Clinical trial results:
An international, multicenter, randomized, double-blind, placebo-controlled phase 3 trial investigating the efficacy and safety of rivaroxaban to reduce the risk of major thrombotic vascular events in patients with symptomatic peripheral artery disease undergoing lower extremity revascularization procedures

Summary

EudraCT number	2014-005569-58
Trial protocol	CZ AT ES HU GB FR PT SE BE BG DK DE NL PL SK LT LV RO EE FI IT
Global end of trial date	09 January 2020

Results information

Result version number	v1 (current)
This version publication date	26 November 2020
First version publication date	26 November 2020

Trial information

Trial identification

Sponsor protocol code	17454

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02504216
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Bayer AG
Sponsor organisation address	Kaiser-Wilhelm-Allee, Leverkusen, Germany, D-51368
Public contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com
Scientific contact	Therapeutic Area Head, Bayer AG, clinical-trials-contact@bayer.com

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	31 March 2020
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	09 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary efficacy objective of the study was: - to evaluate whether rivaroxaban added to ASA is superior to ASA alone in reducing the risk of major thrombotic vascular events (defined as MI, ischemic stroke, CV (Cardiovascular) death, ALI (Acute limb ischemia), and major amputation of a vascular etiology) in symptomatic PAD (Peripheral artery disease) patients with a recent lower extremity revascularization procedure. The primary safety objective of the study was: - to evaluate the overall safety and tolerability of rivaroxaban added to ASA compared to ASA alone.

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	18 August 2015
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	China: 287
Country: Number of subjects enrolled	Japan: 459
Country: Number of subjects enrolled	Korea, Republic of: 148
Country: Number of subjects enrolled	Bulgaria: 737
Country: Number of subjects enrolled	Czechia: 243
Country: Number of subjects enrolled	Estonia: 9
Country: Number of subjects enrolled	Hungary: 261
Country: Number of subjects enrolled	Latvia: 202
Country: Number of subjects enrolled	Lithuania: 84
Country: Number of subjects enrolled	Poland: 168
Country: Number of subjects enrolled	Romania: 214
Country: Number of subjects enrolled	Russian Federation: 188
Country: Number of subjects enrolled	Serbia: 68
Country: Number of subjects enrolled	Slovakia: 126

Country: Number of subjects enrolled	Ukraine: 299
Country: Number of subjects enrolled	Canada: 170
Country: Number of subjects enrolled	United States: 524
Country: Number of subjects enrolled	Argentina: 299
Country: Number of subjects enrolled	Brazil: 185
Country: Number of subjects enrolled	Austria: 212
Country: Number of subjects enrolled	Belgium: 126
Country: Number of subjects enrolled	Denmark: 78
Country: Number of subjects enrolled	Thailand: 67
Country: Number of subjects enrolled	Finland: 17
Country: Number of subjects enrolled	France: 107
Country: Number of subjects enrolled	Germany: 593
Country: Number of subjects enrolled	Italy: 184
Country: Number of subjects enrolled	Netherlands: 77
Country: Number of subjects enrolled	Portugal: 74
Country: Number of subjects enrolled	Spain: 96
Country: Number of subjects enrolled	Sweden: 42
Country: Number of subjects enrolled	Switzerland: 91
Country: Number of subjects enrolled	United Kingdom: 129
Worldwide total number of subjects	6564
EEA total number of subjects	3779

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)	2622
From 65 to 84 years	3801
85 years and over	141

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 548 centers which screened subjects (534 sites randomized subjects) world-wide between 31 Jul 2015 (first patient's first visit) and 27 Nov 2019 (last patient's last visit).

Pre-assignment

Screening details:

A total of 6772 subjects were screened, of which 6564 were randomly assigned to either of the two treatment arms.

Period 1

Period 1 title	Overall (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	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od

Arm description:

Subjects were treated with Rivaroxaban 2.5 mg twice-daily (bid) and aspirin (ASA: Acetylsalicylic Acid) 100 mg once-daily (od)

Arm type	Experimental
Investigational medicinal product name	Acetylsalicylic Acid (ASA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg once-daily (od)

Investigational medicinal product name	Rivaroxaban (Xarelto, BAY59-7939)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

2.5 mg twice-daily (bid) (5 mg/day)

Arm title	Rivaroxaban placebo bid + Aspirin 100 mg od

Arm description:

Subjects were treated with Rivaroxaban-placebo twice-daily and aspirin (ASA: Acetylsalicylic Acid) 100 mg once-daily

Arm type	Placebo
Investigational medicinal product name	Acetylsalicylic Acid (ASA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg once-daily (od)

Investigational medicinal product name	Rivaroxaban-Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Matching placebo, twice daily,

Number of subjects in period 1	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od	Rivaroxaban placebo bid + Aspirin 100 mg od
Started	3286	3278
Received treatment	3256 [1]	3248 [2]
Completed	3275	3263
Not completed	11	15
Consent withdrawn by subject	8	12
Lost to follow-up	3	3

Notes:

[1] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: 30 subjects were never administered study drug.

[2] - The number of subjects at this milestone seems inconsistent with the number of subjects in the arm. It is expected that the number of subjects will be greater than, or equal to the number that completed, minus those who left.

Justification: 30 subjects were never administered study drug.

Baseline characteristics

Reporting groups	
Reporting group title	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od
Reporting group description:	
Subjects were treated with Rivaroxaban 2.5 mg twice-daily (bid) and aspirin (ASA: Acetylsalicylic Acid) 100 mg once-daily (od)	
Reporting group title	Rivaroxaban placebo bid + Aspirin 100 mg od
Reporting group description:	
Subjects were treated with Rivaroxaban-placebo twice-daily and aspirin (ASA: Acetylsalicylic Acid) 100 mg once-daily	

Reporting group values	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od	Rivaroxaban placebo bid + Aspirin 100 mg od	Total
Number of subjects	3286	3278	6564
Age Categorical Units: Subjects			
Age Continuous Units: years			
median	67.0	67.0	
full range (min-max)	49 to 93	50 to 95	-
Gender Categorical Units: Subjects			
Female	847	857	1704
Male	2439	2421	4860
Race Units: Subjects			
White	2647	2656	5303
Black or African American	84	71	155
Asian	484	482	966
American Indian or Alaska native	1	4	5
Native Hawaiian or other Pacific islander	0	1	1
Not reported	69	62	131
Multiple	1	2	3

End points

End points reporting groups

Reporting group title	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od
Reporting group description:	
Subjects were treated with Rivaroxaban 2.5 mg twice-daily (bid) and aspirin (ASA: Acetylsalicylic Acid) 100 mg once-daily (od)	
Reporting group title	Rivaroxaban placebo bid + Aspirin 100 mg od
Reporting group description:	
Subjects were treated with Rivaroxaban-placebo twice-daily and aspirin (ASA: Acetylsalicylic Acid) 100 mg once-daily	
Subject analysis set title	Intention-to-treat analysis set (ITT Set)
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
The ITT population comprised all randomized subjects.	
Subject analysis set title	Safety analysis set (SAF Set)
Subject analysis set type	Safety analysis
Subject analysis set description:	
The SAF comprised all treated subjects, i.e. randomized subjects who received at least one dose of study drug (rivaroxaban or rivaroxaban placebo).	

Primary: Primary efficacy outcome: Composite of Myocardial infarction (MI), ischemic stroke, cardiovascular death, acute limb ischemia (ALI) and major amputation due to a vascular etiology

End point title	Primary efficacy outcome: Composite of Myocardial infarction (MI), ischemic stroke, cardiovascular death, acute limb ischemia (ALI) and major amputation due to a vascular etiology
End point description:	
Only the first occurrence of the outcome event under analysis within the data scope from a subject is considered.	
End point type	Primary
End point timeframe:	
For each participant, the first occurrence of the composite primary efficacy outcome after randomization up until the efficacy cut-off date (08-Sep-2019) was considered. The mean time in follow-up survival time until ECOD that date was 1109.76 days.	

End point values	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od	Rivaroxaban placebo bid + Aspirin 100 mg od		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3286	3278		
Units: Subject	508	584		

Statistical analyses

Statistical analysis title	Primary efficacy outcome
Comparison groups	Rivaroxaban placebo bid + Aspirin 100 mg od v Rivaroxaban

	2.5 mg bid + Aspirin 100 mg od
Number of subjects included in analysis	6564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0043 [1]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.85
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	0.96

Notes:

[1] - P-value (1-sided) is based on the log rank test stratified by type of procedure and clopidogrel use per IxRS (Interactive web/voice response system) assignment with treatment as a factor.

Primary: Primary safety outcome: Number of participants with TIMI Major bleeding

End point title	Primary safety outcome: Number of participants with TIMI Major bleeding

End point description:

TIMI: Thrombolysis in Myocardial Infarction Only the first occurrence of the outcome event under analysis within the data scope from a subject is considered.

End point type	Primary

End point timeframe:

For each participant, the first occurrence of the primary safety outcome after randomization up until 2 days after permanent stop of study drug (rivaroxaban or rivaroxaban placebo).

End point values	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od	Rivaroxaban placebo bid + Aspirin 100 mg od		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3256	3248		
Units: Subject	62	44		

Statistical analyses

Statistical analysis title	TIMI major bleeding
Comparison groups	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od v Rivaroxaban placebo bid + Aspirin 100 mg od
Number of subjects included in analysis	6504
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0695 [2]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.43

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.97
upper limit	2.1

Notes:

[2] - P−value (2-sided) is based on the log rank test stratified by type of procedure and clopidogrel use per IxRS assignment with treatment as a factor.

Secondary: Composite of MI, ischemic stroke, Coronary heart disease (CHD) death, ALI, and major amputation of a vascular etiology

End point title	Composite of MI, ischemic stroke, Coronary heart disease (CHD) death, ALI, and major amputation of a vascular etiology

End point description:

MI, stroke, mortality, ALI, and major amputation of a vascular etiology, and events leading to hospitalization are adjudicated.

End point type	Secondary

End point timeframe:

For each participant, the first occurrence of the composite primary efficacy outcome after randomization up until the efficacy cut-off date (08-Sep-2019) was considered. The mean survival time until ECOD was 1108.79 days.

End point values	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od	Rivaroxaban placebo bid + Aspirin 100 mg od		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3286	3278		
Units: Subject	433	528		

Statistical analyses

Statistical analysis title	Secondary efficacy outcome
Comparison groups	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od v Rivaroxaban placebo bid + Aspirin 100 mg od
Number of subjects included in analysis	6564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0004 [3]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.8
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.71
upper limit	0.91

Notes:

[3] - P-value (1-sided) is based on the log rank test stratified by type of procedure and clopidogrel use per IxRS assignment with treatment as a factor.

Secondary: Number of participants with an unplanned index limb revascularization for recurrent limb ischemia (subsequent index leg revascularization that was not planned or considered as part of the initial treatment plan at the time of randomization)

End point title	Number of participants with an unplanned index limb revascularization for recurrent limb ischemia (subsequent index leg revascularization that was not planned or considered as part of the initial treatment plan at the time of randomization)

End point description:

Index limb revascularization is defined as subsequent index leg revascularization that was not planned or considered as part of the initial treatment plan at the time of randomization. index limb revascularization were reported by investigator only.

End point type	Secondary

End point timeframe:

For each participant, the first occurrence of the composite primary efficacy outcome after randomization up until the efficacy cut-off date (08-Sep-2019) was considered. The mean survival time until ECOD was 1062.48 days.

End point values	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od	Rivaroxaban placebo bid + Aspirin 100 mg od		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3286	3278		
Units: Subject	584	655		

Statistical analyses

Statistical analysis title	Secondary efficacy outcome
Comparison groups	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od v Rivaroxaban placebo bid + Aspirin 100 mg od
Number of subjects included in analysis	6564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.014 [4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.88
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	0.99

Notes:

[4] - P-value (1-sided) is based on the log rank test stratified by type of procedure and clopidogrel use per IxRS assignment with treatment as a factor.

Secondary: Number of participants with hospitalization for a coronary or peripheral cause (either lower limb) of a thrombotic nature

End point title	Number of participants with hospitalization for a coronary or peripheral cause (either lower limb) of a thrombotic nature

End point description:

Events leading to hospitalization are adjudicated.

End point type	Secondary

End point timeframe:

For each participant, the first occurrence of the composite primary efficacy outcome after randomization up until the efficacy cut-off date (08-Sep-2019) was considered. The mean survival time until ECOD was 1154.04 days

End point values	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od	Rivaroxaban placebo bid + Aspirin 100 mg od		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3286	3278		
Units: Subject	262	356		

Statistical analyses

Statistical analysis title	Secondary efficacy outcome
Comparison groups	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od v Rivaroxaban placebo bid + Aspirin 100 mg od
Number of subjects included in analysis	6564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [5]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.62
upper limit	0.85

Notes:

[5] - P-value (1-sided) is based on the log rank test stratified by type of procedure and clopidogrel use per IxRS assignment with treatment as a factor.

Secondary: Composite of MI, ischemic stroke, All-cause mortality (ACM), ALI, and major amputation of a vascular etiology

End point title	Composite of MI, ischemic stroke, All-cause mortality (ACM), ALI, and major amputation of a vascular etiology

End point description:

MI, stroke, mortality, ALI, and major amputation of a vascular etiology are adjudicated.

End point type	Secondary

End point timeframe:

For each participant, the first occurrence of the composite primary efficacy outcome after randomization up until the efficacy cut-off date (08-Sep-2019) was considered. The mean survival time until ECOD was 1085.13 days

End point values	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od	Rivaroxaban placebo bid + Aspirin 100 mg od		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3286	3278		
Units: Subject	614	679		

Statistical analyses

Statistical analysis title	Secondary efficacy outcome
Comparison groups	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od v Rivaroxaban placebo bid + Aspirin 100 mg od
Number of subjects included in analysis	6564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0145 [6]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.89
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.79
upper limit	0.99

Notes:

[6] - P-value (1-sided) is based on the log rank test stratified by type of procedure and clopidogrel use per IxRS assignment with treatment as a factor.

Secondary: Composite of MI, all-cause stroke, Cardiovascular (CV) death, Acute limb ischemia (ALI), and major amputation of a vascular etiology

End point title	Composite of MI, all-cause stroke, Cardiovascular (CV) death, Acute limb ischemia (ALI), and major amputation of a vascular etiology

End point description:

MI, stroke, mortality, ALI, and major amputation of a vascular etiology are adjudicated.

End point type	Secondary

End point timeframe:

For each participant, the first occurrence of the composite primary efficacy outcome after randomization up until the efficacy cut-off date (08-Sep-2019) was considered. The mean survival time until ECOD was 1108.29 days

End point values	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od	Rivaroxaban placebo bid + Aspirin 100 mg od		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3286	3278		
Units: Subject	514	588		

Statistical analyses

Statistical analysis title	Secondary efficacy outcome
Comparison groups	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od v Rivaroxaban placebo bid + Aspirin 100 mg od
Number of subjects included in analysis	6564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0051 [7]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.86
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.76
upper limit	0.96

Notes:

[7] - P-value (1-sided) is based on the log rank test stratified by type of procedure and clopidogrel use per IxRS assignment with treatment as a factor.

Secondary: Mortality (all-cause)

End point title	Mortality (all-cause)

End point description:

Mortality are adjudicated.

End point type	Secondary

End point timeframe:

For each participant, the first occurrence of the composite primary efficacy outcome after randomization up until the efficacy cut-off date (08-Sep-2019) was considered. The mean survival time until ECOD was 1188.48 days

End point values	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od	Rivaroxaban placebo bid + Aspirin 100 mg od		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3286	3278		
Units: Subject	321	297		

Statistical analyses

Statistical analysis title	Secondary efficacy outcome
Comparison groups	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od v Rivaroxaban placebo bid + Aspirin 100 mg od
Number of subjects included in analysis	6564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8322 [8]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.92
upper limit	1.27

Notes:

[8] - P-value (1-sided) is based on the log rank test stratified by type of procedure and clopidogrel use per IxRS assignment with treatment as a factor.

Secondary: Number of participants with venous thromboembolic (VTE) events

End point title	Number of participants with venous thromboembolic (VTE) events

End point description:

Venous thromboembolic events were reported by investigator only.

End point type	Secondary

End point timeframe:

For each participant, the first occurrence of the composite primary efficacy outcome after randomization up until the efficacy cut-off date (08-Sep-2019) was considered. The mean survival time until ECOD was 1187.65 days

End point values	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od	Rivaroxaban placebo bid + Aspirin 100 mg od		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3286	3278		
Units: Subject	25	41		

Statistical analyses

Statistical analysis title	Secondary efficacy outcome
Comparison groups	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od v Rivaroxaban placebo bid + Aspirin 100 mg od

Number of subjects included in analysis	6564
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0235 [9]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.61
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	1

Notes:

[9] - P-value (1-sided) is based on the log rank test stratified by type of procedure and clopidogrel use per IxRS assignment with treatment as a factor.

Secondary: Secondary safety outcome: Number of participants with ISTH major bleeding

End point title	Secondary safety outcome: Number of participants with ISTH major bleeding

End point description:

ISTH: International Society on Thrombosis and Haemostasis Only the first occurrence of the outcome event under analysis within the data scope from a subject is considered.

End point type	Secondary

End point timeframe:

For each participant, the first occurrence of the major bleeding events according to the ISTH classification after randomization up until 2 days after permanent stop of study drug (rivaroxaban or rivaroxaban placebo).

End point values	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od	Rivaroxaban placebo bid + Aspirin 100 mg od		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3256	3248		
Units: Subject	140	100		

Statistical analyses

Statistical analysis title	ISTH major bleeding
Comparison groups	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od v Rivaroxaban placebo bid + Aspirin 100 mg od
Number of subjects included in analysis	6504
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0068
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.42

Confidence interval	
level	95 %
sides	2-sided
lower limit	1.1
upper limit	1.84

Secondary: Secondary safety outcome: Number of participants with BARC Type 3b and above bleeding events

End point title	Secondary safety outcome: Number of participants with BARC Type 3b and above bleeding events

End point description:

BARC: Bleeding Academic Research Consortium Only the first occurrence of the outcome event under analysis within the data scope from a subject is considered

End point type	Secondary

End point timeframe:

For each participant, the first occurrence of the type 3b and above bleeding events according to the BARC classification after randomization up until 2 days after permanent stop of study drug (rivaroxaban or rivaroxaban placebo)

End point values	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od	Rivaroxaban placebo bid + Aspirin 100 mg od		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	3256	3248		
Units: Subject	93	73		

Statistical analyses

Statistical analysis title	BARC Type 3b and above bleeding events
Comparison groups	Rivaroxaban 2.5 mg bid + Aspirin 100 mg od v Rivaroxaban placebo bid + Aspirin 100 mg od
Number of subjects included in analysis	6504
Analysis specification	Pre-specified
Analysis type	other
P-value	= 0.0979
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	1.76

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
From randomization until 2 days following permanent discontinuation of the study drug	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	22.1

Reporting groups	
Reporting group title	Rivaroxaban 2.5 mg bid + ASA 100 mg od
Reporting group description:	
Subjects were treated with Rivaroxaban 2.5 mg twice-daily (bid) and ASA (Acetylsalicylic Acid) 100 mg once-daily (od)	
Reporting group title	Rivaroxaban placebo bid + ASA 100 mg od
Reporting group description:	
Subjects were treated with Rivaroxaban-placebo twice-daily and ASA (Acetylsalicylic Acid) 100 mg once-daily	

Serious adverse events	Rivaroxaban 2.5 mg bid + ASA 100 mg od	Rivaroxaban placebo bid + ASA 100 mg od	
Total subjects affected by serious adverse events			
subjects affected / exposed	948 / 3256 (29.12%)	927 / 3248 (28.54%)	
number of deaths (all causes)	327	304	
number of deaths resulting from adverse events	76	79	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma gastric			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Adenocarcinoma of colon			

subjects affected / exposed	3 / 3256 (0.09%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
B-cell lymphoma			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Basal cell carcinoma			
subjects affected / exposed	3 / 3256 (0.09%)	7 / 3248 (0.22%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign laryngeal neoplasm			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign neoplasm of skin			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Benign ovarian tumour			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct cancer			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer			
subjects affected / exposed	4 / 3256 (0.12%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder cancer stage IV			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Bladder neoplasm			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder transitional cell carcinoma			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone cancer			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Breast cancer			
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchial carcinoma			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Central nervous system lymphoma			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cervix carcinoma			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangiocarcinoma			

subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholesteatoma			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myeloid leukaemia			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic myelomonocytic leukaemia			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colon cancer			
subjects affected / exposed	5 / 3256 (0.15%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Endometrial cancer			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Follicular thyroid cancer			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gallbladder cancer			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			

subjects affected / exposed	5 / 3256 (0.15%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastric cancer stage I			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer stage II			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal cancer			
subjects affected / exposed	1 / 3256 (0.03%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngeal neoplasm			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung adenocarcinoma			
subjects affected / exposed	4 / 3256 (0.12%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung adenocarcinoma recurrent			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung adenocarcinoma stage IV			

subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung carcinoma cell type unspecified recurrent			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung carcinoma cell type unspecified stage IV			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung squamous cell carcinoma stage IV			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to liver			
subjects affected / exposed	3 / 3256 (0.09%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Metastases to lung			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to lymph nodes			
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to neck			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myelodysplastic syndrome			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Neoplasm malignant			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Neoplasm skin			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal adenocarcinoma			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal carcinoma			
subjects affected / exposed	3 / 3256 (0.09%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Oesophageal carcinoma recurrent			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oropharyngeal cancer			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			

subjects affected / exposed	2 / 3256 (0.06%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 2	0 / 2	
Papillary serous endometrial carcinoma			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Plasma cell myeloma			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural mesothelioma			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Prostate cancer stage III			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenocarcinoma			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rectal cancer			
subjects affected / exposed	2 / 3256 (0.06%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Rectal cancer stage I			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal cancer stage IV			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Rectosigmoid cancer			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal cancer			
subjects affected / exposed	3 / 3256 (0.09%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell carcinoma			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small cell lung cancer			
subjects affected / exposed	3 / 3256 (0.09%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 3	0 / 1	
Squamous cell carcinoma			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of lung			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Squamous cell carcinoma of skin			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the oral cavity			

subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma of the tongue			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
T-cell lymphoma			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Transitional cell carcinoma			
subjects affected / exposed	2 / 3256 (0.06%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal adenoma			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colon adenoma			
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung cancer metastatic			
subjects affected / exposed	3 / 3256 (0.09%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 3	0 / 2	
Salivary gland adenoma			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to peritoneum			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colorectal adenocarcinoma			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Adenocarcinoma pancreas			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Oesophageal cancer metastatic			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Neuroendocrine carcinoma			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lung neoplasm malignant			
subjects affected / exposed	8 / 3256 (0.25%)	14 / 3248 (0.43%)	
occurrences causally related to treatment / all	0 / 8	0 / 16	
deaths causally related to treatment / all	0 / 4	0 / 7	
Metastases to central nervous system			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma stage IV			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Non-small cell lung cancer metastatic			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Prostate cancer			
subjects affected / exposed	9 / 3256 (0.28%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 9	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain neoplasm			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thymoma malignant			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic neoplasm			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Colorectal cancer			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract neoplasm			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lip and/or oral cavity cancer			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adrenal neoplasm			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hodgkin's disease stage IV			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal neoplasm			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Pancreatic neoplasm			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Lung neoplasm			
subjects affected / exposed	4 / 3256 (0.12%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 3	
Rectal neoplasm			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastatic squamous cell carcinoma			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gingival cancer			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head and neck cancer			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammatory pseudotumour			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenolymphoma			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung squamous cell carcinoma metastatic			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatic cancer			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hepatocellular carcinoma			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ductal adenocarcinoma of pancreas			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Malignant genitourinary tract neoplasm			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant neoplasm papilla of Vater			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal adenocarcinoma			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin squamous cell carcinoma recurrent			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	2 / 3256 (0.06%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic dissection			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic stenosis			

subjects affected / exposed	6 / 3256 (0.18%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriovenous fistula			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	1 / 3256 (0.03%)	5 / 3248 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	5 / 3256 (0.15%)	6 / 3248 (0.18%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	4 / 3256 (0.12%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication			

subjects affected / exposed	43 / 3256 (1.32%)	52 / 3248 (1.60%)	
occurrences causally related to treatment / all	0 / 51	0 / 58	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoedema			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orthostatic hypotension			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral coldness			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral ischaemia			
subjects affected / exposed	34 / 3256 (1.04%)	29 / 3248 (0.89%)	
occurrences causally related to treatment / all	0 / 44	1 / 46	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral vascular disorder			
subjects affected / exposed	3 / 3256 (0.09%)	5 / 3248 (0.15%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Poor peripheral circulation			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Renovascular hypertension			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Temporal arteritis			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphocele			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dry gangrene			
subjects affected / exposed	2 / 3256 (0.06%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subclavian artery stenosis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphorrhoea			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iliac artery stenosis			
subjects affected / exposed	4 / 3256 (0.12%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stenosis			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery occlusion			
subjects affected / exposed	7 / 3256 (0.21%)	9 / 3248 (0.28%)	
occurrences causally related to treatment / all	0 / 9	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive emergency			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive urgency			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Venous occlusion			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angiopathy			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extremity necrosis			
subjects affected / exposed	12 / 3256 (0.37%)	8 / 3248 (0.25%)	
occurrences causally related to treatment / all	0 / 14	0 / 9	
deaths causally related to treatment / all	0 / 1	0 / 0	
Peripheral embolism			

subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	125 / 3256 (3.84%)	130 / 3248 (4.00%)	
occurrences causally related to treatment / all	1 / 156	0 / 182	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial occlusive disease			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic limb pain			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphatic fistula			
subjects affected / exposed	0 / 3256 (0.00%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stenosis			
subjects affected / exposed	25 / 3256 (0.77%)	14 / 3248 (0.43%)	
occurrences causally related to treatment / all	0 / 29	0 / 17	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery thrombosis			
subjects affected / exposed	2 / 3256 (0.06%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral venous disease			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Bladder calculus removal			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blepharoplasty			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid endarterectomy			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot amputation			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Knee arthroplasty			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia repair			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitrectomy			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Radical prostatectomy			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus management			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transurethral bladder resection			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral revascularisation			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain tumour operation			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystoprostatectomy			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery angioplasty			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Amputation			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder polypectomy			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bladder neoplasm surgery			

subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb reconstructive surgery			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery bypass			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery stent insertion			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eventration repair			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest discomfort			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	4 / 3256 (0.12%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crepitations			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gait disturbance			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Granuloma			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired healing			
subjects affected / exposed	3 / 3256 (0.09%)	7 / 3248 (0.22%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral swelling			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Puncture site haemorrhage			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Organ failure			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Inflammation			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug intolerance			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	3 / 3256 (0.09%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent thrombosis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stent-graft endoleak			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent occlusion			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular stent stenosis			
subjects affected / exposed	11 / 3256 (0.34%)	8 / 3248 (0.25%)	
occurrences causally related to treatment / all	2 / 11	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Vascular device occlusion			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Anaphylactic reaction			

subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypersensitivity			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Social circumstances			
Disease risk factor			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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	3 / 3256 (0.09%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical polyp			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic prolapse			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spermatocele			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Uterine prolapse			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vulvar dysplasia			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Prostatic obstruction			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vulval eczema			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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	2 / 3256 (0.06%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	2 / 3256 (0.06%)	5 / 3248 (0.15%)	
occurrences causally related to treatment / all	0 / 2	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 1	
Aspiration			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Asthma			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	

Chronic obstructive pulmonary disease			
subjects affected / exposed	16 / 3256 (0.49%)	9 / 3248 (0.28%)	
occurrences causally related to treatment / all	0 / 23	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cough			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	4 / 3256 (0.12%)	6 / 3248 (0.18%)	
occurrences causally related to treatment / all	0 / 5	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Emphysema			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoxia			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Interstitial lung disease			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal polyps			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nasal septum deviation			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			

subjects affected / exposed	3 / 3256 (0.09%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	5 / 3256 (0.15%)	6 / 3248 (0.18%)	
occurrences causally related to treatment / all	0 / 6	0 / 6	
deaths causally related to treatment / all	0 / 1	0 / 3	
Pneumothorax			
subjects affected / exposed	3 / 3256 (0.09%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax spontaneous			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary congestion			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary fibrosis			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pulmonary hypertension			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory distress			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Respiratory failure			
subjects affected / exposed	5 / 3256 (0.15%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 5	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 3	
Sinus polyp			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vocal cord polyp			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngeal lesion			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary mass			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillar cyst			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic respiratory disease			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Acute interstitial pneumonitis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Acute psychosis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol abuse			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholism			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Completed suicide			
subjects affected / exposed	4 / 3256 (0.12%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 4	0 / 0	
Depression			
subjects affected / exposed	3 / 3256 (0.09%)	5 / 3248 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug abuse			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intentional self-injury			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	1 / 3256 (0.03%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol withdrawal syndrome			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient psychosis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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 breakage			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device dislocation			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device occlusion			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patient-device incompatibility			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device battery issue			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	3 / 3256 (0.09%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	1 / 3256 (0.03%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis acute			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	7 / 3256 (0.21%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 7	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	2 / 3256 (0.06%)	12 / 3248 (0.37%)	
occurrences causally related to treatment / all	0 / 2	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cirrhosis alcoholic			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	3 / 3256 (0.09%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Hepatic failure			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic steatosis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatorenal syndrome			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bile duct obstruction			
subjects affected / exposed	0 / 3256 (0.00%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary dyskinesia			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Steatohepatitis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Primary biliary cholangitis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Blood creatinine increased			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood glucose increased			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood potassium increased			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood pressure increased			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiovascular function test abnormal			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystoscopy			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immunoglobulins decreased			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbohydrate antigen 19-9 increased			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac stress test abnormal			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular test			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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			
Accidental overdose			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcohol poisoning			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ankle fracture			

subjects affected / exposed	2 / 3256 (0.06%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain herniation			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbon monoxide poisoning			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compression fracture			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Concussion			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial bones fracture			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to anastomose			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	5 / 3256 (0.15%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Femoral neck fracture			

subjects affected / exposed	4 / 3256 (0.12%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	10 / 3256 (0.31%)	12 / 3248 (0.37%)	
occurrences causally related to treatment / all	0 / 10	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	3 / 3256 (0.09%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot fracture			
subjects affected / exposed	2 / 3256 (0.06%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Forearm fracture			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fractured sacrum			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Head injury			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			
subjects affected / exposed	5 / 3256 (0.15%)	5 / 3248 (0.15%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Humerus fracture			

subjects affected / exposed	1 / 3256 (0.03%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intentional overdose			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Joint dislocation			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple injuries			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Open fracture			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Patella fracture			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Penetrating abdominal trauma			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Radius fracture				
subjects affected / exposed	3 / 3256 (0.09%)	2 / 3248 (0.06%)		
occurrences causally related to treatment / all	0 / 3	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
Rib fracture				
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)		
occurrences causally related to treatment / all	0 / 2	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Road traffic accident				
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)		
occurrences causally related to treatment / all	0 / 1	0 / 0		
deaths causally related to treatment / all	0 / 1	0 / 0		
Seroma				
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)		
occurrences causally related to treatment / all	0 / 1	0 / 2		
deaths causally related to treatment / all	0 / 0	0 / 0		
Skull fractured base				
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	1 / 3256 (0.03%)	4 / 3248 (0.12%)		
occurrences causally related to treatment / all	0 / 1	0 / 5		
deaths causally related to treatment / all	0 / 0	0 / 0		
Spinal fracture				
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)		
occurrences causally related to treatment / all	0 / 0	0 / 1		
deaths causally related to treatment / all	0 / 0	0 / 0		
Tendon rupture				

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	3 / 3256 (0.09%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic ulcer			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound dehiscence			
subjects affected / exposed	4 / 3256 (0.12%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft occlusion			
subjects affected / exposed	1 / 3256 (0.03%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic fracture			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar vertebral fracture			
subjects affected / exposed	2 / 3256 (0.06%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thoracic vertebral fracture			

subjects affected / exposed	2 / 3256 (0.06%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anastomotic stenosis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft thrombosis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound complication			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound necrosis			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery restenosis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative thoracic procedure complication			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post laminectomy syndrome			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Underdose			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular procedure complication			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Post procedural bile leak			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural discharge			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural complication			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chemical burn of skin			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural complication			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Limb injury			
subjects affected / exposed	2 / 3256 (0.06%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest injury			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Traumatic intracranial haemorrhage			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural oedema			

subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft complication			
subjects affected / exposed	5 / 3256 (0.15%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral hyperperfusion syndrome			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal anastomotic leak			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone contusion			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periprosthetic fracture			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial reocclusion			
subjects affected / exposed	4 / 3256 (0.12%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column injury			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft thrombosis			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pubis fracture			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral artery restenosis			
subjects affected / exposed	16 / 3256 (0.49%)	15 / 3248 (0.46%)	
occurrences causally related to treatment / all	0 / 22	0 / 18	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	2 / 3256 (0.06%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin scar contracture			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Procedural intestinal perforation			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft stenosis			
subjects affected / exposed	2 / 3256 (0.06%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular graft restenosis			

subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular access site haematoma			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial bypass thrombosis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial bypass occlusion			
subjects affected / exposed	2 / 3256 (0.06%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial bypass stenosis			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foreign body in gastrointestinal tract			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Congenital bladder neck obstruction			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocele			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Phimosis			

subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenomatous polyposis coli			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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 myocardial infarction			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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	10 / 3256 (0.31%)	10 / 3248 (0.31%)	
occurrences causally related to treatment / all	0 / 11	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Angina unstable			
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aortic valve stenosis			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia			
subjects affected / exposed	3 / 3256 (0.09%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arrhythmia supraventricular			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerosis coronary artery			

subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	19 / 3256 (0.58%)	20 / 3248 (0.62%)	
occurrences causally related to treatment / all	0 / 19	0 / 21	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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	3 / 3256 (0.09%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block first degree			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac arrest			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			

subjects affected / exposed	14 / 3256 (0.43%)	14 / 3248 (0.43%)	
occurrences causally related to treatment / all	0 / 16	0 / 15	
deaths causally related to treatment / all	0 / 1	0 / 2	
Cardiac failure acute			
subjects affected / exposed	3 / 3256 (0.09%)	6 / 3248 (0.18%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure chronic			
subjects affected / exposed	6 / 3256 (0.18%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 8	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure congestive			
subjects affected / exposed	10 / 3256 (0.31%)	8 / 3248 (0.25%)	
occurrences causally related to treatment / all	0 / 11	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiac tamponade			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardio-respiratory arrest			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Cardiogenic shock			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery disease			
subjects affected / exposed	15 / 3256 (0.46%)	21 / 3248 (0.65%)	
occurrences causally related to treatment / all	0 / 18	0 / 21	
deaths causally related to treatment / all	0 / 1	0 / 0	
Coronary artery occlusion			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery stenosis			
subjects affected / exposed	4 / 3256 (0.12%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cyanosis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive heart disease			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial infarction			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial effusion			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pericardial haemorrhage			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Pericarditis			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrest			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	3 / 3256 (0.09%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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 / 3256 (0.00%)	1 / 3248 (0.03%)	
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 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Congestive cardiomyopathy			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachyarrhythmia			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stress cardiomyopathy			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	22 / 3256 (0.68%)	24 / 3248 (0.74%)	
occurrences causally related to treatment / all	0 / 23	0 / 26	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			

subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral atrophy			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral haemorrhage			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebral infarction			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia			
subjects affected / exposed	3 / 3256 (0.09%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic neuropathy			
subjects affected / exposed	2 / 3256 (0.06%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	5 / 3256 (0.15%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness postural			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drop attacks			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Epilepsy			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Guillain-Barre syndrome			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydrocephalus			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental impairment			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelopathy			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nerve compression			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neuralgia			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinsonism			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polyneuropathy			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Presyncope			
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sciatica			
subjects affected / exposed	2 / 3256 (0.06%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Somnolence			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal claudication			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Status epilepticus			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Syncope			
subjects affected / exposed	9 / 3256 (0.28%)	11 / 3248 (0.34%)	
occurrences causally related to treatment / all	1 / 9	0 / 12	
deaths causally related to treatment / all	0 / 1	0 / 0	
Tension headache			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonic convulsion			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical radiculopathy			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar radiculopathy			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Facial paresis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic neuropathy			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Restless legs syndrome			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Putamen haemorrhage			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cranial nerve disorder			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Parkinson's disease			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery disease			

subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular encephalopathy			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudoradicular syndrome			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Brain injury			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Colloid brain cyst			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sacral radiculopathy			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	14 / 3256 (0.43%)	10 / 3248 (0.31%)	
occurrences causally related to treatment / all	10 / 16	4 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	4 / 3256 (0.12%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	2 / 4	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Microcytic anaemia			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normochromic normocytic anaemia			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normocytic anaemia			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytosis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrogenic anaemia			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood loss anaemia			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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			

subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden hearing loss			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Cataract			
subjects affected / exposed	8 / 3256 (0.25%)	8 / 3248 (0.25%)	
occurrences causally related to treatment / all	0 / 9	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract subcapsular			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic retinopathy			
subjects affected / exposed	3 / 3256 (0.09%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eyelid ptosis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glaucoma			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iridocyclitis			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular degeneration			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular oedema			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myopia			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Retinal detachment			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreous haemorrhage			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular hole			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Detachment of macular retinal pigment epithelium			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vitreoretinal traction syndrome			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular detachment			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal adhesions			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal mass			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	3 / 3256 (0.09%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain lower			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fissure			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal stenosis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ascites			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic gastritis			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis ischaemic			
subjects affected / exposed	2 / 3256 (0.06%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Crohn's disease			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dental alveolar anomaly			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diaphragmatic hernia			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	3 / 3256 (0.09%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulum intestinal haemorrhagic			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dry mouth			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	3 / 3256 (0.09%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gallstone ileus			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric polyps			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer			
subjects affected / exposed	3 / 3256 (0.09%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric ulcer haemorrhage			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	3 / 3256 (0.09%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal necrosis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hiatus hernia			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Impaired gastric emptying			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia			
subjects affected / exposed	4 / 3256 (0.12%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 4	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal angina			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ischaemia			
subjects affected / exposed	4 / 3256 (0.12%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 4	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 2	
Intestinal obstruction			
subjects affected / exposed	3 / 3256 (0.09%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Intestinal perforation			

subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal ulcer			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine perforation			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophagitis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis			
subjects affected / exposed	4 / 3256 (0.12%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 4	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 3256 (0.03%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis chronic			
subjects affected / exposed	0 / 3256 (0.00%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis necrotising			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peptic ulcer perforation			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periodontal disease			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal obstruction			
subjects affected / exposed	0 / 3256 (0.00%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small intestinal perforation			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tooth loss			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia, obstructive			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper gastrointestinal haemorrhage			

subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Volvulus			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic mass			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mechanical ileus			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric antral vascular ectasia			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine polyp			

subjects affected / exposed	10 / 3256 (0.31%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 10	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedematous pancreatitis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alcoholic pancreatitis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestinal obstruction			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterovesical fistula			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic duct stenosis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal incarcerated hernia			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obstructive pancreatitis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Angioedema			

subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decubitus ulcer			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermal cyst			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis allergic			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermatitis contact			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhage subcutaneous			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hidradenitis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pemphigoid			

subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pemphigus			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin exfoliation			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin lesion			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin necrosis			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	10 / 3256 (0.31%)	12 / 3248 (0.37%)	
occurrences causally related to treatment / all	0 / 11	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urticaria			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ulcer			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toxic skin eruption			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	9 / 3256 (0.28%)	9 / 3248 (0.28%)	
occurrences causally related to treatment / all	0 / 9	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic skin ulcer			
subjects affected / exposed	1 / 3256 (0.03%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myxoid cyst			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Calculus bladder			
subjects affected / exposed	3 / 3256 (0.09%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Calculus urinary			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nephrolithiasis			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
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	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal artery stenosis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal colic			
subjects affected / exposed	4 / 3256 (0.12%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	6 / 3256 (0.18%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	1 / 8	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ureteric fistula			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract obstruction			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal impairment			

subjects affected / exposed	3 / 3256 (0.09%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	1 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	5 / 3256 (0.15%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 0	
Urethral stenosis			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	9 / 3256 (0.28%)	17 / 3248 (0.52%)	
occurrences causally related to treatment / all	0 / 9	1 / 17	
deaths causally related to treatment / all	0 / 0	0 / 1	
End stage renal disease			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ureterolithiasis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Goitre			
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thyroid mass			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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			

Arthritis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	3 / 3256 (0.09%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone disorder			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone formation increased			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical spinal stenosis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Compartment syndrome			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fracture nonunion			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gouty arthritis			

subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaw cyst			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lumbar spinal stenosis			
subjects affected / exposed	3 / 3256 (0.09%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metatarsalgia			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle disorder			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle spasms			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteitis			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	14 / 3256 (0.43%)	13 / 3248 (0.40%)	
occurrences causally related to treatment / all	2 / 18	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteonecrosis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoporotic fracture			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			
subjects affected / exposed	6 / 3256 (0.18%)	14 / 3248 (0.43%)	
occurrences causally related to treatment / all	0 / 6	1 / 15	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polymyalgia rheumatica			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rotator cuff syndrome			

subjects affected / exposed	0 / 3256 (0.00%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	2 / 3256 (0.06%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Synovial cyst			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tendon disorder			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudarthrosis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	6 / 3256 (0.18%)	6 / 3248 (0.18%)	
occurrences causally related to treatment / all	0 / 7	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondyloarthropathy			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertebral column mass			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acquired claw toe			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Foot deformity			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ligament disorder			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue disorder			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spondylolisthesis			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone loss			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Soft tissue necrosis			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic scleroderma			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal stenosis			
subjects affected / exposed	6 / 3256 (0.18%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 6	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abscess			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute sinusitis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	4 / 3256 (0.12%)	5 / 3248 (0.15%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arteriosclerotic gangrene			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blister infected			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchiolitis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carbuncle			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	19 / 3256 (0.58%)	18 / 3248 (0.55%)	
occurrences causally related to treatment / all	0 / 19	1 / 20	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis gangrenous			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	2 / 3256 (0.06%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic gangrene			
subjects affected / exposed	2 / 3256 (0.06%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea infectious			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	4 / 3256 (0.12%)	5 / 3248 (0.15%)	
occurrences causally related to treatment / all	0 / 4	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear infection			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eczema infected			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	1 / 3256 (0.03%)	0 / 3248 (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	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			

subjects affected / exposed	1 / 3256 (0.03%)	10 / 3248 (0.31%)	
occurrences causally related to treatment / all	0 / 1	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Escherichia sepsis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fournier's gangrene			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal cystitis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fungal skin infection			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gangrene			
subjects affected / exposed	16 / 3256 (0.49%)	20 / 3248 (0.62%)	
occurrences causally related to treatment / all	0 / 18	0 / 22	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	3 / 3256 (0.09%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis salmonella			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis viral			

subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected skin ulcer			
subjects affected / exposed	6 / 3256 (0.18%)	4 / 3248 (0.12%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Localised infection			
subjects affected / exposed	19 / 3256 (0.58%)	11 / 3248 (0.34%)	
occurrences causally related to treatment / all	0 / 19	0 / 11	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphangitis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mastoiditis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal candidiasis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ophthalmic herpes zoster			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	11 / 3256 (0.34%)	12 / 3248 (0.37%)	
occurrences causally related to treatment / all	0 / 15	0 / 14	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis chronic			
subjects affected / exposed	3 / 3256 (0.09%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Otitis media			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perinephric abscess			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periodontitis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pharyngitis			

subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	40 / 3256 (1.23%)	45 / 3248 (1.39%)	
occurrences causally related to treatment / all	0 / 49	0 / 50	
deaths causally related to treatment / all	0 / 5	0 / 4	
Postoperative wound infection			
subjects affected / exposed	27 / 3256 (0.83%)	25 / 3248 (0.77%)	
occurrences causally related to treatment / all	0 / 28	0 / 26	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pseudomembranous colitis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis			
subjects affected / exposed	1 / 3256 (0.03%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyelonephritis acute			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sepsis			
subjects affected / exposed	12 / 3256 (0.37%)	13 / 3248 (0.40%)	
occurrences causally related to treatment / all	0 / 12	0 / 13	
deaths causally related to treatment / all	0 / 3	0 / 4	
Septic shock			

subjects affected / exposed	1 / 3256 (0.03%)	5 / 3248 (0.15%)	
occurrences causally related to treatment / all	0 / 1	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 4	
Sinusitis			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin infection			
subjects affected / exposed	2 / 3256 (0.06%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subcutaneous abscess			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (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	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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	13 / 3256 (0.40%)	11 / 3248 (0.34%)	
occurrences causally related to treatment / all	0 / 17	0 / 13	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	17 / 3256 (0.52%)	15 / 3248 (0.46%)	
occurrences causally related to treatment / all	0 / 19	0 / 16	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			

subjects affected / exposed	0 / 3256 (0.00%)	5 / 3248 (0.15%)	
occurrences causally related to treatment / all	0 / 0	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal sepsis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Scrotal abscess			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin abscess			
subjects affected / exposed	3 / 3256 (0.09%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess limb			
subjects affected / exposed	6 / 3256 (0.18%)	5 / 3248 (0.15%)	
occurrences causally related to treatment / all	0 / 8	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin infection			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Lymph gland infection			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periumbilical abscess			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Burn infection			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haematoma infection			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary sepsis			
subjects affected / exposed	1 / 3256 (0.03%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 1	0 / 1	
Perineal abscess			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis bacterial			
subjects affected / exposed	2 / 3256 (0.06%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal infection			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Graft infection			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric infection			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of chronic obstructive airways disease			

subjects affected / exposed	3 / 3256 (0.09%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected lymphocele			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot infection			
subjects affected / exposed	1 / 3256 (0.03%)	6 / 3248 (0.18%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia bacterial			
subjects affected / exposed	2 / 3256 (0.06%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arthritis infective			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extradural abscess			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Soft tissue infection			
subjects affected / exposed	2 / 3256 (0.06%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Respiratory tract infection			

subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis infective			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
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	2 / 3256 (0.06%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cystitis bacterial			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteomyelitis bacterial			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermo-hypodermitis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Post procedural sepsis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Superinfection bacterial			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			

subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bone abscess			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infectious pleural effusion			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumocystis jirovecii pneumonia			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infected seroma			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site infection			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site joint infection			
subjects affected / exposed	0 / 3256 (0.00%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Perineal cellulitis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular device infection			

subjects affected / exposed	2 / 3256 (0.06%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Complicated appendicitis			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Large intestine infection			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	6 / 3256 (0.18%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 6	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	6 / 3256 (0.18%)	8 / 3248 (0.25%)	
occurrences causally related to treatment / all	0 / 6	0 / 9	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic ketoacidosis			
subjects affected / exposed	2 / 3256 (0.06%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	1 / 3256 (0.03%)	3 / 3248 (0.09%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			

subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypoglycaemia			
subjects affected / exposed	3 / 3256 (0.09%)	6 / 3248 (0.18%)	
occurrences causally related to treatment / all	0 / 3	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	3 / 3256 (0.09%)	5 / 3248 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ketoacidosis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lactic acidosis			
subjects affected / exposed	1 / 3256 (0.03%)	0 / 3248 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metabolic disorder			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemic hyperosmolar nonketotic syndrome			

subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypophagia			
subjects affected / exposed	0 / 3256 (0.00%)	1 / 3248 (0.03%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Type 1 diabetes mellitus			
subjects affected / exposed	0 / 3256 (0.00%)	2 / 3248 (0.06%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	3 / 3256 (0.09%)	5 / 3248 (0.15%)	
occurrences causally related to treatment / all	0 / 3	0 / 6	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic metabolic decompensation			
subjects affected / exposed	1 / 3256 (0.03%)	1 / 3248 (0.03%)	
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: 0.1 %

Non-serious adverse events	Rivaroxaban 2.5 mg bid + ASA 100 mg od	Rivaroxaban placebo bid + ASA 100 mg od	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	725 / 3256 (22.27%)	729 / 3248 (22.44%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Prostate cancer			
subjects affected / exposed	1 / 3256 (0.03%)	4 / 3248 (0.12%)	
occurrences (all)	1	4	
Vascular disorders			
Hypertension			
subjects affected / exposed	49 / 3256 (1.50%)	50 / 3248 (1.54%)	
occurrences (all)	54	56	

Hypotension			
subjects affected / exposed	7 / 3256 (0.21%)	3 / 3248 (0.09%)	
occurrences (all)	7	3	
Hypertensive crisis			
subjects affected / exposed	11 / 3256 (0.34%)	13 / 3248 (0.40%)	
occurrences (all)	13	15	
Peripheral ischaemia			
subjects affected / exposed	3 / 3256 (0.09%)	11 / 3248 (0.34%)	
occurrences (all)	3	14	
Intermittent claudication			
subjects affected / exposed	39 / 3256 (1.20%)	43 / 3248 (1.32%)	
occurrences (all)	48	48	
Peripheral vascular disorder			
subjects affected / exposed	6 / 3256 (0.18%)	5 / 3248 (0.15%)	
occurrences (all)	8	5	
Dry gangrene			
subjects affected / exposed	1 / 3256 (0.03%)	4 / 3248 (0.12%)	
occurrences (all)	1	4	
Peripheral artery occlusion			
subjects affected / exposed	6 / 3256 (0.18%)	12 / 3248 (0.37%)	
occurrences (all)	6	13	
Extremity necrosis			
subjects affected / exposed	6 / 3256 (0.18%)	5 / 3248 (0.15%)	
occurrences (all)	7	5	
Peripheral arterial occlusive disease			
subjects affected / exposed	34 / 3256 (1.04%)	31 / 3248 (0.95%)	
occurrences (all)	45	37	
Peripheral artery stenosis			
subjects affected / exposed	13 / 3256 (0.40%)	10 / 3248 (0.31%)	
occurrences (all)	16	13	
Surgical and medical procedures			
Tooth extraction			
subjects affected / exposed	6 / 3256 (0.18%)	5 / 3248 (0.15%)	
occurrences (all)	7	5	
Cataract operation			

subjects affected / exposed	5 / 3256 (0.15%)	8 / 3248 (0.25%)	
occurrences (all)	6	10	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	6 / 3256 (0.18%)	4 / 3248 (0.12%)	
occurrences (all)	6	4	
Chest discomfort			
subjects affected / exposed	6 / 3256 (0.18%)	1 / 3248 (0.03%)	
occurrences (all)	6	1	
Chest pain			
subjects affected / exposed	11 / 3256 (0.34%)	16 / 3248 (0.49%)	
occurrences (all)	12	16	
Fatigue			
subjects affected / exposed	11 / 3256 (0.34%)	12 / 3248 (0.37%)	
occurrences (all)	11	14	
Gait disturbance			
subjects affected / exposed	5 / 3256 (0.15%)	2 / 3248 (0.06%)	
occurrences (all)	5	2	
Impaired healing			
subjects affected / exposed	4 / 3256 (0.12%)	2 / 3248 (0.06%)	
occurrences (all)	4	2	
Oedema peripheral			
subjects affected / exposed	16 / 3256 (0.49%)	20 / 3248 (0.62%)	
occurrences (all)	17	21	
Peripheral swelling			
subjects affected / exposed	9 / 3256 (0.28%)	10 / 3248 (0.31%)	
occurrences (all)	10	10	
Non-cardiac chest pain			
subjects affected / exposed	5 / 3256 (0.15%)	3 / 3248 (0.09%)	
occurrences (all)	5	3	
Vascular stent stenosis			
subjects affected / exposed	9 / 3256 (0.28%)	10 / 3248 (0.31%)	
occurrences (all)	10	10	
Immune system disorders			

Hypersensitivity			
subjects affected / exposed	1 / 3256 (0.03%)	5 / 3248 (0.15%)	
occurrences (all)	1	5	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	5 / 3256 (0.15%)	9 / 3248 (0.28%)	
occurrences (all)	5	9	
Respiratory, thoracic and mediastinal disorders			
Chronic obstructive pulmonary disease			
subjects affected / exposed	6 / 3256 (0.18%)	4 / 3248 (0.12%)	
occurrences (all)	6	5	
Cough			
subjects affected / exposed	8 / 3256 (0.25%)	14 / 3248 (0.43%)	
occurrences (all)	8	14	
Dyspnoea			
subjects affected / exposed	11 / 3256 (0.34%)	15 / 3248 (0.46%)	
occurrences (all)	11	15	
Dyspnoea exertional			
subjects affected / exposed	3 / 3256 (0.09%)	5 / 3248 (0.15%)	
occurrences (all)	3	5	
Epistaxis			
subjects affected / exposed	9 / 3256 (0.28%)	3 / 3248 (0.09%)	
occurrences (all)	14	3	
Psychiatric disorders			
Delirium			
subjects affected / exposed	0 / 3256 (0.00%)	4 / 3248 (0.12%)	
occurrences (all)	0	4	
Depression			
subjects affected / exposed	11 / 3256 (0.34%)	14 / 3248 (0.43%)	
occurrences (all)	12	14	
Investigations			
Blood pressure increased			
subjects affected / exposed	4 / 3256 (0.12%)	6 / 3248 (0.18%)	
occurrences (all)	5	6	
Haemoglobin decreased			

subjects affected / exposed	5 / 3256 (0.15%)	2 / 3248 (0.06%)	
occurrences (all)	5	2	
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	6 / 3256 (0.18%)	6 / 3248 (0.18%)	
occurrences (all)	6	6	
Foot fracture			
subjects affected / exposed	5 / 3256 (0.15%)	2 / 3248 (0.06%)	
occurrences (all)	5	2	
Ligament sprain			
subjects affected / exposed	0 / 3256 (0.00%)	5 / 3248 (0.15%)	
occurrences (all)	0	5	
Rib fracture			
subjects affected / exposed	2 / 3256 (0.06%)	6 / 3248 (0.18%)	
occurrences (all)	2	6	
Muscle strain			
subjects affected / exposed	4 / 3256 (0.12%)	3 / 3248 (0.09%)	
occurrences (all)	4	3	
Contusion			
subjects affected / exposed	9 / 3256 (0.28%)	10 / 3248 (0.31%)	
occurrences (all)	11	11	
Limb injury			
subjects affected / exposed	11 / 3256 (0.34%)	11 / 3248 (0.34%)	
occurrences (all)	11	11	
Peripheral artery restenosis			
subjects affected / exposed	5 / 3256 (0.15%)	6 / 3248 (0.18%)	
occurrences (all)	8	8	
Meniscus injury			
subjects affected / exposed	2 / 3256 (0.06%)	4 / 3248 (0.12%)	
occurrences (all)	2	4	
Arterial bypass occlusion			
subjects affected / exposed	2 / 3256 (0.06%)	5 / 3248 (0.15%)	
occurrences (all)	2	5	
Cardiac disorders			

Angina pectoris			
subjects affected / exposed	9 / 3256 (0.28%)	7 / 3248 (0.22%)	
occurrences (all)	10	7	
Atrial fibrillation			
subjects affected / exposed	31 / 3256 (0.95%)	48 / 3248 (1.48%)	
occurrences (all)	33	49	
Atrial flutter			
subjects affected / exposed	7 / 3256 (0.21%)	2 / 3248 (0.06%)	
occurrences (all)	7	2	
Cardiac failure			
subjects affected / exposed	3 / 3256 (0.09%)	7 / 3248 (0.22%)	
occurrences (all)	4	7	
Coronary artery disease			
subjects affected / exposed	12 / 3256 (0.37%)	9 / 3248 (0.28%)	
occurrences (all)	13	9	
Myocardial ischaemia			
subjects affected / exposed	6 / 3256 (0.18%)	1 / 3248 (0.03%)	
occurrences (all)	6	1	
Palpitations			
subjects affected / exposed	3 / 3256 (0.09%)	4 / 3248 (0.12%)	
occurrences (all)	3	4	
Sinus tachycardia			
subjects affected / exposed	4 / 3256 (0.12%)	0 / 3248 (0.00%)	
occurrences (all)	4	0	
Nervous system disorders			
Carotid artery stenosis			
subjects affected / exposed	3 / 3256 (0.09%)	8 / 3248 (0.25%)	
occurrences (all)	3	10	
Carpal tunnel syndrome			
subjects affected / exposed	2 / 3256 (0.06%)	6 / 3248 (0.18%)	
occurrences (all)	2	6	
Diabetic neuropathy			
subjects affected / exposed	3 / 3256 (0.09%)	4 / 3248 (0.12%)	
occurrences (all)	3	4	
Dizziness			

subjects affected / exposed	23 / 3256 (0.71%)	26 / 3248 (0.80%)	
occurrences (all)	27	28	
Headache			
subjects affected / exposed	18 / 3256 (0.55%)	19 / 3248 (0.58%)	
occurrences (all)	20	21	
Hypoaesthesia			
subjects affected / exposed	6 / 3256 (0.18%)	8 / 3248 (0.25%)	
occurrences (all)	7	9	
Neuropathy peripheral			
subjects affected / exposed	5 / 3256 (0.15%)	1 / 3248 (0.03%)	
occurrences (all)	5	1	
Paraesthesia			
subjects affected / exposed	4 / 3256 (0.12%)	9 / 3248 (0.28%)	
occurrences (all)	4	9	
Sciatica			
subjects affected / exposed	6 / 3256 (0.18%)	13 / 3248 (0.40%)	
occurrences (all)	6	14	
Syncope			
subjects affected / exposed	3 / 3256 (0.09%)	9 / 3248 (0.28%)	
occurrences (all)	3	10	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	29 / 3256 (0.89%)	23 / 3248 (0.71%)	
occurrences (all)	29	23	
Iron deficiency anaemia			
subjects affected / exposed	8 / 3256 (0.25%)	3 / 3248 (0.09%)	
occurrences (all)	9	3	
Ear and labyrinth disorders			
Tinnitus			
subjects affected / exposed	4 / 3256 (0.12%)	3 / 3248 (0.09%)	
occurrences (all)	5	3	
Vertigo			
subjects affected / exposed	7 / 3256 (0.21%)	11 / 3248 (0.34%)	
occurrences (all)	7	13	
Eye disorders			

Cataract			
subjects affected / exposed	14 / 3256 (0.43%)	9 / 3248 (0.28%)	
occurrences (all)	17	9	
Diabetic retinopathy			
subjects affected / exposed	4 / 3256 (0.12%)	0 / 3248 (0.00%)	
occurrences (all)	4	0	
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	6 / 3256 (0.18%)	3 / 3248 (0.09%)	
occurrences (all)	7	3	
Abdominal pain			
subjects affected / exposed	6 / 3256 (0.18%)	6 / 3248 (0.18%)	
occurrences (all)	6	6	
Abdominal pain upper			
subjects affected / exposed	19 / 3256 (0.58%)	15 / 3248 (0.46%)	
occurrences (all)	19	16	
Constipation			
subjects affected / exposed	11 / 3256 (0.34%)	13 / 3248 (0.40%)	
occurrences (all)	11	13	
Diarrhoea			
subjects affected / exposed	23 / 3256 (0.71%)	22 / 3248 (0.68%)	
occurrences (all)	24	22	
Diverticulum intestinal			
subjects affected / exposed	1 / 3256 (0.03%)	4 / 3248 (0.12%)	
occurrences (all)	1	4	
Duodenal ulcer			
subjects affected / exposed	4 / 3256 (0.12%)	0 / 3248 (0.00%)	
occurrences (all)	4	0	
Dyspepsia			
subjects affected / exposed	15 / 3256 (0.46%)	8 / 3248 (0.25%)	
occurrences (all)	16	8	
Gastric ulcer			
subjects affected / exposed	4 / 3256 (0.12%)	5 / 3248 (0.15%)	
occurrences (all)	4	5	
Gastritis			

subjects affected / exposed	15 / 3256 (0.46%)	8 / 3248 (0.25%)	
occurrences (all)	15	8	
Gastritis erosive			
subjects affected / exposed	2 / 3256 (0.06%)	5 / 3248 (0.15%)	
occurrences (all)	2	5	
Gastrooesophageal reflux disease			
subjects affected / exposed	8 / 3256 (0.25%)	8 / 3248 (0.25%)	
occurrences (all)	8	9	
Hiatus hernia			
subjects affected / exposed	4 / 3256 (0.12%)	2 / 3248 (0.06%)	
occurrences (all)	4	2	
Inguinal hernia			
subjects affected / exposed	1 / 3256 (0.03%)	5 / 3248 (0.15%)	
occurrences (all)	1	5	
Nausea			
subjects affected / exposed	14 / 3256 (0.43%)	10 / 3248 (0.31%)	
occurrences (all)	14	10	
Vomiting			
subjects affected / exposed	7 / 3256 (0.21%)	13 / 3248 (0.40%)	
occurrences (all)	7	13	
Large intestine polyp			
subjects affected / exposed	6 / 3256 (0.18%)	4 / 3248 (0.12%)	
occurrences (all)	6	4	
Hepatobiliary disorders			
Hepatic steatosis			
subjects affected / exposed	4 / 3256 (0.12%)	2 / 3248 (0.06%)	
occurrences (all)	4	2	
Skin and subcutaneous tissue disorders			
Dermatitis allergic			
subjects affected / exposed	1 / 3256 (0.03%)	4 / 3248 (0.12%)	
occurrences (all)	1	4	
Ecchymosis			
subjects affected / exposed	5 / 3256 (0.15%)	2 / 3248 (0.06%)	
occurrences (all)	5	2	
Eczema			

subjects affected / exposed	2 / 3256 (0.06%)	4 / 3248 (0.12%)	
occurrences (all)	2	4	
Erythema			
subjects affected / exposed	2 / 3256 (0.06%)	5 / 3248 (0.15%)	
occurrences (all)	2	5	
Pruritus			
subjects affected / exposed	10 / 3256 (0.31%)	7 / 3248 (0.22%)	
occurrences (all)	11	7	
Rash			
subjects affected / exposed	16 / 3256 (0.49%)	18 / 3248 (0.55%)	
occurrences (all)	16	20	
Skin ulcer			
subjects affected / exposed	16 / 3256 (0.49%)	18 / 3248 (0.55%)	
occurrences (all)	17	18	
Urticaria			
subjects affected / exposed	7 / 3256 (0.21%)	5 / 3248 (0.15%)	
occurrences (all)	7	5	
Diabetic foot			
subjects affected / exposed	6 / 3256 (0.18%)	1 / 3248 (0.03%)	
occurrences (all)	6	1	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	3 / 3256 (0.09%)	4 / 3248 (0.12%)	
occurrences (all)	3	4	
Haematuria			
subjects affected / exposed	4 / 3256 (0.12%)	2 / 3248 (0.06%)	
occurrences (all)	4	2	
Renal failure			
subjects affected / exposed	2 / 3256 (0.06%)	5 / 3248 (0.15%)	
occurrences (all)	2	6	
Renal impairment			
subjects affected / exposed	4 / 3256 (0.12%)	6 / 3248 (0.18%)	
occurrences (all)	5	6	
Chronic kidney disease			
subjects affected / exposed	8 / 3256 (0.25%)	1 / 3248 (0.03%)	
occurrences (all)	8	1	

Acute kidney injury			
subjects affected / exposed	7 / 3256 (0.21%)	4 / 3248 (0.12%)	
occurrences (all)	8	4	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	18 / 3256 (0.55%)	32 / 3248 (0.99%)	
occurrences (all)	19	37	
Bursitis			
subjects affected / exposed	5 / 3256 (0.15%)	7 / 3248 (0.22%)	
occurrences (all)	6	7	
Back pain			
subjects affected / exposed	23 / 3256 (0.71%)	30 / 3248 (0.92%)	
occurrences (all)	25	33	
Joint swelling			
subjects affected / exposed	6 / 3256 (0.18%)	2 / 3248 (0.06%)	
occurrences (all)	6	2	
Lumbar spinal stenosis			
subjects affected / exposed	5 / 3256 (0.15%)	2 / 3248 (0.06%)	
occurrences (all)	6	4	
Muscle spasms			
subjects affected / exposed	13 / 3256 (0.40%)	13 / 3248 (0.40%)	
occurrences (all)	14	16	
Muscular weakness			
subjects affected / exposed	4 / 3256 (0.12%)	5 / 3248 (0.15%)	
occurrences (all)	4	6	
Musculoskeletal pain			
subjects affected / exposed	10 / 3256 (0.31%)	11 / 3248 (0.34%)	
occurrences (all)	10	11	
Myalgia			
subjects affected / exposed	6 / 3256 (0.18%)	4 / 3248 (0.12%)	
occurrences (all)	6	4	
Osteoarthritis			
subjects affected / exposed	12 / 3256 (0.37%)	14 / 3248 (0.43%)	
occurrences (all)	12	14	
Pain in extremity			

subjects affected / exposed	47 / 3256 (1.44%)	52 / 3248 (1.60%)	
occurrences (all)	58	53	
Rotator cuff syndrome			
subjects affected / exposed	4 / 3256 (0.12%)	2 / 3248 (0.06%)	
occurrences (all)	4	3	
Spinal osteoarthritis			
subjects affected / exposed	2 / 3256 (0.06%)	5 / 3248 (0.15%)	
occurrences (all)	2	6	
Intervertebral disc protrusion			
subjects affected / exposed	7 / 3256 (0.21%)	5 / 3248 (0.15%)	
occurrences (all)	7	5	
Spinal pain			
subjects affected / exposed	1 / 3256 (0.03%)	4 / 3248 (0.12%)	
occurrences (all)	1	4	
Spinal stenosis			
subjects affected / exposed	4 / 3256 (0.12%)	5 / 3248 (0.15%)	
occurrences (all)	4	5	
Infections and infestations			
Bronchitis			
subjects affected / exposed	15 / 3256 (0.46%)	17 / 3248 (0.52%)	
occurrences (all)	17	21	
Cellulitis			
subjects affected / exposed	10 / 3256 (0.31%)	6 / 3248 (0.18%)	
occurrences (all)	11	7	
Gangrene			
subjects affected / exposed	5 / 3256 (0.15%)	2 / 3248 (0.06%)	
occurrences (all)	5	2	
Herpes zoster			
subjects affected / exposed	5 / 3256 (0.15%)	7 / 3248 (0.22%)	
occurrences (all)	5	7	
Influenza			
subjects affected / exposed	10 / 3256 (0.31%)	7 / 3248 (0.22%)	
occurrences (all)	11	8	
Localised infection			
subjects affected / exposed	11 / 3256 (0.34%)	7 / 3248 (0.22%)	
occurrences (all)	11	7	

Nasopharyngitis			
subjects affected / exposed	21 / 3256 (0.64%)	30 / 3248 (0.92%)	
occurrences (all)	23	32	
Osteomyelitis			
subjects affected / exposed	4 / 3256 (0.12%)	1 / 3248 (0.03%)	
occurrences (all)	4	1	
Pneumonia			
subjects affected / exposed	9 / 3256 (0.28%)	14 / 3248 (0.43%)	
occurrences (all)	9	14	
Postoperative wound infection			
subjects affected / exposed	9 / 3256 (0.28%)	9 / 3248 (0.28%)	
occurrences (all)	9	9	
Sinusitis			
subjects affected / exposed	6 / 3256 (0.18%)	3 / 3248 (0.09%)	
occurrences (all)	6	4	
Upper respiratory tract infection			
subjects affected / exposed	4 / 3256 (0.12%)	2 / 3248 (0.06%)	
occurrences (all)	4	2	
Urinary tract infection			
subjects affected / exposed	22 / 3256 (0.68%)	21 / 3248 (0.65%)	
occurrences (all)	23	27	
Wound infection			
subjects affected / exposed	9 / 3256 (0.28%)	4 / 3248 (0.12%)	
occurrences (all)	9	4	
Respiratory tract infection viral			
subjects affected / exposed	2 / 3256 (0.06%)	4 / 3248 (0.12%)	
occurrences (all)	2	4	
Respiratory tract infection			
subjects affected / exposed	5 / 3256 (0.15%)	2 / 3248 (0.06%)	
occurrences (all)	5	3	
Metabolism and nutrition disorders			
Diabetes mellitus			
subjects affected / exposed	6 / 3256 (0.18%)	12 / 3248 (0.37%)	
occurrences (all)	6	12	
Gout			

subjects affected / exposed	5 / 3256 (0.15%)	11 / 3248 (0.34%)	
occurrences (all)	5	11	
Hyperkalaemia			
subjects affected / exposed	0 / 3256 (0.00%)	4 / 3248 (0.12%)	
occurrences (all)	0	4	
Vitamin D deficiency			
subjects affected / exposed	5 / 3256 (0.15%)	1 / 3248 (0.03%)	
occurrences (all)	5	1	
Dyslipidaemia			
subjects affected / exposed	1 / 3256 (0.03%)	5 / 3248 (0.15%)	
occurrences (all)	1	5	
Decreased appetite			
subjects affected / exposed	6 / 3256 (0.18%)	4 / 3248 (0.12%)	
occurrences (all)	6	4	
Type 2 diabetes mellitus			
subjects affected / exposed	13 / 3256 (0.40%)	7 / 3248 (0.22%)	
occurrences (all)	13	7	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 February 2016	First global amendment including 25 changes.
20 March 2017	Second global amendment including 7 changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported