Clinical trial results:
Reduced-dosed rivaroxaban and standard-dosed rivaroxaban versus ASA in the long-term prevention of recurrent symptomatic venous thromboembolism in patients with symptomatic deep-vein thrombosis and/or pulmonary embolism

Summary

EudraCT number	2013-000619-26
Trial protocol	BE SE AT IT ES GB CZ DE HU DK NL NO PL
Global end of trial date	04 November 2016

Results information

Result version number	v2 (current)
This version publication date	17 February 2019
First version publication date	08 November 2017
Version creation reason	• Correction of full data set Control of data.

Trial information

Trial identification

Sponsor protocol code	BAY59-7939/16416

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02064439
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	04 November 2016
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	04 November 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary efficacy objective is to evaluate whether rivaroxaban, in doses of 10 mg or 20 mg, is superior to acetylsalicylic acid (ASA) 100 mg in the prevention of the primary efficacy outcome (i.e. fatal or non-fatal symptomatic recurrent venous thromboembolism).
The secondary efficacy objective is to evaluate whether rivaroxaban 10 mg and rivaroxaban 20 mg are superior to ASA 100 mg in the prevention of the secondary efficacy outcome (i.e. fatal or non-fatal symptomatic recurrent venous thromboembolism, myocardial infarction, ischemic stroke, systemic non-CNS embolism).

Protection of trial subjects:

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

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	05 March 2014
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 76
Country: Number of subjects enrolled	Austria: 28
Country: Number of subjects enrolled	Belgium: 81
Country: Number of subjects enrolled	Brazil: 88
Country: Number of subjects enrolled	Canada: 154
Country: Number of subjects enrolled	China: 323
Country: Number of subjects enrolled	Czech Republic: 203
Country: Number of subjects enrolled	Denmark: 152
Country: Number of subjects enrolled	France: 516
Country: Number of subjects enrolled	Germany: 142
Country: Number of subjects enrolled	Hungary: 80
Country: Number of subjects enrolled	Israel: 75
Country: Number of subjects enrolled	Italy: 104
Country: Number of subjects enrolled	Mexico: 23

Country: Number of subjects enrolled	Netherlands: 250
Country: Number of subjects enrolled	New Zealand: 62
Country: Number of subjects enrolled	Norway: 14
Country: Number of subjects enrolled	Philippines: 4
Country: Number of subjects enrolled	Poland: 23
Country: Number of subjects enrolled	Russian Federation: 368
Country: Number of subjects enrolled	South Africa: 143
Country: Number of subjects enrolled	Korea, Republic of: 62
Country: Number of subjects enrolled	Spain: 111
Country: Number of subjects enrolled	Sweden: 67
Country: Number of subjects enrolled	Switzerland: 37
Country: Number of subjects enrolled	Taiwan: 35
Country: Number of subjects enrolled	Thailand: 28
Country: Number of subjects enrolled	Turkey: 8
Country: Number of subjects enrolled	United Kingdom: 24
Country: Number of subjects enrolled	United States: 70
Country: Number of subjects enrolled	Vietnam: 14
Worldwide total number of subjects	3365
EEA total number of subjects	1795

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)	2053
From 65 to 84 years	1262
85 years and over	50

Subject disposition

Recruitment

Recruitment details:

In total 3439 subjects were screened at 244 sites in 31 countries from 05-Mar-2014 (First Patient First Visit) to 15-Mar-2016 (Last Patient First Visit).

Pre-assignment

Screening details:

Of the 3439 subjects screened 43 did not complete screening. Thus, 3396 subjects were randomly assigned to treatment, 31 of the randomized subjects never received study medication because either withdrew consent or were withdrawn from the study based on protocol violations.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD

Arm description:

Subjects were randomized, stratified by country and by index event, to receive rivaroxaban 10 mg tablet or matching placebo once daily (OD) with food for 12, or 9 to less than 12, or 6 months depending on the date of randomization. Treatment of all subjects stopped 6 months after the last subject was randomized.

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

Dosage and administration details:

10 mg tablet, OD

Arm title	Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD

Arm description:

Subjects were randomized, stratified by country and by index event, to receive rivaroxaban 20 mg tablet or matching placebo OD with food for 12, or 9 to less than 12, or 6 months depending on the date of randomization. Treatment of all subjects stopped 6 months after the last subject was randomized.

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

Dosage and administration details:

20 mg tablet, OD

Arm title	Acetylsalicylic (ASA) 100 mg, OD

Arm description:

Subjects were randomized, stratified by country and by index event, to receive ASA 100 mg tablet or matching placebo OD with food for 12, or 9 to less than 12, or 6 months depending on the date of randomization. Treatment of all subjects stopped 6 months after the last subject was randomized.

Arm type	Active comparator
Investigational medicinal product name	Acetylsalicylic (ASA)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg tablet, OD

Number of subjects in period 1	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD	Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD	Acetylsalicylic (ASA) 100 mg, OD
Started	1127	1107	1131
Completed	984	969	949
Not completed	143	138	182
Adverse event, serious fatal	-	2	3
Consent withdrawn by subject	29	18	26
Physician decision	-	1	1
Logistical difficulties	6	5	2
Adverse event, non-fatal	51	47	46
Safety outcome reached	12	20	10
Other	2	2	7
Non-compliance with study medication	21	19	23
Efficacy outcome reached	18	16	57
Lost to follow-up	1	3	4
Protocol deviation	3	5	3

Baseline characteristics

Reporting groups	
Reporting group title	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD
Reporting group description:	
Subjects were randomized, stratified by country and by index event, to receive rivaroxaban 10 mg tablet or matching placebo once daily (OD) with food for 12, or 9 to less than 12, or 6 months depending on the date of randomization. Treatment of all subjects stopped 6 months after the last subject was randomized.	
Reporting group title	Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD
Reporting group description:	
Subjects were randomized, stratified by country and by index event, to receive rivaroxaban 20 mg tablet or matching placebo OD with food for 12, or 9 to less than 12, or 6 months depending on the date of randomization. Treatment of all subjects stopped 6 months after the last subject was randomized.	
Reporting group title	Acetylsalicylic (ASA) 100 mg, OD
Reporting group description:	
Subjects were randomized, stratified by country and by index event, to receive ASA 100 mg tablet or matching placebo OD with food for 12, or 9 to less than 12, or 6 months depending on the date of randomization. Treatment of all subjects stopped 6 months after the last subject was randomized.	

Reporting group values	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD	Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD	Acetylsalicylic (ASA) 100 mg, OD
Number of subjects	1127	1107	1131
Age Categorical Units: Subjects			
Adults (18-64 years)	678	691	684
From 65-75 years	316	301	301
75 years and over	133	115	146
Age Continuous Units: years			
arithmetic mean	58.8	57.9	58.8
standard deviation	± 14.7	± 14.7	± 14.7
Gender Categorical Units: Subjects			
Female	507	505	488
Male	620	602	643
Ethnicity Units: Subjects			
Hispanic or Latino	31	31	30
Not Hispanic or Latino	892	899	889
Unknown or Not Reported	204	177	212
Race Units: Subjects			
American Indian or Alaska Native	2	0	2
Asian	161	159	159
Native Hawaiian or Other Pacific Islander	1	1	2
Black or African American	41	49	36
White	786	772	786
More than one race	1	0	5
Unknown or Not Reported	135	126	141

Reporting group values	Total		
Number of subjects	3365		
Age Categorical Units: Subjects			
Adults (18-64 years)	2053		
From 65-75 years	918		
75 years and over	394		
Age Continuous Units: years arithmetic mean standard deviation	- -		
Gender Categorical Units: Subjects			
Female	1500		
Male	1865		
Ethnicity Units: Subjects			
Hispanic or Latino	92		
Not Hispanic or Latino	2680		
Unknown or Not Reported	593		
Race Units: Subjects			
American Indian or Alaska Native	4		
Asian	479		
Native Hawaiian or Other Pacific Islander	4		
Black or African American	126		
White	2344		
More than one race	6		
Unknown or Not Reported	402		

Subject analysis sets

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

Full analysis set (FAS) includes all randomized subjects who received at least one dose of study medication.

Reporting group values	FAS		
Number of subjects	3365		
Age Categorical Units: Subjects			
Adults (18-64 years)	2053		
From 65-75 years	918		
75 years and over	364		
Age Continuous Units: years arithmetic mean standard deviation	 58.5 ± 14.7		

Gender Categorical Units: Subjects			
Female	1500		
Male	1865		
Ethnicity Units: Subjects			
Hispanic or Latino	2680		
Not Hispanic or Latino	92		
Unknown or Not Reported	593		
Race Units: Subjects			
American Indian or Alaska Native	4		
Asian	479		
Native Hawaiian or Other Pacific Islander	4		
Black or African American	126		
White	2344		
More than one race	6		
Unknown or Not Reported	402		

End points

End points reporting groups

Reporting group title	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD

Reporting group description:

Subjects were randomized, stratified by country and by index event, to receive rivaroxaban 10 mg tablet or matching placebo once daily (OD) with food for 12, or 9 to less than 12, or 6 months depending on the date of randomization. Treatment of all subjects stopped 6 months after the last subject was randomized.

Reporting group title	Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD

Reporting group description:

Subjects were randomized, stratified by country and by index event, to receive rivaroxaban 20 mg tablet or matching placebo OD with food for 12, or 9 to less than 12, or 6 months depending on the date of randomization. Treatment of all subjects stopped 6 months after the last subject was randomized.

Reporting group title	Acetylsalicylic (ASA) 100 mg, OD

Reporting group description:

Subjects were randomized, stratified by country and by index event, to receive ASA 100 mg tablet or matching placebo OD with food for 12, or 9 to less than 12, or 6 months depending on the date of randomization. Treatment of all subjects stopped 6 months after the last subject was randomized.

Subject analysis set title	FAS
Subject analysis set type	Full analysis

Subject analysis set description:

Full analysis set (FAS) includes all randomized subjects who received at least one dose of study medication.

Primary: Number of subjects with the composite of fatal or non-fatal symptomatic recurrent venous thromboembolism

End point title	Number of subjects with the composite of fatal or non-fatal symptomatic recurrent venous thromboembolism

End point description:

The primary efficacy outcomes (i.e., recurrent venous thromboembolism [VTE] defined as composite of fatal or non-fatal symptomatic recurrent VTE, including unexplained death for which pulmonary embolism [PE] could not be ruled out) as confirmed by the central independent adjudication committee (CIAC) were considered up to the end of the individual intended duration of treatment.

End point type	Primary

End point timeframe:

Up to 12 months

End point values	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD	Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD	Acetylsalicylic (ASA) 100 mg, OD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1127	1107	1131	
Units: subjects				
Composite	13	17	50	
Symptomatic recurrent Deep vein thrombosis (DVT)	8	9	29	
Symptomatic recurrent PE	5	6	19	
Death (PE)	0	0	1	
Death (unexplained and PE cannot be ruled out)	0	2	1	

Statistical analyses

Statistical analysis title	Rivaroxaban 20 mg vs. ASA 100 mg
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD v Acetylsalicylic (ASA) 100 mg, OD
Number of subjects included in analysis	2238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0001 [1]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.59

Notes:

[1] - P-value and hazard ratio estimates based on stratified proportional hazards model, with stratification based index event (DVT or PE with or without DVT).

Statistical analysis title	Rivaroxaban 10 mg vs. ASA 100 mg
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD v Acetylsalicylic (ASA) 100 mg, OD
Number of subjects included in analysis	2258
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [2]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.26
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.14
upper limit	0.47

Notes:

[2] - P-value and hazard ratio estimates based on stratified proportional hazards model, with stratification based index event (DVT or PE with or without DVT).

Statistical analysis title	Rivaroxaban 20 mg vs. Rivaroxaban 10 mg
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD v Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD

Number of subjects included in analysis	2234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.4328 [3]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.34
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	2.75

Notes:

[3] - P-value and hazard ratio estimates based on stratified proportional hazards model, with stratification based index event (DVT or PE with or without DVT).

Primary: Number of subjects with first treatment-emergent major bleeding

End point title	Number of subjects with first treatment-emergent major bleeding

End point description:

The principal safety outcome was major bleeding which was defined according to the criteria of the International Society on Thrombosis and Hemostasis (ISTH) as clinically overt bleeding and associated with a fall in hemoglobin of 2 gram per deciliter (g/dL) or more, or leading to a transfusion of 2 or more units of packed red blood cells or whole blood, or occurring in a critical site, e.g. intracranial, intraspinal, intraocular, pericardial, intra articular, intramuscular with compartment syndrome, retroperitoneal, or contributing to death.

End point type	Primary

End point timeframe:

Up to 12 months

End point values	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD	Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD	Acetylsalicylic (ASA) 100 mg, OD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1127	1107	1131	
Units: subjects				
Any major bleeding	5	6	3	
Fatal bleeding	0	1	1	
Non-fatal critical organ bleed	2	4	1	
Non-fatal non-critical organ bleeding	3	1	1	

Statistical analyses

Statistical analysis title	Rivaroxaban 20 mg vs. ASA 100 mg
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD v Acetylsalicylic (ASA) 100 mg, OD

Number of subjects included in analysis	2238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3235 [4]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	2.01
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.5
upper limit	8.04

Notes:

[4] - P-value and hazard ratio estimates based on stratified proportional hazards model, with stratification based index event (DVT or PE with or without DVT).

Statistical analysis title	Rivaroxaban 20 mg vs. Rivaroxaban 10 mg
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD v Acetylsalicylic (ASA) 100 mg, OD
Number of subjects included in analysis	2258
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.5005 [5]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.64
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.39
upper limit	6.84

Notes:

[5] - P-value and hazard ratio estimates based on stratified proportional hazards model, with stratification based index event (DVT or PE with or without DVT).

Statistical analysis title	Rivaroxaban 20 mg vs. Rivaroxaban 10 mg
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD v Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD
Number of subjects included in analysis	2234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7337 [6]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.23
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.37
upper limit	4.03

Notes:

[6] - P-value and hazard ratio estimates based on stratified proportional hazards model, with stratification based index event (DVT or PE with or without DVT).

Secondary: Number of subjects with the composite of the primary efficacy outcome, myocardial infarction, ischemic stroke or systemic non-CNS embolism

End point title	Number of subjects with the composite of the primary efficacy outcome, myocardial infarction, ischemic stroke or systemic non-CNS embolism

End point description:

The secondary efficacy outcome is the composite of the primary efficacy outcome, myocardial infarction (MI), ischemic stroke or non-central nervous system (CNS) systemic embolism.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD	Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD	Acetylsalicylic (ASA) 100 mg, OD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1127	1107	1131	
Units: subjects				
Composite	18	19	56	
Ischemic stroke	4	2	2	
Non-CNS systemic embolism	1	0	1	
Myocardial infarction	0	1	4	
Symptomatic recurrent DVT	8	9	29	
Symptomatic recurrent PE	5	6	18	
Death (PE)	0	0	1	
Death (unexplained and PE cannot be ruled out)	0	1	1	
Death (cardiovascular: myocardial infarction)	0	0	0	
Death (cardiovascular: ischemic stroke)	0	0	0	

Statistical analyses

Statistical analysis title	Rivaroxaban 20 mg vs. ASA 100 mg
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD v Acetylsalicylic (ASA) 100 mg, OD
Number of subjects included in analysis	2238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [7]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.34

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.2
upper limit	0.57

Notes:

[7] - P-value and hazard ratio estimates based on stratified proportional hazards model, with stratification based index event (DVT or PE with or without DVT).

Statistical analysis title	Rivaroxaban 10 mg vs. ASA 100 mg
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD v Acetylsalicylic (ASA) 100 mg, OD
Number of subjects included in analysis	2258
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.0001 [8]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.32
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	0.54

Notes:

[8] - P-value and hazard ratio estimates based on stratified proportional hazards model, with stratification based index event (DVT or PE with or without DVT).

Statistical analysis title	Rivaroxaban 20 mg vs. Rivaroxaban 10 mg
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD v Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD
Number of subjects included in analysis	2234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.8172 [9]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.08
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.57
upper limit	2.06

Notes:

[9] - P-value and hazard ratio estimates based on stratified proportional hazards model, with stratification based index event (DVT or PE with or without DVT).

Secondary: Number of subjects with non-major bleeding associated with study drug interruption for > 14 days

End point title	Number of subjects with non-major bleeding associated with study drug interruption for > 14 days

End point description:

The secondary safety outcome was clinically relevant non-major (CRNM) bleeding, which was adjudicated by the CIAC using the ASA criteria: the bleeding was non-major and the bleeding was

associated with a study medication interruption of more than 14 days.

End point type	Secondary

End point timeframe:

Up to 12 months

End point values	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD	Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD	Acetylsalicylic (ASA) 100 mg, OD	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	1127	1107	1131	
Units: subjects	12	17	12	

Statistical analyses

Statistical analysis title	Rivaroxaban 20 mg vs. ASA 100 mg
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD v Acetylsalicylic (ASA) 100 mg, OD
Number of subjects included in analysis	2238
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3318 [10]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	1.44
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.69
upper limit	3.02

Notes:

[10] - P-value and hazard ratio estimates based on stratified proportional hazards model, with stratification based index event (DVT or PE with or without DVT).

Statistical analysis title	Rivaroxaban 10 mg vs. ASA 100 mg
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD v Acetylsalicylic (ASA) 100 mg, OD
Number of subjects included in analysis	2258
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.9726 [11]
Method	Wald test
Parameter estimate	Hazard ratio (HR)
Point estimate	0.99

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.44
upper limit	2.2

Notes:

[11] - P-value and hazard ratio estimates based on stratified proportional hazards model, with stratification based index event (DVT or PE with or without DVT).

Statistical analysis title	Rivaroxaban 20 mg vs. Rivaroxaban 10 mg
Comparison groups	Rivaroxaban (Xarelto, BAY59-7939) 10 mg, OD v Rivaroxaban (Xarelto, BAY59-7939) 20 mg, OD
Number of subjects included in analysis	2234
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.3137
Method	Wald te
Parameter estimate	Hazard ratio (HR)
Point estimate	1.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.7
upper limit	3.06

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From after start of study medication but not more than 2 days after stop of study medication.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.1

Reporting groups

Reporting group title	Rivaroxaban (Xarelto, BAY59-7939) 10 mg

Reporting group description:

Subjects were randomized, stratified by country and by index event, to receive rivaroxaban 10 mg tablet or matching placebo once daily (OD) with food for 12, or 9 to less than 12, or 6 months depending on the date of randomization. Treatment of all subjects stopped 6 months after the last subject was randomized.

Reporting group title	Rivaroxaban (Xarelto, BAY59-7939) 20 mg

Reporting group description:

Subjects were randomized, stratified by country and by index event, to receive rivaroxaban 20 mg tablet or matching placebo OD with food for 12, or 9 to less than 12, or 6 months depending on the date of randomization. Treatment of all subjects stopped 6 months after the last subject was randomized.

Reporting group title	Acetylsalicylic (ASA) 100 mg

Reporting group description:

Subjects were randomized, stratified by country and by index event, to receive ASA 100 mg tablet or matching placebo OD with food for 12, or 9 to less than 12, or 6 months depending on the date of randomization. Treatment of all subjects stopped 6 months after the last subject was randomized.

Serious adverse events	Rivaroxaban (Xarelto, BAY59-7939) 10 mg	Rivaroxaban (Xarelto, BAY59-7939) 20 mg	Acetylsalicylic (ASA) 100 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	78 / 1127 (6.92%)	82 / 1107 (7.41%)	79 / 1131 (6.98%)
number of deaths (all causes)	3	10	7
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Adenocarcinoma of colon			
subjects affected / exposed	1 / 1127 (0.09%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal cell carcinoma			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Benign gastric neoplasm			

subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder cancer recurrent			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder transitional cell carcinoma			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Breast cancer			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix carcinoma recurrent			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Endometrial cancer			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastric cancer			

subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Leiomyosarcoma			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung carcinoma cell type unspecified stage IV			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Malignant melanoma stage I			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma stage IV			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Meningioma			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lung			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to lymph nodes			
subjects affected / exposed	1 / 1127 (0.09%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal carcinoma			

subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal carcinoma stage 0			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasma cell myeloma			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal cancer recurrent			
subjects affected / exposed	1 / 1127 (0.09%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric cancer			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine cancer			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine leiomyoma			
subjects affected / exposed	1 / 1127 (0.09%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon cancer metastatic			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate cancer			

subjects affected / exposed	3 / 1127 (0.27%)	1 / 1107 (0.09%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervix warts			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant glioma			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian cancer stage IV			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Vascular disorders			
Aortic aneurysm			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aortic dissection			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Aortic stenosis			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			

subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peripheral arterial occlusive disease			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Surgical and medical procedures			
Hysterectomy			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningioma surgery			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Overlap syndrome			

subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Asthma			
subjects affected / exposed	1 / 1127 (0.09%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 1127 (0.09%)	3 / 1107 (0.27%)	3 / 1131 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 1127 (0.09%)	2 / 1107 (0.18%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 2	0 / 0
Interstitial lung disease			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasal polyps			

subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleurisy			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary hypertension			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mass			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Organising pneumonia			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Adjustment disorder with depressed mood			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcohol abuse			

subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Alcoholism			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anxiety			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	2 / 1131 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Paranoia			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicide attempt			
subjects affected / exposed	3 / 1127 (0.27%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			
Cystoscopy			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoglobin decreased			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
White blood cell count decreased			

subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
B-lymphocyte count increased			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clavicle fracture			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	3 / 1131 (0.27%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femoral neck fracture			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	3 / 1131 (0.27%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fibula fracture			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Head injury			

subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Humerus fracture			
subjects affected / exposed	2 / 1127 (0.18%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint dislocation			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Radius fracture			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road traffic accident			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal compression fracture			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tendon rupture			

subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	1 / 1127 (0.09%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cervical vertebral fracture			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lower limb fracture			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomal hernia			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pubis fracture			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Craniocerebral injury			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Arteriosclerosis coronary artery			

subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Atrial fibrillation			
subjects affected / exposed	1 / 1127 (0.09%)	3 / 1107 (0.27%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block second degree			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bradycardia			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure chronic			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery disease			

subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	2 / 1131 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mitral valve incompetence			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericarditis constrictive			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Axonal neuropathy			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyskinesia			

subjects affected / exposed	2 / 1127 (0.18%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Headache			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Migraine			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Presyncope			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	2 / 1131 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paresis			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 1127 (0.00%)	2 / 1107 (0.18%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Iron deficiency anaemia			
subjects affected / exposed	0 / 1127 (0.00%)	2 / 1107 (0.18%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vestibular disorder			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden hearing loss			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Corneal degeneration			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Ascites			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0

Diverticulum			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulum intestinal			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastritis			
subjects affected / exposed	1 / 1127 (0.09%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhoids			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 1127 (0.09%)	2 / 1107 (0.18%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis relapsing			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Umbilical hernia			

subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subileus			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertrophic anal papilla			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal hernia			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eosinophilic oesophagitis			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colon dysplasia			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Bile duct stone			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary colic			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			

subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	2 / 1131 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seborrhoea			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urticaria			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pruritus generalised			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cutaneous lupus erythematosus			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Nephrolithiasis			
subjects affected / exposed	2 / 1127 (0.18%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neurogenic bladder			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal colic			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial nephritis			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral stenosis			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute kidney injury			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	2 / 1131 (0.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
End stage renal disease			

subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureterolithiasis			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Cushing's syndrome			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Joint ankylosis			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteitis			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	3 / 1127 (0.27%)	0 / 1107 (0.00%)	5 / 1131 (0.44%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 6
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rheumatoid arthritis			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Spinal column stenosis			
subjects affected / exposed	0 / 1127 (0.00%)	2 / 1107 (0.18%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mobility decreased			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meniscal degeneration			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal pain			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Appendicitis			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	1 / 1127 (0.09%)	2 / 1107 (0.18%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			

subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea infectious			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	2 / 1127 (0.18%)	0 / 1107 (0.00%)	2 / 1131 (0.18%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	2 / 1127 (0.18%)	1 / 1107 (0.09%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Influenza			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nasopharyngitis			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Orchitis			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			

subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasmodium falciparum infection			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	2 / 1127 (0.18%)	5 / 1107 (0.45%)	3 / 1131 (0.27%)
occurrences causally related to treatment / all	0 / 2	0 / 6	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomembranous colitis			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelitis			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis acute			
subjects affected / exposed	0 / 1127 (0.00%)	0 / 1107 (0.00%)	1 / 1131 (0.09%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	1 / 1127 (0.09%)	3 / 1107 (0.27%)	2 / 1131 (0.18%)
occurrences causally related to treatment / all	0 / 1	0 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Septic shock			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Urethral abscess			

subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	2 / 1127 (0.18%)	4 / 1107 (0.36%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 6	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis bacterial			
subjects affected / exposed	0 / 1127 (0.00%)	2 / 1107 (0.18%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infective exacerbation of chronic obstructive airways disease			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pseudomonal sepsis			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Pneumonia bacterial			

subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Borrelia infection			
subjects affected / exposed	1 / 1127 (0.09%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural infection			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Diabetes mellitus inadequate control			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obesity			
subjects affected / exposed	0 / 1127 (0.00%)	1 / 1107 (0.09%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Type 2 diabetes mellitus			
subjects affected / exposed	2 / 1127 (0.18%)	0 / 1107 (0.00%)	0 / 1131 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Frequency threshold for reporting non-serious adverse events: 0.3 %

Non-serious adverse events	Rivaroxaban (Xarelto, BAY59-7939) 10 mg	Rivaroxaban (Xarelto, BAY59-7939) 20 mg	Acetylsalicylic (ASA) 100 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 1127 (3.55%)	35 / 1107 (3.16%)	38 / 1131 (3.36%)
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	6 / 1127 (0.53%)	2 / 1107 (0.18%)	3 / 1131 (0.27%)
occurrences (all)	6	2	3
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 1127 (0.35%)	4 / 1107 (0.36%)	3 / 1131 (0.27%)
occurrences (all)	5	4	3
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	2 / 1127 (0.18%)	2 / 1107 (0.18%)	5 / 1131 (0.44%)
occurrences (all)	3	2	5
Constipation			
subjects affected / exposed	2 / 1127 (0.18%)	0 / 1107 (0.00%)	7 / 1131 (0.62%)
occurrences (all)	2	0	8
Diarrhoea			
subjects affected / exposed	4 / 1127 (0.35%)	4 / 1107 (0.36%)	1 / 1131 (0.09%)
occurrences (all)	4	5	1
Dyspepsia			
subjects affected / exposed	1 / 1127 (0.09%)	3 / 1107 (0.27%)	4 / 1131 (0.35%)
occurrences (all)	1	3	4
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 1127 (0.09%)	5 / 1107 (0.45%)	6 / 1131 (0.53%)
occurrences (all)	1	5	6
Vomiting			
subjects affected / exposed	0 / 1127 (0.00%)	4 / 1107 (0.36%)	2 / 1131 (0.18%)
occurrences (all)	0	4	2
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	5 / 1127 (0.44%)	3 / 1107 (0.27%)	3 / 1131 (0.27%)
occurrences (all)	5	3	3
Pruritus			

subjects affected / exposed	8 / 1127 (0.71%)	3 / 1107 (0.27%)	3 / 1131 (0.27%)
occurrences (all)	8	3	3
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	3 / 1127 (0.27%)	3 / 1107 (0.27%)	4 / 1131 (0.35%)
occurrences (all)	3	3	4
Myalgia			
subjects affected / exposed	2 / 1127 (0.18%)	2 / 1107 (0.18%)	4 / 1131 (0.35%)
occurrences (all)	2	2	4
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	4 / 1127 (0.35%)	2 / 1107 (0.18%)	0 / 1131 (0.00%)
occurrences (all)	4	2	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 1127 (0.09%)	4 / 1107 (0.36%)	3 / 1131 (0.27%)
occurrences (all)	1	6	4

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported