Clinical trial results:
A Randomised, Double-Blind, Multinational Study to Prevent Major Vascular Events with Ticagrelor Compared to Aspirin (ASA) in Patients with Acute Ischaemic Stroke or TIA. [SOCRATES –Acute Stroke Or Transient IsChaemic Attack TReated with Aspirin or Ticagrelor and Patient OutcomES].

Summary

EudraCT number	2012-003895-38
Trial protocol	CZ SK BE SE DE IT ES BG FR
Global end of trial date	18 March 2016

Results information

Result version number	v1 (current)
This version publication date	23 March 2017
First version publication date	23 March 2017

Trial information

Trial identification

Sponsor protocol code	D5134C00001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	AstraZeneca R&D
Sponsor organisation address	Pepparedsleden 1, Mölndal, Sweden, 431 83
Public contact	Brilinta Global Clinical Lead, AstraZeneca R&D, +46 31776000, ClinicalTrialTransparency@astrazeneca.com
Scientific contact	Brilinta Global Clinical Lead, AstraZeneca R&D, +46 31776000, ClinicalTrialTransparency@astrazeneca.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	23 March 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 March 2016
Global end of trial reached?	Yes
Global end of trial date	18 March 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study is to compare the effect of 90-day treatment with ticagrelor (180 mg [two 90 mg tablets] loading dose on Day 1 followed by 90 mg twice daily maintenance dose for the remainder of the study) vs acetylsalicylic acid (ASA)-aspirinTM2 (300 mg [three 100 mg tablets] loading dose on Day 1 followed by 100 mg once daily maintenance dose for the remainder of the study) for the prevention of major vascular events (composite of stroke, MI and death) in patients with acute ischaemic stroke or TIA.

The primary efficacy variable is time from randomisation to first occurrence of any event from the composite of all strokes (including haemorrhagic stroke), MI and all cause death. This will be referred to as stroke, MI and death in the protocol.

Protection of trial subjects:

The PI at each site ensured that the patient was given full and adequate oral and written information about the nature, purpose, possible benefit, and risk of the study. The Investigator, whether the PI or another investigator at the study site, also notified patients that they were free to withdraw from the study at any time. The Investigator gave the patient the opportunity to ask questions and time to consider the information provided. The Investigator obtained the patient’s signed and dated ICF before conducting any procedure specifically for the study. The Investigator stored the original, signed ICF, and gave a copy to the patient. Samples of written patient information and consent forms are provided in Appendix 12.1.3.

The ICF incorporated (or, in some cases, was accompanied by a separate document incorporating) wording that complied with relevant data protection and privacy legislation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	07 January 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 96
Country: Number of subjects enrolled	Australia: 113
Country: Number of subjects enrolled	Belgium: 221
Country: Number of subjects enrolled	Brazil: 114
Country: Number of subjects enrolled	Bulgaria: 800
Country: Number of subjects enrolled	Canada: 220
Country: Number of subjects enrolled	Chile: 252
Country: Number of subjects enrolled	China: 1175

Country: Number of subjects enrolled	Czech Republic: 554
Country: Number of subjects enrolled	France: 660
Country: Number of subjects enrolled	Germany: 395
Country: Number of subjects enrolled	Hong Kong: 97
Country: Number of subjects enrolled	Hungary: 513
Country: Number of subjects enrolled	Israel: 64
Country: Number of subjects enrolled	Italy: 283
Country: Number of subjects enrolled	Japan: 995
Country: Number of subjects enrolled	Mexico: 36
Country: Number of subjects enrolled	Peru: 135
Country: Number of subjects enrolled	Philippines: 240
Country: Number of subjects enrolled	Poland: 536
Country: Number of subjects enrolled	Romania: 183
Country: Number of subjects enrolled	Russian Federation: 990
Country: Number of subjects enrolled	Slovakia: 476
Country: Number of subjects enrolled	Korea, Republic of: 264
Country: Number of subjects enrolled	Spain: 844
Country: Number of subjects enrolled	Sweden: 211
Country: Number of subjects enrolled	Switzerland: 234
Country: Number of subjects enrolled	Taiwan: 297
Country: Number of subjects enrolled	Thailand: 313
Country: Number of subjects enrolled	Turkey: 230
Country: Number of subjects enrolled	United States: 834
Country: Number of subjects enrolled	Ukraine: 347
Country: Number of subjects enrolled	Vietnam: 477
Worldwide total number of subjects	13199
EEA total number of subjects	5676

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)	6028
From 65 to 84 years	6577
85 years and over	594

Subject disposition

Recruitment

Recruitment details:

In total, 13307 patients were enrolled from 674 study sites in 33 countries. The first patient was enrolled on 07 January 2014. The last patient visit took place on 02 March 2016.

Pre-assignment

Screening details:

Enrolled patients randomised to study drug: 99.2%; n=13199
Patients who were not randomised: 0.8%; n=108
Patients with eligibility criteria not fulfilled: 0.7%; n=93
Patient decision: 0.1%; n=15

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Ticagrelor 90 mg

Arm description:

Ticagrelor 90 mg twice daily (BD)

Arm type	Experimental
Investigational medicinal product name	Ticagrelor
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Not mentioned

Dosage and administration details:

90 mg twice daily

Arm title	ASA 100 mg

Arm description:

ASA 100 mg once daily (OD)

Arm type	Active comparator
Investigational medicinal product name	Acetylsalicylic acid
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Coated tablet
Routes of administration	Not mentioned

Dosage and administration details:

100 mg once daily

Number of subjects in period 1	Ticagrelor 90 mg	ASA 100 mg
Started	6589	6610
Completed	6543	6554
Not completed	46	56
Consent withdrawn by subject	46	56

Baseline characteristics

Reporting groups	
Reporting group title	Ticagrelor 90 mg
Reporting group description: Ticagrelor 90 mg twice daily (BD)	
Reporting group title	ASA 100 mg
Reporting group description: ASA 100 mg once daily (OD)	

Reporting group values	Ticagrelor 90 mg	ASA 100 mg	Total
Number of subjects	6589	6610	13199
Age categorical Units: Subjects			
Adults (18-64 years)	3021	3007	6028
From 65-75 years	2064	2112	4176
76 years and over	1504	1491	2995
Age Continuous | Units: Years			
arithmetic mean	65.8	65.9	
standard deviation	± 11.23	± 11.37	-
Gender, Male/Female Units: Participants			
Male	3830	3886	7716
Female	2759	2724	5483
Race/Ethnicity, Customized Units: Subjects			
American Indian or Alaska Native	69	74	143
Asian	1957	1949	3906
Native Hawaiian or Other Pacific Islander	4	1	5
Black or African American	119	120	239
White	4374	4410	8784
Other	66	56	122
Ethnicity (NIH/OMB) Units: Subjects			
Hispanic or Latino	566	558	1124
Not Hispanic or Latino	6023	6050	12073
Unknown or Not Reported	0	2	2

End points

End points reporting groups	
Reporting group title	Ticagrelor 90 mg
Reporting group description:	
Ticagrelor 90 mg twice daily (BD)	
Reporting group title	ASA 100 mg
Reporting group description:	
ASA 100 mg once daily (OD)	

Primary: Composite of stroke/MI/death	
End point title	Composite of stroke/MI/death
End point description:	
Participants with stroke, MI or death. If no event, censoring occures at the minimum of (last date of event assessment, end of treatment date, day 97).	
End point type	Primary
End point timeframe:	
From randomization up to 97 days	

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6589	6610		
Units: Participants	442	497		

Statistical analyses

Statistical analysis title	Composite of stroke/MI/death
Comparison groups	Ticagrelor 90 mg v ASA 100 mg
Number of subjects included in analysis	13199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.067 [1]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.01

Notes:

[1] - In order to address the issue of multiple testing, a hierarchical test sequence will be used. Tested at 4.98% level.

Secondary: Ischaemic stroke

End point title	Ischaemic stroke

End point description:

Participants with ischaemic stroke. If no event, censoring occures at the minimum of (last date of event assessment, date of death, end of treatment date, day 97).

End point type	Secondary

End point timeframe:

From randomization up to 97 days

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6589	6610		
Units: Participants	385	441		

Statistical analyses

Statistical analysis title	Ischemic stroke
Comparison groups	Ticagrelor 90 mg v ASA 100 mg
Number of subjects included in analysis	13199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0462 [2]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.87
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	1

Notes:

[2] - If the treatment effect on the primary efficacy variable is significant at the 4.98% level, the secondary efficacy variable will be tested in a confirmatory sense. Otherwise it will be tested in an exploratory manner.

Secondary: Net Clinical Outcome

End point title	Net Clinical Outcome

End point description:

Participants with stroke, MI, death or life-threatening bleeding. If no event, censoring occures at the minimum of (last date of event assessment, end of treatment date, day 97).

End point type	Secondary

End point timeframe:

From randomization up to 97 days

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6589	6610		
Units: Participants	457	508		

Statistical analyses

Statistical analysis title	Net Clinical Outcome
Comparison groups	Ticagrelor 90 mg v ASA 100 mg
Number of subjects included in analysis	13199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0928
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	1.02

Secondary: Composite of ischaemic stroke, MI and CV death

End point title	Composite of ischaemic stroke, MI and CV death
End point description:	
Participants with ischaemic stroke, MI or CV death. If no event, censoring at the minimum of (last date of event assessment, date of death from non-CV causes, end of treatment date, day 97).	
End point type	Secondary
End point timeframe:	
From randomization up to 97 days	

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6589	6610		
Units: Participants	423	475		

Statistical analyses

Statistical analysis title	Composite of ischemic stroke, MI and CV death
Comparison groups	Ticagrelor 90 mg v ASA 100 mg
Number of subjects included in analysis	13199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0771
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.78
upper limit	1.01

Secondary: All-cause death	
End point title	All-cause death
End point description:	
Participants with all-cause death. If no event, censoring at the minimum of (last date of event assessment, end of treatment date, day 97).	
End point type	Secondary
End point timeframe:	
From randomization up to 97 days	

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6589	6610		
Units: Participants	68	58		

Statistical analyses

Statistical analysis title	All-cause death
Comparison groups	Ticagrelor 90 mg v ASA 100 mg
Number of subjects included in analysis	13199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3641
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.18

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.83
upper limit	1.67

Secondary: CV death

End point title	CV death

End point description:

Participants with CV death. If no event, censoring at the minimum of (last date of event assessment, date of death from non-CV causes, end of treatment date, day 97).

End point type	Secondary

End point timeframe:

From randomization up to 97 days

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6589	6610		
Units: Participants	41	35		

Statistical analyses

Statistical analysis title	CV death
Comparison groups	Ticagrelor 90 mg v ASA 100 mg
Number of subjects included in analysis	13199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4828
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.18
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	1.85

Secondary: MI

End point title	MI

End point description:

Participants with MI. If no event, censoring at the minimum of (last date of event assessment, date of

death, end of treatment date, day 97)

End point type	Secondary

End point timeframe:

From randomization up to 97 days

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6589	6610		
Units: Participants	25	21		

Statistical analyses

Statistical analysis title	MI
Comparison groups	Ticagrelor 90 mg v ASA 100 mg
Number of subjects included in analysis	13199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5457
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.67
upper limit	2.14

Secondary: Severity of stroke and overall disability

End point title	Severity of stroke and overall disability

End point description:

Analysis of severity of stroke and overall disability of patients, using modified Rankin Score, mRS. Disability defined as mRS>1.

End point type	Secondary

End point timeframe:

From randomization up to 97 days

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6589	6610		
Units: Participants	1107	1194		

Statistical analyses

Statistical analysis title	Severity of stroke and overall disability
Comparison groups	Ticagrelor 90 mg v ASA 100 mg
Number of subjects included in analysis	13199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.1393
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.93
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.85
upper limit	1.02

Secondary: Stroke

End point title	Stroke
End point description:	
Participants with stroke. If no event, censoring at the minimum of (last date of event assessment, date of death, end of treatment date, day 97)	
End point type	Secondary
End point timeframe:	
From randomization up to 97 days	

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6589	6610		
Units: Participants	390	450		

Statistical analyses

Statistical analysis title	Stroke
Comparison groups	Ticagrelor 90 mg v ASA 100 mg

Number of subjects included in analysis	13199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0342
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.75
upper limit	0.99

Secondary: Fatal stroke

End point title	Fatal stroke

End point description:

Participants with fatal stroke. If no event, censoring at the minimum of (last date of event assessment, date of death from non-CV causes, end of treatment date, day 97).

End point type	Secondary

End point timeframe:

From randomization up to 97 days

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6589	6610		
Units: Participants	18	17		

Statistical analyses

Statistical analysis title	Fatal stroke
Comparison groups	Ticagrelor 90 mg v ASA 100 mg
Number of subjects included in analysis	13199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8557
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1.06
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.55
upper limit	2.06

Secondary: Disabling stroke

End point title	Disabling stroke
End point description:	
Participants with disabling stroke. If no event, censoring at the minimum of (last date of event assessment, date of death, end of treatment date, day 97).	
End point type	Secondary
End point timeframe:	
From randomization up to 97 days	

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6589	6610		
Units: Participants	277	307		

Statistical analyses

Statistical analysis title	Disabling stroke
Comparison groups	Ticagrelor 90 mg v ASA 100 mg
Number of subjects included in analysis	13199
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.2126
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.9
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.77
upper limit	1.06

Secondary: NIHSS

End point title	NIHSS
End point description:	
Change from baseline to end of treatment visit	
End point type	Secondary
End point timeframe:	
From randomization up to 97 days	

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	4798	4869		
Units: Participants				
Change in NIHSS <=-5	132	127		
Change in NIHSS = -4	403	438		
Change in NIHSS = -3	779	810		
Change in NIHSS = -2	1088	1073		
Change in NIHSS = -1	1099	1131		
Change in NIHSS = 0	681	683		
Change in NIHSS = 1	67	79		
Change in NIHSS = 2	28	31		
Change in NIHSS = 3	18	16		
Change in NIHSS = 4	13	11		
Change in NIHSS = 5	6	6		
Change in NIHSS >5	10	14		
Missing	474	450		

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D at Visit 1 (Enrolment)

End point title	EQ-5D at Visit 1 (Enrolment)
End point description: EQ-5D index score using the UK tariff	
End point type	Secondary
End point timeframe: Visit 1	

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6497	6512		
Units: Index score				
arithmetic mean (standard deviation)	0.7 (± 0.297)	0.7 (± 0.298)		

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D at Visit 2 (Day 7+-2d)

End point title	EQ-5D at Visit 2 (Day 7+-2d)
End point description: EQ-5D index score using the UK tariff	
End point type	Secondary
End point timeframe: Visit 2	

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5883	5909		
Units: Index score				
arithmetic mean (standard deviation)	0.8 (± 0.244)	0.79 (± 0.262)		

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D at End of treatment visit

End point title	EQ-5D at End of treatment visit
End point description: EQ-5D index score using the UK tariff	
End point type	Secondary
End point timeframe: End of treatment visit	

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5817	5893		
Units: Index score				
arithmetic mean (standard deviation)	0.85 (± 0.203)	0.84 (± 0.208)		

Statistical analyses

No statistical analyses for this end point

Secondary: EQ-5D at Premature treatment discontinuation visit

End point title	EQ-5D at Premature treatment discontinuation visit
End point description: EQ-5D index score using the UK tariff	
End point type	Secondary
End point timeframe: Premature treatment discontinuation visit	

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	787	633		
Units: Index score				
arithmetic mean (standard deviation)	0.72 (± 0.33)	0.68 (± 0.364)		

Statistical analyses

No statistical analyses for this end point

Secondary: PLATO Major bleeding event

End point title	PLATO Major bleeding event
End point description: Participants with PLATO Major bleeding. If no event, censoring occures at the minimum of (last date of event assessment, date of death, end of treatment date, day 97).	
End point type	Secondary
End point timeframe: From randomization up to 97 days	

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6549	6581		
Units: Participants	31	38		

Statistical analyses

Statistical analysis title	PLATO Major bleeding
Comparison groups	Ticagrelor 90 mg v ASA 100 mg

Number of subjects included in analysis	13130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4511
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.52
upper limit	1.34

Secondary: Premature discontinuation of study drug due to any bleeding adverse event

End point title	Premature discontinuation of study drug due to any bleeding adverse event

End point description:

Participants discontinuation of study drug due to any bleeding adverse event. If no event, censoring occures at the minimum of (last date of event assessment, date of death, end of treatment date, day 97).

End point type	Secondary

End point timeframe:

Time from first dose and up to and inclusing 7 days following the date of last dose of the study

End point values	Ticagrelor 90 mg	ASA 100 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	6549	6581		
Units: Participants	82	37		

Statistical analyses

Statistical analysis title	Prem disc of study drug due to any bl AE
Comparison groups	Ticagrelor 90 mg v ASA 100 mg
Number of subjects included in analysis	13130
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	2.26

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.53
upper limit	3.34

Adverse events

Adverse events information

Timeframe for reporting adverse events:

On or after the date of first dose and up to and including 7 days following the date of last dose of study medication

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.1

Reporting groups

Reporting group title	TICAGRELOR 90mg BID
Reporting group description: -	
Reporting group title	ASA 100mg

Reporting group description: -

Serious adverse events	TICAGRELOR 90mg BID	ASA 100mg	
Total subjects affected by serious adverse events			
subjects affected / exposed	532 / 6549 (8.12%)	533 / 6581 (8.10%)	
number of deaths (all causes)	38	37	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Anaplastic astrocytoma			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basal cell carcinoma			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer recurrent			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm			
subjects affected / exposed	4 / 6549 (0.06%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Breast cancer female			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac myxoma			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac neoplasm unspecified			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac valve fibroelastoma			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system neoplasm			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clear cell renal cell carcinoma			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
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	2 / 6549 (0.03%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon neoplasm			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endometrial adenocarcinoma			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Extraskeletal myxoid chondrosarcoma			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
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 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Glioblastoma			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glioma			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cancer			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukaemia recurrent			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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	2 / 6549 (0.03%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			
subjects affected / exposed	1 / 6549 (0.02%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	3 / 6549 (0.05%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Metastases to central nervous system			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			

subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastases to spine			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nodular melanoma			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ocular neoplasm			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian neoplasm			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 6549 (0.00%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 2	
Pituitary tumour benign			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polycythaemia vera			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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 / 6549 (0.02%)	0 / 6581 (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	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cancer			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal neoplasm			

subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid cancer			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Accelerated hypertension			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm			
subjects affected / exposed	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic aneurysm rupture			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic dissection			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure fluctuation			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure inadequately controlled			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	3 / 6549 (0.05%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic infarction			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	12 / 6549 (0.18%)	11 / 6581 (0.17%)	
occurrences causally related to treatment / all	1 / 13	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	7 / 6549 (0.11%)	7 / 6581 (0.11%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemia			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leriche syndrome			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery aneurysm			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phlebitis			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian artery aneurysm			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian artery stenosis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous thrombosis limb			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	2 / 6549 (0.03%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised oedema			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	2 / 6549 (0.03%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multi-organ failure			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Non-cardiac chest pain			
subjects affected / exposed	5 / 6549 (0.08%)	7 / 6581 (0.11%)	
occurrences causally related to treatment / all	0 / 5	2 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic shock			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menorrhagia			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metrorrhagia			
subjects affected / exposed	2 / 6549 (0.03%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatitis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vaginal haemorrhage			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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 respiratory failure			
subjects affected / exposed	2 / 6549 (0.03%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Asthma			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
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	1 / 6549 (0.02%)	5 / 6581 (0.08%)	
occurrences causally related to treatment / all	1 / 1	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chronic respiratory failure			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	11 / 6549 (0.17%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	6 / 11	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	2 / 6549 (0.03%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hypoxia			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal oedema			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platypnoea			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	3 / 6549 (0.05%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumothorax			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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	4 / 6549 (0.06%)	10 / 6581 (0.15%)	
occurrences causally related to treatment / all	0 / 4	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sarcoidosis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 6549 (0.02%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 2	
Sleep apnoea syndrome			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheal stenosis			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Abnormal behaviour			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety disorder			

subjects affected / exposed	3 / 6549 (0.05%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bipolar disorder			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Confusional state			
subjects affected / exposed	1 / 6549 (0.02%)	4 / 6581 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	2 / 6549 (0.03%)	4 / 6581 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disorientation			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised anxiety disorder			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Major depression			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervousness			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Personality disorder			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric decompensation			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somatoform disorder			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood urea increased			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac function test abnormal			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Flavivirus test positive			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
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 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet count increased			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
White blood cell count decreased			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back injury			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
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	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural haematoma			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 6549 (0.02%)	4 / 6581 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	1 / 6549 (0.02%)	4 / 6581 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
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 / 6549 (0.02%)	0 / 6581 (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	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional overdose			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament sprain			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	3 / 6549 (0.05%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nerve root injury			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematoma			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haematuria			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural haemorrhage			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 6549 (0.02%)	4 / 6581 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal fracture			

subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	2 / 6549 (0.03%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tendon injury			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haematoma			
subjects affected / exposed	2 / 6549 (0.03%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic haemothorax			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound necrosis			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
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	3 / 6549 (0.05%)	6 / 6581 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute left ventricular failure			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina pectoris			
subjects affected / exposed	3 / 6549 (0.05%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	0 / 3	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	11 / 6549 (0.17%)	4 / 6581 (0.06%)	
occurrences causally related to treatment / all	0 / 11	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			
subjects affected / exposed	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	1 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	24 / 6549 (0.37%)	21 / 6581 (0.32%)	
occurrences causally related to treatment / all	1 / 25	1 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	

Atrial flutter			
subjects affected / exposed	3 / 6549 (0.05%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial thrombosis			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	6 / 6549 (0.09%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradyarrhythmia			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	1 / 6549 (0.02%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	1 / 1	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	7 / 6549 (0.11%)	7 / 6581 (0.11%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 1	0 / 1	
Cardiac failure acute			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
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	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac ventricular thrombosis			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Congestive cardiomyopathy			
subjects affected / exposed	2 / 6549 (0.03%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	2 / 6549 (0.03%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	4 / 6549 (0.06%)	4 / 6581 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive heart disease			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracardiac mass			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracardiac thrombus			
subjects affected / exposed	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	3 / 6549 (0.05%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve disease			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
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	4 / 6549 (0.06%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericarditis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrest			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	2 / 6549 (0.03%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular asystole			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Aphasia			
subjects affected / exposed	2 / 6549 (0.03%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Basilar artery stenosis			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Capsular warning syndrome			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid arteriosclerosis			
subjects affected / exposed	2 / 6549 (0.03%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery aneurysm			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery dissection			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	28 / 6549 (0.43%)	27 / 6581 (0.41%)	
occurrences causally related to treatment / all	0 / 28	0 / 27	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery thrombosis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid sinus syndrome			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral amyloid angiopathy			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral artery occlusion			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	2 / 6549 (0.03%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular disorder			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervicobrachial syndrome			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clumsiness			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depressed level of consciousness			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	6 / 6549 (0.09%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	1 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysaesthesia			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysarthria			
subjects affected / exposed	1 / 6549 (0.02%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	0 / 1	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalopathy			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			

subjects affected / exposed	4 / 6549 (0.06%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paresis			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Generalised tonic-clonic seizure			
subjects affected / exposed	2 / 6549 (0.03%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	0 / 6549 (0.00%)	4 / 6581 (0.06%)	
occurrences causally related to treatment / all	0 / 0	2 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic transformation stroke			
subjects affected / exposed	2 / 6549 (0.03%)	6 / 6581 (0.09%)	
occurrences causally related to treatment / all	0 / 2	2 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	1 / 6549 (0.02%)	5 / 6581 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemianopia			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiparesis			

subjects affected / exposed	1 / 6549 (0.02%)	4 / 6581 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemiplegia			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive encephalopathy			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Internal carotid artery kinking			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial haematoma			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intracranial venous sinus thrombosis			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			

subjects affected / exposed	5 / 6549 (0.08%)	7 / 6581 (0.11%)	
occurrences causally related to treatment / all	0 / 5	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbosacral radiculopathy			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningeal disorder			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine with aura			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mononeuropathy			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Monoparesis			

subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple sclerosis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurodegenerative disorder			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological decompensation			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological symptom			
subjects affected / exposed	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Paraesthesia			
subjects affected / exposed	3 / 6549 (0.05%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reversible ischaemic neurological deficit			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal claudication			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Stroke in evolution			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subarachnoid haemorrhage			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	6 / 6549 (0.09%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tension headache			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic encephalopathy			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	55 / 6549 (0.84%)	68 / 6581 (1.03%)	
occurrences causally related to treatment / all	5 / 57	8 / 74	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tremor			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trigeminal nerve disorder			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
VIIth nerve paralysis			
subjects affected / exposed	1 / 6549 (0.02%)	5 / 6581 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular encephalopathy			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis cerebral			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord paresis			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Antiphospholipid syndrome			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochromic anaemia			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
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 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytosis			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Deafness permanent			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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	3 / 6549 (0.05%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	2 / 6549 (0.03%)	4 / 6581 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Conjunctival haemorrhage			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinopathy			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intraocular haematoma			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Optic neuropathy			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal haemorrhage			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vision blurred			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual acuity reduced			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous detachment			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic gastritis			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
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 / 6549 (0.03%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	0 / 2	1 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	3 / 6549 (0.05%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	1 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	0 / 6549 (0.00%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Enteritis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			

subjects affected / exposed	2 / 6549 (0.03%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	1 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer perforation			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	2 / 6549 (0.03%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	1 / 2	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis haemorrhagic			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 6549 (0.03%)	5 / 6581 (0.08%)	
occurrences causally related to treatment / all	2 / 2	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic erosive gastritis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Incarcerated inguinal hernia			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal haemorrhage			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intestinal perforation			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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	2 / 6549 (0.03%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mallory-Weiss syndrome			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis haemorrhagic			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	0 / 6549 (0.00%)	4 / 6581 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Rectal haemorrhage			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			

subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	2 / 6549 (0.03%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	1 / 2	2 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	3 / 6549 (0.05%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	1 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	2 / 6549 (0.03%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	2 / 6549 (0.03%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	3 / 6549 (0.05%)	5 / 6581 (0.08%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug-induced liver injury			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular injury			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis allergic			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ecchymosis			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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	3 / 6549 (0.05%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash papular			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Swelling face			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	6 / 6549 (0.09%)	7 / 6581 (0.11%)	
occurrences causally related to treatment / all	1 / 6	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus bladder			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus ureteric			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis noninfective			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	2 / 6549 (0.03%)	5 / 6581 (0.08%)	
occurrences causally related to treatment / all	2 / 2	4 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malacoplakia vesicae			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephritis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvi-ureteric obstruction			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst haemorrhage			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			

subjects affected / exposed	2 / 6549 (0.03%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 2	2 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renal impairment			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tubulointerstitial nephritis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot deformity			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc degeneration			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc disorder			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
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	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular weakness			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myalgia			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periostitis			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rheumatoid arthritis			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	3 / 6549 (0.05%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sympathetic posterior cervical syndrome			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
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 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute endocarditis			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute hepatitis C			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute sinusitis			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendiceal abscess			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary sepsis			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Biliary tract infection			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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	3 / 6549 (0.05%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridial infection			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
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	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Encephalitis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endophthalmitis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epididymitis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			

subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	2 / 6549 (0.03%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	1 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis B			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	3 / 6549 (0.05%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
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 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	1 / 6549 (0.02%)	5 / 6581 (0.08%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 1	
Lyme disease			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningoencephalitis herpetic			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuroborreliosis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otosalpingitis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	19 / 6549 (0.29%)	23 / 6581 (0.35%)	
occurrences causally related to treatment / all	0 / 19	1 / 25	
deaths causally related to treatment / all	0 / 5	0 / 4	
Pneumonia influenzal			

subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound infection			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary tuberculosis			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	0 / 6549 (0.00%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	3 / 6549 (0.05%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	1 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	4 / 6549 (0.06%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	2 / 6549 (0.03%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sinusitis			
subjects affected / exposed	2 / 6549 (0.03%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural empyema			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	8 / 6549 (0.12%)	4 / 6581 (0.06%)	
occurrences causally related to treatment / all	1 / 8	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	4 / 6549 (0.06%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular neuronitis			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			

subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	0 / 6549 (0.00%)	5 / 6581 (0.08%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 6549 (0.02%)	2 / 6581 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 6549 (0.02%)	0 / 6581 (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 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	0 / 6549 (0.00%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			

subjects affected / exposed	1 / 6549 (0.02%)	3 / 6581 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	3 / 6549 (0.05%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	3 / 6549 (0.05%)	4 / 6581 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemia			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tetany			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 6549 (0.02%)	1 / 6581 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	TICAGRELOR 90mg BID	ASA 100mg	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	383 / 6549 (5.85%)	85 / 6581 (1.29%)	
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	383 / 6549 (5.85%)	85 / 6581 (1.29%)	
occurrences (all)	425	86	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
20 February 2014	Principal Investigator address details were updated; The sample size was increased from 9600 to 13600 patients; Clarification that concomitant anticoagulation therapy is prohibited

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported