Sponsor protocol code	BAY59-7939/16573

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02313909
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, D-51368 Leverkusen, Germany,
Public contact	Therapeutic Area Head, Bayer AG , clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG , clinical-trials-contact@bayer.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	15 February 2018
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	15 February 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary efficacy objective of this study was to evaluate whether rivaroxaban (Xarelto, BAY59-7939) was superior to acetylsalicylic acid (Aspirin) in reducing the risk of recurrent stroke and systemic embolism in subjects with a recent embolic stroke of undetermined source (ESUS).

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization guideline E6: Good Clinical Practice. Before entering the study, the informed consent form was read by and explained to all subjects. Participating subjects signed informed consent form and could withdraw from the study at any time without any disadvantage and without having to provide a reason for this decision. Only investigators qualified by training and experience were selected as appropriate experts to investigate the study drug.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 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	Poland: 284
Country: Number of subjects enrolled	Portugal: 154
Country: Number of subjects enrolled	Spain: 618
Country: Number of subjects enrolled	Sweden: 71
Country: Number of subjects enrolled	United Kingdom: 435
Country: Number of subjects enrolled	Austria: 174
Country: Number of subjects enrolled	Belgium: 90
Country: Number of subjects enrolled	Czech Republic: 243
Country: Number of subjects enrolled	Denmark: 146
Country: Number of subjects enrolled	Finland: 131
Country: Number of subjects enrolled	France: 288
Country: Number of subjects enrolled	Germany: 198
Country: Number of subjects enrolled	Greece: 76
Country: Number of subjects enrolled	Hungary: 224

Country: Number of subjects enrolled	Ireland: 13
Country: Number of subjects enrolled	Italy: 334
Country: Number of subjects enrolled	Australia: 119
Country: Number of subjects enrolled	Israel: 60
Country: Number of subjects enrolled	South Africa: 49
Country: Number of subjects enrolled	Switzerland: 125
Country: Number of subjects enrolled	Russian Federation: 328
Country: Number of subjects enrolled	Turkey: 39
Country: Number of subjects enrolled	China: 491
Country: Number of subjects enrolled	Japan: 647
Country: Number of subjects enrolled	Korea, Democratic People's Republic of: 212
Country: Number of subjects enrolled	Canada: 573
Country: Number of subjects enrolled	United States: 345
Country: Number of subjects enrolled	Argentina: 265
Country: Number of subjects enrolled	Brazil: 179
Country: Number of subjects enrolled	Chile: 194
Country: Number of subjects enrolled	Mexico: 108
Worldwide total number of subjects	7213
EEA total number of subjects	3479

Notes:

Subjects enrolled per age group	
In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	2943
From 65 to 84 years	4047
85 years and over	223

Subject disposition

Recruitment

Recruitment details:

Study was conducted at multiple centers in 31 countries between 23 December 2014 (first subject first visit) and 15 February 2018 (last subject last visit).

Pre-assignment

Screening details:

Overall, 7582 subjects were screened; of these 369 subjects were screen failures. A total of 7213 subjects were randomized, of which 92 never took study drug; 3562 were treated with rivaroxaban/placebo and 3559 were treated with acetylsalicylic acid/placebo.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Rivaroxaban 15 mg OD

Arm description:

Subjects received rivaroxaban 15 milligram (mg) immediate-release film-coated tablet and matching placebo of acetylsalicylic acid orally once daily (OD).

Arm type	Experimental
Investigational medicinal product name	Rivaroxaban
Investigational medicinal product code	BAY59-7939
Other name	Xarelto
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received rivaroxaban 15 mg immediate-release film-coated tablet orally OD.

Investigational medicinal product name	Placebo matched to acetylsalicylic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received matching placebo of acetylsalicylic acid 100 mg enteric-coated tablet orally OD.

Arm title	Acetylsalicylic acid 100 mg OD

Arm description:

Subjects received acetylsalicylic acid 100 mg enteric-coated tablet and matching placebo of rivaroxaban orally OD.

Arm type	Experimental
Investigational medicinal product name	Acetylsalicylic acid
Investigational medicinal product code	BAY1019036
Other name	Aspirin
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received acetylsalicylic acid 100 mg enteric-coated tablet orally OD.

Investigational medicinal product name	Placebo matched to rivaroxaban
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received matching placebo of rivaroxaban 15 mg immediate-release film-coated tablet orally OD.

Number of subjects in period 1	Rivaroxaban 15 mg OD	Acetylsalicylic acid 100 mg OD
Started	3609	3604
Treated	3562	3559
Completed	3552	3554
Not completed	57	50
Consent withdrawn by subject	33	33
Lost to follow-up	24	17

Baseline characteristics

Reporting groups	
Reporting group title	Rivaroxaban 15 mg OD
Reporting group description:	
Subjects received rivaroxaban 15 milligram (mg) immediate-release film-coated tablet and matching placebo of acetylsalicylic acid orally once daily (OD).	
Reporting group title	Acetylsalicylic acid 100 mg OD
Reporting group description:	
Subjects received acetylsalicylic acid 100 mg enteric-coated tablet and matching placebo of rivaroxaban orally OD.	

Reporting group values	Rivaroxaban 15 mg OD	Acetylsalicylic acid 100 mg OD	Total
Number of subjects	3609	3604	7213
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	66.9	66.9	
standard deviation	± 9.8	± 9.8	-
Gender categorical			
Units: Subjects			
Female	1377	1400	2777
Male	2232	2204	4436
Race			
Units: Subjects			
White	2613	2605	5218
Black or African American	51	60	111
Asian	716	698	1414
Other	229	241	470
Stroke or TIA (prior to qualifying stroke) or Other medical history			
The other medical history refers to number of subjects with one medical history finding other than stroke or Transient ischemic attack (TIA).			
Units: Subjects			
Stroke or TIA (prior to qualifying stroke)	620	643	1263
Other medical history	2989	2961	5950
Time from qualifying stroke to randomization			
Units: days			
median	38.0	36.0	
inter-quartile range (Q1-Q3)	15.0 to 89.0	14.0 to 86.5	-

End points

End points reporting groups

Reporting group title	Rivaroxaban 15 mg OD
Reporting group description:	
Subjects received rivaroxaban 15 milligram (mg) immediate-release film-coated tablet and matching placebo of acetylsalicylic acid orally once daily (OD).	
Reporting group title	Acetylsalicylic acid 100 mg OD
Reporting group description:	
Subjects received acetylsalicylic acid 100 mg enteric-coated tablet and matching placebo of rivaroxaban orally OD.	
Subject analysis set title	Intention-to-treat analysis set (ITT)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
ITT included all randomized subjects (N= 7213).	
Subject analysis set title	Safety analysis set (SAF)
Subject analysis set type	Safety analysis
Subject analysis set description:	
SAF included all randomized subjects who received at least one dose of study drug (N= 7121).	

Primary: Incidence Rate of the Composite Efficacy Outcome (Adjudicated)

End point title	Incidence Rate of the Composite Efficacy Outcome (Adjudicated)
End point description:	
Components of composite efficacy outcome (adjudicated) includes stroke (ischemic, hemorrhagic, and undefined stroke, TIA with positive neuroimaging) and systemic embolism. Incidence rate estimated as number of subjects with incident events divided by cumulative at-risk time, where subject is no longer at risk once an incident event occurred.	
End point type	Primary
End point timeframe:	
From randomization until the efficacy cut-off date (median 326 days)	

End point values	Rivaroxaban 15 mg OD	Acetylsalicylic acid 100 mg OD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3609[1]	3604[2]		
Units: event/100 subject-years				
number (confidence interval 95%)	5.14 (4.40 to 5.97)	4.78 (4.07 to 5.58)		

Notes:

[1] - ITT

[2] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis: Stroke + Systemic embolism

Statistical analysis description:

Risk reduction was estimated with the stratified Cox proportional hazards model. Hazard ratios (95% confidence interval) as compared to acetylsalicylic acid arm were reported. Rivaroxaban treatment was compared with the Acetylsalicylic acid control group using a stratified log-rank test. P-values (two-sided)

as compared to acetylsalicylic acid arm were based on the log-rank test.

Comparison groups	Rivaroxaban 15 mg OD v Acetylsalicylic acid 100 mg OD
Number of subjects included in analysis	7213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.51884
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.07
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.33

Primary: Incidence Rate of a Major Bleeding Event According to the International Society on Thrombosis and Haemostasis (ISTH) Criteria (Adjudicated)

End point title	Incidence Rate of a Major Bleeding Event According to the International Society on Thrombosis and Haemostasis (ISTH) Criteria (Adjudicated)

End point description:

Major bleeding event (as per ISTH), defined as bleeding event that met at least one of following: fatal bleeding; symptomatic bleeding in a critical area or organ (intraarticular, intramuscular with compartment syndrome, intraocular, intraspinal, pericardial, or retroperitoneal); symptomatic intracranial haemorrhage; clinically overt bleeding associated with a recent decrease in the hemoglobin level of greater than or equal to (>=) 2 grams per decilitre (g/dL) (20 grams per liter [g/L]; 1.24 millimoles per liter [mmol/L]) compared to the most recent hemoglobin value available before the event; clinically overt bleeding leading to transfusion of 2 or more units of packed red blood cells or whole blood. The results were based on classification of events that have been positively adjudicated as major bleeding events. Incidence rate estimated as number of subjects with incident events divided by cumulative at-risk time, where subject is no longer at risk once an incident event occurred.

End point type	Primary

End point timeframe:

From randomization until the efficacy cut-off date (median 326 days)

End point values	Rivaroxaban 15 mg OD	Acetylsalicylic acid 100 mg OD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3609[3]	3604[4]		
Units: event/100 subject-years				
number (confidence interval 95%)	1.82 (1.39 to 2.33)	0.67 (0.42 to 1.00)		

Notes:

[3] - ITT

[4] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis: ISTH major bleeding events

Statistical analysis description:

Risk reduction was estimated with the stratified Cox proportional hazards model. Hazard ratios (95% confidence interval) as compared to acetylsalicylic acid arm were reported. Rivaroxaban treatment was compared with the Acetylsalicylic acid control group using a stratified log-rank test. P-values (two-sided) as compared to acetylsalicylic acid arm were based on the log-rank test.

Comparison groups	Rivaroxaban 15 mg OD v Acetylsalicylic acid 100 mg OD
Number of subjects included in analysis	7213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00002
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	2.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.68
upper limit	4.39

Secondary: Incidence Rate of Any of the Following: Cardiovascular Death, Recurrent Stroke, Systemic Embolism and Myocardial Infarction

End point title	Incidence Rate of Any of the Following: Cardiovascular Death, Recurrent Stroke, Systemic Embolism and Myocardial Infarction

End point description:

Incidence rate estimated as number of subjects with incident events divided by cumulative at-risk time, where subject is no longer at risk once an incident event occurred. Cardiovascular death includes death due to haemorrhage and death with undetermined/unknown cause. Systemic embolism is defined as abrupt vascular insufficiency associated with clinical or radiological evidence of arterial occlusion in the absence of other likely mechanisms. The diagnosis of myocardial infarction requires the combination of: 1)evidence of myocardial necrosis (either changes in cardiac biomarkers or post-mortem pathological findings); and 2)supporting information derived from the clinical presentation, electrocardiographic changes, or the results of myocardial or coronary artery imaging.

End point type	Secondary

End point timeframe:

From randomization until the efficacy cut-off date (median 326 days)

End point values	Rivaroxaban 15 mg OD	Acetylsalicylic acid 100 mg OD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3609[5]	3604[6]		
Units: event/100 subject-years				
number (confidence interval 95%)	6.20 (5.38 to 7.10)	5.85 (5.05 to 6.73)		

Notes:

[5] - ITT

[6] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis

Statistical analysis description:

Risk reduction was estimated with the stratified Cox proportional hazards model. Hazard ratios (95% confidence interval) as compared to acetylsalicylic acid arm were reported. Confidence intervals were calculated, if at least 1 event in each treatment arm existed. Rivaroxaban treatment was compared with the Acetylsalicylic acid control group using a stratified log-rank test. P-values (two-sided) as compared to acetylsalicylic acid arm were based on the log-rank test.

Comparison groups	Acetylsalicylic acid 100 mg OD v Rivaroxaban 15 mg OD
Number of subjects included in analysis	7213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.56922
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.29

Secondary: Incidence Rate of All-Cause Mortality

End point title	Incidence Rate of All-Cause Mortality

End point description:

All-cause mortality includes all deaths of subjects due to any cause.

End point type	Secondary

End point timeframe:

From randomization until the efficacy cut-off date (median 326 days)

End point values	Rivaroxaban 15 mg OD	Acetylsalicylic acid 100 mg OD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3609[7]	3604[8]		
Units: event/100 subject-years				
number (confidence interval 95%)	1.88 (1.45 to 2.40)	1.50 (1.12 to 1.97)		

Notes:

[7] - ITT

[8] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis: All-cause mortality

Statistical analysis description:

Risk reduction was estimated with the stratified Cox proportional hazards model. Hazard ratios (95% confidence interval) as compared to acetylsalicylic acid arm were reported. Confidence intervals were calculated, if at least 1 event in each treatment arm existed. Rivaroxaban treatment was compared with the Acetylsalicylic acid control group using a stratified log-rank test. P-values (two-sided) as compared

to acetylsalicylic acid arm were based on the log-rank test.

Comparison groups	Rivaroxaban 15 mg OD v Acetylsalicylic acid 100 mg OD
Number of subjects included in analysis	7213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.22078
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.81

Secondary: Incidence Rate of the Following: Stroke, Ischemic Stroke, Disabling Stroke (Modified Rankin Score >= 4), Cardiovascular Death (Including Death due to Hemorrhage and Death with Undetermined/Unknown Cause), Myocardial Infarction

End point title	Incidence Rate of the Following: Stroke, Ischemic Stroke, Disabling Stroke (Modified Rankin Score >= 4), Cardiovascular Death (Including Death due to Hemorrhage and Death with Undetermined/Unknown Cause), Myocardial Infarction

End point description:

Disabling stroke is defined as stroke with modified Rankin score (mRS) greater than or equal to (>=) 4 as assessed by investigator. mRS spans 0-6, running from perfect health to death. A score of 0-3 indicates functional status ranging from no symptoms to "moderate disability" (defined in the mRS as requiring some help, but able to walk without assistance); mRS 4-6 indicates functional status ranging from "moderately severe disability" (unable to walk or to attend to own bodily needs without assistance) through to death. CV death includes death due to haemorrhage and death with undetermined/unknown cause. Diagnosis of myocardial infarction requires combination of: 1) evidence of myocardial necrosis (either changes in cardiac biomarkers or post-mortem pathological findings); 2) supporting information derived from clinical presentation, electrocardiographic changes, or results of myocardial or coronary artery imaging.

End point type	Secondary

End point timeframe:

From randomization until the efficacy cut-off date (median 326 days)

End point values	Rivaroxaban 15 mg OD	Acetylsalicylic acid 100 mg OD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3609[9]	3604[10]		
Units: event/100 subject-years				
number (confidence interval 95%)				
Stroke	5.11 (4.37 to 5.93)	4.71 (4.01 to 5.51)		
Ischemic stroke	4.71 (4.01 to 5.51)	4.56 (3.87 to 5.34)		
Disabling stroke	1.20 (0.86 to 1.62)	0.84 (0.56 to 1.21)		
CVdeath (includes death due to hemorrhage)	0.99 (0.68 to 1.38)	0.66 (0.42 to 1.00)		

Myocardial infarction	0.49 (0.29 to 0.79)	0.67 (0.42 to 1.00)		

Notes:

[9] - ITT

[10] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis 1: Stroke

Statistical analysis description:

Risk reduction was estimated with the stratified Cox proportional hazards model. Hazard ratios (95% confidence interval) as compared to acetylsalicylic acid arm were reported. Rivaroxaban treatment was compared with the Acetylsalicylic acid control group using a stratified log-rank test. P-values (two-sided) as compared to acetylsalicylic acid arm were based on the log-rank test.

Comparison groups	Rivaroxaban 15 mg OD v Acetylsalicylic acid 100 mg OD
Number of subjects included in analysis	7213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4797
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	1.34

Statistical analysis title	Statistical analysis 2: Ischemic stroke

Statistical analysis description:

Risk reduction was estimated with the stratified Cox proportional hazards model. Hazard ratios (95% confidence interval) as compared to acetylsalicylic acid arm were reported. Rivaroxaban treatment was compared with the Acetylsalicylic acid control group using a stratified log-rank test. P-values (two-sided) as compared to acetylsalicylic acid arm were based on the log-rank test.

Comparison groups	Rivaroxaban 15 mg OD v Acetylsalicylic acid 100 mg OD
Number of subjects included in analysis	7213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.78738
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.03
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.29

Statistical analysis title	Statistical analysis 3: Disabling stroke

Statistical analysis description:

Risk reduction was estimated with the stratified Cox proportional hazards model. Hazard ratios (95% confidence interval) as compared to acetylsalicylic acid arm were reported. Rivaroxaban treatment was compared with the Acetylsalicylic acid control group using a stratified log-rank test. P-values (two-sided) as compared to acetylsalicylic acid arm were based on the log-rank test.

Comparison groups	Rivaroxaban 15 mg OD v Acetylsalicylic acid 100 mg OD
Number of subjects included in analysis	7213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.14822
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.42
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.88
upper limit	2.28

Statistical analysis title	Statistical analysis 4: CV death

Statistical analysis description:

Risk reduction was estimated with the stratified Cox proportional hazards model. Hazard ratios (95% confidence interval) as compared to acetylsalicylic acid arm were reported. Rivaroxaban treatment was compared with the Acetylsalicylic acid control group using a stratified log-rank test. P-values (two-sided) as compared to acetylsalicylic acid arm were based on the log-rank test.

Comparison groups	Rivaroxaban 15 mg OD v Acetylsalicylic acid 100 mg OD
Number of subjects included in analysis	7213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.14051
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.48
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.87
upper limit	2.52

Statistical analysis title	Statistical analysis 5: Myocardial infarction

Statistical analysis description:

Risk reduction was estimated with the stratified Cox proportional hazards model. Hazard ratios (95% confidence interval) as compared to acetylsalicylic acid arm were reported. Rivaroxaban treatment was compared with the Acetylsalicylic acid control group using a stratified log-rank test. P-values (two-sided) as compared to acetylsalicylic acid arm were based on the log-rank test.

Comparison groups	Rivaroxaban 15 mg OD v Acetylsalicylic acid 100 mg OD

Number of subjects included in analysis	7213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.34284
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.74
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	1.38

Secondary: Incidence Rate of Life-Threatening Bleeding Events

End point title	Incidence Rate of Life-Threatening Bleeding Events

End point description:

Life-threatening bleeding was defined as a subset of major bleeding that met at least one of the following criteria: 1) fatal bleeding; 2) symptomatic intracranial haemorrhage; 3) reduction in hemoglobin of at least 5 g/dl (50 g/l; 3.10 mmol/L); 4) transfusion of at least 4 units of packed red cells or whole blood; 5) associated with hypotension requiring the use of intravenous inotropic agents; 6) necessitated surgical intervention. Incidence rate estimated as number of subjects with incident events divided by cumulative at-risk time, where subject is no longer at risk once an incident event occurred.

End point type	Secondary

End point timeframe:

From randomization until the efficacy cut-off date (median 326 days)

End point values	Rivaroxaban 15 mg OD	Acetylsalicylic acid 100 mg OD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3609[11]	3604[12]		
Units: event/100 subject-years				
number (confidence interval 95%)	1.02 (0.71 to 1.42)	0.43 (0.24 to 0.72)		

Notes:

[11] - ITT

[12] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis

Statistical analysis description:

Risk reduction was estimated with the stratified Cox proportional hazards model. Hazard ratios (95% confidence interval) as compared to acetylsalicylic acid arm were reported. Rivaroxaban treatment was compared with the Acetylsalicylic acid control group using a stratified log-rank test. P-values (two-sided) as compared to acetylsalicylic acid arm were based on the log-rank test.

Comparison groups	Rivaroxaban 15 mg OD v Acetylsalicylic acid 100 mg OD

Number of subjects included in analysis	7213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00443
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	2.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.28
upper limit	4.29

Secondary: Incidence Rate of Clinically Relevant Non-Major Bleeding Events

End point title	Incidence Rate of Clinically Relevant Non-Major Bleeding Events

End point description:

Non-major clinically relevant bleeding was defined as non-major overt bleeding but required medical attention (example: hospitalization, medical treatment for bleeding), and/or was associated with the study drug interruption of more than 14 days. The results were based on the outcome events at or after randomization until the efficacy cut-off date. Incidence rate estimated as number of subjects with incident events divided by cumulative at-risk time, where subject is no longer at risk once an incident event occurred.

End point type	Secondary

End point timeframe:

From randomization until the efficacy cut-off date (median 326 days)

End point values	Rivaroxaban 15 mg OD	Acetylsalicylic acid 100 mg OD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3609[13]	3604[14]		
Units: event/100 subject-years				
number (confidence interval 95%)	3.52 (2.91 to 4.21)	2.32 (1.84 to 2.90)		

Notes:

[13] - ITT

[14] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis

Statistical analysis description:

Risk reduction was estimated with the stratified Cox proportional hazards model. Hazard ratios (95% confidence interval) as compared to acetylsalicylic acid arm were reported. Rivaroxaban treatment was compared with the Acetylsalicylic acid control group using a stratified log-rank test. P-values (two-sided) as compared to acetylsalicylic acid arm were based on the log-rank test.

Comparison groups	Rivaroxaban 15 mg OD v Acetylsalicylic acid 100 mg OD

Number of subjects included in analysis	7213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.00451
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.51
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.13
upper limit	2

Secondary: Incidence Rate of Intracranial Hemorrhage

End point title	Incidence Rate of Intracranial Hemorrhage

End point description:

Intracranial hemorrhage included all bleeding events that occurred in intracerebral, subarachnoidal as well as subdural or epidural sites. The below table displays results for all randomized subjects and the outcomes at or after randomization until the efficacy cut-off date. Incidence rate estimated as number of subjects with incident events divided by cumulative at-risk time, where subject is no longer at risk once an incident event occurred.

End point type	Secondary

End point timeframe:

From randomization until the efficacy cut-off date (median 326 days)

End point values	Rivaroxaban 15 mg OD	Acetylsalicylic acid 100 mg OD		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3609[15]	3604[16]		
Units: event/100 subject-years				
number (confidence interval 95%)	0.70 (0.45 to 1.04)	0.35 (0.18 to 0.61)		

Notes:

[15] - ITT

[16] - ITT

Statistical analyses

Statistical analysis title	Statistical analysis

Statistical analysis description:

Risk reduction was estimated with the stratified Cox proportional hazards model. Hazard ratios (95% confidence interval) as compared to acetylsalicylic acid arm were reported. Rivaroxaban treatment was compared with the Acetylsalicylic acid control group using a stratified log-rank test. P-values (two-sided) as compared to acetylsalicylic acid arm were based on the log-rank test.

Comparison groups	Rivaroxaban 15 mg OD v Acetylsalicylic acid 100 mg OD

Number of subjects included in analysis	7213
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04409
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	2.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	1
upper limit	4.02

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From start of study drug administration until 2 days after the last dose of study drug	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	20.1

Reporting groups	
Reporting group title	Rivaroxaban 15 mg OD
Reporting group description:	
Subjects received rivaroxaban 15 mg immediate-release film-coated tablet and matching placebo of acetylsalicylic acid orally OD up to end of treatment.	
Reporting group title	Acetylsalicylic acid 100 mg OD
Reporting group description:	
Subjects received acetylsalicylic acid 100 mg enteric-coated tablet and matching placebo of rivaroxaban orally OD up to end of treatment.	

Serious adverse events	Rivaroxaban 15 mg OD	Acetylsalicylic acid 100 mg OD	
Total subjects affected by serious adverse events			
subjects affected / exposed	466 / 3562 (13.08%)	434 / 3559 (12.19%)	
number of deaths (all causes)	73	58	
number of deaths resulting from adverse events	15	20	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute lymphocytic leukaemia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma of colon			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma gastric			

subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
B-cell lymphoma			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	3 / 3562 (0.08%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct adenocarcinoma			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bladder cancer			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Bladder neoplasm			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm malignant			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cervix carcinoma			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic lymphocytic leukaemia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon cancer			
subjects affected / exposed	3 / 3562 (0.08%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colorectal cancer stage IV			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fallopian tube cancer			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder cancer			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal carcinoma			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Kaposi's sarcoma			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung adenocarcinoma stage IV			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung carcinoma cell type unspecified stage IV			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lymphoma			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to bone			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal adenocarcinoma			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oropharyngeal cancer			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma metastatic			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Papillary thyroid cancer			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parathyroid tumour			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer stage III			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal meningioma benign			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
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	3 / 3562 (0.08%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
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 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenoma			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to peritoneum			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal adenocarcinoma			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
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	1 / 3562 (0.03%)	5 / 3559 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neuroendocrine tumour			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma stage IV			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			
subjects affected / exposed	1 / 3562 (0.03%)	8 / 3559 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign bone neoplasm			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal neoplasm			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal squamous cell carcinoma			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pituitary tumour benign			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic neoplasm			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Thyroid cancer			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cell carcinoma			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic uterine cancer			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Inflammatory pseudotumour			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm of unknown primary site			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatic cancer			

subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive breast carcinoma			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	3 / 3562 (0.08%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm rupture			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Embolism venous			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	4 / 3562 (0.11%)	6 / 3559 (0.17%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoedema			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Temporal arteritis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post thrombotic syndrome			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
May-Thurner syndrome			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	5 / 3562 (0.14%)	5 / 3559 (0.14%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Finger amputation			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial septal defect repair			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	0 / 3562 (0.00%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza like illness			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral swelling			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	3 / 3562 (0.08%)	4 / 3559 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal graft rejection			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	4 / 3562 (0.11%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Menorrhagia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peyronie's disease			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial dysplasia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Genital haemorrhage			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chronic obstructive pulmonary disease			
subjects affected / exposed	3 / 3562 (0.08%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiccups			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic pulmonary fibrosis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung disorder			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
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	3 / 3562 (0.08%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 3562 (0.03%)	8 / 3559 (0.22%)	
occurrences causally related to treatment / all	0 / 1	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pulmonary oedema			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep apnoea syndrome			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial disorder			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Alcohol abuse			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adjustment disorder with mixed anxiety and depressed mood			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholism			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Conversion disorder			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	2 / 3562 (0.06%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	3 / 3562 (0.08%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression suicidal			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination, visual			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional self-injury			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mania			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obsessive-compulsive personality disorder			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic disorder			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic reaction			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Schizophrenia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnambulism			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
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	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol use disorder			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurologic somatic symptom disorder			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device malfunction			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	4 / 3562 (0.11%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary colic			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			

subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	3 / 3562 (0.08%)	4 / 3559 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	6 / 3562 (0.17%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
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 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
C-reactive protein increased			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eosinophil count increased			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
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 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic specific antigen increased			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza A virus test positive			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver function test increased			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Accidental overdose			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic ulcer haemorrhage			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			
subjects affected / exposed	3 / 3562 (0.08%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbon monoxide poisoning			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compression fracture			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	3 / 3562 (0.08%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	6 / 3562 (0.17%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			

subjects affected / exposed	5 / 3562 (0.14%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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	1 / 3562 (0.03%)	5 / 3559 (0.14%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			
subjects affected / exposed	2 / 3562 (0.06%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laceration			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medication error			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Overdose			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radius fracture			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Road traffic accident			
subjects affected / exposed	0 / 3562 (0.00%)	4 / 3559 (0.11%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Spinal compression fracture			
subjects affected / exposed	3 / 3562 (0.08%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic fracture			
subjects affected / exposed	0 / 3562 (0.00%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle strain			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Face injury			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial restenosis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain contusion			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transplant failure			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament rupture			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone contusion			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column injury			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	0 / 3562 (0.00%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incorrect dosage administered			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haemothorax			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb fracture			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bicuspid aortic valve			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocele			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary arteriovenous fistula			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia supraventricular			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			

subjects affected / exposed	36 / 3562 (1.01%)	37 / 3559 (1.04%)	
occurrences causally related to treatment / all	0 / 36	0 / 37	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	5 / 3562 (0.14%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac amyloidosis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
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	3 / 3562 (0.08%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conduction disorder			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
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	3 / 3562 (0.08%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive heart disease			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 3562 (0.03%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			

subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	3 / 3562 (0.08%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial thrombosis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular hypokinesia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery insufficiency			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis noninfective			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Amyotrophic lateral sclerosis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Autonomic nervous system imbalance			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem haemorrhage			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Cerebellar haemorrhage			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral venous thrombosis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			

subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chorea			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Demyelination			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	2 / 3562 (0.06%)	4 / 3559 (0.11%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	7 / 3562 (0.20%)	8 / 3559 (0.22%)	
occurrences causally related to treatment / all	0 / 8	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paralysis			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			

subjects affected / exposed	2 / 3562 (0.06%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine with aura			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorder			
subjects affected / exposed	1 / 3562 (0.03%)	4 / 3559 (0.11%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelopathy			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post herpetic neuralgia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			

subjects affected / exposed	9 / 3562 (0.25%)	9 / 3559 (0.25%)	
occurrences causally related to treatment / all	0 / 10	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Syncope			
subjects affected / exposed	10 / 3562 (0.28%)	8 / 3559 (0.22%)	
occurrences causally related to treatment / all	0 / 10	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient global amnesia			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tension headache			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebrobasilar insufficiency			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalamus haemorrhage			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Putamen haemorrhage			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stroke in evolution			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	5 / 3562 (0.14%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson's disease			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral artery stenosis			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral arteriosclerosis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central pain syndrome			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post stroke seizure			

subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemianaesthesia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudostroke			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
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 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparaesthesia			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	8 / 3562 (0.22%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	3 / 8	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Anaemia macrocytic			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Antiphospholipid syndrome			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	4 / 3562 (0.11%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	1 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcytic anaemia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombotic thrombocytopenic purpura			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Meniere's disease			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			

subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Blindness			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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 / 3562 (0.11%)	8 / 3559 (0.22%)	
occurrences causally related to treatment / all	0 / 5	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diplopia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eyelid ptosis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular oedema			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular fibrosis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic vein thrombosis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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 pain			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dental caries			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			

subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	1 / 1	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal fistula			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	7 / 3562 (0.20%)	5 / 3559 (0.14%)	
occurrences causally related to treatment / all	0 / 7	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Large intestinal ulcer			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	0 / 3562 (0.00%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatolithiasis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			
subjects affected / exposed	4 / 3562 (0.11%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric volvulus			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Abdominal hernia			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric mucosal lesion			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erosive duodenitis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal fissure			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatomyositis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erythema multiforme			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psoriasis			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin reaction			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute prerenal failure			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			

subjects affected / exposed	2 / 3562 (0.06%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal haematoma			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal hypertension			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
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 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Costovertebral angle tenderness			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urethral stenosis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			

subjects affected / exposed	4 / 3562 (0.11%)	6 / 3559 (0.17%)	
occurrences causally related to treatment / all	0 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ureterolithiasis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Basedow's disease			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
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 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperparathyroidism			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroiditis subacute			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Back pain			
subjects affected / exposed	1 / 3562 (0.03%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fasciitis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle spasms			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neck pain			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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	11 / 3562 (0.31%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 12	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periarthritis			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			

subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myofascial pain syndrome			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle tightness			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
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 / 3562 (0.08%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb discomfort			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
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 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plica syndrome			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral foraminal stenosis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis perforated			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atypical pneumonia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain abscess			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cellulitis			

subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Corneal abscess			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gangrene			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis viral			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endophthalmitis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	6 / 3562 (0.17%)	3 / 3559 (0.08%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis A			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Influenza			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Kidney infection			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningitis			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis externa			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paronychia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritoneal abscess			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (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	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	14 / 3562 (0.39%)	14 / 3559 (0.39%)	
occurrences causally related to treatment / all	0 / 14	0 / 14	
deaths causally related to treatment / all	0 / 1	0 / 2	
Postoperative wound infection			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal abscess			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	3 / 3562 (0.08%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Septic shock			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth abscess			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	6 / 3562 (0.17%)	6 / 3559 (0.17%)	
occurrences causally related to treatment / all	0 / 6	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	3 / 3562 (0.08%)	4 / 3559 (0.11%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal abscess			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia bacteraemia			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia necrotising			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal infection			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	3 / 3562 (0.08%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurocysticercosis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis infectious			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal abscess			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis infective			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			

subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perichondritis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	3 / 3562 (0.08%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acarodermatitis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster oticus			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection viral			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary tract infection bacterial			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Diabetes mellitus			

subjects affected / exposed	4 / 3562 (0.11%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to thrive			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 3562 (0.03%)	6 / 3559 (0.17%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obesity			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock hypoglycaemic			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic complication			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adult failure to thrive			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Rivaroxaban 15 mg OD	Acetylsalicylic acid 100 mg OD	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	308 / 3562 (8.65%)	294 / 3559 (8.26%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basosquamous carcinoma			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Breast cancer			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Breast neoplasm			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Essential thrombocythaemia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Superficial spreading melanoma stage unspecified			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Metastases to bone			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Vascular disorders			
Flushing			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	11 / 3562 (0.31%)	7 / 3559 (0.20%)	
occurrences (all)	11	8	
Aortic aneurysm			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences (all)	2	1	
Hypertensive crisis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Hypotension			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences (all)	2	1	
Intermittent claudication			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Varicose vein			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Phlebitis superficial			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Thrombophlebitis superficial			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences (all)	0	2	
Peripheral arterial occlusive disease			
subjects affected / exposed	3 / 3562 (0.08%)	0 / 3559 (0.00%)	
occurrences (all)	3	0	
Deep vein thrombosis			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences (all)	2	1	

Vascular pain			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences (all)	3	2	
Implantable cardiac monitor insertion			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Cataract operation			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Chest discomfort			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	3 / 3562 (0.08%)	4 / 3559 (0.11%)	
occurrences (all)	3	4	
Discomfort			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Fatigue			
subjects affected / exposed	2 / 3562 (0.06%)	3 / 3559 (0.08%)	
occurrences (all)	2	3	
Chills			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Malaise			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences (all)	1	2	
Gait disturbance			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Oedema peripheral			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences (all)	1	2	
Non-cardiac chest pain			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Peripheral swelling			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences (all)	2	2	
Immune system disorders			
Allergy to arthropod sting			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Hypersensitivity			
subjects affected / exposed	3 / 3562 (0.08%)	1 / 3559 (0.03%)	
occurrences (all)	3	3	
Social circumstances			
Treatment noncompliance			
subjects affected / exposed	2 / 3562 (0.06%)	5 / 3559 (0.14%)	
occurrences (all)	2	5	
Reproductive system and breast disorders			
Breast mass			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Prostatomegaly			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Prostatitis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			

Asthma			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Dyspnoea			
subjects affected / exposed	4 / 3562 (0.11%)	1 / 3559 (0.03%)	
occurrences (all)	4	1	
Dry throat			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Epistaxis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Cough			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Hiccups			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Pharyngeal ulceration			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Pulmonary embolism			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Pulmonary microemboli			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Depression			
subjects affected / exposed	3 / 3562 (0.08%)	2 / 3559 (0.06%)	
occurrences (all)	3	2	
Anxiety			

subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Impatience			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Abulia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Anxiety disorder			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Panic attack			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Mental disorder due to a general medical condition			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Adjustment disorder			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Post stroke depression			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Hepatobiliary disorders			
Biliary colic			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Hepatic function abnormal			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences (all)	2	2	
Hypertransaminasaemia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Hepatitis			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Blood creatine phosphokinase increased			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Blood creatinine increased			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Coagulation factor VIII level increased			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Glomerular filtration rate decreased			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Visual acuity tests abnormal			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Heart rate increased			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Haemoglobin decreased			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Transaminases increased			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Weight decreased			

subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences (all)	1	2	
Liver function test increased			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Injury, poisoning and procedural complications			
Accident			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences (all)	0	2	
Alcohol poisoning			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Concussion			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Foot fracture			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Head injury			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Humerus fracture			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Inappropriate schedule of drug administration			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Medication error			

subjects affected / exposed	10 / 3562 (0.28%)	9 / 3559 (0.25%)	
occurrences (all)	10	9	
Overdose			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Radius fracture			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Rib fracture			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Face injury			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Tendon rupture			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Post procedural haemorrhage			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Contusion			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Limb injury			
subjects affected / exposed	3 / 3562 (0.08%)	1 / 3559 (0.03%)	
occurrences (all)	3	1	
Drug administration error			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Incorrect dose administered			
subjects affected / exposed	6 / 3562 (0.17%)	4 / 3559 (0.11%)	
occurrences (all)	6	4	
Upper limb fracture			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Incorrect dosage administered			

subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences (all)	2	1	
Skin wound			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Labelled drug-drug interaction medication error			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Intentional product misuse			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences (all)	2	1	
Medication monitoring error			
subjects affected / exposed	1 / 3562 (0.03%)	3 / 3559 (0.08%)	
occurrences (all)	1	3	
Congenital, familial and genetic disorders			
Atrial septal defect			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Factor V Leiden mutation			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Fabry's disease			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Atrial fibrillation			
subjects affected / exposed	60 / 3562 (1.68%)	60 / 3559 (1.69%)	
occurrences (all)	60	60	
Atrial flutter			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Atrial tachycardia			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Cardiac failure			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Coronary artery disease			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Cardiac failure congestive			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Myocardial ischaemia			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Palpitations			
subjects affected / exposed	3 / 3562 (0.08%)	1 / 3559 (0.03%)	
occurrences (all)	3	1	
Sinus arrhythmia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Sinus tachycardia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Supraventricular extrasystoles			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Intracardiac thrombus			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Ventricular fibrillation			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Tachycardia			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Cardiac flutter			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Amnesia			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Aphasia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Cerebrovascular accident			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Dizziness postural			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Dementia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Dizziness			
subjects affected / exposed	5 / 3562 (0.14%)	7 / 3559 (0.20%)	
occurrences (all)	6	7	
Dysarthria			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Facial paralysis			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Epilepsy			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Dysgeusia			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences (all)	1	2	

Migraine			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Lethargy			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Hypoaesthesia			
subjects affected / exposed	1 / 3562 (0.03%)	3 / 3559 (0.08%)	
occurrences (all)	1	3	
Headache			
subjects affected / exposed	10 / 3562 (0.28%)	8 / 3559 (0.22%)	
occurrences (all)	10	9	
Parkinsonism			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Presyncope			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences (all)	1	2	
Paraesthesia			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Sensory disturbance			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Seizure			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Sciatica			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Syncope			
subjects affected / exposed	2 / 3562 (0.06%)	3 / 3559 (0.08%)	
occurrences (all)	2	4	

Speech disorder			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Vertebral artery occlusion			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Cervical radiculopathy			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Facial paresis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
IIIrd nerve paresis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Cognitive disorder			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Hyposmia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Stroke in evolution			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Partial seizures			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Parkinson's disease			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Vascular dementia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Autonomic neuropathy			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	

Cerebral artery stenosis			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Occipital neuralgia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences (all)	2	2	
Iron deficiency anaemia			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Antiphospholipid syndrome			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Thrombocytosis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Thrombocytopenia			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences (all)	2	1	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Vertigo positional			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences (all)	2	2	
Vertigo			
subjects affected / exposed	2 / 3562 (0.06%)	4 / 3559 (0.11%)	
occurrences (all)	2	4	
Eye disorders			
Diabetic retinopathy			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences (all)	1	2	
Conjunctival haemorrhage			

subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Cataract			
subjects affected / exposed	1 / 3562 (0.03%)	2 / 3559 (0.06%)	
occurrences (all)	2	2	
Episcleritis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Dry eye			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Eyelid ptosis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Keratitis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Pterygium			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Retinal vein occlusion			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Vision blurred			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Conjunctival hyperaemia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Abdominal pain lower			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	

Abdominal pain			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Abdominal pain upper			
subjects affected / exposed	5 / 3562 (0.14%)	7 / 3559 (0.20%)	
occurrences (all)	5	7	
Cheilitis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Chronic gastritis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Constipation			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences (all)	2	1	
Diarrhoea			
subjects affected / exposed	8 / 3562 (0.22%)	3 / 3559 (0.08%)	
occurrences (all)	8	3	
Defaecation urgency			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	2 / 3562 (0.06%)	3 / 3559 (0.08%)	
occurrences (all)	2	4	
Eructation			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Gastritis erosive			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences (all)	0	2	
Gastritis			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences (all)	2	2	
Gastric ulcer			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences (all)	0	2	

Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Gastrointestinal disorder			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Gingival swelling			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	2	
Gingival bleeding			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Hyperchlorhydria			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Haemorrhoids			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Inguinal hernia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Lip swelling			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Inflammatory bowel disease			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	5 / 3562 (0.14%)	1 / 3559 (0.03%)	
occurrences (all)	5	1	
Oesophagitis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Toothache			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	

Vomiting			
subjects affected / exposed	2 / 3562 (0.06%)	4 / 3559 (0.11%)	
occurrences (all)	2	4	
Retching			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Palatal disorder			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Colitis microscopic			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Dermatitis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Angioedema			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	2	
Alopecia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Dermatitis allergic			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Drug eruption			
subjects affected / exposed	0 / 3562 (0.00%)	3 / 3559 (0.08%)	
occurrences (all)	0	3	
Eczema			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Erythema			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Rash erythematous			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	4 / 3562 (0.11%)	4 / 3559 (0.11%)	
occurrences (all)	4	4	
Pruritus			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Rash pruritic			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Skin lesion			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Urticaria			
subjects affected / exposed	2 / 3562 (0.06%)	3 / 3559 (0.08%)	
occurrences (all)	2	3	
Rash papular			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Solar lentigo			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Precancerous skin lesion			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Skin swelling			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	

Nephrolithiasis			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Renal colic			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Renal failure			
subjects affected / exposed	3 / 3562 (0.08%)	0 / 3559 (0.00%)	
occurrences (all)	3	0	
Renal impairment			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences (all)	2	2	
Chronic kidney disease			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Ureterolithiasis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Urinary incontinence			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Thyroiditis subacute			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Thyroid mass			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	4 / 3562 (0.11%)	3 / 3559 (0.08%)	
occurrences (all)	4	3	
Arthralgia			

subjects affected / exposed	1 / 3562 (0.03%)	4 / 3559 (0.11%)	
occurrences (all)	1	4	
Arthritis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Bursitis			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Gouty arthritis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Joint swelling			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Metatarsalgia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Haemarthrosis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences (all)	2	2	
Musculoskeletal pain			
subjects affected / exposed	1 / 3562 (0.03%)	4 / 3559 (0.11%)	
occurrences (all)	1	4	
Muscular weakness			
subjects affected / exposed	2 / 3562 (0.06%)	2 / 3559 (0.06%)	
occurrences (all)	2	2	
Muscle spasms			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Myopathy			

subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Osteoarthritis			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences (all)	2	1	
Osteochondrosis			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Pain in extremity			
subjects affected / exposed	3 / 3562 (0.08%)	1 / 3559 (0.03%)	
occurrences (all)	3	1	
Periostitis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Plantar fasciitis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Tenosynovitis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Spinal osteoarthritis			
subjects affected / exposed	0 / 3562 (0.00%)	2 / 3559 (0.06%)	
occurrences (all)	0	2	
Synovial cyst			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Tendonitis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Limb mass			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Infections and infestations			
Bronchitis			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	

Diarrhoea infectious			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	3 / 3562 (0.08%)	1 / 3559 (0.03%)	
occurrences (all)	3	1	
Influenza			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	2	
Herpes zoster			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Lower respiratory tract infection			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Oesophageal candidiasis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Pneumonia viral			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Upper respiratory tract infection			
subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences (all)	2	2	
Urinary tract infection			
subjects affected / exposed	3 / 3562 (0.08%)	4 / 3559 (0.11%)	
occurrences (all)	3	4	
Vaginal infection			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	

Vulvovaginitis trichomonal			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Helicobacter infection			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Respiratory tract infection viral			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Alveolar osteitis			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Lung infection			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	2 / 3562 (0.06%)	0 / 3559 (0.00%)	
occurrences (all)	2	0	
Haemochromatosis			
subjects affected / exposed	1 / 3562 (0.03%)	0 / 3559 (0.00%)	
occurrences (all)	1	0	
Hypercholesterolaemia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Electrolyte imbalance			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Gout			
subjects affected / exposed	1 / 3562 (0.03%)	1 / 3559 (0.03%)	
occurrences (all)	1	1	
Hyperglycaemia			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	
Type 2 diabetes mellitus			

subjects affected / exposed	2 / 3562 (0.06%)	1 / 3559 (0.03%)	
occurrences (all)	2	1	
Decreased appetite			
subjects affected / exposed	0 / 3562 (0.00%)	1 / 3559 (0.03%)	
occurrences (all)	0	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 November 2015	The following eligibility criteria were revised: •More details were provided in definition of a lacunar stroke. •Subjects were to be included if there was no stenosis greater than (>) 50% rather than greater than or equal to (>=) 50%. •They were to be excluded if there was an intracranial stenosis > 50%. •For subjects with intracranial arterial occlusions in territory of qualifying stroke, it was clarified that a subject was eligible if investigator believed the occlusion was due to embolism, and not atherosclerotic based on absence of intracranial atherosclerosis elsewhere. •For 24-hour cardiac rhythm monitoring assessment to exclude the presence of Atrial fibrillation (AF), an allowance was added to accept a 20-hour recording to reflect routine practice. •For determination of intra-cardiac thrombus, allowance of transesophageal echocardiography was added as well as transthoracic echocardiography. •Recruitment of subjects was changed from 18 years or older to 50 years of age or older. •Additional clarifications were made to the inclusion criteria regarding subjects enrolled with certain risk factors: •Clarification that covert/silent strokes on neuroimaging and current tobacco smoker counted as risk factors. •Clarification that each risk factor counted separately (for example, "stroke or Transient ischemic attack (TIA) prior to index stroke, diabetes, hypertension, and heart failure" changed to "stroke or TIA prior to index stroke [includes covert/silent strokes on neuroimaging], diabetes, hypertension, current tobacco smoker, or heart failure"). •Age restriction changed from less than (<) 60 years of age with a cap at 10% of the total study population to ≥ 50 years and requirement for an additional risk factor for subjects between 50-59 years. •A statement was added that enrollment in the age group 50-59 years might have been stopped based on a blinded review of the observed overall event rate of confirmed primary efficacy outcomes during the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
05 October 2017	The study was terminated early on recommendation of the IDMC and concurrence of the co-principal investigators and the sponsor due to no efficacy improvement over aspirin at an interim analysis and very little chance of showing overall benefit if study were completed.	-

Notes:

Limitations and caveats

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

Decimal places were automatically truncated if last decimals is equals to zero.

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/29525076

http://www.ncbi.nlm.nih.gov/pubmed/29766772