



Clinical trial results:

A Randomised, Double-Blind, Placebo-Controlled, International, Multicentre, Phase III Study to Investigate the Efficacy and Safety of Ticagrelor and ASA Compared with ASA in the Prevention of Stroke and Death in Patients with Acute Ischaemic Stroke or Transient Ischaemic Attack

Summary

EudraCT number	2016-004232-37
Trial protocol	SE CZ HU BG FR DE ES BE PL SK IT RO
Global end of trial date	13 December 2019

Results information

Result version number	v1 (current)
This version publication date	04 December 2020
First version publication date	04 December 2020

Trial information

Trial identification

Sponsor protocol code	D5134C00003
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03354429
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	AstraZeneca AB
Sponsor organisation address	Södertälje, Södertälje, Sweden, SE 151 85
Public contact	Information Center, AstraZeneca AB, 1 877-240-9479, Information.Center@astrazeneca.com
Scientific contact	Information Center, AstraZeneca AB, 1 877-240-9479, Information.Center@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	16 January 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 December 2019
Global end of trial reached?	Yes
Global end of trial date	13 December 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate superior efficacy of ticagrelor and ASA compared with placebo and ASA in patients with acute ischaemic stroke (AIS) or TIA in the prevention of the composite of stroke and death at 30 days

Protection of trial subjects:

Patients treated with aspirin as part of standard of care. An independent data monitoring committee was responsible for safeguarding the interests of the patients by assessing the benefit/risk profile of the intervention during the study, and for reviewing the overall conduct of the study

Background therapy:

Aspirin as part of standard of care. Loading dose of 300-325 mg day 1, followed by 75-100 mg once daily

Evidence for comparator: -

Actual start date of recruitment	22 January 2018
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: 98
Country: Number of subjects enrolled	Australia: 54
Country: Number of subjects enrolled	Belgium: 162
Country: Number of subjects enrolled	Brazil: 143
Country: Number of subjects enrolled	Bulgaria: 401
Country: Number of subjects enrolled	Canada: 23
Country: Number of subjects enrolled	China: 1480
Country: Number of subjects enrolled	Czechia: 147
Country: Number of subjects enrolled	France: 444
Country: Number of subjects enrolled	Germany: 192
Country: Number of subjects enrolled	Hong Kong: 69
Country: Number of subjects enrolled	Hungary: 692
Country: Number of subjects enrolled	India: 329
Country: Number of subjects enrolled	Italy: 154
Country: Number of subjects enrolled	Mexico: 105
Country: Number of subjects enrolled	Peru: 301
Country: Number of subjects enrolled	Poland: 406
Country: Number of subjects enrolled	Romania: 66
Country: Number of subjects enrolled	Russian Federation: 1293

Country: Number of subjects enrolled	Saudi Arabia: 27
Country: Number of subjects enrolled	Slovakia: 269
Country: Number of subjects enrolled	Korea, Republic of: 282
Country: Number of subjects enrolled	Spain: 857
Country: Number of subjects enrolled	Sweden: 157
Country: Number of subjects enrolled	Taiwan: 248
Country: Number of subjects enrolled	Thailand: 968
Country: Number of subjects enrolled	Ukraine: 350
Country: Number of subjects enrolled	Vietnam: 1299
Worldwide total number of subjects	11016
EEA total number of subjects	3947

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)	5308
From 65 to 84 years	5312
85 years and over	396

Subject disposition

Recruitment

Recruitment details:

414 study sites in 28 countries enrolled patients. The first patient was enrolled on 22 January 2018. The last patient visit took place on 13 December 2019.

Pre-assignment

Screening details:

11073 patients enrolled; 11016 patients randomised. 57 patients who were not randomised (patient did not meet inclusion/exclusion criteria n=52, patient decision n=5).

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, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	TICAGRELOR

Arm description:

Ticagrelor 180 mg day 1, followed by 90 mg twice daily day 2-30

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

Dosage and administration details:

180 mg loading dose followed by 90 mg twice daily

Arm title	PLACEBO
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Arm description:

Placebo 180 mg day 1, followed by 90 mg twice daily day 2-30

Arm type	Placebo
Investigational medicinal product name	Placebo (matching ticagrelor)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Matching 180 mg loading dose followed by 90 mg twice daily

Number of subjects in period 1	TICAGRELOR	PLACEBO
Started	5523	5493
Completed	5514	5486
Not completed	9	7
Consent withdrawn by subject	8	7
Lost to follow-up	1	-

Baseline characteristics

Reporting groups

Reporting group title	TICAGRELOR
Reporting group description:	
Ticagrelor 180 mg day 1, followed by 90 mg twice daily day 2-30	
Reporting group title	PLACEBO
Reporting group description:	
Placebo 180 mg day 1, followed by 90 mg twice daily day 2-30	

Reporting group values	TICAGRELOR	PLACEBO	Total
Number of subjects	5523	5493	11016
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	2676	2632	5308
From 65-84 years	2642	2670	5312
85 years and over	205	191	396
Age Continuous Units: Years			
arithmetic mean	65.2	65.1	
standard deviation	± 11.0	± 11.1	-
Sex: Female, Male Units: Participants			
Female	2108	2171	4279
Male	3415	3322	6737
Race/Ethnicity, Customized Units: Subjects			
White	2973	2948	5921
Black or African American	21	32	53
Asian	2353	2339	4692
Native Hawaiian or other Pacific Islander	1	3	4
American Indian or Alaska Native	173	168	341
Other	2	3	5

End points

End points reporting groups

Reporting group title	TICAGRELOR
Reporting group description:	
Ticagrelor 180 mg day 1, followed by 90 mg twice daily day 2-30	
Reporting group title	PLACEBO
Reporting group description:	
Placebo 180 mg day 1, followed by 90 mg twice daily day 2-30	

Primary: Composite of subsequent stroke or death

End point title	Composite of subsequent stroke or death
End point description:	
Participants with subsequent stroke or death	
End point type	Primary
End point timeframe:	
From randomisation (day 1) to visit 3 (day 30-34)	

End point values	TICAGRELOR	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5523	5493		
Units: Number of participants with event	303	362		

Statistical analyses

Statistical analysis title	Prevention of the composite of stroke and death
Statistical analysis description:	
Time from randomisation to first subsequent stroke or death	
Comparison groups	TICAGRELOR v PLACEBO
Number of subjects included in analysis	11016
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.015 ^[1]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.83
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	0.96

Notes:

[1] - The hypothesis was tested at the 4.996% two-sided significance level to account for the planned interim analysis with the overall type I error preserved at 5%. A hierarchical test sequence was used to address the issue of multiple testing

Secondary: Ischaemic stroke

End point title	Ischaemic stroke
End point description:	
Number of participants with ischaemic stroke	
End point type	Secondary
End point timeframe:	
From randomisation (day 1) to visit 3 (day 30-34)	

End point values	TICAGRELOR	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5523	5493		
Units: Participants with event	276	345		

Statistical analyses

Statistical analysis title	Prevention of ischaemic stroke
Statistical analysis description:	
Time from randomisation to first subsequent ischaemic stroke (including strokes classified as "Undetermined")	
Comparison groups	TICAGRELOR v PLACEBO
Number of subjects included in analysis	11016
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.004 ^[2]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	0.79
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.68
upper limit	0.93

Notes:

[2] - The hypothesis was tested at the 4.996% two-sided significance level to account for the planned interim analysis with the overall type I error preserved at 5%. A hierarchical test sequence was used to address the issue of multiple testing

Secondary: The modified Rankin Scale (mRS) score >1 at Visit 3

End point title	The modified Rankin Scale (mRS) score >1 at Visit 3
End point description:	
The modified Rankin Scale (mRS) is a scale for measuring the degree of disability or dependence in the daily activities of people who have suffered a stroke or other causes of neurological disability. The scale runs from 0-6, running from perfect health without symptoms to death. 0 - No symptoms, 1 - No significant disability. Able to carry out all usual activities, despite some symptoms. 2 - Slight disability.	

Able to look after own affairs without assistance, but unable to carry out all previous activities. 3 - Moderate disability. Requires some help, but able to walk unassisted. 4 - Moderately severe disability. Unable to attend to own bodily needs without assistance, and unable to walk unassisted. 5 - Severe disability. Requires constant nursing care and attention, bedridden, incontinent. 6 - Dead.

End point type	Secondary
End point timeframe:	
Visit 3 (day 30-34)	

End point values	TICAGRELOR	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5386	5333		
Units: Participants with mRS score >1	1282	1284		

Statistical analyses

Statistical analysis title	Reduction of overall disability
Statistical analysis description:	
Modified Rankin Scale (mRS) score >1 at Visit 3	
Comparison groups	TICAGRELOR v PLACEBO
Number of subjects included in analysis	10719
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.613 ^[3]
Method	Regression, Logistic
Parameter estimate	Odds ratio (OR)
Point estimate	0.98
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.07

Notes:

[3] - The hypothesis was tested at the 4.996% two-sided significance level to account for the planned interim analysis with the overall type I error preserved at 5%. A hierarchical test sequence was used to address the issue of multiple testing

Other pre-specified: Bleeding event that fulfils SAE criteria and is categorised as GUSTO Severe

End point title	Bleeding event that fulfils SAE criteria and is categorised as GUSTO Severe
End point description:	
Participants with bleeding event that fulfils SAE criteria and is categorised as GUSTO Severe	
End point type	Other pre-specified
End point timeframe:	
From randomisation (day 1) to visit 3 (day 30-34)	

End point values	TICAGRELOR	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5523	5493		
Units: Participants with event	28	7		

Statistical analyses

Statistical analysis title	GUSTO Severe bleeding
Statistical analysis description:	
Time from randomisation to first bleeding event that fulfils SAE criteria and is categorised as GUSTO Severe	
Comparison groups	TICAGRELOR v PLACEBO
Number of subjects included in analysis	11016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.001
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	3.99
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.74
upper limit	9.14

Other pre-specified: ICH or fatal bleeding event

End point title	ICH or fatal bleeding event
End point description:	
Participants with ICH or fatal bleeding event	
End point type	Other pre-specified
End point timeframe:	
From randomisation (day 1) to visit 3 (day 30-34)	

End point values	TICAGRELOR	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5523	5493		
Units: Participants with event	22	6		

Statistical analyses

Statistical analysis title	ICH or fatal bleeding
Statistical analysis description:	
Time from randomisation to first intracranial haemorrhage or fatal bleeding event	
Comparison groups	TICAGRELOR v PLACEBO
Number of subjects included in analysis	11016
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.005
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	3.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.48
upper limit	9.02

Other pre-specified: Bleeding event that fulfils SAE criteria and is categorised as GUSTO Moderate/Severe

End point title	Bleeding event that fulfils SAE criteria and is categorised as GUSTO Moderate/Severe
End point description:	
Participants with bleeding event that fulfils SAE criteria and is categorised as GUSTO Moderate/Severe	
End point type	Other pre-specified
End point timeframe:	
From randomisation (day 1) to visit 3 (day 30-34)	

End point values	TICAGRELOR	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5523	5493		
Units: Participants with event	36	11		

Statistical analyses

Statistical analysis title	GUSTO Moderate/Severe bleeding
Statistical analysis description:	
Time from randomisation to first bleeding event that fulfils SAE criteria and is categorised as GUSTO Moderate/Severe	
Comparison groups	TICAGRELOR v PLACEBO
Number of subjects included in analysis	11016
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	3.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.67
upper limit	6.43

Other pre-specified: Premature permanent discontinuation of IP due to bleeding

End point title	Premature permanent discontinuation of IP due to bleeding
End point description:	
Participants with premature permanent discontinuation of IP due to bleeding	
End point type	Other pre-specified
End point timeframe:	
From randomisation (day 1) to visit 3 (day 30-34)	

End point values	TICAGRELOR	PLACEBO		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	5523	5493		
Units: Participants with event	152	32		

Statistical analyses

Statistical analysis title	Permanent discontinuation of IP due to bleeding
Statistical analysis description:	
Time from randomisation to premature permanent discontinuation of IP due to bleeding	
Comparison groups	TICAGRELOR v PLACEBO

Number of subjects included in analysis	11016
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.001
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	4.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	3.28
upper limit	7.02

Adverse events

Adverse events information^[1]

Timeframe for reporting adverse events:

From randomisation (day 1) up to visit 3 (day 30-34)

Adverse event reporting additional description:

Systematic assessment of serious adverse events and adverse events leading to premature permanent discontinuation of study drug. Other non-serious adverse events were not to be reported

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	22.1
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Reporting groups

Reporting group title	Ticagrelor 90 mg bd
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Reporting group description: -

Reporting group title	Placebo
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Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Only serious adverse events and adverse events leading to discontinuation of study drug were to be collected. Hence, the number of non-serious events were limited and no preferred term reached the 5% threshold.

Serious adverse events	Ticagrelor 90 mg bd	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	571 / 5523 (10.34%)	609 / 5493 (11.09%)	
number of deaths (all causes)	36	27	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute leukaemia			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Brain neoplasm			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm malignant			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (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 / 5523 (0.00%)	1 / 5493 (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	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal adenocarcinoma			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Focal nodular hyperplasia			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (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 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Glioma			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (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 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung adenocarcinoma			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung carcinoma cell type unspecified recurrent			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	2 / 5523 (0.04%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant mediastinal neoplasm			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meningioma			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to central nervous system			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic gastric cancer			

subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelofibrosis			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myeloproliferative neoplasm			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (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 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pancreatic carcinoma metastatic			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phaeochromocytoma			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal cancer			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pituitary tumour benign			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer			

subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostate cancer metastatic			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (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	0 / 5523 (0.00%)	1 / 5493 (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	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine cancer			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Vascular disorders			
Aortic dissection			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic intramural haematoma			

subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Aortic stenosis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial stenosis			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteritis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Circulatory collapse			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (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	0 / 5523 (0.00%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (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	5 / 5523 (0.09%)	5 / 5493 (0.09%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			

subjects affected / exposed	3 / 5523 (0.05%)	4 / 5493 (0.07%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive urgency			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penetrating aortic ulcer			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 5523 (0.02%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian artery stenosis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vasculitis			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vena cava thrombosis			

subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (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			
Chest discomfort			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	4 / 5523 (0.07%)	4 / 5493 (0.07%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 4	0 / 4	
Device related thrombosis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Necrosis			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			

subjects affected / exposed	2 / 5523 (0.04%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden cardiac death			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 5523 (0.02%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	1 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaphylactic shock			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug hypersensitivity			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Endometrial hyperplasia			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Menorrhagia			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine haemorrhage			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory failure			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Bronchitis chronic			
subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			
subjects affected / exposed	3 / 5523 (0.05%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epistaxis			
subjects affected / exposed	6 / 5523 (0.11%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	4 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (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	0 / 5523 (0.00%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pneumonitis			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pulmonary embolism			
subjects affected / exposed	9 / 5523 (0.16%)	5 / 5493 (0.09%)	
occurrences causally related to treatment / all	1 / 9	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pulmonary granuloma			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (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 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract haemorrhage			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anxiety disorder			
subjects affected / exposed	0 / 5523 (0.00%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			

subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Confusional state			
subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Conversion disorder			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			
subjects affected / exposed	1 / 5523 (0.02%)	3 / 5493 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination, visual			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuropsychiatric symptoms			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organic brain syndrome			
subjects affected / exposed	0 / 5523 (0.00%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic disorder			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			

subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sleep disorder			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somatic symptom disorder			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Device dislocation			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood glucose increased			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
International normalised ratio increased			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Occult blood positive			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Arterial bypass occlusion			

subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	0 / 5523 (0.00%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	0 / 5523 (0.00%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Open globe injury			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periprocedural myocardial infarction			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural haemorrhage			

subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rib fracture			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal compression fracture			
subjects affected / exposed	0 / 5523 (0.00%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subdural haematoma			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thermal burn			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxicity to various agents			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (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	1 / 5523 (0.02%)	4 / 5493 (0.07%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular malformation			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute left ventricular failure			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute myocardial infarction			
subjects affected / exposed	4 / 5523 (0.07%)	5 / 5493 (0.09%)	
occurrences causally related to treatment / all	0 / 4	1 / 5	
deaths causally related to treatment / all	0 / 2	0 / 0	
Angina unstable			
subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve disease mixed			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			

subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	18 / 5523 (0.33%)	15 / 5493 (0.27%)	
occurrences causally related to treatment / all	0 / 18	0 / 17	
deaths causally related to treatment / all	0 / 1	0 / 0	
Atrial tachycardia			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial thrombosis			
subjects affected / exposed	4 / 5523 (0.07%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	1 / 5523 (0.02%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	3 / 5523 (0.05%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	1 / 5523 (0.02%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac asthma			

subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	0 / 5523 (0.00%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiac failure acute			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	3 / 5523 (0.05%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac ventricular thrombosis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	0 / 5523 (0.00%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cardiomyopathy			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congestive cardiomyopathy			

subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	2 / 5523 (0.04%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery occlusion			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (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	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve disease			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve disease mixed			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			

subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 5523 (0.00%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sinoatrial block			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			

subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular fibrillation			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Autonomic neuropathy			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balance disorder			
subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain oedema			
subjects affected / exposed	3 / 5523 (0.05%)	3 / 5493 (0.05%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 3	0 / 1	
Basal ganglia haemorrhage			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem stroke			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain stem syndrome			

subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid arteriosclerosis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery occlusion			
subjects affected / exposed	0 / 5523 (0.00%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	8 / 5523 (0.14%)	7 / 5493 (0.13%)	
occurrences causally related to treatment / all	0 / 8	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central pain syndrome			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar infarction			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cerebral artery stenosis			
subjects affected / exposed	2 / 5523 (0.04%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			

subjects affected / exposed	4 / 5523 (0.07%)	3 / 5493 (0.05%)	
occurrences causally related to treatment / all	2 / 4	2 / 3	
deaths causally related to treatment / all	2 / 4	1 / 2	
Cerebral infarction			
subjects affected / exposed	6 / 5523 (0.11%)	8 / 5493 (0.15%)	
occurrences causally related to treatment / all	3 / 6	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral ischaemia			
subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral venous sinus thrombosis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral venous thrombosis			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular accident			
subjects affected / exposed	6 / 5523 (0.11%)	7 / 5493 (0.13%)	
occurrences causally related to treatment / all	0 / 6	1 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular disorder			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cerebrovascular insufficiency			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic inflammatory demyelinating polyradiculoneuropathy			

subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	2 / 5523 (0.04%)	3 / 5493 (0.05%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia Alzheimer's type			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysgraphia			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysmetria			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	5 / 5523 (0.09%)	3 / 5493 (0.05%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Haemorrhage intracranial			
subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic stroke			

subjects affected / exposed	7 / 5523 (0.13%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	5 / 7	0 / 0	
deaths causally related to treatment / all	4 / 6	0 / 0	
Haemorrhagic transformation stroke			
subjects affected / exposed	8 / 5523 (0.14%)	6 / 5493 (0.11%)	
occurrences causally related to treatment / all	6 / 8	4 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Headache			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hemianaesthesia			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (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	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic encephalopathy			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoaesthesia			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemic seizure			

subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intracranial aneurysm			
subjects affected / exposed	1 / 5523 (0.02%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cerebral infarction			
subjects affected / exposed	4 / 5523 (0.07%)	6 / 5493 (0.11%)	
occurrences causally related to treatment / all	1 / 4	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	254 / 5523 (4.60%)	324 / 5493 (5.90%)	
occurrences causally related to treatment / all	19 / 258	36 / 330	
deaths causally related to treatment / all	0 / 8	0 / 7	
Lacunar stroke			
subjects affected / exposed	0 / 5523 (0.00%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lacunar infarction			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Memory impairment			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			

subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurological symptom			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paresis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson's disease			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post stroke seizure			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychomotor hyperactivity			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			

subjects affected / exposed	4 / 5523 (0.07%)	3 / 5493 (0.05%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			
subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Spondylitic myelopathy			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stroke in evolution			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (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 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tension headache			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thalamic infarction			

subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic attack			
subjects affected / exposed	12 / 5523 (0.22%)	30 / 5493 (0.55%)	
occurrences causally related to treatment / all	0 / 12	3 / 31	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular dementia			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral artery stenosis			
subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphadenopathy mediastinal			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normochromic normocytic anaemia			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normocytic anaemia			

subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polycythaemia			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spontaneous haematoma			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo positional			
subjects affected / exposed	2 / 5523 (0.04%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 2	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vestibular ataxia			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Angle closure glaucoma			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinopathy			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Idiopathic orbital inflammation			

subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Visual impairment			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticular perforation			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (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	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			

subjects affected / exposed	1 / 5523 (0.02%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric disorder			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (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	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	6 / 5523 (0.11%)	6 / 5493 (0.11%)	
occurrences causally related to treatment / all	5 / 6	3 / 6	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gingival bleeding			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoidal haemorrhage			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	3 / 5523 (0.05%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Melaena			

subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal haemorrhage			
subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal ulcer haemorrhage			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	3 / 5523 (0.05%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	3 / 3	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal ulcer haemorrhage			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal haemorrhage			
subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			
subjects affected / exposed	5 / 5523 (0.09%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	4 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			

subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Acute hepatic failure			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct stone			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	1 / 5523 (0.02%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	1 / 5523 (0.02%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic function abnormal			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatitis acute			

subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular injury			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ecchymosis			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	4 / 5523 (0.07%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	2 / 5523 (0.04%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cystitis haemorrhagic			

subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysuria			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
End stage renal disease			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematuria			
subjects affected / exposed	8 / 5523 (0.14%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	6 / 8	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephropathy toxic			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prerenal failure			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			

subjects affected / exposed	1 / 5523 (0.02%)	3 / 5493 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal injury			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urethral stenosis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder polyp			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Costochondritis			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (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	0 / 5523 (0.00%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb discomfort			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (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	1 / 5523 (0.02%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sympathetic posterior cervical syndrome			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (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			
Anal abscess			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Brain abscess			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	1 / 5523 (0.02%)	3 / 5493 (0.05%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium colitis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Endocarditis			
subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia urinary tract infection			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal bacterial infection			

subjects affected / exposed	1 / 5523 (0.02%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal infection			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella sepsis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neurosyphilis			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	25 / 5523 (0.45%)	28 / 5493 (0.51%)	
occurrences causally related to treatment / all	1 / 25	2 / 29	
deaths causally related to treatment / all	0 / 2	0 / 4	
Pseudomembranous colitis			

subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis chronic			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory syncytial virus infection			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Sepsis			
subjects affected / exposed	3 / 5523 (0.05%)	5 / 5493 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 2	0 / 1	
Septic shock			
subjects affected / exposed	2 / 5523 (0.04%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tracheobronchitis			

subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tuberculosis			
subjects affected / exposed	2 / 5523 (0.04%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	6 / 5523 (0.11%)	7 / 5493 (0.13%)	
occurrences causally related to treatment / all	0 / 6	2 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection enterococcal			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (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	1 / 5523 (0.02%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic metabolic decompensation			
subjects affected / exposed	0 / 5523 (0.00%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (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	2 / 5523 (0.04%)	2 / 5493 (0.04%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	3 / 5523 (0.05%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 5523 (0.02%)	0 / 5493 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	3 / 5523 (0.05%)	1 / 5493 (0.02%)	
occurrences causally related to treatment / all	0 / 3	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 90 mg bd	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 5523 (0.00%)	0 / 5493 (0.00%)	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 May 2019	Number of randomised subjects reduced from 13000 to 11000

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

None

Notes:

Online references

<http://www.ncbi.nlm.nih.gov/pubmed/32668111>