



Clinical trial results:

Global multicenter, open-label, randomized, event-driven, active-controlled study comparing a rivaroxaban-based antithrombotic strategy to an antiplatelet-based strategy after transcatheter aortic valve replacement (TAVR) to optimize clinical outcomes

Summary

EudraCT number	2015-001975-30
Trial protocol	DE ES BE NO AT DK SE NL GB FR CZ IT
Global end of trial date	27 November 2018

Results information

Result version number	v1 (current)
This version publication date	18 December 2019
First version publication date	18 December 2019

Trial information

Trial identification

Sponsor protocol code	BAY59-7939/17938
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02556203
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 January 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	27 November 2018
Global end of trial reached?	Yes
Global end of trial date	27 November 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

•Assess whether a rivaroxaban-based anticoagulation strategy, following successful TAVR, compared to an antiplatelet-based strategy, is superior in reducing death or first thromboembolic events (DTE). This comparison was hierarchically preceded by a non-inferiority test that had to be satisfied (i.e., the null hypothesis had to be rejected). •Assess the primary bleeding events (PBE) of the rivaroxaban-based strategy, following TAVR, compared to an antiplatelet-based strategy. PBE was defined as the composite of life-threatening, disabling, or major bleeding events and was classified according to the Valve Academic Research Consortium (VARC) definitions.

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	16 December 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	Canada: 61
Country: Number of subjects enrolled	United States: 318
Country: Number of subjects enrolled	Czech Republic: 17
Country: Number of subjects enrolled	Poland: 19
Country: Number of subjects enrolled	Austria: 78
Country: Number of subjects enrolled	Belgium: 32
Country: Number of subjects enrolled	Denmark: 149
Country: Number of subjects enrolled	France: 128
Country: Number of subjects enrolled	Germany: 520
Country: Number of subjects enrolled	Italy: 58
Country: Number of subjects enrolled	Netherlands: 27
Country: Number of subjects enrolled	Norway: 38
Country: Number of subjects enrolled	Spain: 51
Country: Number of subjects enrolled	Sweden: 7

Country: Number of subjects enrolled	Switzerland: 69
Country: Number of subjects enrolled	United Kingdom: 72
Worldwide total number of subjects	1644
EEA total number of subjects	1196

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)	34
From 65 to 84 years	1138
85 years and over	472

Subject disposition

Recruitment

Recruitment details:

Study was conducted at 136 centers world-wide between 16 Dec 2015 (first patient's first visit) and 27 Nov 2018 (last patient's last visit).

Pre-assignment

Screening details:

A total of 1674 subjects were screened, of which 1644 were randomly assigned to either of the two treatment arms and 1608 subjects started treatment with study medication.

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Rivaroxaban (Xarelto, BAY59-7939)

Arm description:

Subjects were treated with Rivaroxaban (10mg once-daily) and ASA (75-100mg once-daily) within first 90 days after randomization. After 90 days, ASA was discontinued and rivaroxaban (10mg once-daily) was to be continued alone. In the event of NOAF (New Onset of Atrial Fibrillation), subjects should be switched to rivaroxaban (20/15mg once-daily) and ASA (75-100mg once-daily) within first 90 days. After 90 days, ASA was discontinued and rivaroxaban (20/15mg once-daily) was to be continued alone.

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

Dosage and administration details:

10 mg OD (once-daily)

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:

75-100mg OD (once-daily)

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

Dosage and administration details:

In case of NOAF, 20/15 mg OD (once-daily)

Arm title	Antiplatelet
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Arm description:

Subjects were treated with clopidogrel (75mg once-daily) and ASA (75-100mg once-daily) within first 90 days after randomization. After 90 days, clopidogrel was discontinued and ASA (75-100mg once-daily) was to be continued alone. In the event of NOAF, subjects should start treatment of open-label VKA to

target INR 2 to 3 (according to guidelines) and ASA (75-100mg once-daily) within first 90 days. After 90 days, ASA was discontinued and VKA was to be continued alone.

Arm type	Active comparator
Investigational medicinal product name	Clopidogrel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

75mg OD (once-daily)

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:

75-100mg OD (once-daily)

Investigational medicinal product name	Vitamin K antagonist (VKA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

In case of NOAF, Open-label VKA therapy to target international normalized ratio (INR) 2-3, according to guidelines

Number of subjects in period 1	Rivaroxaban (Xarelto, BAY59-7939)	Antiplatelet
	Started	826
Received treatment	801	807
Completed	799	792
Not completed	27	26
Adverse event, serious fatal	1	-
Consent withdrawn by subject	21	21
Lost to follow-up	5	5

Baseline characteristics

Reporting groups

Reporting group title	Rivaroxaban (Xarelto, BAY59-7939)
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Reporting group description:

Subjects were treated with Rivaroxaban (10mg once-daily) and ASA (75-100mg once-daily) within first 90 days after randomization. After 90 days, ASA was discontinued and rivaroxaban (10mg once-daily) was to be continued alone. In the event of NOAF (New Onset of Atrial Fibrillation), subjects should be switched to rivaroxaban (20/15mg once-daily) and ASA (75-100mg once-daily) within first 90 days. After 90 days, ASA was discontinued and rivaroxaban (20/15mg once-daily) was to be continued alone.

Reporting group title	Antiplatelet
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Reporting group description:

Subjects were treated with clopidogrel (75mg once-daily) and ASA (75-100mg once-daily) within first 90 days after randomization. After 90 days, clopidogrel was discontinued and ASA (75-100mg once-daily) was to be continued alone. In the event of NOAF, subjects should start treatment of open-label VKA to target INR 2 to 3 (according to guidelines) and ASA (75-100mg once-daily) within first 90 days. After 90 days, ASA was discontinued and VKA was to be continued alone.

Reporting group values	Rivaroxaban (Xarelto, BAY59-7939)	Antiplatelet	Total
Number of subjects	826	818	1644
Age Categorical Units: Subjects			

Age Continuous Units: years			
arithmetic mean	80.38	80.77	-
standard deviation	± 7.12	± 5.99	

Gender Categorical Units: Subjects			
Female	400	413	813
Male	426	405	831

Race Units: Subjects			
Asia	2	1	3
Black or African American	9	7	16
Native Hawaiian or other Pacific Islander	0	2	2
Not reported	123	115	238
White	692	693	1385

Ethnicity Units: Subjects			
Hispanic or Latino	26	17	43
Not Hispanic or Latino	677	694	1371
Not reported	123	107	230

End points

End points reporting groups

Reporting group title	Rivaroxaban (Xarelto, BAY59-7939)
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Reporting group description:

Subjects were treated with Rivaroxaban (10mg once-daily) and ASA (75-100mg once-daily) within first 90 days after randomization. After 90 days, ASA was discontinued and rivaroxaban (10mg once-daily) was to be continued alone. In the event of NOAF (New Onset of Atrial Fibrillation), subjects should be switched to rivaroxaban (20/15mg once-daily) and ASA (75-100mg once-daily) within first 90 days. After 90 days, ASA was discontinued and rivaroxaban (20/15mg once-daily) was to be continued alone.

Reporting group title	Antiplatelet
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Reporting group description:

Subjects were treated with clopidogrel (75mg once-daily) and ASA (75-100mg once-daily) within first 90 days after randomization. After 90 days, clopidogrel was discontinued and ASA (75-100mg once-daily) was to be continued alone. In the event of NOAF, subjects should start treatment of open-label VKA to target INR 2 to 3 (according to guidelines) and ASA (75-100mg once-daily) within first 90 days. After 90 days, ASA was discontinued and VKA was to be continued alone.

Subject analysis set title	Full analysis set (FAS)
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Subject analysis set type	Full analysis
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Subject analysis set description:

Included all randomized subjects and results presented according to randomized treatment arm (1644 subjects overall)

Subject analysis set title	Safety analysis set (SAF)
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Subject analysis set type	Safety analysis
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Subject analysis set description:

Included all randomized subjects and results presented according to actual treatment arm that matches the randomized arm (1608 subjects).

Primary: Number of subjects with death or adjudicated thromboembolic event (DTE)

End point title	Number of subjects with death or adjudicated thromboembolic event (DTE)
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End point description:

Death or first adjudicated thromboembolic event (DTE), defined as composite of all-cause death, any stroke, myocardial infarction (MI), symptomatic valve thrombosis, pulmonary embolism (PE), deep vein thrombosis (DVT), and non-central nervous system (CNS) systemic embolism (per adjudication).

End point type	Primary
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End point timeframe:

From randomization until end of study medication + 2 days

End point values	Rivaroxaban (Xarelto, BAY59-7939)	Antiplatelet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	801	807		
Units: Subjects	68	63		

Statistical analyses

Statistical analysis title	DTE (non-inferiority)
Statistical analysis description: Non-inferiority was tested in Safety analysis set (SAF)	
Comparison groups	Antiplatelet v Rivaroxaban (Xarelto, BAY59-7939)
Number of subjects included in analysis	1608
Analysis specification	Pre-specified
Analysis type	non-inferiority
P-value	> 0.05
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Confidence interval	
level	Other: 97.5 %
sides	1-sided
upper limit	1.7040824

Primary: Number of subjects with death or adjudicated thromboembolic event (DTE)

End point title	Number of subjects with death or adjudicated thromboembolic event (DTE)
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End point description:

Death or first adjudicated thromboembolic event (DTE), defined as composite of all-cause death, any stroke, myocardial infarction (MI), symptomatic valve thrombosis, pulmonary embolism (PE), deep vein thrombosis (DVT), and non-central nervous system (CNS) systemic embolism (per adjudication).

End point type	Primary
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End point timeframe:

From randomization until efficacy cut-off date (13-Aug-2018)

End point values	Rivaroxaban (Xarelto, BAY59-7939)	Antiplatelet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	826	818		
Units: Subjects	105	78		

Statistical analyses

Statistical analysis title	DTE (superiority)
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Statistical analysis description:

Superiority test was analyzed on Full Analysis Set (FAS)

Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) v Antiplatelet
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Number of subjects included in analysis	1644
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.04223
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.01
upper limit	1.81

Primary: Number of participants with primary bleeding event (PBE)

End point title	Number of participants with primary bleeding event (PBE)
End point description:	
PBE is defined according to VARC (Valve Academic Research Consortium) definitions as the adjudicated composite of: Life-threatening, disabling or major bleeding.	
End point type	Primary
End point timeframe:	
From randomization until efficacy cut-off date (13-Aug-2018)	

End point values	Rivaroxaban (Xarelto, BAY59-7939)	Antiplatelet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	826	818		
Units: Subjects	46	31		

Statistical analyses

Statistical analysis title	Primary bleeding event
Statistical analysis description:	
PBE was described in Full analysis set (FAS)	
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) v Antiplatelet
Number of subjects included in analysis	1644
Analysis specification	Pre-specified
Analysis type	other ^[1]
P-value	= 0.07745
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.5

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.95
upper limit	2.37

Notes:

[1] - Descriptive

Secondary: Number of participants with Net-clinical benefit

End point title	Number of participants with Net-clinical benefit
End point description:	
The net-clinical-benefit defined as the adjudicated composite of all-cause death, any stroke, myocardial infarction, symptomatic valve thrombosis, pulmonary embolism, deep vein thrombosis, non-CNS systemic embolism (efficacy); VARC life-threatening, disabling and VARC major bleeds (safety).	
End point type	Secondary
End point timeframe:	
From randomization until efficacy cut-off date (13-Aug-2018)	

End point values	Rivaroxaban (Xarelto, BAY59-7939)	Antiplatelet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	826	818		
Units: Subjects	137	100		

Statistical analyses

Statistical analysis title	Net-clinical benefit
Statistical analysis description:	
Net-clinical benefit was tested in Full analysis set (FAS)	
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) v Antiplatelet
Number of subjects included in analysis	1644
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.01156
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.39
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	1.8

Secondary: Number of participants with cardiovascular death or thromboembolic event

End point title	Number of participants with cardiovascular death or thromboembolic event
End point description: Composite of CV-death, any stroke, myocardial infarction (MI), symptomatic valve thrombosis, pulmonary embolism (PE), deep vein thrombosis (DVT), and non-central nervous system (CNS) systemic embolism (per adjudication).	
End point type	Secondary
End point timeframe: From randomization until efficacy cut-off date (13-Aug-2018)	

End point values	Rivaroxaban (Xarelto, BAY59-7939)	Antiplatelet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	826	818		
Units: Subjects	83	68		

Statistical analyses

Statistical analysis title	Cardiovascular death or thromboembolic event
Statistical analysis description: Secondary efficacy endpoint was tested in Full analysis set (FAS)	
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) v Antiplatelet
Number of subjects included in analysis	1644
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.21595
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.22
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.89
upper limit	1.69

Secondary: Number of participants with TIMI (Thrombolysis In Myocardial Infarction) major / minor bleeds

End point title	Number of participants with TIMI (Thrombolysis In Myocardial Infarction) major / minor bleeds
End point description: Composite of TIMI major and minor bleedings	
End point type	Secondary

End point timeframe:

From randomization until efficacy cut-off date (13 August 2018)

End point values	Rivaroxaban (Xarelto, BAY59-7939)	Antiplatelet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	826	818		
Units: Subjects	42	24		

Statistical analyses

Statistical analysis title	TIMI major / minor bleeds
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Statistical analysis description:

TIMI major and minor bleeds were described in Full analysis set (FAS)

Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) v Antiplatelet
Number of subjects included in analysis	1644
Analysis specification	Pre-specified
Analysis type	other ^[2]
P-value	= 0.02216
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.78
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.08
upper limit	2.94

Notes:

[2] - Descriptive

Secondary: Number of participants with ISTH (International Society on Thrombosis and Haemostasis) major bleeds

End point title	Number of participants with ISTH (International Society on Thrombosis and Haemostasis) major bleeds
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End point description:

ISTH major bleeds

End point type	Secondary
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End point timeframe:

From randomization until efficacy cut-off date (13 August 2018)

End point values	Rivaroxaban (Xarelto, BAY59-7939)	Antiplatelet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	826	818		
Units: Subjects	49	30		

Statistical analyses

Statistical analysis title	ISTH major bleeds
Statistical analysis description: ISTH major bleeds were described in Full analysis set (FAS)	
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) v Antiplatelet
Number of subjects included in analysis	1644
Analysis specification	Pre-specified
Analysis type	other ^[3]
P-value	= 0.02702
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.05
upper limit	2.62

Notes:

[3] - Descriptive

Secondary: Number of participants with composite bleeding endpoint of BARC (Bleeding Academic Research Consortium) 2, 3, or 5 bleeds

End point title	Number of participants with composite bleeding endpoint of BARC (Bleeding Academic Research Consortium) 2, 3, or 5 bleeds			
End point description: Composite of BARC 2,3 or 5 bleedings				
End point type	Secondary			
End point timeframe: From randomization until efficacy cut-off date (13 August 2018)				

End point values	Rivaroxaban (Xarelto, BAY59-7939)	Antiplatelet		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	826	818		
Units: Subjects	148	85		

Statistical analyses

Statistical analysis title	BARC 2, 3 or 5 bleedings
Statistical analysis description: BARC 2, 3 or 5 bleedings were described in Full analysis set (FAS)	
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) v Antiplatelet
Number of subjects included in analysis	1644
Analysis specification	Pre-specified
Analysis type	other ^[4]
P-value	= 0.00001
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.84
Confidence interval	
level	95 %
sides	2-sided
lower limit	1.41
upper limit	2.41

Notes:

[4] - Descriptive

Adverse events

Adverse events information

Timeframe for reporting adverse events:

After study medication start until end of study medication plus 2 days.

Timeframe for number of death (all causes): After study medication start until last contact date.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21
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Reporting groups

Reporting group title	Antiplatelet arm
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Reporting group description:

Subjects were treated with clopidogrel (75mg once-daily) and ASA (75-100mg once-daily) within first 90 days after randomization. After 90 days, clopidogrel was discontinued and ASA (75-100mg once-daily) was to be continued alone. In the event of NOAF, subjects should start treatment of open-label VKA (Vitamin K antagonist) to target INR (international normalized ratio) 2 to 3 (according to guidelines) and ASA (75-100mg once-daily) within first 90 days. After 90 days, ASA was discontinued and VKA was to be continued alone.

Reporting group title	Rivaroxaban arm
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Reporting group description:

Subjects were treated with Rivaroxaban (10mg once-daily) and ASA (75-100mg once-daily) within first 90 days after randomization. After 90 days, ASA was discontinued and rivaroxaban (10mg once-daily) was to be continued alone. In the event of NOAF (New Onset of Atrial Fibrillation), subjects should be switched to rivaroxaban (20/15 mg once-daily) and ASA (75-100mg once-daily) within first 90 days. After 90 days, ASA was discontinued and rivaroxaban (20/15 mg once-daily) was to be continued alone.

Serious adverse events	Antiplatelet arm	Rivaroxaban arm	
Total subjects affected by serious adverse events			
subjects affected / exposed	282 / 807 (34.94%)	296 / 801 (36.95%)	
number of deaths (all causes)	43	70	
number of deaths resulting from adverse events	26	39	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Acute myeloid leukaemia			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Adenocarcinoma gastric			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Adenocarcinoma of colon			

subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Basal cell carcinoma		
subjects affected / exposed	3 / 807 (0.37%)	2 / 801 (0.25%)
occurrences causally related to treatment / all	0 / 4	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Benign salivary gland neoplasm		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bladder cancer		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bladder cancer recurrent		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Bladder neoplasm		
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Breast cancer		
subjects affected / exposed	3 / 807 (0.37%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Breast cancer recurrent		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Colon cancer		

subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic neoplasm			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Liposarcoma			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant melanoma			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelodysplastic syndrome			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myeloid leukaemia			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Neoplasm malignant			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Non-Hodgkin's lymphoma			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatic carcinoma			

subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Plasmacytoma		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Rectal cancer		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Squamous cell carcinoma of skin		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Uterine cancer		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Ear neoplasm malignant		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Prostate cancer		
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Brain neoplasm		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Colon neoplasm		

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Renal neoplasm			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-small cell lung cancer			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatocellular carcinoma			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Invasive lobular breast carcinoma			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Aortic dissection			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (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	0 / 807 (0.00%)	1 / 801 (0.12%)	
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 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			

subjects affected / exposed	5 / 807 (0.62%)	3 / 801 (0.37%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertension			
subjects affected / exposed	5 / 807 (0.62%)	3 / 801 (0.37%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotension			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intermittent claudication			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypovolaemic shock			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Varicose vein			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombophlebitis superficial			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peripheral arterial occlusive disease			
subjects affected / exposed	8 / 807 (0.99%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 8	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Carotid endarterectomy			

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cochlea implant			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip arthroplasty			
subjects affected / exposed	3 / 807 (0.37%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Incisional hernia repair			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inguinal hernia repair			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (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 / 807 (0.00%)	3 / 801 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin cyst excision			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Toe amputation			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac pacemaker replacement			

subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Shoulder arthroplasty		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hip surgery		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Peripheral artery angioplasty		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac resynchronisation therapy		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac ablation		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Dental operation		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Eyelid operation		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Ear operation		

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac pacemaker adjustment			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia repair			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transcatheter arterial chemoembolisation			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 807 (0.00%)	3 / 801 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Death			
subjects affected / exposed	5 / 807 (0.62%)	5 / 801 (0.62%)	
occurrences causally related to treatment / all	0 / 5	0 / 5	
deaths causally related to treatment / all	0 / 5	0 / 5	
Fatigue			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gait disturbance			

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
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	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Malaise			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oedema peripheral			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (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 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Strangulated hernia			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 2	0 / 0	
Sudden cardiac death			

subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
General physical health deterioration			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac death			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Exercise tolerance decreased			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Systemic inflammatory response syndrome			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pacemaker generated arrhythmia			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammation			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-cardiac chest pain			
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple organ dysfunction syndrome			

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Sarcoidosis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemophagocytic lymphohistiocytosis			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Reproductive system and breast disorders			
Benign prostatic hyperplasia			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ovarian cyst			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectocele			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Female genital tract fistula			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			

subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Acute respiratory distress syndrome		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Acute respiratory failure		
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Aspiration		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 1
Asthma		
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Chronic obstructive pulmonary disease		
subjects affected / exposed	7 / 807 (0.87%)	7 / 801 (0.87%)
occurrences causally related to treatment / all	0 / 9	0 / 9
deaths causally related to treatment / all	0 / 0	0 / 0
Cough		
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Dyspnoea		
subjects affected / exposed	6 / 807 (0.74%)	5 / 801 (0.62%)
occurrences causally related to treatment / all	0 / 6	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Dyspnoea exertional		

subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hiccups		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lung disorder		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Lung infiltration		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (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	2 / 807 (0.25%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pneumonia aspiration		
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 2
Pneumothorax		
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary fibrosis		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary hypertension		

subjects affected / exposed	2 / 807 (0.25%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary oedema			
subjects affected / exposed	1 / 807 (0.12%)	3 / 801 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory arrest			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory failure			
subjects affected / exposed	1 / 807 (0.12%)	5 / 801 (0.62%)	
occurrences causally related to treatment / all	0 / 1	0 / 7	
deaths causally related to treatment / all	0 / 0	0 / 1	
Wheezing			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
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	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Organising pneumonia			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Delirium			

subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Depression			
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hallucination			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Panic disorder			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Suicide attempt			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mental status changes			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychotic disorder			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product issues			
Undersensing			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (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	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	1 / 807 (0.12%)	3 / 801 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis acute			
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis chronic			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholelithiasis			
subjects affected / exposed	3 / 807 (0.37%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic cirrhosis			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Jaundice			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

Haemoglobin decreased			
subjects affected / exposed	1 / 807 (0.12%)	3 / 801 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Heart rate irregular			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Weight decreased			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ejection fraction decreased			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Troponin increased			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inflammatory marker increased			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza A virus test positive			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transvalvular pressure gradient increased			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			

Accident			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clavicle fracture			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
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 / 807 (0.12%)	1 / 801 (0.12%)	
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	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fall			
subjects affected / exposed	5 / 807 (0.62%)	12 / 801 (1.50%)	
occurrences causally related to treatment / all	0 / 5	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femoral neck fracture			
subjects affected / exposed	0 / 807 (0.00%)	3 / 801 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Femur fracture			
subjects affected / exposed	2 / 807 (0.25%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fibula fracture			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hip fracture			

subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Humerus fracture		
subjects affected / exposed	3 / 807 (0.37%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Joint dislocation		
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Muscle injury		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pancreatic injury		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Radius fracture		
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Rib fracture		
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Splenic rupture		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Stress fracture		

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
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 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tibia fracture			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wrist fracture			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia postoperative			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular pseudoaneurysm			
subjects affected / exposed	2 / 807 (0.25%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Traumatic fracture			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cervical vertebral fracture			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
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	0 / 807 (0.00%)	3 / 801 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	2 / 807 (0.25%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin laceration			
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pelvic fracture			
subjects affected / exposed	1 / 807 (0.12%)	3 / 801 (0.37%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Upper limb fracture			
subjects affected / exposed	0 / 807 (0.00%)	3 / 801 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin abrasion			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Periprosthetic fracture			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Craniocerebral injury			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin wound			

subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Meniscus injury			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary bypass stenosis			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Arterial bypass stenosis			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural hypoparathyroidism			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Product administration error			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Congenital, familial and genetic disorders			
Neuroacanthocytosis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Angina pectoris			
subjects affected / exposed	3 / 807 (0.37%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arrhythmia			
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)	
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	25 / 807 (3.10%)	17 / 801 (2.12%)	
occurrences causally related to treatment / all	0 / 27	0 / 19	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial flutter			
subjects affected / exposed	2 / 807 (0.25%)	4 / 801 (0.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Atrial tachycardia			
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block complete			
subjects affected / exposed	15 / 807 (1.86%)	12 / 801 (1.50%)	
occurrences causally related to treatment / all	0 / 15	0 / 12	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block first degree			
subjects affected / exposed	3 / 807 (0.37%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrioventricular block second degree			
subjects affected / exposed	2 / 807 (0.25%)	4 / 801 (0.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			

subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0
Bundle branch block left		
subjects affected / exposed	6 / 807 (0.74%)	4 / 801 (0.50%)
occurrences causally related to treatment / all	0 / 6	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac arrest		
subjects affected / exposed	1 / 807 (0.12%)	4 / 801 (0.50%)
occurrences causally related to treatment / all	0 / 1	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 2
Cardiac failure		
subjects affected / exposed	16 / 807 (1.98%)	16 / 801 (2.00%)
occurrences causally related to treatment / all	0 / 22	0 / 19
deaths causally related to treatment / all	0 / 3	0 / 1
Cardiac failure acute		
subjects affected / exposed	5 / 807 (0.62%)	2 / 801 (0.25%)
occurrences causally related to treatment / all	0 / 10	0 / 2
deaths causally related to treatment / all	0 / 2	0 / 0
Cardiac failure chronic		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Cardiac failure congestive		
subjects affected / exposed	3 / 807 (0.37%)	8 / 801 (1.00%)
occurrences causally related to treatment / all	0 / 4	0 / 8
deaths causally related to treatment / all	0 / 0	0 / 3
Cardio-respiratory arrest		
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1
Cardiovascular disorder		

subjects affected / exposed	2 / 807 (0.25%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Conduction disorder			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery disease			
subjects affected / exposed	3 / 807 (0.37%)	5 / 801 (0.62%)	
occurrences causally related to treatment / all	0 / 5	0 / 8	
deaths causally related to treatment / all	0 / 0	0 / 1	
Coronary artery stenosis			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary ostial stenosis			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Extrasystoles			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Left ventricular failure			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mitral valve incompetence			
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocarditis			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Palpitations			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Right ventricular failure			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus arrest			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus bradycardia			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular extrasystoles			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular tachycardia			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tachycardia			

subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Torsade de pointes			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Trifascicular block			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular arrhythmia			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular extrasystoles			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ventricular tachycardia			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary artery dissection			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic cardiomyopathy			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			

subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiopulmonary failure			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Acute left ventricular failure			
subjects affected / exposed	4 / 807 (0.50%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Cardiorenal syndrome			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinus node dysfunction			
subjects affected / exposed	2 / 807 (0.25%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Axonal neuropathy			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carotid artery stenosis			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Carpal tunnel syndrome			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dementia			

subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Dementia Alzheimer's type		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Dizziness		
subjects affected / exposed	4 / 807 (0.50%)	9 / 801 (1.12%)
occurrences causally related to treatment / all	0 / 4	4 / 9
deaths causally related to treatment / all	0 / 0	0 / 0
Encephalopathy		
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Epilepsy		
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)
occurrences causally related to treatment / all	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Extrapyramidal disorder		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Headache		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Hepatic encephalopathy		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Hypoglycaemic coma		

subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypotonia			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Loss of consciousness			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
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	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Migraine			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myasthenia gravis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myelopathy			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nerve compression			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Normal pressure hydrocephalus			

subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Parkinsonism		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Petit mal epilepsy		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Presyncope		
subjects affected / exposed	0 / 807 (0.00%)	3 / 801 (0.37%)
occurrences causally related to treatment / all	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Sciatica		
subjects affected / exposed	2 / 807 (0.25%)	4 / 801 (0.50%)
occurrences causally related to treatment / all	0 / 2	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0
Seizure		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Syncope		
subjects affected / exposed	23 / 807 (2.85%)	19 / 801 (2.37%)
occurrences causally related to treatment / all	0 / 25	0 / 20
deaths causally related to treatment / all	0 / 0	0 / 0
Transient ischaemic attack		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Vertebrobasilar insufficiency		

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vlth nerve paralysis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Balance disorder			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intercostal neuralgia			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular dementia			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ballismus			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parkinson's disease			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolic encephalopathy			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (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	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Blood and lymphatic system disorders			
Anaemia			
alternative assessment type: Systematic			
subjects affected / exposed	0 / 807 (0.00%)	5 / 801 (0.62%)	
occurrences causally related to treatment / all	0 / 0	1 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anaemia macrocytic			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypochromic anaemia			
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Iron deficiency anaemia			
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukocytosis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Polycythaemia			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Thrombocytopenia			
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic anaemia			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vertigo positional			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Blindness			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cataract			
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Keratitis			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular degeneration			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
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 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neovascular age-related macular degeneration			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Macular detachment			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal ulcer			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Colitis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Diarrhoea			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal ulcer			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dysphagia			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enteritis			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastritis erosive			
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhoids			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ileus			

subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Incarcerated inguinal hernia		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Inguinal hernia		
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Intestinal ischaemia		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Intestinal obstruction		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Nausea		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Oesophageal obstruction		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Oesophagitis		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (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	1 / 807 (0.12%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancreatitis acute			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (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	3 / 807 (0.37%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Umbilical hernia			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coeliac artery stenosis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemorrhagic erosive gastritis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Dermatitis atopic			

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug eruption			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lichen sclerosus			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pemphigus			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin ulcer			
subjects affected / exposed	3 / 807 (0.37%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Renal failure			
subjects affected / exposed	0 / 807 (0.00%)	3 / 801 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary incontinence			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (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 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary bladder polyp			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (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	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic kidney disease			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	17 / 807 (2.11%)	10 / 801 (1.25%)	
occurrences causally related to treatment / all	0 / 17	1 / 10	
deaths causally related to treatment / all	0 / 0	0 / 1	
Endocrine disorders			
Primary adrenal insufficiency			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Inappropriate antidiuretic hormone secretion			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Arthritis			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Back pain			
subjects affected / exposed	4 / 807 (0.50%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chondrocalcinosis pyrophosphate			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
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	1 / 807 (0.12%)	0 / 801 (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	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteoarthritis			
subjects affected / exposed	10 / 807 (1.24%)	3 / 801 (0.37%)	
occurrences causally related to treatment / all	0 / 10	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain in extremity			

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rhabdomyolysis			
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	3 / 807 (0.37%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal osteoarthritis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Osteopenia			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral disc protrusion			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal pain			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Bacteraemia			

subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Campylobacter gastroenteritis			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			
subjects affected / exposed	4 / 807 (0.50%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium difficile colitis			
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis			
subjects affected / exposed	7 / 807 (0.87%)	8 / 801 (1.00%)	
occurrences causally related to treatment / all	0 / 7	0 / 8	
deaths causally related to treatment / all	0 / 1	0 / 1	
Endocarditis bacterial			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocarditis enterococcal			

subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Enterococcal bacteraemia		
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Erysipelas		
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gangrene		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroenteritis		
subjects affected / exposed	4 / 807 (0.50%)	3 / 801 (0.37%)
occurrences causally related to treatment / all	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0
Gastroenteritis viral		
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Gastrointestinal infection		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Herpes zoster		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Infected skin ulcer		

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Influenza			
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Liver abscess			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 807 (0.00%)	3 / 801 (0.37%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Orchitis			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Parotitis			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			

subjects affected / exposed	22 / 807 (2.73%)	23 / 801 (2.87%)
occurrences causally related to treatment / all	0 / 23	0 / 28
deaths causally related to treatment / all	0 / 3	0 / 3
Pneumonia influenzal		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0
Postoperative wound infection		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Pyelonephritis acute		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Sepsis		
subjects affected / exposed	3 / 807 (0.37%)	7 / 801 (0.87%)
occurrences causally related to treatment / all	0 / 3	0 / 7
deaths causally related to treatment / all	0 / 0	0 / 2
Sialoadenitis		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Tooth abscess		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Tracheobronchitis		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Typhoid fever		

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
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	3 / 807 (0.37%)	5 / 801 (0.62%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral infection			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Viral upper respiratory tract infection			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 807 (0.12%)	4 / 801 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Groin infection			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Staphylococcal bacteraemia			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal bacteraemia			

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
occurrences causally related to treatment / all	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0
Pulmonary sepsis		
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)
occurrences causally related to treatment / all	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0
Escherichia urinary tract infection		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Arthritis bacterial		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Escherichia bacteraemia		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Staphylococcal sepsis		
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)
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	1 / 807 (0.12%)	2 / 801 (0.25%)
occurrences causally related to treatment / all	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0
Biliary sepsis		
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0
Abdominal sepsis		

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Wound abscess			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal cyst infection			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intervertebral discitis			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic foot infection			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung infection			
subjects affected / exposed	3 / 807 (0.37%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal infection			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis bacterial			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection viral			

subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection pseudomonal			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac valve abscess			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dermo-hypodermatitis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Post procedural infection			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic encephalopathy			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infective exacerbation of bronchiectasis			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Streptococcal endocarditis			

subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Medical device site joint infection			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
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	1 / 807 (0.12%)	4 / 801 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus			
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 807 (0.00%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte imbalance			
subjects affected / exposed	1 / 807 (0.12%)	1 / 801 (0.12%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gout			
subjects affected / exposed	3 / 807 (0.37%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	3 / 807 (0.37%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			

subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	2 / 807 (0.25%)	5 / 801 (0.62%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Type 2 diabetes mellitus			
subjects affected / exposed	1 / 807 (0.12%)	0 / 801 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0.2 %

Non-serious adverse events	Antiplatelet arm	Rivaroxaban arm	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	302 / 807 (37.42%)	359 / 801 (44.82%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences (all)	0	2	
Vascular disorders			
Blood pressure fluctuation			
subjects affected / exposed	2 / 807 (0.25%)	3 / 801 (0.37%)	
occurrences (all)	2	3	
Haematoma			
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)	
occurrences (all)	2	1	
Hypertensive crisis			

subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	4 / 801 (0.50%) 4	
Hypertension subjects affected / exposed occurrences (all)	28 / 807 (3.47%) 28	26 / 801 (3.25%) 26	
Hypotension subjects affected / exposed occurrences (all)	10 / 807 (1.24%) 11	3 / 801 (0.37%) 3	
Intermittent claudication subjects affected / exposed occurrences (all)	1 / 807 (0.12%) 1	2 / 801 (0.25%) 2	
Lymphoedema subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	4 / 801 (0.50%) 4	
Orthostatic hypotension subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	2 / 801 (0.25%) 2	
Peripheral vascular disorder subjects affected / exposed occurrences (all)	1 / 807 (0.12%) 1	2 / 801 (0.25%) 2	
Peripheral arterial occlusive disease subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	6 / 801 (0.75%) 6	
Peripheral venous disease subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	0 / 801 (0.00%) 0	
Surgical and medical procedures			
Cataract operation subjects affected / exposed occurrences (all)	1 / 807 (0.12%) 1	6 / 801 (0.75%) 9	
Tooth extraction subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	10 / 801 (1.25%) 10	
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	2 / 807 (0.25%)	4 / 801 (0.50%)	
occurrences (all)	2	4	
Chest pain			
subjects affected / exposed	12 / 807 (1.49%)	10 / 801 (1.25%)	
occurrences (all)	12	10	
Fatigue			
subjects affected / exposed	7 / 807 (0.87%)	13 / 801 (1.62%)	
occurrences (all)	7	15	
Gait disturbance			
subjects affected / exposed	2 / 807 (0.25%)	2 / 801 (0.25%)	
occurrences (all)	2	2	
Oedema			
subjects affected / exposed	3 / 807 (0.37%)	2 / 801 (0.25%)	
occurrences (all)	3	2	
Oedema peripheral			
subjects affected / exposed	20 / 807 (2.48%)	16 / 801 (2.00%)	
occurrences (all)	21	16	
Pyrexia			
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)	
occurrences (all)	4	1	
Peripheral swelling			
subjects affected / exposed	3 / 807 (0.37%)	0 / 801 (0.00%)	
occurrences (all)	3	0	
General physical health deterioration			
subjects affected / exposed	3 / 807 (0.37%)	0 / 801 (0.00%)	
occurrences (all)	3	0	
Non-cardiac chest pain			
subjects affected / exposed	5 / 807 (0.62%)	4 / 801 (0.50%)	
occurrences (all)	5	4	
Drug intolerance			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences (all)	0	2	
Immune system disorders			
Drug hypersensitivity			

subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	0 / 801 (0.00%) 0	
Reproductive system and breast disorders Benign prostatic hyperplasia subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	1 / 801 (0.12%) 1	
Respiratory, thoracic and mediastinal disorders Chronic obstructive pulmonary disease subjects affected / exposed occurrences (all)	6 / 807 (0.74%) 7	8 / 801 (1.00%) 9	
Cough subjects affected / exposed occurrences (all)	6 / 807 (0.74%) 6	2 / 801 (0.25%) 2	
Dyspnoea subjects affected / exposed occurrences (all)	6 / 807 (0.74%) 6	17 / 801 (2.12%) 17	
Pleural effusion subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 4	4 / 801 (0.50%) 4	
Dyspnoea exertional subjects affected / exposed occurrences (all)	1 / 807 (0.12%) 1	3 / 801 (0.37%) 3	
Respiratory failure subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	2 / 801 (0.25%) 2	
Psychiatric disorders Anxiety subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	1 / 801 (0.12%) 1	
Confusional state subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	2 / 801 (0.25%) 2	
Depression subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	2 / 801 (0.25%) 2	

Insomnia subjects affected / exposed occurrences (all)	1 / 807 (0.12%) 1	3 / 801 (0.37%) 3	
Mental status changes subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	2 / 801 (0.25%) 2	
Product issues Device dislocation subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	0 / 801 (0.00%) 0	
Investigations Blood creatinine increased subjects affected / exposed occurrences (all)	4 / 807 (0.50%) 4	2 / 801 (0.25%) 2	
Blood glucose increased subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	3 / 801 (0.37%) 3	
C-reactive protein increased subjects affected / exposed occurrences (all)	3 / 807 (0.37%) 3	1 / 801 (0.12%) 1	
Blood pressure increased subjects affected / exposed occurrences (all)	4 / 807 (0.50%) 4	4 / 801 (0.50%) 4	
Electrocardiogram QRS complex prolonged subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	2 / 801 (0.25%) 2	
Glomerular filtration rate decreased subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	2 / 801 (0.25%) 2	
International normalised ratio abnormal subjects affected / exposed occurrences (all)	3 / 807 (0.37%) 3	0 / 801 (0.00%) 0	
Haemoglobin decreased subjects affected / exposed occurrences (all)	3 / 807 (0.37%) 3	1 / 801 (0.12%) 1	
Intraocular pressure increased			

subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	0 / 801 (0.00%) 0	
Weight increased subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	0 / 801 (0.00%) 0	
Ejection fraction decreased subjects affected / exposed occurrences (all)	5 / 807 (0.62%) 5	2 / 801 (0.25%) 2	
Transvalvular pressure gradient increased subjects affected / exposed occurrences (all)	1 / 807 (0.12%) 1	3 / 801 (0.37%) 3	
Injury, poisoning and procedural complications			
Fall subjects affected / exposed occurrences (all)	16 / 807 (1.98%) 16	18 / 801 (2.25%) 18	
Ligament sprain subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	0 / 801 (0.00%) 0	
Rib fracture subjects affected / exposed occurrences (all)	4 / 807 (0.50%) 4	0 / 801 (0.00%) 0	
Anaemia postoperative subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	2 / 801 (0.25%) 2	
Contusion subjects affected / exposed occurrences (all)	8 / 807 (0.99%) 11	11 / 801 (1.37%) 11	
Skin laceration subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	5 / 801 (0.62%) 5	
Skin abrasion subjects affected / exposed occurrences (all)	1 / 807 (0.12%) 1	3 / 801 (0.37%) 3	
Cardiac disorders			

Angina pectoris		
subjects affected / exposed	4 / 807 (0.50%)	2 / 801 (0.25%)
occurrences (all)	5	2
Atrial fibrillation		
subjects affected / exposed	44 / 807 (5.45%)	43 / 801 (5.37%)
occurrences (all)	45	44
Atrial flutter		
subjects affected / exposed	5 / 807 (0.62%)	2 / 801 (0.25%)
occurrences (all)	5	2
Atrial tachycardia		
subjects affected / exposed	0 / 807 (0.00%)	3 / 801 (0.37%)
occurrences (all)	0	3
Atrioventricular block first degree		
subjects affected / exposed	8 / 807 (0.99%)	7 / 801 (0.87%)
occurrences (all)	8	7
Bradycardia		
subjects affected / exposed	2 / 807 (0.25%)	3 / 801 (0.37%)
occurrences (all)	2	3
Bundle branch block left		
subjects affected / exposed	7 / 807 (0.87%)	6 / 801 (0.75%)
occurrences (all)	7	6
Cardiac failure		
subjects affected / exposed	11 / 807 (1.36%)	14 / 801 (1.75%)
occurrences (all)	11	15
Cardiac failure chronic		
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)
occurrences (all)	0	2
Cardiac failure congestive		
subjects affected / exposed	3 / 807 (0.37%)	5 / 801 (0.62%)
occurrences (all)	3	5
Left ventricular failure		
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)
occurrences (all)	0	2
Mitral valve incompetence		
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)
occurrences (all)	1	2

Palpitations			
subjects affected / exposed	3 / 807 (0.37%)	1 / 801 (0.12%)	
occurrences (all)	3	1	
Sinus bradycardia			
subjects affected / exposed	3 / 807 (0.37%)	2 / 801 (0.25%)	
occurrences (all)	3	2	
Sinus tachycardia			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences (all)	0	2	
Supraventricular tachycardia			
subjects affected / exposed	1 / 807 (0.12%)	3 / 801 (0.37%)	
occurrences (all)	1	3	
Tachycardia			
subjects affected / exposed	2 / 807 (0.25%)	7 / 801 (0.87%)	
occurrences (all)	2	7	
Ventricular extrasystoles			
subjects affected / exposed	2 / 807 (0.25%)	2 / 801 (0.25%)	
occurrences (all)	2	2	
Ventricular tachycardia			
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences (all)	2	0	
Left ventricular dysfunction			
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences (all)	2	0	
Acute left ventricular failure			
subjects affected / exposed	2 / 807 (0.25%)	2 / 801 (0.25%)	
occurrences (all)	2	2	
Nervous system disorders			
Amnesia			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences (all)	0	2	
Dementia			
subjects affected / exposed	2 / 807 (0.25%)	4 / 801 (0.50%)	
occurrences (all)	2	4	
Carpal tunnel syndrome			

subjects affected / exposed occurrences (all)	1 / 807 (0.12%) 1	2 / 801 (0.25%) 3
Dementia Alzheimer's type subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	2 / 801 (0.25%) 2
Dizziness subjects affected / exposed occurrences (all)	16 / 807 (1.98%) 16	32 / 801 (4.00%) 32
Headache subjects affected / exposed occurrences (all)	4 / 807 (0.50%) 4	10 / 801 (1.25%) 10
Hypoaesthesia subjects affected / exposed occurrences (all)	3 / 807 (0.37%) 3	2 / 801 (0.25%) 2
Normal pressure hydrocephalus subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	0 / 801 (0.00%) 0
Presyncope subjects affected / exposed occurrences (all)	3 / 807 (0.37%) 3	5 / 801 (0.62%) 5
Sciatica subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	3 / 801 (0.37%) 3
Seizure subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	2 / 801 (0.25%) 2
Syncope subjects affected / exposed occurrences (all)	15 / 807 (1.86%) 16	10 / 801 (1.25%) 10
Cognitive disorder subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	2 / 801 (0.25%) 2
Blood and lymphatic system disorders Anaemia subjects affected / exposed occurrences (all)	3 / 807 (0.37%) 3	10 / 801 (1.25%) 10

Iron deficiency anaemia subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	5 / 801 (0.62%) 5	
Normochromic normocytic anaemia subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	2 / 801 (0.25%) 2	
Splenomegaly subjects affected / exposed occurrences (all)	1 / 807 (0.12%) 1	2 / 801 (0.25%) 2	
Ear and labyrinth disorders			
Vertigo subjects affected / exposed occurrences (all)	8 / 807 (0.99%) 8	17 / 801 (2.12%) 17	
Vertigo positional subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	1 / 801 (0.12%) 1	
Cerumen impaction subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	2 / 801 (0.25%) 2	
Sudden hearing loss subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	2 / 801 (0.25%) 2	
Eye disorders			
Cataract subjects affected / exposed occurrences (all)	5 / 807 (0.62%) 6	2 / 801 (0.25%) 2	
Lacrimation increased subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	0 / 801 (0.00%) 0	
Vision blurred subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	3 / 801 (0.37%) 3	
Visual impairment subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	6 / 801 (0.75%) 6	
Gastrointestinal disorders			

Abdominal distension		
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)
occurrences (all)	2	0
Abdominal pain		
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)
occurrences (all)	0	2
Abdominal pain upper		
subjects affected / exposed	6 / 807 (0.74%)	8 / 801 (1.00%)
occurrences (all)	6	8
Constipation		
subjects affected / exposed	5 / 807 (0.62%)	7 / 801 (0.87%)
occurrences (all)	5	7
Diarrhoea		
subjects affected / exposed	9 / 807 (1.12%)	11 / 801 (1.37%)
occurrences (all)	11	12
Dyspepsia		
subjects affected / exposed	2 / 807 (0.25%)	3 / 801 (0.37%)
occurrences (all)	2	3
Dysphagia		
subjects affected / exposed	1 / 807 (0.12%)	3 / 801 (0.37%)
occurrences (all)	1	3
Gastritis		
subjects affected / exposed	2 / 807 (0.25%)	2 / 801 (0.25%)
occurrences (all)	2	2
Gastrooesophageal reflux disease		
subjects affected / exposed	3 / 807 (0.37%)	1 / 801 (0.12%)
occurrences (all)	3	1
Nausea		
subjects affected / exposed	4 / 807 (0.50%)	10 / 801 (1.25%)
occurrences (all)	4	10
Toothache		
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)
occurrences (all)	0	2
Vomiting		
subjects affected / exposed	4 / 807 (0.50%)	1 / 801 (0.12%)
occurrences (all)	4	1

Hepatobiliary disorders			
Hepatic cirrhosis			
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)	
occurrences (all)	2	0	
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences (all)	0	2	
Erythema			
subjects affected / exposed	0 / 807 (0.00%)	3 / 801 (0.37%)	
occurrences (all)	0	3	
Pruritus			
subjects affected / exposed	3 / 807 (0.37%)	4 / 801 (0.50%)	
occurrences (all)	3	4	
Rash			
subjects affected / exposed	5 / 807 (0.62%)	5 / 801 (0.62%)	
occurrences (all)	5	6	
Skin ulcer			
subjects affected / exposed	0 / 807 (0.00%)	3 / 801 (0.37%)	
occurrences (all)	0	3	
Rash pruritic			
subjects affected / exposed	3 / 807 (0.37%)	0 / 801 (0.00%)	
occurrences (all)	3	0	
Urticaria			
subjects affected / exposed	1 / 807 (0.12%)	3 / 801 (0.37%)	
occurrences (all)	1	3	
Renal and urinary disorders			
Nocturia			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences (all)	0	2	
Renal failure			
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)	
occurrences (all)	2	2	
Urinary retention			
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)	
occurrences (all)	1	2	
Chronic kidney disease			

subjects affected / exposed occurrences (all)	3 / 807 (0.37%) 3	4 / 801 (0.50%) 4	
Acute kidney injury subjects affected / exposed occurrences (all)	8 / 807 (0.99%) 8	6 / 801 (0.75%) 6	
Endocrine disorders			
Hyperthyroidism subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	2 / 801 (0.25%) 2	
Hypothyroidism subjects affected / exposed occurrences (all)	7 / 807 (0.87%) 7	3 / 801 (0.37%) 3	
Musculoskeletal and connective tissue disorders			
Arthralgia subjects affected / exposed occurrences (all)	5 / 807 (0.62%) 5	9 / 801 (1.12%) 10	
Arthritis subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	1 / 801 (0.12%) 1	
Back pain subjects affected / exposed occurrences (all)	5 / 807 (0.62%) 6	11 / 801 (1.37%) 12	
Bursitis subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	0 / 801 (0.00%) 0	
Groin pain subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	1 / 801 (0.12%) 1	
Joint swelling subjects affected / exposed occurrences (all)	2 / 807 (0.25%) 2	4 / 801 (0.50%) 4	
Muscle spasms subjects affected / exposed occurrences (all)	0 / 807 (0.00%) 0	5 / 801 (0.62%) 5	
Muscular weakness			

subjects affected / exposed	3 / 807 (0.37%)	3 / 801 (0.37%)	
occurrences (all)	3	3	
Musculoskeletal pain			
subjects affected / exposed	4 / 807 (0.50%)	7 / 801 (0.87%)	
occurrences (all)	4	7	
Myalgia			
subjects affected / exposed	2 / 807 (0.25%)	4 / 801 (0.50%)	
occurrences (all)	2	4	
Osteoarthritis			
subjects affected / exposed	1 / 807 (0.12%)	7 / 801 (0.87%)	
occurrences (all)	1	7	
Neck pain			
subjects affected / exposed	3 / 807 (0.37%)	2 / 801 (0.25%)	
occurrences (all)	3	2	
Osteoporosis			
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)	
occurrences (all)	1	2	
Polymyalgia rheumatica			
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)	
occurrences (all)	2	1	
Pain in extremity			
subjects affected / exposed	9 / 807 (1.12%)	7 / 801 (0.87%)	
occurrences (all)	9	7	
Rhabdomyolysis			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences (all)	0	2	
Rheumatoid arthritis			
subjects affected / exposed	1 / 807 (0.12%)	3 / 801 (0.37%)	
occurrences (all)	1	3	
Spinal column stenosis			
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)	
occurrences (all)	1	2	
Infections and infestations			
Bronchitis			
subjects affected / exposed	12 / 807 (1.49%)	9 / 801 (1.12%)	
occurrences (all)	12	10	

Conjunctivitis		
subjects affected / exposed	2 / 807 (0.25%)	2 / 801 (0.25%)
occurrences (all)	2	2
Cellulitis		
subjects affected / exposed	4 / 807 (0.50%)	1 / 801 (0.12%)
occurrences (all)	4	1
Cystitis		
subjects affected / exposed	3 / 807 (0.37%)	3 / 801 (0.37%)
occurrences (all)	3	3
Erysipelas		
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)
occurrences (all)	2	1
Fungal infection		
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)
occurrences (all)	0	2
Gastroenteritis		
subjects affected / exposed	0 / 807 (0.00%)	4 / 801 (0.50%)
occurrences (all)	0	4
Gastrointestinal infection		
subjects affected / exposed	2 / 807 (0.25%)	0 / 801 (0.00%)
occurrences (all)	2	0
Gingivitis		
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)
occurrences (all)	0	2
Herpes zoster		
subjects affected / exposed	2 / 807 (0.25%)	3 / 801 (0.37%)
occurrences (all)	2	3
Infection		
subjects affected / exposed	2 / 807 (0.25%)	3 / 801 (0.37%)
occurrences (all)	2	3
Influenza		
subjects affected / exposed	3 / 807 (0.37%)	4 / 801 (0.50%)
occurrences (all)	3	4
Lower respiratory tract infection		
subjects affected / exposed	2 / 807 (0.25%)	2 / 801 (0.25%)
occurrences (all)	2	2

Nasopharyngitis			
subjects affected / exposed	5 / 807 (0.62%)	0 / 801 (0.00%)	
occurrences (all)	5	0	
Oesophageal candidiasis			
subjects affected / exposed	0 / 807 (0.00%)	2 / 801 (0.25%)	
occurrences (all)	0	2	
Pneumonia			
subjects affected / exposed	10 / 807 (1.24%)	5 / 801 (0.62%)	
occurrences (all)	10	6	
Pulpitis dental			
subjects affected / exposed	0 / 807 (0.00%)	4 / 801 (0.50%)	
occurrences (all)	0	4	
Upper respiratory tract infection			
subjects affected / exposed	1 / 807 (0.12%)	2 / 801 (0.25%)	
occurrences (all)	1	2	
Sinusitis			
subjects affected / exposed	0 / 807 (0.00%)	4 / 801 (0.50%)	
occurrences (all)	0	4	
Urinary tract infection			
subjects affected / exposed	19 / 807 (2.35%)	30 / 801 (3.75%)	
occurrences (all)	21	33	
Respiratory tract infection			
subjects affected / exposed	1 / 807 (0.12%)	3 / 801 (0.37%)	
occurrences (all)	1	3	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	5 / 807 (0.62%)	3 / 801 (0.37%)	
occurrences (all)	5	3	
Diabetes mellitus			
subjects affected / exposed	2 / 807 (0.25%)	5 / 801 (0.62%)	
occurrences (all)	2	5	
Gout			
subjects affected / exposed	1 / 807 (0.12%)	7 / 801 (0.87%)	
occurrences (all)	1	8	
Hypokalaemia			

subjects affected / exposed	2 / 807 (0.25%)	3 / 801 (0.37%)	
occurrences (all)	3	3	
Hyponatraemia			
subjects affected / exposed	5 / 807 (0.62%)	3 / 801 (0.37%)	
occurrences (all)	5	3	
Decreased appetite			
subjects affected / exposed	2 / 807 (0.25%)	1 / 801 (0.12%)	
occurrences (all)	2	1	
Vitamin D deficiency			
subjects affected / exposed	0 / 807 (0.00%)	3 / 801 (0.37%)	
occurrences (all)	0	3	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
25 June 2015	Amendment 1, dated 25-Jun-2015: The first amendment occurred before start of the trial. Amendment 1 specified 2 minor modifications to remove the terms IMP and NIMP because of different local requirements in the participating countries, and to clarify the supply and labeling of clopidogrel, ASA, and VKA.
17 August 2016	Amendment 3, dated 17-Aug-2016, Amendment 3 mainly addressed changes in standard of care due to a changing clinical setting for the patient population in GALILEO, wording updates in the inclusion/exclusion criteria for clarification, removal of interim analysis and inferiority margin of safety analysis in the statistical analysis section.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

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

The study was terminated prematurely following a DSMB recommendation on 07-Aug-2018 to stop the study due to imbalance in the efficacy and safety endpoints between treatment arms in favor of comparator. The study termination date was 13-Aug-2018.

Notes: