



Clinical trial results:

Efficacy and Safety of Rivaroxaban Prophylaxis Compared with Placebo in Ambulatory

Cancer Subjects Initiating Systemic Cancer Therapy and at High Risk for Venous

Thromboembolism

Summary

EudraCT number	2015-001630-21
Trial protocol	GB BE DE CZ BG IT
Global end of trial date	24 August 2018

Results information

Result version number	v1 (current)
This version publication date	24 August 2019
First version publication date	24 August 2019

Trial information

Trial identification

Sponsor protocol code	39039039STM4001
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02555878
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Janssen Scientific Affairs, LLC
Sponsor organisation address	1125 Trenton-Harbourton Road, Titusville, United States, 08560-0200
Public contact	Clinical Registry Group, Janssen Scientific Affairs, LLC, ClinicalTrialsEU@its.jnj.com
Scientific contact	Clinical Registry Group, Janssen Scientific Affairs, LLC, ClinicalTrialsEU@its.jnj.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	24 August 2018
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	24 August 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary efficacy objective was to demonstrate that rivaroxaban is superior to placebo for reducing the risk of the primary composite outcome as defined by objectively confirmed symptomatic lower extremity proximal deep vein thrombosis (DVT), asymptomatic lower extremity proximal DVT, symptomatic lower extremity distal DVT, symptomatic upper extremity DVT, symptomatic non-fatal pulmonary embolism (PE), incidental PE, and venous thromboembolism (VTE)-related death in ambulatory adult subjects with various cancer types receiving systemic cancer therapy who were at high risk of developing a VTE.

Protection of trial subjects:

This study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practices (GCP) and applicable regulatory requirements. Safety was assessed by the evaluation of bleeding event assessment and classification, clinical laboratory tests (hematology and serum chemistry), vital sign measurements, physical examinations, and adverse events.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	08 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	Brazil: 103
Country: Number of subjects enrolled	Bulgaria: 34
Country: Number of subjects enrolled	Canada: 3
Country: Number of subjects enrolled	Czech Republic: 37
Country: Number of subjects enrolled	France: 63
Country: Number of subjects enrolled	Belgium: 13
Country: Number of subjects enrolled	Germany: 113
Country: Number of subjects enrolled	Italy: 32
Country: Number of subjects enrolled	Russian Federation: 120
Country: Number of subjects enrolled	United Kingdom: 49
Country: Number of subjects enrolled	United States: 274
Worldwide total number of subjects	841
EEA total number of subjects	341

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)	471
From 65 to 84 years	363
85 years and over	7

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

A total of 841 subjects were enrolled in the study to receive either of the 2 treatments: rivaroxaban or matching placebo.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

Subjects received placebo tablet matched to rivaroxaban orally once daily for 180 days.

Arm type	Experimental
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received placebo matched to rivaroxaban orally once daily.

Arm title	Rivaroxaban 10 mg
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Arm description:

Subjects received rivaroxaban 10 milligram (mg) tablet orally once daily for 180 days.

Arm type	Experimental
Investigational medicinal product name	Rivaroxaban
Investigational medicinal product code	BAY-59-7939
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subjects received 10 mg of rivaroxaban tablet orally once daily.

Number of subjects in period 1	Placebo	Rivaroxaban 10 mg
Started	421	420
Completed	255	270
Not completed	166	150
Adverse event, serious fatal	4	1

Consent withdrawn by subject	48	48
Physician decision	12	13
Adverse event, non-fatal	4	5
Adverse event, non-fatal	4	2
Death	74	59
Unspecified	17	17
Lost to follow-up	2	3
Protocol deviation	1	2

Baseline characteristics

Reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received placebo tablet matched to rivaroxaban orally once daily for 180 days.	
Reporting group title	Rivaroxaban 10 mg
Reporting group description:	
Subjects received rivaroxaban 10 milligram (mg) tablet orally once daily for 180 days.	

Reporting group values	Placebo	Rivaroxaban 10 mg	Total
Number of subjects	421	420	841
Title for AgeCategorical Units: subjects			
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	234	237	471
From 65 to 84 years	182	181	363
85 years and over	5	2	7
Title for AgeContinuous Units: years			
arithmetic mean	61.9	62.1	
standard deviation	± 11.19	± 11.22	-
Title for Gender Units: subjects			
Female	215	198	413
Male	206	222	428

End points

End points reporting groups

Reporting group title	Placebo
Reporting group description:	
Subjects received placebo tablet matched to rivaroxaban orally once daily for 180 days.	
Reporting group title	Rivaroxaban 10 mg
Reporting group description:	
Subjects received rivaroxaban 10 milligram (mg) tablet orally once daily for 180 days.	

Primary: Percentage of Subjects with Time to First Occurrence of Primary Efficacy Endpoint (Composite and Components)

End point title	Percentage of Subjects with Time to First Occurrence of Primary Efficacy Endpoint (Composite and Components)
End point description:	
Percentage of subjects with time to the first occurrence of primary efficacy endpoint (composite and components) was reported. The primary efficacy composite endpoint is time to first occurrence of objectively confirmed symptomatic and asymptomatic lower extremity proximal DVT, symptomatic lower extremity distal DVT, symptomatic upper extremity DVT, symptomatic non-fatal PE, incidental PE, or VTE-related death as adjudicated by an independent blinded Clinical Endpoint Committee (CEC). The Intent-to-treat (ITT) population consisted of all randomized subjects.	
End point type	Primary
End point timeframe:	
Up to Day 180	

End point values	Placebo	Rivaroxaban 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	421	420		
Units: Percentage of Subjects				
number (not applicable)				
Primary efficacy composite endpoint	8.79	5.95		
Symptomatic lower extremity proximal DVT	1.90	2.14		
Symptomatic lower extremity distal DVT	1.19	0.48		
Symptomatic upper extremity DVT	1.43	0.95		
Symptomatic non-fatal PE	1.19	1.19		
Asymptomatic lower extremity proximal DVT	2.61	0.95		
Incidental PE	2.38	1.43		
VTE-related death	0.71	0.24		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
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Statistical analysis description:

Statistical analysis for primary efficacy composite endpoint.

Comparison groups	Placebo v Rivaroxaban 10 mg
Number of subjects included in analysis	841
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.101
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.66
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.4
upper limit	1.09

Statistical analysis title	Statistical Analysis 2
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Statistical analysis description:

Statistical analysis for Symptomatic lower extremity proximal DVT.

Comparison groups	Placebo v Rivaroxaban 10 mg
Number of subjects included in analysis	841
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.814
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.12
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.43
upper limit	2.91

Statistical analysis title	Statistical Analysis 3
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Statistical analysis description:

Statistical analysis for symptomatic lower extremity distal DVT.

Comparison groups	Placebo v Rivaroxaban 10 mg
Number of subjects included in analysis	841
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.26
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.4

Confidence interval	
level	95 %
sides	2-sided
lower limit	0.08
upper limit	2.07

Statistical analysis title	Statistical Analysis 4
Statistical analysis description: Statistical analysis for symptomatic upper extremity DVT.	
Comparison groups	Placebo v Rivaroxaban 10 mg
Number of subjects included in analysis	841
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.538
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.67
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.19
upper limit	2.39

Statistical analysis title	Statistical Analysis 5
Statistical analysis description: Statistical analysis for symptomatic non-fatal PE.	
Comparison groups	Placebo v Rivaroxaban 10 mg
Number of subjects included in analysis	841
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.977
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.02
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.29
upper limit	3.52

Statistical analysis title	Statistical Analysis 6
Statistical analysis description: Statistical analysis for asymptomatic lower extremity proximal DVT.	
Comparison groups	Placebo v Rivaroxaban 10 mg

Number of subjects included in analysis	841
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.063
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.35
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.11
upper limit	1.11

Statistical analysis title	Statistical Analysis 7
Statistical analysis description: Statistical analysis for incidental PE.	
Comparison groups	Placebo v Rivaroxaban 10 mg
Number of subjects included in analysis	841
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.301
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.59
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.21
upper limit	1.62

Statistical analysis title	Statistical Analysis 8
Statistical analysis description: Statistical analysis for VTE-related death.	
Comparison groups	Placebo v Rivaroxaban 10 mg
Number of subjects included in analysis	841
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.314
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.33
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.03
upper limit	3.18

Primary: Percentage of Subjects with Time to the First Occurrence of Major Bleeding Events as Defined by International Society of Thrombosis and Haemostasis (ISTH)

End point title	Percentage of Subjects with Time to the First Occurrence of Major Bleeding Events as Defined by International Society of Thrombosis and Haemostasis (ISTH)
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End point description:

Major bleeding is defined as clinically overt bleeding that is associated with a reduction in hemoglobin of 2 gram per deciliter (g/dL) or more, or a transfusion of 2 or more units of packed red blood cells or whole blood, or occurrence at a critical site defined as intracranial, intra-spinal, intraocular, pericardial, intra-articular, intra-muscular with compartment syndrome, retroperitoneal, or fatal outcome. The safety analysis population consisted of all randomized subjects who received at least 1 dose of study drug.

End point type	Primary
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End point timeframe:

From first dose of study drug to 2 days after the last dose of the study drug (up to 32 weeks)

End point values	Placebo	Rivaroxaban 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	404	405		
Units: Percentage of subjects				
number (not applicable)	0.99	1.98		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo v Rivaroxaban 10 mg
Number of subjects included in analysis	809
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.265
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	1.96
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.59
upper limit	6.49

Secondary: Percentage of Subjects with Time to the First Occurrence of Symptomatic VTE Events or VTE-Related Deaths

End point title	Percentage of Subjects with Time to the First Occurrence of
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End point description:

Percentage of subjects with time to first occurrence of the composite endpoint of symptomatic VTE events (symptomatic lower extremity proximal DVT, symptomatic lower extremity distal DVT, symptomatic upper extremity DVT, or symptomatic non-fatal PE) or VTE-related deaths as adjudicated by an independent blinded CEC up-to-Day 180 observation period was reported. The ITT population consisted of all randomized subjects.

End point type	Secondary
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End point timeframe:

Up to Day 180

End point values	Placebo	Rivaroxaban 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	421	420		
Units: Percentage of subjects				
number (not applicable)	5.23	3.81		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Time to the First Occurrence of All-Cause Mortality

End point title	Percentage of Subjects with Time to the First Occurrence of All-Cause Mortality
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End point description:

Percentage of subjects with time to the first occurrence of all-cause mortality as adjudicated by an independent blinded CEC up-to-Day 180 observation period was reported. The ITT population consisted of all randomized subjects.

End point type	Secondary
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End point timeframe:

Up to Day 180

End point values	Placebo	Rivaroxaban 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	421	420		
Units: Percentage of subjects				
number (not applicable)	23.8	20.0		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Time to the First Occurrence of Fatal or Non-fatal Arterial Thromboembolic Events (ATE)

End point title	Percentage of Subjects with Time to the First Occurrence of Fatal or Non-fatal Arterial Thromboembolic Events (ATE)
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End point description:

Percentage of subjects with time to first occurrence of fatal/non-fatal ATE (a composite of occurrence of myocardial infarction (MI), stroke [ischemic infarction with or without hemorrhagic conversion or primary hemorrhagic events – intraparenchymal hemorrhage, subdural hematoma or epidural hematoma] or any other ATE recorded) event as adjudicated by an independent blinded CEC up-to-Day 180 observation period was reported. The ITT population consisted of all randomized subjects.

End point type	Secondary
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End point timeframe:

Up to Day 180

End point values	Placebo	Rivaroxaban 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	421	420		
Units: Percentage of subjects				
number (not applicable)	1.66	0.95		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Time to the First Occurrence of Fatal or Non-fatal Visceral VTE

End point title	Percentage of Subjects with Time to the First Occurrence of Fatal or Non-fatal Visceral VTE
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End point description:

Percentage of subjects with time to the first occurrence of fatal or non-fatal visceral VTE as adjudicated by an independent blinded CEC up-to-Day 180 observation period was reported. The ITT population consisted of all randomized subjects.

End point type	Secondary
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End point timeframe:

Up to Day 180

End point values	Placebo	Rivaroxaban 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	421	420		
Units: Percentage of subjects				
number (not applicable)	0.48	0.24		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Time to the First Occurrence of Composite Efficacy Endpoint 1

End point title	Percentage of Subjects with Time to the First Occurrence of Composite Efficacy Endpoint 1
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End point description:

Percentage of subjects with time to first occurrence of composite efficacy endpoint 1 (composite of objectively confirmed symptomatic and asymptomatic lower extremity proximal DVT, symptomatic lower extremity distal DVT, symptomatic upper extremity DVT, symptomatic non-fatal PE, incidental PE or all-cause mortality) as adjudicated by an independent blinded CEC up-to-Day 180 observation period was reported. The ITT population consisted of all randomized subjects.

End point type	Secondary
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End point timeframe:

Up to Day 180

End point values	Placebo	Rivaroxaban 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	421	420		
Units: Percentage of subjects				
number (not applicable)	29.5	23.1		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Time to First Occurrence of Composite Efficacy Endpoint 2

End point title	Percentage of Subjects with Time to First Occurrence of Composite Efficacy Endpoint 2
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End point description:

Percentage of subjects with time to first occurrence of composite efficacy endpoint 2 (composite of objectively confirmed symptomatic lower extremity proximal DVT, symptomatic lower extremity distal DVT, symptomatic upper extremity DVT, symptomatic non-fatal PE or VTE-related deaths) as adjudicated by an independent blinded CEC up-to-Day 180 observation period was reported. The ITT population consisted of all randomized subjects.

End point type	Secondary
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End point timeframe:

Up to Day 180

End point values	Placebo	Rivaroxaban 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	421	420		
Units: Percentage of subjects				
number (not applicable)	5.23	3.81		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Time to First Occurrence of Composite Efficacy Endpoint 3

End point title	Percentage of Subjects with Time to First Occurrence of Composite Efficacy Endpoint 3
End point description: Percentage of subjects with time to first occurrence of composite efficacy endpoint 3 (composite of objectively confirmed symptomatic lower extremity proximal DVT, symptomatic lower extremity distal DVT, symptomatic upper extremity DVT, asymptomatic lower extremity proximal DVT, symptomatic non-fatal PE, incidental PE, VTE-related deaths, fatal/non-fatal ATE [MI, stroke {ischemic infarction with or without hemorrhagic conversion or primary hemorrhagic events – intraparenchymal hemorrhage, subdural hematoma or epidural hematoma} or any ATE] or fatal/non-fatal visceral VTE) as adjudicated by an independent blinded CEC up-to-Day 180 observation period was reported. The ITT population consisted of all randomized subjects.	
End point type	Secondary
End point timeframe: Up to Day 180	

End point values	Placebo	Rivaroxaban 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	421	420		
Units: Percentage of subjects				
number (not applicable)	10.7	6.90		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Time to First Occurrence of Composite Efficacy Endpoint 4

End point title	Percentage of Subjects with Time to First Occurrence of Composite Efficacy Endpoint 4
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End point description:

Percentage of subjects with time to first occurrence of composite efficacy endpoint 4 (composite of objectively confirmed symptomatic lower extremity proximal DVT, symptomatic lower extremity distal DVT, symptomatic upper extremity DVT, symptomatic non-fatal PE, VTE-related deaths or major bleeding events up to day 180) as adjudicated by an independent blinded CEC up-to-Day 180 observation period was reported. The ITT population consisted of all randomized subjects.

End point type	Secondary
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End point timeframe:

Up to Day 180

End point values	Placebo	Rivaroxaban 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	421	420		
Units: Percentage of subjects				
number (not applicable)	6.89	5.71		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Time to the First Occurrence of Clinically Relevant Non-major Bleeding

End point title	Percentage of Subjects with Time to the First Occurrence of Clinically Relevant Non-major Bleeding
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End point description:

Percentage of subjects with time to the first occurrence of clinically relevant non-major bleeding was reported. Clinically relevant non-major bleeding is defined as overt bleeding not meeting the criteria for major bleeding but associated with medical intervention, or unscheduled contact with a physician, or temporary cessation of study treatment, or discomfort such as pain, or impairment of activities of daily life. The safety analysis population consisted of all randomized subjects who received at least 1 dose of study drug.

End point type	Secondary
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End point timeframe:

From first dose of study drug to 2 days after the last dose of the study drug (up to 32 weeks)

End point values	Placebo	Rivaroxaban 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	404	405		
Units: Percentage of subjects				
number (not applicable)	1.98	2.72		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Time to the First Occurrence of Minor bleeding

End point title	Percentage of Subjects with Time to the First Occurrence of Minor bleeding
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End point description:

Percentage of subjects with time to the first occurrence of minor bleeding was reported. Minor bleeding (that is, minimal bleeding) is defined as overt bleeding episodes not meeting the criteria for major or clinically relevant non-major bleeding event. The safety analysis population consisted of all randomized subjects who received at least 1 dose of study drug.

End point type	Secondary
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End point timeframe:

From first dose of study drug to 2 days after the last dose of the study drug (up to 32 weeks)

End point values	Placebo	Rivaroxaban 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	404	405		
Units: Percentage of subjects				
number (not applicable)	3.96	6.91		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Subjects with Time to the First Occurrence of Any Bleeding

End point title	Percentage of Subjects with Time to the First Occurrence of Any Bleeding
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End point description:

Percentage of subjects with time to the first occurrence of any bleeding event was reported. Any bleeding is defined as a composite of major bleeding, clinically relevant non-major bleeding, or minor bleeding. The safety analysis population consisted of all randomized subjects who received at least 1 dose of study drug.

End point type	Secondary
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End point timeframe:

From first dose of study drug to 2 days after the last dose of the study drug (up to 32 weeks)

End point values	Placebo	Rivaroxaban 10 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	404	405		
Units: Percentage of subjects				
number (not applicable)	6.44	11.1		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Up to 32 weeks

Adverse event reporting additional description:

The safety analysis population consisted of all randomized subjects who received at least 1 dose of study drug.

Assessment type	Non-systematic
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Dictionary used

Dictionary name	MedDRA
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Dictionary version	21.0
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Reporting groups

Reporting group title	Rivaroxaban 10 mg
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Reporting group description:

Subjects received rivaroxaban 10 milligram (mg) tablet orally once daily for 180 days.

Reporting group title	Placebo
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Reporting group description:

Subjects received placebo tablet matched to rivaroxaban orally once daily for 180 days.

Serious adverse events	Rivaroxaban 10 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	134 / 405 (33.09%)	128 / 404 (31.68%)	
number of deaths (all causes)	85	106	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Lung Adenocarcinoma			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cancer Pain			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metastases to Liver			
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Metastases to Central Nervous			

System			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malignant Neoplasm Progression			
subjects affected / exposed	29 / 405 (7.16%)	33 / 404 (8.17%)	
occurrences causally related to treatment / all	0 / 29	0 / 33	
deaths causally related to treatment / all	0 / 28	0 / 29	
Metastases to Lymph Nodes			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm Progression			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ovarian Cancer			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tumour Associated Fever			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Superior Vena Cava Syndrome			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Chest Pain			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Death			
subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 2	
Condition Aggravated			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease Progression			
subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
General Physical Health Deterioration			
subjects affected / exposed	5 / 405 (1.23%)	4 / 404 (0.99%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 2	0 / 2	
Generalised Oedema			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Malaise			
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Mucosal Inflammation			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Multiple Organ Dysfunction Syndrome			

subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	8 / 405 (1.98%)	8 / 404 (1.98%)	
occurrences causally related to treatment / all	0 / 9	0 / 10	
deaths causally related to treatment / all	0 / 0	0 / 0	
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Immune system disorders			
Drug Hypersensitivity			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Female Genital Tract Fistula			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Failure			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	3 / 405 (0.74%)	5 / 404 (1.24%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 1	0 / 1	
Pleural Effusion			
subjects affected / exposed	3 / 405 (0.74%)	3 / 404 (0.74%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Laryngospasm			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Distress			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory Failure			
subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Psychiatric disorders			
Confusional State			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			

Aspiration Bronchial subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Blood Bilirubin Increased subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General Physical Condition Abnormal subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Glomerular Filtration Rate Decreased subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Platelet Count Decreased subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
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			
Hip Fracture subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pubis Fracture subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Atrial Fibrillation subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiotoxicity			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Coronary Artery Disease			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pericardial Effusion			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Supraventricular Tachycardia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Headache			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lethargy			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraesthesia			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle Contractions Involuntary			

subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient Global Amnesia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 405 (0.74%)	3 / 404 (0.74%)	
occurrences causally related to treatment / all	0 / 3	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile Neutropenia			
subjects affected / exposed	6 / 405 (1.48%)	4 / 404 (0.99%)	
occurrences causally related to treatment / all	0 / 6	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 405 (0.25%)	3 / 404 (0.74%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pancytopenia			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal disorders			

Abdominal Pain Upper			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal Pain			
subjects affected / exposed	5 / 405 (1.23%)	3 / 404 (0.74%)	
occurrences causally related to treatment / all	0 / 5	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 1	
Ascites			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	2 / 405 (0.49%)	2 / 404 (0.50%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Duodenal Obstruction			
subjects affected / exposed	3 / 405 (0.74%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspepsia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocolitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (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 / 405 (0.25%)	4 / 404 (0.99%)	
occurrences causally related to treatment / all	0 / 1	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 1	
Faecaloma			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Disorder			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal Obstruction			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal Perforation			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Gastrointestinal Toxicity			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Infarction			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Intestinal Ischaemia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal Obstruction			

subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nausea			
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 405 (0.49%)	3 / 404 (0.74%)	
occurrences causally related to treatment / all	0 / 2	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Small Intestinal Obstruction			
subjects affected / exposed	3 / 405 (0.74%)	3 / 404 (0.74%)	
occurrences causally related to treatment / all	0 / 3	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Bile Duct Obstruction			
subjects affected / exposed	1 / 405 (0.25%)	3 / 404 (0.74%)	
occurrences causally related to treatment / all	0 / 1	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholangitis			
subjects affected / exposed	2 / 405 (0.49%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholestasis			
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Hypertransaminaemia			

subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Decubitus Ulcer			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Drug Eruption			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rash Macular			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute Kidney Injury			
subjects affected / exposed	3 / 405 (0.74%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Dysuria			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal Failure			

subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hydronephrosis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Endocrine disorders			
Inappropriate Antidiuretic Hormone Secretion			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back Pain			
subjects affected / exposed	2 / 405 (0.49%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bursitis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscular Weakness			
subjects affected / exposed	2 / 405 (0.49%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Muscle Tightness			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal Pain			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
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 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Abdominal Sepsis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abscess Limb			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal Abscess			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Appendicitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atypical Pneumonia			
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bacteraemia			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Biliary Sepsis			
subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cellulitis			

subjects affected / exposed	3 / 405 (0.74%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 5	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cholecystitis Infective			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Clostridium Difficile Colitis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device Related Infection			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile Infection			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diverticulitis			
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Klebsiella Sepsis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis Viral			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower Respiratory Tract Infection			

subjects affected / exposed	0 / 405 (0.00%)	3 / 404 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lung Infection			
subjects affected / exposed	2 / 405 (0.49%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neutropenic Sepsis			
subjects affected / exposed	0 / 405 (0.00%)	3 / 404 (0.74%)	
occurrences causally related to treatment / all	0 / 0	0 / 3	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oral Candidiasis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	10 / 405 (2.47%)	4 / 404 (0.99%)	
occurrences causally related to treatment / all	0 / 10	0 / 4	
deaths causally related to treatment / all	0 / 1	0 / 0	
Sepsis			
subjects affected / exposed	6 / 405 (1.48%)	4 / 404 (0.99%)	
occurrences causally related to treatment / all	0 / 6	0 / 5	
deaths causally related to treatment / all	0 / 2	0 / 1	
Respiratory Tract Infection			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia Bacterial			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sinusitis			

subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic Shock			
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 1	
Tracheobronchitis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
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 / 405 (0.74%)	2 / 404 (0.50%)	
occurrences causally related to treatment / all	0 / 3	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	3 / 405 (0.74%)	5 / 404 (1.24%)	
occurrences causally related to treatment / all	0 / 3	0 / 5	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diabetic Ketoacidosis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrolyte Imbalance			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Failure to Thrive			

subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Feeding Intolerance			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypercalcaemia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperglycaemia			
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyponatraemia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (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 %

Non-serious adverse events	Rivaroxaban 10 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	221 / 405 (54.57%)	225 / 404 (55.69%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Brain Cancer Metastatic			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Cancer Pain			

subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)	
occurrences (all)	0	2	
Malignant Neoplasm Progression			
subjects affected / exposed	7 / 405 (1.73%)	4 / 404 (0.99%)	
occurrences (all)	7	5	
Metastases to Central Nervous System			
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)	
occurrences (all)	1	2	
Testicular Neoplasm			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Tumour Pain			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Vascular disorders			
Flushing			
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)	
occurrences (all)	1	2	
Haematoma			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Hyperaemia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Hot Flush			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Hypertension			
subjects affected / exposed	6 / 405 (1.48%)	8 / 404 (1.98%)	
occurrences (all)	7	9	
Hypotension			
subjects affected / exposed	3 / 405 (0.74%)	6 / 404 (1.49%)	
occurrences (all)	3	6	
Pallor			

subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Peripheral Coldness			
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)	
occurrences (all)	1	1	
Peripheral Vascular Disorder			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Phlebitis Superficial			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Phlebitis			
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)	
occurrences (all)	4	1	
Varicose Vein			
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)	
occurrences (all)	2	0	
Surgical and medical procedures			
Thrombosis Prophylaxis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Tooth Extraction			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	16 / 405 (3.95%)	19 / 404 (4.70%)	
occurrences (all)	18	38	
Chest Pain			
subjects affected / exposed	4 / 405 (0.99%)	1 / 404 (0.25%)	
occurrences (all)	4	1	
Chills			
subjects affected / exposed	2 / 405 (0.49%)	2 / 404 (0.50%)	
occurrences (all)	2	2	
Extravasation			

subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Fatigue		
subjects affected / exposed	44 / 405 (10.86%)	32 / 404 (7.92%)
occurrences (all)	55	41
Gait Disturbance		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Feeling Cold		
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)
occurrences (all)	1	1
General Physical Health Deterioration		
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)
occurrences (all)	2	0
Induration		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Inflammation		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Influenza Like Illness		
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)
occurrences (all)	1	1
Malaise		
subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)
occurrences (all)	0	2
Localised Oedema		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Mucosal Dryness		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Non-Cardiac Chest Pain		
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)
occurrences (all)	1	2
Mucosal Inflammation		

subjects affected / exposed	8 / 405 (1.98%)	5 / 404 (1.24%)	
occurrences (all)	10	5	
Oedema			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Oedema Peripheral			
subjects affected / exposed	9 / 405 (2.22%)	19 / 404 (4.70%)	
occurrences (all)	10	23	
Pain			
subjects affected / exposed	6 / 405 (1.48%)	7 / 404 (1.73%)	
occurrences (all)	6	8	
Performance Status Decreased			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Peripheral Swelling			
subjects affected / exposed	0 / 405 (0.00%)	4 / 404 (0.99%)	
occurrences (all)	0	5	
Pyrexia			
subjects affected / exposed	9 / 405 (2.22%)	16 / 404 (3.96%)	
occurrences (all)	12	19	
Immune system disorders			
Drug Hypersensitivity			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Food Allergy			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Seasonal Allergy			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Reproductive system and breast disorders			
Genital Pain			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Pelvic Pain			

subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Prostatitis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Vaginal Discharge			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Atelectasis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Bronchopneumopathy			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Chylothorax			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	2	
Chronic Obstructive Pulmonary Disease			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Cough			
subjects affected / exposed	9 / 405 (2.22%)	14 / 404 (3.47%)	
occurrences (all)	9	17	
Dysaesthesia Pharynx			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Epistaxis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Dyspnoea Exertional			
subjects affected / exposed	0 / 405 (0.00%)	4 / 404 (0.99%)	
occurrences (all)	0	4	
Dyspnoea			

subjects affected / exposed	17 / 405 (4.20%)	9 / 404 (2.23%)
occurrences (all)	19	11
Dysphonia		
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)
occurrences (all)	1	1
Mediastinal Shift		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Lung Disorder		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Hypoxia		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Hiccups		
subjects affected / exposed	2 / 405 (0.49%)	2 / 404 (0.50%)
occurrences (all)	2	2
Nasal Congestion		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Pleural Effusion		
subjects affected / exposed	2 / 405 (0.49%)	3 / 404 (0.74%)
occurrences (all)	3	3
Oropharyngeal Pain		
subjects affected / exposed	4 / 405 (0.99%)	3 / 404 (0.74%)
occurrences (all)	4	3
Pleural Thickening		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Nasal Dryness		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Rhinitis Allergic		
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)
occurrences (all)	1	1
Productive Cough		

subjects affected / exposed	0 / 405 (0.00%)	7 / 404 (1.73%)	
occurrences (all)	0	7	
Respiratory Disorder			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Respiratory Tract Congestion			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Wheezing			
subjects affected / exposed	2 / 405 (0.49%)	1 / 404 (0.25%)	
occurrences (all)	2	1	
Upper-Airway Cough Syndrome			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Sinus Congestion			
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)	
occurrences (all)	2	0	
Psychiatric disorders			
Confusional State			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Anxiety			
subjects affected / exposed	4 / 405 (0.99%)	3 / 404 (0.74%)	
occurrences (all)	4	3	
Insomnia			
subjects affected / exposed	8 / 405 (1.98%)	5 / 404 (1.24%)	
occurrences (all)	8	5	
Depression			
subjects affected / exposed	2 / 405 (0.49%)	4 / 404 (0.99%)	
occurrences (all)	2	4	
Irritability			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Mood Swings			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	

Sleep Disorder subjects affected / exposed occurrences (all)	2 / 405 (0.49%) 2	4 / 404 (0.99%) 4	
Restlessness subjects affected / exposed occurrences (all)	1 / 405 (0.25%) 1	2 / 404 (0.50%) 2	
Stress subjects affected / exposed occurrences (all)	1 / 405 (0.25%) 1	0 / 404 (0.00%) 0	
Product issues Thrombosis in Device subjects affected / exposed occurrences (all)	0 / 405 (0.00%) 0	1 / 404 (0.25%) 1	
Investigations Alanine Aminotransferase Increased subjects affected / exposed occurrences (all)	9 / 405 (2.22%) 14	10 / 404 (2.48%) 12	
Aspartate Aminotransferase Increased subjects affected / exposed occurrences (all)	6 / 405 (1.48%) 11	12 / 404 (2.97%) 15	
Bilirubin Conjugated Decreased subjects affected / exposed occurrences (all)	4 / 405 (0.99%) 4	10 / 404 (2.48%) 10	
Blood Albumin Decreased subjects affected / exposed occurrences (all)	1 / 405 (0.25%) 1	1 / 404 (0.25%) 1	
Blood Alkaline Phosphatase Decreased subjects affected / exposed occurrences (all)	1 / 405 (0.25%) 1	0 / 404 (0.00%) 0	
Blood Alkaline Phosphatase Increased subjects affected / exposed occurrences (all)	6 / 405 (1.48%) 6	6 / 404 (1.49%) 6	
Blood Bicarbonate Increased subjects affected / exposed occurrences (all)	1 / 405 (0.25%) 1	0 / 404 (0.00%) 0	

Blood Bilirubin Decreased subjects affected / exposed occurrences (all)	0 / 405 (0.00%) 0	1 / 404 (0.25%) 1
Blood Bilirubin Increased subjects affected / exposed occurrences (all)	1 / 405 (0.25%) 1	6 / 404 (1.49%) 7
Blood Calcium Decreased subjects affected / exposed occurrences (all)	0 / 405 (0.00%) 0	1 / 404 (0.25%) 1
Blood Calcium Increased subjects affected / exposed occurrences (all)	0 / 405 (0.00%) 0	1 / 404 (0.25%) 1
Blood Chloride Decreased subjects affected / exposed occurrences (all)	1 / 405 (0.25%) 1	0 / 404 (0.00%) 0
Blood Creatinine Decreased subjects affected / exposed occurrences (all)	1 / 405 (0.25%) 1	0 / 404 (0.00%) 0
Blood Creatinine Increased subjects affected / exposed occurrences (all)	3 / 405 (0.74%) 3	2 / 404 (0.50%) 2
Blood Glucose Decreased subjects affected / exposed occurrences (all)	0 / 405 (0.00%) 0	1 / 404 (0.25%) 1
Blood Glucose Increased subjects affected / exposed occurrences (all)	5 / 405 (1.23%) 5	12 / 404 (2.97%) 14
Blood Potassium Decreased subjects affected / exposed occurrences (all)	2 / 405 (0.49%) 2	1 / 404 (0.25%) 1
Blood Potassium Increased subjects affected / exposed occurrences (all)	2 / 405 (0.49%) 2	6 / 404 (1.49%) 6
Blood Sodium Decreased subjects affected / exposed occurrences (all)	1 / 405 (0.25%) 1	0 / 404 (0.00%) 0

Blood Sodium Increased		
subjects affected / exposed	0 / 405 (0.00%)	3 / 404 (0.74%)
occurrences (all)	0	3
Blood Urea Increased		
subjects affected / exposed	0 / 405 (0.00%)	4 / 404 (0.99%)
occurrences (all)	0	4
Blood Uric Acid Increased		
subjects affected / exposed	3 / 405 (0.74%)	1 / 404 (0.25%)
occurrences (all)	3	2
C-Reactive Protein Increased		
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)
occurrences (all)	1	2
Creatinine Renal Clearance Decreased		
subjects affected / exposed	3 / 405 (0.74%)	8 / 404 (1.98%)
occurrences (all)	4	8
Creatinine Renal Clearance Increased		
subjects affected / exposed	4 / 405 (0.99%)	4 / 404 (0.99%)
occurrences (all)	4	5
Gamma-Glutamyltransferase Increased		
subjects affected / exposed	2 / 405 (0.49%)	1 / 404 (0.25%)
occurrences (all)	2	1
Haematocrit Decreased		
subjects affected / exposed	5 / 405 (1.23%)	0 / 404 (0.00%)
occurrences (all)	5	0
Haemoglobin Decreased		
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)
occurrences (all)	1	1
Hepatic Enzyme Increased		
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)
occurrences (all)	1	1
Lymphocyte Count Decreased		
subjects affected / exposed	5 / 405 (1.23%)	7 / 404 (1.73%)
occurrences (all)	7	9
Lymphocyte Count Increased		

subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)
occurrences (all)	0	2
Monocyte Count Decreased		
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)
occurrences (all)	1	1
Monocyte Count Increased		
subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)
occurrences (all)	0	2
Neutrophil Count Decreased		
subjects affected / exposed	4 / 405 (0.99%)	10 / 404 (2.48%)
occurrences (all)	6	11
Platelet Count Decreased		
subjects affected / exposed	4 / 405 (0.99%)	10 / 404 (2.48%)
occurrences (all)	4	17
Neutrophil Count Increased		
subjects affected / exposed	2 / 405 (0.49%)	2 / 404 (0.50%)
occurrences (all)	2	2
Platelet Count Increased		
subjects affected / exposed	6 / 405 (1.48%)	4 / 404 (0.99%)
occurrences (all)	6	4
Protein Total Decreased		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Red Blood Cell Count Decreased		
subjects affected / exposed	7 / 405 (1.73%)	5 / 404 (1.24%)
occurrences (all)	7	5
Transaminases Increased		
subjects affected / exposed	2 / 405 (0.49%)	1 / 404 (0.25%)
occurrences (all)	2	3
Vascular Resistance Systemic Increased		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Troponin Increased		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0

Vitamin B12 Decreased subjects affected / exposed occurrences (all)	0 / 405 (0.00%) 0	1 / 404 (0.25%) 1	
Weight Decreased subjects affected / exposed occurrences (all)	10 / 405 (2.47%) 10	9 / 404 (2.23%) 10	
Weight Increased subjects affected / exposed occurrences (all)	0 / 405 (0.00%) 0	1 / 404 (0.25%) 1	
White Blood Cell Count Decreased subjects affected / exposed occurrences (all)	6 / 405 (1.48%) 8	9 / 404 (2.23%) 10	
White Blood Cell Count Increased subjects affected / exposed occurrences (all)	3 / 405 (0.74%) 3	4 / 404 (0.99%) 4	
Injury, poisoning and procedural complications			
Contusion subjects affected / exposed occurrences (all)	1 / 405 (0.25%) 1	0 / 404 (0.00%) 0	
Face Injury subjects affected / exposed occurrences (all)	1 / 405 (0.25%) 1	0 / 404 (0.00%) 0	
Fall subjects affected / exposed occurrences (all)	2 / 405 (0.49%) 2	3 / 404 (0.74%) 3	
Head Injury subjects affected / exposed occurrences (all)	0 / 405 (0.00%) 0	1 / 404 (0.25%) 1	
Limb Injury subjects affected / exposed occurrences (all)	0 / 405 (0.00%) 0	1 / 404 (0.25%) 1	
Lumbar Vertebral Fracture subjects affected / exposed occurrences (all)	0 / 405 (0.00%) 0	1 / 404 (0.25%) 1	
Procedural Headache			

subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Radiation Injury			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Radiation Skin Injury			
subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)	
occurrences (all)	0	2	
Scar			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Scratch			
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)	
occurrences (all)	2	0	
Thermal Burn			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	2	
Tooth Fracture			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Cardiac disorders			
Angina Pectoris			
subjects affected / exposed	2 / 405 (0.49%)	1 / 404 (0.25%)	
occurrences (all)	2	1	
Arrhythmia			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Atrial Fibrillation			
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)	
occurrences (all)	1	1	
Bradycardia			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Cardiac Failure Congestive			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	

Cardiovascular Disorder			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Left Ventricular Hypertrophy			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Myocardial Ischaemia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Palpitations			
subjects affected / exposed	0 / 405 (0.00%)	3 / 404 (0.74%)	
occurrences (all)	0	3	
Sinus Tachycardia			
subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)	
occurrences (all)	0	2	
Supraventricular Extrasystoles			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	2	0	
Tachycardia			
subjects affected / exposed	2 / 405 (0.49%)	3 / 404 (0.74%)	
occurrences (all)	2	3	
Nervous system disorders			
Ageusia			
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)	
occurrences (all)	1	2	
Anosmia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Ataxia			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Balance Disorder			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Coordination Abnormal			

subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Depressed Level of Consciousness		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Encephalopathy		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Dysgeusia		
subjects affected / exposed	5 / 405 (1.23%)	3 / 404 (0.74%)
occurrences (all)	6	3
Dysaesthesia		
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)
occurrences (all)	2	1
Dizziness		
subjects affected / exposed	2 / 405 (0.49%)	4 / 404 (0.99%)
occurrences (all)	2	4
Hypotonia		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Hypoaesthesia		
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)
occurrences (all)	1	3
Headache		
subjects affected / exposed	5 / 405 (1.23%)	6 / 404 (1.49%)
occurrences (all)	5	6
Memory Impairment		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Epilepsy		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Neuralgia		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Migraine		

subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)
occurrences (all)	0	2
Neuropathy Peripheral		
subjects affected / exposed	16 / 405 (3.95%)	12 / 404 (2.97%)
occurrences (all)	17	12
Orthostatic Intolerance		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	2
Peripheral Motor Neuropathy		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Paraesthesia		
subjects affected / exposed	4 / 405 (0.99%)	18 / 404 (4.46%)
occurrences (all)	4	22
Peripheral Sensory Neuropathy		
subjects affected / exposed	8 / 405 (1.98%)	5 / 404 (1.24%)
occurrences (all)	8	8
Polyneuropathy		
subjects affected / exposed	7 / 405 (1.73%)	8 / 404 (1.98%)
occurrences (all)	9	8
Psychomotor Hyperactivity		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Sciatica		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Seizure		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Sinus Headache		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Thermohyperaesthesia		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Tremor		

subjects affected / exposed occurrences (all)	0 / 405 (0.00%) 0	1 / 404 (0.25%) 1	
Blood and lymphatic system disorders			
Anaemia Macrocytic			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Anaemia			
subjects affected / exposed	46 / 405 (11.36%)	59 / 404 (14.60%)	
occurrences (all)	56	75	
Febrile Bone Marrow Aplasia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	2	0	
Haemorrhagic Diathesis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Hypochromic Anaemia			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Increased Tendency to Bruise			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Hypocoagulable State			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Leukocytosis			
subjects affected / exposed	2 / 405 (0.49%)	2 / 404 (0.50%)	
occurrences (all)	3	2	
Iron Deficiency Anaemia			
subjects affected / exposed	2 / 405 (0.49%)	1 / 404 (0.25%)	
occurrences (all)	4	1	
Lymphadenopathy			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Leukopenia			
subjects affected / exposed	7 / 405 (1.73%)	11 / 404 (2.72%)	
occurrences (all)	11	22	

Pancytopenia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Lymphopenia			
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)	
occurrences (all)	1	1	
Neutropenia			
subjects affected / exposed	25 / 405 (6.17%)	24 / 404 (5.94%)	
occurrences (all)	33	43	
Splenic Infarction			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Thrombocytopenia			
subjects affected / exposed	12 / 405 (2.96%)	19 / 404 (4.70%)	
occurrences (all)	14	30	
Thrombocytosis			
subjects affected / exposed	1 / 405 (0.25%)	6 / 404 (1.49%)	
occurrences (all)	1	6	
Ear and labyrinth disorders			
Deafness			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Hypoacusis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Tinnitus			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Vertigo			
subjects affected / exposed	2 / 405 (0.49%)	3 / 404 (0.74%)	
occurrences (all)	2	3	
Eye disorders			
Blepharospasm			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Dry Eye			

subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Eye Discharge			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Eye Irritation			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Eye Pain			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Lacrimation Increased			
subjects affected / exposed	3 / 405 (0.74%)	0 / 404 (0.00%)	
occurrences (all)	3	0	
Photopsia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Vision Blurred			
subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)	
occurrences (all)	0	2	
Visual Impairment			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Abdominal Discomfort			
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)	
occurrences (all)	2	0	
Abdominal Distension			
subjects affected / exposed	2 / 405 (0.49%)	1 / 404 (0.25%)	
occurrences (all)	2	1	
Abdominal Pain			
subjects affected / exposed	14 / 405 (3.46%)	14 / 404 (3.47%)	
occurrences (all)	14	15	
Abdominal Pain Lower			
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)	
occurrences (all)	2	0	

Abdominal Pain Upper		
subjects affected / exposed	7 / 405 (1.73%)	6 / 404 (1.49%)
occurrences (all)	8	8
Abdominal Rigidity		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Anal Incontinence		
subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)
occurrences (all)	0	2
Aphthous Ulcer		
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)
occurrences (all)	2	0
Cheilitis		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Ascites		
subjects affected / exposed	1 / 405 (0.25%)	4 / 404 (0.99%)
occurrences (all)	1	4
Constipation		
subjects affected / exposed	29 / 405 (7.16%)	12 / 404 (2.97%)
occurrences (all)	30	12
Dental Pulp Disorder		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Diarrhoea		
subjects affected / exposed	34 / 405 (8.40%)	36 / 404 (8.91%)
occurrences (all)	40	44
Dry Mouth		
subjects affected / exposed	4 / 405 (0.99%)	2 / 404 (0.50%)
occurrences (all)	4	2
Dyspepsia		
subjects affected / exposed	8 / 405 (1.98%)	5 / 404 (1.24%)
occurrences (all)	9	5
Dysphagia		
subjects affected / exposed	3 / 405 (0.74%)	2 / 404 (0.50%)
occurrences (all)	3	2

Flatulence		
subjects affected / exposed	2 / 405 (0.49%)	3 / 404 (0.74%)
occurrences (all)	2	3
Gastritis		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Gastrointestinal Pain		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Gastrooesophageal Reflux Disease		
subjects affected / exposed	5 / 405 (1.23%)	2 / 404 (0.50%)
occurrences (all)	5	2
Haemorrhoids		
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)
occurrences (all)	1	1
Nausea		
subjects affected / exposed	55 / 405 (13.58%)	55 / 404 (13.61%)
occurrences (all)	78	63
Oesophageal Compression		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Oesophageal Spasm		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Oesophagitis		
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)
occurrences (all)	1	3
Pancreatic Failure		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Oral Pain		
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)
occurrences (all)	2	0
Proctalgia		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1

Stomatitis			
subjects affected / exposed	8 / 405 (1.98%)	7 / 404 (1.73%)	
occurrences (all)	8	8	
Rectal Prolapse			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Toothache			
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)	
occurrences (all)	1	2	
Tongue Coated			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Vomiting			
subjects affected / exposed	28 / 405 (6.91%)	17 / 404 (4.21%)	
occurrences (all)	32	18	
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Cholestasis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Hepatic Steatosis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Hepatitis Toxic			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	2	0	
Hepatocellular Injury			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Hepatotoxicity			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Hyperbilirubinaemia			

subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)	
occurrences (all)	1	1	
Liver Injury			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Jaundice			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Decubitus Ulcer			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Butterfly Rash			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Blister			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Dermatitis Acneiform			
subjects affected / exposed	1 / 405 (0.25%)	3 / 404 (0.74%)	
occurrences (all)	1	3	
Alopecia			
subjects affected / exposed	14 / 405 (3.46%)	12 / 404 (2.97%)	
occurrences (all)	14	12	
Ecchymosis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Dry Skin			
subjects affected / exposed	4 / 405 (0.99%)	0 / 404 (0.00%)	
occurrences (all)	4	0	
Dermatitis Allergic			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	

Dermatitis Exfoliative Generalised		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Nail Discolouration		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Lividity		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Hyperhidrosis		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Erythema		
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)
occurrences (all)	1	2
Nail Disorder		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Palmar-Plantar Erythrodysesthesia Syndrome		
subjects affected / exposed	10 / 405 (2.47%)	9 / 404 (2.23%)
occurrences (all)	10	9
Pain of Skin		
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)
occurrences (all)	2	0
Night Sweats		
subjects affected / exposed	2 / 405 (0.49%)	5 / 404 (1.24%)
occurrences (all)	2	6
Nail Dystrophy		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Rash Generalised		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	2	0
Rash		

subjects affected / exposed	5 / 405 (1.23%)	7 / 404 (1.73%)
occurrences (all)	5	7
Pruritus		
subjects affected / exposed	4 / 405 (0.99%)	3 / 404 (0.74%)
occurrences (all)	4	3
Rash Maculo-Papular		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Photosensitivity Reaction		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Seborrhoea		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Rash Pruritic		
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)
occurrences (all)	1	2
Skin Exfoliation		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Skin Irritation		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Skin Lesion		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Skin Mass		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Skin Reaction		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	2	0
Solar Dermatitis		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Urticaria		

subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	2	
Yellow Skin			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Renal and urinary disorders			
Bladder Spasm			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Acute Kidney Injury			
subjects affected / exposed	0 / 405 (0.00%)	4 / 404 (0.99%)	
occurrences (all)	0	4	
Dysuria			
subjects affected / exposed	0 / 405 (0.00%)	5 / 404 (1.24%)	
occurrences (all)	0	5	
Hypertonic Bladder			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Kidney Congestion			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Nephrolithiasis			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Nephropathy Toxic			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Renal Failure			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Renal Cyst			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Pollakiuria			
subjects affected / exposed	3 / 405 (0.74%)	2 / 404 (0.50%)	
occurrences (all)	3	2	

Renal Infarct			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Urinary Incontinence			
subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)	
occurrences (all)	0	2	
Urinary Retention			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Urinary Tract Pain			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Endocrine disorders			
Hypercalcaemia of Malignancy			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Hypothyroidism			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	10 / 405 (2.47%)	1 / 404 (0.25%)	
occurrences (all)	12	1	
Back Pain			
subjects affected / exposed	5 / 405 (1.23%)	6 / 404 (1.49%)	
occurrences (all)	5	6	
Bone Pain			
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)	
occurrences (all)	1	2	
Flank Pain			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Hypercreatinaemia			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Joint Swelling			

subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)	
occurrences (all)	1	1	
Muscle Mass			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Muscle Spasms			
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)	
occurrences (all)	1	1	
Muscular Weakness			
subjects affected / exposed	2 / 405 (0.49%)	5 / 404 (1.24%)	
occurrences (all)	2	7	
Muscle Tightness			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Musculoskeletal Pain			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)	
occurrences (all)	0	2	
Myalgia			
subjects affected / exposed	3 / 405 (0.74%)	2 / 404 (0.50%)	
occurrences (all)	3	2	
Osteoarthritis			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Pain in Extremity			
subjects affected / exposed	6 / 405 (1.48%)	8 / 404 (1.98%)	
occurrences (all)	6	9	
Pain in Jaw			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Spinal Pain			
subjects affected / exposed	2 / 405 (0.49%)	2 / 404 (0.50%)	
occurrences (all)	2	2	
Infections and infestations			

Abscess		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Abscess Limb		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Angular Cheilitis		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Biliary Sepsis		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Bronchitis		
subjects affected / exposed	1 / 405 (0.25%)	5 / 404 (1.24%)
occurrences (all)	1	6
Candida Infection		
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)
occurrences (all)	1	1
Catheter Site Infection		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Cellulitis		
subjects affected / exposed	2 / 405 (0.49%)	2 / 404 (0.50%)
occurrences (all)	3	2
Clostridium Difficile Colitis		
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)
occurrences (all)	2	0
Clostridium Difficile Infection		
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)
occurrences (all)	1	1
Coccidioidomycosis		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Conjunctivitis		
subjects affected / exposed	3 / 405 (0.74%)	0 / 404 (0.00%)
occurrences (all)	3	0

Device Related Infection		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Ear Infection		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Folliculitis		
subjects affected / exposed	4 / 405 (0.99%)	0 / 404 (0.00%)
occurrences (all)	4	0
Fungal Infection		
subjects affected / exposed	0 / 405 (0.00%)	2 / 404 (0.50%)
occurrences (all)	0	3
Fungal Skin Infection		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	2	0
Furuncle		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Gastroenteritis Viral		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Genital Infection Fungal		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Influenza		
subjects affected / exposed	2 / 405 (0.49%)	1 / 404 (0.25%)
occurrences (all)	2	1
Oesophageal Candidiasis		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Nasopharyngitis		
subjects affected / exposed	3 / 405 (0.74%)	2 / 404 (0.50%)
occurrences (all)	3	2
Oral Candidiasis		
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)
occurrences (all)	2	0

Oral Fungal Infection		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Oral Herpes		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Oral Infection		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Paronychia		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Perirectal Abscess		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Pharyngitis Streptococcal		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Pneumonia		
subjects affected / exposed	1 / 405 (0.25%)	3 / 404 (0.74%)
occurrences (all)	1	3
Pneumonia Bacterial		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Pulpitis Dental		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Postoperative Wound Infection		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Pyelonephritis Chronic		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Respiratory Tract Infection		
subjects affected / exposed	3 / 405 (0.74%)	0 / 404 (0.00%)
occurrences (all)	3	0

Rhinitis		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Rhinovirus Infection		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Sepsis		
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)
occurrences (all)	1	2
Septic Shock		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Sinusitis		
subjects affected / exposed	1 / 405 (0.25%)	4 / 404 (0.99%)
occurrences (all)	1	4
Spinal Cord Infection		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Tooth Infection		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Upper Respiratory Tract Infection		
subjects affected / exposed	4 / 405 (0.99%)	4 / 404 (0.99%)
occurrences (all)	4	4
Urinary Tract Infection		
subjects affected / exposed	6 / 405 (1.48%)	6 / 404 (1.49%)
occurrences (all)	6	9
Urinary Tract Infection Bacterial		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Viral Infection		
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)
occurrences (all)	0	1
Vulvovaginal Mycotic Infection		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0

Metabolism and nutrition disorders			
Abnormal Loss of Weight			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Decreased Appetite			
subjects affected / exposed	21 / 405 (5.19%)	25 / 404 (6.19%)	
occurrences (all)	23	30	
Dehydration			
subjects affected / exposed	9 / 405 (2.22%)	7 / 404 (1.73%)	
occurrences (all)	10	8	
Diabetes Mellitus			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Electrolyte Depletion			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Fluid Retention			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Folate Deficiency			
subjects affected / exposed	2 / 405 (0.49%)	1 / 404 (0.25%)	
occurrences (all)	2	1	
Hypercalcaemia			
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)	
occurrences (all)	3	0	
Gout			
subjects affected / exposed	1 / 405 (0.25%)	1 / 404 (0.25%)	
occurrences (all)	1	1	
Hyperglycaemia			
subjects affected / exposed	5 / 405 (1.23%)	1 / 404 (0.25%)	
occurrences (all)	6	1	
Hyperlipidaemia			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Hyperuricaemia			

subjects affected / exposed	2 / 405 (0.49%)	2 / 404 (0.50%)
occurrences (all)	2	2
Hypoalbuminaemia		
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)
occurrences (all)	1	2
Hypocalcaemia		
subjects affected / exposed	6 / 405 (1.48%)	2 / 404 (0.50%)
occurrences (all)	7	2
Hypokalaemia		
subjects affected / exposed	18 / 405 (4.44%)	10 / 404 (2.48%)
occurrences (all)	21	11
Hypoglycaemia		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Hypomagnesaemia		
subjects affected / exposed	11 / 405 (2.72%)	4 / 404 (0.99%)
occurrences (all)	11	4
Hypophosphataemia		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Hyponatraemia		
subjects affected / exposed	4 / 405 (0.99%)	3 / 404 (0.74%)
occurrences (all)	4	3
Iron Deficiency		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Hypovolaemia		
subjects affected / exposed	1 / 405 (0.25%)	2 / 404 (0.50%)
occurrences (all)	1	2
Lactic Acidosis		
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)
occurrences (all)	1	0
Malnutrition		
subjects affected / exposed	2 / 405 (0.49%)	0 / 404 (0.00%)
occurrences (all)	2	0
Metabolic Acidosis		

subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Protein Deficiency			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Type 2 Diabetes Mellitus			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Vitamin B12 Deficiency			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Vitamin D Deficiency			
subjects affected / exposed	2 / 405 (0.49%)	1 / 404 (0.25%)	
occurrences (all)	2	1	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
16 February 2018	This amendment included an increase in the planned enrollment to approximately 800 subjects to account for the high subject discontinuation rate, the addition of symptomatic lower extremity distal DVT to the primary efficacy composite endpoint and secondary efficacy composite endpoint, clarifications to the statistical analysis methods, corrections to the efficacy evaluations, outcomes, and endpoints (that is, symptomatic proximal upper extremity DVT was corrected to symptomatic upper extremity DVT and non-fatal PE was corrected to symptomatic non-fatal PE), and minor editorial changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported