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

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

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

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
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
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)

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

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

	Symptomatic VTE Events or VTE-Related Deaths

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

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

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

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)

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

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

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

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

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

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

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

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

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

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

End point description:

Percentage of subjects with time 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

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

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

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

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

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

Dictionary used	
Dictionary name	MedDRA
Dictionary version	21.0

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

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

Blood Bilirubin Decreased				
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)		
occurrences (all)	0	1		
Blood Bilirubin Increased				
subjects affected / exposed	1 / 405 (0.25%)	6 / 404 (1.49%)		
occurrences (all)	1	7		
Blood Calcium Decreased				
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)		
occurrences (all)	0	1		
Blood Calcium Increased				
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)		
occurrences (all)	0	1		
Blood Chloride Decreased				
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)		
occurrences (all)	1	0		
Blood Creatinine Decreased				
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)		
occurrences (all)	1	0		
Blood Creatinine Increased				
subjects affected / exposed	3 / 405 (0.74%)	2 / 404 (0.50%)		
occurrences (all)	3	2		
Blood Glucose Decreased				
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)		
occurrences (all)	0	1		
Blood Glucose Increased				
subjects affected / exposed	5 / 405 (1.23%)	12 / 404 (2.97%)		
occurrences (all)	5	14		
Blood Potassium Decreased				
subjects affected / exposed	2 / 405 (0.49%)	1 / 404 (0.25%)		
occurrences (all)	2	1		
Blood Potassium Increased				
subjects affected / exposed	2 / 405 (0.49%)	6 / 404 (1.49%)		
occurrences (all)	2	6		
Blood Sodium Decreased				
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)		
occurrences (all)	1	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	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Weight Decreased			
subjects affected / exposed	10 / 405 (2.47%)	9 / 404 (2.23%)	
occurrences (all)	10	10	
Weight Increased			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
White Blood Cell Count Decreased			
subjects affected / exposed	6 / 405 (1.48%)	9 / 404 (2.23%)	
occurrences (all)	8	10	
White Blood Cell Count Increased			
subjects affected / exposed	3 / 405 (0.74%)	4 / 404 (0.99%)	
occurrences (all)	3	4	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Face Injury			
subjects affected / exposed	1 / 405 (0.25%)	0 / 404 (0.00%)	
occurrences (all)	1	0	
Fall			
subjects affected / exposed	2 / 405 (0.49%)	3 / 404 (0.74%)	
occurrences (all)	2	3	
Head Injury			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Limb Injury			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	1	
Lumbar Vertebral Fracture			
subjects affected / exposed	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	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	0 / 405 (0.00%)	1 / 404 (0.25%)	
occurrences (all)	0	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 Erythrodysaesthesia 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