Clinical trial results:
A Multicenter, Randomized, Double- Blind, Placebo-Controlled, Phase 3 Trial of Lenvatinib (E7080) in 131I- Refractory Differentiated Thyroid Cancer

Summary

EudraCT number	2010-023783-41
Trial protocol	BE CZ PT GB DE ES PL DK AT IT SE
Global end of trial date	19 March 2019

Results information

Result version number	v1 (current)
This version publication date	03 April 2020
First version publication date	03 April 2020

Trial information

Trial identification

Sponsor protocol code	E7080-G000-303

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01321554
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Eisai Ltd.
Sponsor organisation address	European Knowledge Centre Mosquito Way, Hatfield, Hertfordshire , United Kingdom, AL10 9SN
Public contact	Medical Information, Eisai Ltd., +1 1-888-274-2378, esi_oncmedinfo@eisai.com
Scientific contact	Medical Information, Eisai Ltd., +1 1-888-274-2378, esi_oncmedinfo@eisai.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	19 March 2019
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	19 March 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To compare the progression-free survival of subjects with 131I-refractory differentiated thyroid cancer with radiographic evidence of disease progression within the prior 12 months treated with E7080 versus placebo.

Protection of trial subjects:

This study was conducted in accordance with standard operating procedures (SOPs) of the sponsor (or designee), which are designed to ensure adherence to Good Clinical Practice (GCP) guidelines as required by the following: - Principles of the World Medical Association Declaration of Helsinki (World Medical Association, 2008) - International Council on Harmonisation (ICH) E6 Guideline for GCP (CPMP/ICH/135/95) of the European Agency for the Evaluation of Medicinal Products, Committee for Proprietary Medicinal Products, International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use -Title 21 of the United States (US) Code of Federal Regulations (US 21 CFR) regarding clinical studies, including Part 50 and Part 56 concerning informed subject consent and Institutional Review Board (IRB) regulations and applicable sections of US 21 CFR Part 312 - European Good Clinical Practice Directive 2005/28/EC and Clinical Trial Directive 2001/20/EC for studies conducted within any European Union (EU) country. All suspected unexpected serious adverse reactions were reported, as required, to the Competent Authorities of all involved EU member states. -Article 14, Paragraph 3, and Article 80-2 of the Pharmaceutical Affairs Law (Law No. 145, 1960) for studies conducted in Japan, in addition to Japan’s GCP Subject Information and Informed Consent.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 March 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 6
Country: Number of subjects enrolled	United Kingdom: 21
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	France: 48
Country: Number of subjects enrolled	Germany: 22
Country: Number of subjects enrolled	Italy: 48
Country: Number of subjects enrolled	Austria: 1
Country: Number of subjects enrolled	Portugal: 2
Country: Number of subjects enrolled	Thailand: 4
Country: Number of subjects enrolled	Australia: 19
Country: Number of subjects enrolled	Brazil: 9

Country: Number of subjects enrolled	Canada: 10
Country: Number of subjects enrolled	Chile: 2
Country: Number of subjects enrolled	Japan: 40
Country: Number of subjects enrolled	Korea, Republic of: 20
Country: Number of subjects enrolled	Romania: 5
Country: Number of subjects enrolled	Russian Federation: 6
Country: Number of subjects enrolled	United States: 87
Country: Number of subjects enrolled	Belgium: 6
Country: Number of subjects enrolled	Spain: 18
Country: Number of subjects enrolled	Poland: 14
Worldwide total number of subjects	392
EEA total number of subjects	195

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)	220
From 65 to 84 years	170
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Subjects took part in the study at 117 investigative sites in Europe, North America, Asia Pacific, Japan, and Latin America from 17 March 2011 to 19 March 2019.

Pre-assignment

Screening details:

A total of 612 subjects were screened for entry into the study. Of these 612 subjects, 220 subjects were screening failures and 392 subjects were randomly assigned to receive either lenvatinib or placebo in a 2:1 ratio.

Period 1

Period 1 title	Randomization Phase
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Randomization Phase: Lenvatinib 24 mg

Arm description:

Subjects received lenvatinib 24 milligram (mg), hard capsule, orally, once daily, until documentation of disease progression (confirmed by Investigator-Initiated Research [IIR]), development of unacceptable toxicity, or withdrawal of consent.

Arm type	Experimental
Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects received lenvatinib 24 mg, hard capsule, orally, once daily, until documentation of disease progression (confirmed by IIR), development of unacceptable toxicity, or withdrawal of consent.

Arm title	Randomization Phase: Placebo

Arm description:

Subjects received matching-placebo, hard capsule, orally, once daily until documentation of disease progression (confirmed by IIR), development of unacceptable toxicity, or withdrawal of consent.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects received matching-placebo, hard capsule, orally, once daily until documentation of disease progression (confirmed by IIR), development of unacceptable toxicity, or withdrawal of consent.

Number of subjects in period 1	Randomization Phase: Lenvatinib 24 mg	Randomization Phase: Placebo
Started	261	131
Completed	261	131

Period 2

Period 2 title	OOL Lenvatinib Treatment Period
Is this the baseline period?	No
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	OOL, Treatment Period: Lenvatinib 24 mg

Arm description:

Subjects received lenvatinib, hard capsule, 24 mg, orally, once daily in Treatment Period. Placebo treated subjects in the Randomization Phase who had progressive disease confirmed by IIR, and who requested treatment with lenvatinib. OOL refers to Optional Open-Label.

Arm type	Experimental
Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects received lenvatinib, hard capsule, 24 mg, orally, once daily in Treatment Period. Placebo treated subjects in the Randomization Phase who had progressive disease confirmed by IIR, and who requested treatment with lenvatinib.

Arm title	OOL, Treatment Period: Lenvatinib 20 mg

Arm description:

Subjects received lenvatinib, hard capsule, 20 mg, orally, once daily in Treatment Period. Placebo treated subjects in the Randomization Phase who had progressive disease confirmed by IIR, and who requested treatment with lenvatinib.

Arm type	Experimental
Investigational medicinal product name	Lenvatinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Subjects received lenvatinib, hard capsule, 20 mg, orally, once daily in Treatment Period. Placebo treated subjects in the Randomization Phase who had progressive disease confirmed by IIR, and who requested treatment with lenvatinib.

Number of subjects in period 2[1]	OOL, Treatment Period: Lenvatinib 24 mg	OOL, Treatment Period: Lenvatinib 20 mg
Started	85	30
Completed	85	30

Notes:

[1] - The number of subjects starting the period is not consistent with the number completing the preceding period. It is expected the number of subjects starting the subsequent period will be the same as the number completing the preceding period.

Justification: Subjects from Randomization phase were re-randomised to OOL Lenvatinib treatment period.

Baseline characteristics

Reporting groups	
Reporting group title	Randomization Phase: Lenvatinib 24 mg
Reporting group description:	
Subjects received lenvatinib 24 milligram (mg), hard capsule, orally, once daily, until documentation of disease progression (confirmed by Investigator-Initiated Research [IIR]), development of unacceptable toxicity, or withdrawal of consent.	
Reporting group title	Randomization Phase: Placebo
Reporting group description:	
Subjects received matching-placebo, hard capsule, orally, once daily until documentation of disease progression (confirmed by IIR), development of unacceptable toxicity, or withdrawal of consent.	

Reporting group values	Randomization Phase: Lenvatinib 24 mg	Randomization Phase: Placebo	Total
Number of subjects	261	131	392
Age categorical			
Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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)			0
From 65-84 years			0
85 years and over			0
Age continuous			
Units: years			
geometric mean	62.1	61.5	
standard deviation	± 10.57	± 10.09	-
Gender categorical			
Units: Subjects			
Female	136	56	192
Male	125	75	200

End points

End points reporting groups

Reporting group title	Randomization Phase: Lenvatinib 24 mg

Reporting group description:

Subjects received lenvatinib 24 milligram (mg), hard capsule, orally, once daily, until documentation of disease progression (confirmed by Investigator-Initiated Research [IIR]), development of unacceptable toxicity, or withdrawal of consent.

Reporting group title	Randomization Phase: Placebo

Reporting group description:

Subjects received matching-placebo, hard capsule, orally, once daily until documentation of disease progression (confirmed by IIR), development of unacceptable toxicity, or withdrawal of consent.

Reporting group title	OOL, Treatment Period: Lenvatinib 24 mg

Reporting group description:

Subjects received lenvatinib, hard capsule, 24 mg, orally, once daily in Treatment Period. Placebo treated subjects in the Randomization Phase who had progressive disease confirmed by IIR, and who requested treatment with lenvatinib. OOL refers to Optional Open-Label.

Reporting group title	OOL, Treatment Period: Lenvatinib 20 mg

Reporting group description:

Subjects received lenvatinib, hard capsule, 20 mg, orally, once daily in Treatment Period. Placebo treated subjects in the Randomization Phase who had progressive disease confirmed by IIR, and who requested treatment with lenvatinib.

Subject analysis set title	Lenvatinib 24 mg
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Subjects received lenvatinib 24 mg, hard capsule, orally, once daily, until documentation of disease progression (confirmed by IIR), development of unacceptable toxicity, or withdrawal of consent.

Primary: Progression Free Survival (PFS)

End point title	Progression Free Survival (PFS)

End point description:

PFS was defined as the time from the date of randomization to the date of first documentation of disease progression or death (whichever occurred first), as determined by blinded IIR using Response Evaluation Criteria In Solid Tumors (RECIST) 1.1 for the double-blind treatment period (Randomization Phase). Disease progression per RECIST v1.1 was defined as at least a 20 percent (%) relative increase and 5 millimeter (mm) absolute increase in the sum of diameters of target lesions (taking as reference the smallest sum on study), recorded since the treatment started or the appearance of 1 or more new lesions. The full analysis set (Intent-to-Treat Analysis Set) included all randomized subjects. Here "99999" refers to data not available and therefore we have added 99999 as space-fillers.

End point type	Primary

End point timeframe:

Date of randomization to the date of disease progression or death (whichever occurred first), assessed up to data cutoff date (15 Nov 2013) or up to approximately 2.5 years

End point values	Randomization Phase: Lenvatinib 24 mg	Randomization Phase: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	131		
Units: months				
median (confidence interval 95%)	18.3 (15.1 to 99999)	3.6 (2.2 to 3.7)		

Statistical analyses

Statistical analysis title	Statistical analysis 1
Comparison groups	Randomization Phase: Lenvatinib 24 mg v Randomization Phase: Placebo
Number of subjects included in analysis	392
Analysis specification	Pre-specified
Analysis type	superiority
Parameter estimate	Cox proportional hazard
Point estimate	0.21
Confidence interval	
level	Other: 99 %
sides	2-sided
lower limit	0.14
upper limit	0.31

Secondary: Overall Response Rate (ORR)

End point title	Overall Response Rate (ORR)

End point description:

ORR, defined as the percentage of subjects who had best overall response (BOR) of complete response (CR) or partial response (PR) as determined by blinded IIR using RECIST 1.1 for target lesions and assessed by magnetic resonance therapy/computed tomography (MRI/CT) scans (for double blind treatment period i.e. Randomization Phase). CR was defined as disappearance of all target lesions. Any pathological lymph nodes (whether target or non-target) had to have reduction in short axis to less than 10 mm. PR was defined as at least a 30% decrease in the sum of diameters of target lesions, taking as reference the baseline sum diameters. ORR = CR + PR. The full analysis set (Intent-to-Treat Analysis Set) included all randomized subjects.

End point type	Secondary

End point timeframe:

Date of randomization to the date of disease progression or death (whichever occurred first), assessed up to data cutoff date (15 Nov 2013) or up to approximately 2.5 years

End point values	Randomization Phase: Lenvatinib 24 mg	Randomization Phase: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	131		
Units: percentage of subjects				
number (confidence interval 95%)	64.8 (59.0 to 70.5)	1.5 (0.0 to 3.6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

Overall survival measured from the date of randomization until date of death from any cause. Overall survival is adjusted with rank preserving structural failure time. The full analysis set (Intent-to-Treat Analysis Set) included all randomized subjects. Here "99999" refers to data not available and therefore we have added 99999 as space-fillers.

End point type	Secondary

End point timeframe:

Date of randomization until date of death from any cause, assessed up to data cutoff date (15 Nov 2013) or up to approximately 2.5 years

End point values	Randomization Phase: Lenvatinib 24 mg	Randomization Phase: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	261	131		
Units: months				
median (confidence interval 95%)	99999 (22.0 to 99999)	99999 (14.3 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic (PK) Profile of Lenvatinib: Area Under the Plasma Concentration Curve

End point title	Pharmacokinetic (PK) Profile of Lenvatinib: Area Under the Plasma Concentration Curve

End point description:

The PK analysis set included all the subjects who received at least one dose of study drug and had evaluable PK data.

End point type	Secondary

End point timeframe:

Cycle 1 Days 1 and 15: 0-10 hours postdose; Cycle 2 Day 1: 0-12 hour postdose (Cycle length =)

End point values	Lenvatinib 24 mg			
Subject group type	Subject analysis set			
Number of subjects analysed	261			
Units: nanogram*hour per milliliter (ng*h/mL)				
median (full range (min-max))	3490 (1410 to 10700)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

For each subject, from the first dose till 30 days up to approximately 8 years

Adverse event reporting additional description:

Safety was assessed by the monitoring and recording of all adverse events (AEs) and serious adverse events (SAEs); regular monitoring of hematology, clinical chemistry, and urine values; physical examinations; and regular measurement of vital signs, electrocardiograms (ECG), and echocardiograms.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Randomization Phase: Lenvatinib 24 mg

Reporting group description:

Subjects received lenvatinib 24 mg, hard capsule, orally, once daily, until documentation of disease progression (confirmed by IIR), development of unacceptable toxicity, or withdrawal of consent.

Reporting group title	Randomization Phase: Placebo

Reporting group description:

Subjects received matching-placebo, hard capsule, orally, once daily until documentation of disease progression (confirmed by IIR), development of unacceptable toxicity, or withdrawal of consent.

Reporting group title	OOL, Treatment Period: Lenvatinib 24 mg

Reporting group description:

Subjects received lenvatinib 24 mg, hard capsule, orally, once daily in Treatment Period. Placebo treated subjects in the Randomization Phase who had progressive disease confirmed by IIR, and who requested treatment with lenvatinib.

Reporting group title	OOL, Treatment Period: Lenvatinib 20 mg

Reporting group description:

Subjects received lenvatinib 20 mg, hard capsule, orally, once daily in Treatment Period. Placebo treated subjects in the Randomization Phase who had progressive disease confirmed by IIR, and who requested treatment with lenvatinib.

Serious adverse events	Randomization Phase: Lenvatinib 24 mg	Randomization Phase: Placebo	OOL, Treatment Period: Lenvatinib 24 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	171 / 261 (65.52%)	31 / 131 (23.66%)	62 / 85 (72.94%)
number of deaths (all causes)	161	13	62
number of deaths resulting from adverse events	29	6	11
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	3 / 261 (1.15%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma gastric			

subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intracranial tumour haemorrhage			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Lymphocytic leukaemia			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant pleural effusion			
subjects affected / exposed	5 / 261 (1.92%)	1 / 131 (0.76%)	3 / 85 (3.53%)
occurrences causally related to treatment / all	0 / 5	0 / 2	3 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant neoplasm progression			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	3 / 85 (3.53%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 3
Metastases to bone			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic pain			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	3 / 85 (3.53%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to spine			

subjects affected / exposed	0 / 261 (0.00%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastatic pulmonary embolism			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Plasmacytoma			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spindle cell sarcoma			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of skin			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tumour pain			
subjects affected / exposed	0 / 261 (0.00%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aneurysm ruptured			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Deep vein thrombosis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive crisis			

subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	2 / 85 (2.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	10 / 261 (3.83%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	11 / 11	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombophlebitis			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	5 / 261 (1.92%)	0 / 131 (0.00%)	2 / 85 (2.35%)
occurrences causally related to treatment / all	4 / 5	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Varicose vein			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vasculitis			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	3 / 261 (1.15%)	0 / 131 (0.00%)	2 / 85 (2.35%)
occurrences causally related to treatment / all	3 / 4	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Death			

subjects affected / exposed	2 / 261 (0.77%)	1 / 131 (0.76%)	3 / 85 (3.53%)
occurrences causally related to treatment / all	2 / 2	0 / 1	1 / 3
deaths causally related to treatment / all	2 / 2	0 / 1	0 / 0
Device breakage			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device failure			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	7 / 261 (2.68%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	3 / 9	0 / 0	0 / 2
deaths causally related to treatment / all	1 / 3	0 / 0	0 / 0
Impaired healing			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Multi-organ failure			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			

subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden death			
subjects affected / exposed	1 / 261 (0.38%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 1	0 / 0
Pyrexia			
subjects affected / exposed	3 / 261 (1.15%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Contrast media allergy			
subjects affected / exposed	0 / 261 (0.00%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Reproductive system and breast disorders			
Cystocele			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Genital prolapse			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postmenopausal haemorrhage			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Rectocele			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Uterine prolapse			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspiration			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute respiratory failure			
subjects affected / exposed	2 / 261 (0.77%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atelectasis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchial secretion retention			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Chronic obstructive pulmonary disease			
subjects affected / exposed	1 / 261 (0.38%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea exertional			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	6 / 261 (2.30%)	5 / 131 (3.82%)	3 / 85 (3.53%)
occurrences causally related to treatment / all	0 / 12	0 / 7	2 / 5
deaths causally related to treatment / all	0 / 2	0 / 2	1 / 1
Haemoptysis			
subjects affected / exposed	0 / 261 (0.00%)	3 / 131 (2.29%)	2 / 85 (2.35%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrothorax			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemothorax			
subjects affected / exposed	1 / 261 (0.38%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal haemorrhage			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoxia			

subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal obstruction			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal necrosis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal oedema			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oropharyngeal pain			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung disorder			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia aspiration			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleuritic pain			

subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax spontaneous			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	6 / 261 (2.30%)	2 / 131 (1.53%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	5 / 8	2 / 2	0 / 0
deaths causally related to treatment / all	1 / 3	0 / 0	0 / 0
Productive cough			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary mass			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary haemorrhage			
subjects affected / exposed	1 / 261 (0.38%)	1 / 131 (0.76%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory depression			

subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	2 / 85 (2.35%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Respiratory failure			
subjects affected / exposed	2 / 261 (0.77%)	2 / 131 (1.53%)	2 / 85 (2.35%)
occurrences causally related to treatment / all	0 / 2	0 / 3	2 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	1 / 1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional state			
subjects affected / exposed	3 / 261 (1.15%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	2 / 4	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	0 / 261 (0.00%)	1 / 131 (0.76%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Delirium			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Suicidal ideation			
subjects affected / exposed	0 / 261 (0.00%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood calcium increased			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatine phosphokinase increased			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood alkaline phosphatase increased			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood uric acid increased			
subjects affected / exposed	2 / 261 (0.77%)	1 / 131 (0.76%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Electrocardiogram T wave inversion			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood creatinine increased			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Platelet count decreased			

subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lipase increased			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Weight decreased			
subjects affected / exposed	2 / 261 (0.77%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Eschar			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hip fracture			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Femur fracture			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Incisional hernia			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Post procedural haemorrhage			

subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal haematoma			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural haematoma			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thermal burn			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic rupture			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Traumatic fracture			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular pseudoaneurysm			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound dehiscence			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound secretion			

subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute coronary syndrome			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute left ventricular failure			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	5 / 261 (1.92%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	4 / 7	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Angina pectoris			
subjects affected / exposed	1 / 261 (0.38%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Angina unstable			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial fibrillation			
subjects affected / exposed	4 / 261 (1.53%)	0 / 131 (0.00%)	3 / 85 (3.53%)
occurrences causally related to treatment / all	0 / 6	0 / 0	1 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrioventricular block complete			

subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac arrest			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Bundle branch block right			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure congestive			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac failure			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-respiratory arrest			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 2	0 / 0	0 / 0
Coronary artery occlusion			
subjects affected / exposed	1 / 261 (0.38%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery stenosis			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coronary artery insufficiency			

subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Myocardial infarction			
subjects affected / exposed	1 / 261 (0.38%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 1	0 / 0
Palpitations			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Right ventricular hypertrophy			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pericardial effusion			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tachycardia			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinus tachycardia			
subjects affected / exposed	0 / 261 (0.00%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular tachycardia			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ventricular hypokinesia			

subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Cauda equina syndrome			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral ischaemia			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular accident			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	3 / 85 (3.53%)
occurrences causally related to treatment / all	1 / 2	0 / 0	2 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Coma			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic encephalopathy			
subjects affected / exposed	0 / 261 (0.00%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dementia			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Facial paresis			

subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epilepsy			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhagic stroke			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Headache			
subjects affected / exposed	4 / 261 (1.53%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	4 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ischaemic stroke			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss of consciousness			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolic encephalopathy			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Monoparesis			
subjects affected / exposed	3 / 261 (1.15%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Parkinson’s disease			

subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osmotic demyelination syndrome			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 1
Posterior reversible encephalopathy syndrome			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Postictal paralysis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	4 / 261 (1.53%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subarachnoid haemorrhage			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord ischaemia			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vocal cord paralysis			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seizure			
subjects affected / exposed	4 / 261 (1.53%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Febrile neutropenia			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anaemia			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Splenic haemorrhage			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neutropenia			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			

Diplopia			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal detachment			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal vein thrombosis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal mass			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain			
subjects affected / exposed	3 / 261 (1.15%)	0 / 131 (0.00%)	4 / 85 (4.71%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal fistula			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis ischaemic			
subjects affected / exposed	0 / 261 (0.00%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			

subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	1 / 261 (0.38%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	2 / 85 (2.35%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dental cyst			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysphagia			
subjects affected / exposed	3 / 261 (1.15%)	3 / 131 (2.29%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis viral			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal inflammation			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Functional gastrointestinal disorder			

subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Inguinal hernia			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal perforation			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intestinal obstruction			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mesenteric artery thrombosis			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Oesophageal stenosis			
subjects affected / exposed	0 / 261 (0.00%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	0 / 261 (0.00%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			

subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumoperitoneum			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumatosis intestinalis			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Stomatitis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vomiting			
subjects affected / exposed	5 / 261 (1.92%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	4 / 5	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	4 / 261 (1.53%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	1 / 5	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis acute			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			

subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder mucocoele			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gallbladder perforation			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic failure			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 2	0 / 0	0 / 0
Hepatic function abnormal			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hydrocholecystis			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatocellular injury			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver injury			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Angioedema			

subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis contact			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Drug eruption			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erythema			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin ulcer			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rash			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	6 / 261 (2.30%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	2 / 6	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Acute prerenal failure			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic kidney disease			

subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dysuria			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nephrotic syndrome			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematuria			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Proteinuria			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal impairment			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal tubular necrosis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			

subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary incontinence			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	3 / 261 (1.15%)	1 / 131 (0.76%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back pain			
subjects affected / exposed	3 / 261 (1.15%)	0 / 131 (0.00%)	3 / 85 (3.53%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mobility decreased			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Foot deformity			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Muscular weakness			

subjects affected / exposed	1 / 261 (0.38%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 261 (0.38%)	1 / 131 (0.76%)	2 / 85 (2.35%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myalgia			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal pain			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	3 / 261 (1.15%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	1 / 261 (0.38%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	2 / 85 (2.35%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis of jaw			

subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Soft tissue necrosis			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rhabdomyolysis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abscess intestinal			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess limb			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abscess soft tissue			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal abscess			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis perforated			

subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bacteraemia			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bartholin’s abscess			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchitis			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary tract infection			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Candida sepsis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cellulitis			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis infective			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest wall abscess			

subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic abscess			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic sinusitis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	2 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Empyema			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Erysipelas			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fungal skin infection			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	2 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Implant site infection			

subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral discitis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	1 / 261 (0.38%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lobar pneumonia			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung infection			
subjects affected / exposed	4 / 261 (1.53%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Lower respiratory tract infection			
subjects affected / exposed	4 / 261 (1.53%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	4 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis viral			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lymph gland infection			

subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteomyelitis			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Perineal abscess			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Phlebitis infective			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	12 / 261 (4.60%)	3 / 131 (2.29%)	5 / 85 (5.88%)
occurrences causally related to treatment / all	7 / 14	0 / 3	0 / 5
deaths causally related to treatment / all	0 / 1	0 / 0	0 / 0
Pneumonia necrotising			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	1 / 1	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia staphylococcal			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			

subjects affected / exposed	6 / 261 (2.30%)	2 / 131 (1.53%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	2 / 6	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Testicular abscess			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous abscess			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Upper respiratory tract infection			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheitis			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	4 / 261 (1.53%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	2 / 261 (0.77%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 261 (0.38%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	2 / 85 (2.35%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	9 / 261 (3.45%)	0 / 131 (0.00%)	2 / 85 (2.35%)
occurrences causally related to treatment / all	4 / 9	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	4 / 261 (1.53%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	2 / 8	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypercalcaemia			
subjects affected / exposed	2 / 261 (0.77%)	1 / 131 (0.76%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			
subjects affected / exposed	1 / 261 (0.38%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypokalaemia			
subjects affected / exposed	3 / 261 (1.15%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	1 / 3	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemia			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	2 / 261 (0.77%)	1 / 131 (0.76%)	1 / 85 (1.18%)
occurrences causally related to treatment / all	0 / 2	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	OOL, Treatment Period: Lenvatinib 20 mg		

Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 30 (53.33%)		
number of deaths (all causes)	15		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Cancer pain			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Adenocarcinoma gastric			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Intracranial tumour haemorrhage			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Lymphocytic leukaemia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant melanoma			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant pleural effusion			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Malignant neoplasm progression			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastases to bone			

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastatic pain				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metastases to spine				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastatic pulmonary embolism				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Plasmacytoma				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spindle cell sarcoma				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of skin				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tumour pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Aneurysm ruptured				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Deep vein thrombosis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive crisis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Thrombophlebitis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Varicose vein				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vasculitis				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	3 / 3			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Asthenia				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 3			
Device breakage				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device failure				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Impaired healing				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multi-organ failure				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-cardiac chest pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sudden death				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Anaphylactic reaction				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Contrast media allergy				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Cystocele				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Genital prolapse				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postmenopausal haemorrhage				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectocele				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Uterine prolapse				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory distress syndrome				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspiration				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute respiratory failure				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atelectasis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Bronchospasm				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchial secretion retention				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic obstructive pulmonary disease				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea exertional				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hydrothorax				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemothorax				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngeal haemorrhage				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngeal obstruction				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngeal necrosis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngeal oedema				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oropharyngeal pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung disorder				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia aspiration				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleuritic pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax spontaneous				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Productive cough				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary mass				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary haemorrhage				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory depression				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Anxiety				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Delirium				

subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				
Alanine aminotransferase increased				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood calcium increased				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood creatine phosphokinase increased				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood alkaline phosphatase increased				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood uric acid increased				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Electrocardiogram T wave inversion				

subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood creatinine increased				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lipase increased				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Weight decreased				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Eschar				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Femur fracture				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lumbar vertebral fracture				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Incisional hernia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post procedural haemorrhage				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Renal haematoma				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thermal burn				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Splenic rupture				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Traumatic fracture				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular pseudoaneurysm				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound dehiscence				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound secretion				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Acute coronary syndrome				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute left ventricular failure				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute myocardial infarction				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina unstable				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial flutter				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block complete				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bundle branch block right				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure congestive				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac failure				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery occlusion				

subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery insufficiency				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial infarction				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Palpitations				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Right ventricular hypertrophy				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial effusion				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tachycardia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus tachycardia				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ventricular tachycardia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ventricular hypokinesia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Cauda equina syndrome				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral ischaemia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Coma				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic encephalopathy				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dementia				

subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Facial paresis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhagic stroke				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ischaemic stroke				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Loss of consciousness				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolic encephalopathy				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Monoparesis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Parkinson’s disease				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osmotic demyelination syndrome				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Posterior reversible encephalopathy syndrome				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postictal paralysis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal cord compression				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subarachnoid haemorrhage				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal cord ischaemia				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Vocal cord paralysis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seizure				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Febrile neutropenia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anaemia				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Splenic haemorrhage				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neutropenia				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Diplopia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retinal detachment				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retinal vein thrombosis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal mass				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal fistula				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis ischaemic				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	2 / 30 (6.67%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticular perforation				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dental cyst				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal inflammation				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Functional gastrointestinal disorder				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrooesophageal reflux disease				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mesenteric artery thrombosis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophageal stenosis				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumoperitoneum				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumatosis intestinalis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stomatitis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Cholecystitis				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis acute				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gallbladder mucocoele				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gallbladder perforation				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic failure				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic function abnormal				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hydrocholecystis				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hepatocellular injury				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver injury				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Angioedema				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dermatitis contact				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug eruption				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erythema				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin ulcer				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				

Acute kidney injury				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute prerenal failure				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic kidney disease				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysuria				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrotic syndrome				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Proteinuria				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal impairment				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal tubular necrosis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary retention				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary incontinence				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal and connective tissue disorders				
Arthralgia				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Back pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Flank pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mobility decreased				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Foot deformity				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal chest pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myalgia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Musculoskeletal pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neck pain				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain in extremity				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis of jaw				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Soft tissue necrosis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rhabdomyolysis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abscess intestinal				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess limb				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess soft tissue				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal abscess				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis perforated				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacteraemia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bartholin’s abscess				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Biliary tract infection				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Candida sepsis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cellulitis				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis infective				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest wall abscess				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colonic abscess				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic sinusitis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Empyema				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fungal skin infection				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Implant site infection				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral discitis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lobar pneumonia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngitis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	2 / 30 (6.67%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis viral				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymph gland infection				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Osteomyelitis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perineal abscess				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Phlebitis infective				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	2 / 30 (6.67%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Pneumonia necrotising				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia staphylococcal				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Testicular abscess				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subcutaneous abscess				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Upper respiratory tract infection				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tracheitis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound infection				

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Decreased appetite				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypocalcaemia				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypomagnesaemia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypokalaemia				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypovolaemia				

subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Randomization Phase: Lenvatinib 24 mg	Randomization Phase: Placebo	OOL, Treatment Period: Lenvatinib 24 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	259 / 261 (99.23%)	118 / 131 (90.08%)	84 / 85 (98.82%)
Vascular disorders			
Hypertension			
subjects affected / exposed	181 / 261 (69.35%)	19 / 131 (14.50%)	52 / 85 (61.18%)
occurrences (all)	720	36	124
Hypotension			
subjects affected / exposed	27 / 261 (10.34%)	3 / 131 (2.29%)	8 / 85 (9.41%)
occurrences (all)	37	3	12
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	116 / 261 (44.44%)	33 / 131 (25.19%)	35 / 85 (41.18%)
occurrences (all)	298	45	64
Asthenia			
subjects affected / exposed	69 / 261 (26.44%)	18 / 131 (13.74%)	21 / 85 (24.71%)
occurrences (all)	209	29	43
Influenza like illness			
subjects affected / exposed	20 / 261 (7.66%)	4 / 131 (3.05%)	0 / 85 (0.00%)
occurrences (all)	25	4	0
Malaise			
subjects affected / exposed	17 / 261 (6.51%)	0 / 131 (0.00%)	5 / 85 (5.88%)
occurrences (all)	29	0	8
General physical health deterioration			

subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	6 / 85 (7.06%)
occurrences (all)	0	0	7
Non-cardiac chest pain			
subjects affected / exposed	14 / 261 (5.36%)	4 / 131 (3.05%)	3 / 85 (3.53%)
occurrences (all)	16	5	3
Pain			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences (all)	0	0	0
Oedema peripheral			
subjects affected / exposed	65 / 261 (24.90%)	10 / 131 (7.63%)	18 / 85 (21.18%)
occurrences (all)	124	12	20
Pyrexia			
subjects affected / exposed	41 / 261 (15.71%)	15 / 131 (11.45%)	10 / 85 (11.76%)
occurrences (all)	58	17	20
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	77 / 261 (29.50%)	24 / 131 (18.32%)	23 / 85 (27.06%)
occurrences (all)	114	36	30
Dysphonia			
subjects affected / exposed	87 / 261 (33.33%)	7 / 131 (5.34%)	33 / 85 (38.82%)
occurrences (all)	135	8	55
Dyspnoea			
subjects affected / exposed	47 / 261 (18.01%)	21 / 131 (16.03%)	16 / 85 (18.82%)
occurrences (all)	65	29	26
Dyspnoea exertional			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	2
Haemoptysis			
subjects affected / exposed	12 / 261 (4.60%)	12 / 131 (9.16%)	9 / 85 (10.59%)
occurrences (all)	17	14	10
Epistaxis			

subjects affected / exposed	36 / 261 (13.79%)	1 / 131 (0.76%)	14 / 85 (16.47%)
occurrences (all)	58	1	20
Oropharyngeal pain			
subjects affected / exposed	43 / 261 (16.48%)	2 / 131 (1.53%)	9 / 85 (10.59%)
occurrences (all)	86	2	13
Productive cough			
subjects affected / exposed	13 / 261 (4.98%)	8 / 131 (6.11%)	3 / 85 (3.53%)
occurrences (all)	23	8	3
Psychiatric disorders			
Anxiety			
subjects affected / exposed	15 / 261 (5.75%)	5 / 131 (3.82%)	5 / 85 (5.88%)
occurrences (all)	16	6	5
Insomnia			
subjects affected / exposed	38 / 261 (14.56%)	4 / 131 (3.05%)	11 / 85 (12.94%)
occurrences (all)	39	5	13
Depression			
subjects affected / exposed	22 / 261 (8.43%)	3 / 131 (2.29%)	5 / 85 (5.88%)
occurrences (all)	31	3	7
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	21 / 261 (8.05%)	0 / 131 (0.00%)	8 / 85 (9.41%)
occurrences (all)	33	0	9
Aspartate aminotransferase increased			
subjects affected / exposed	17 / 261 (6.51%)	2 / 131 (1.53%)	6 / 85 (7.06%)
occurrences (all)	30	2	7
Blood alkaline phosphatase increased			
subjects affected / exposed	18 / 261 (6.90%)	3 / 131 (2.29%)	5 / 85 (5.88%)
occurrences (all)	29	3	5
Blood cholesterol increased			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	1
Blood creatinine increased			
subjects affected / exposed	25 / 261 (9.58%)	2 / 131 (1.53%)	6 / 85 (7.06%)
occurrences (all)	54	2	8
Blood thyroid stimulating hormone increased			

subjects affected / exposed	18 / 261 (6.90%)	0 / 131 (0.00%)	5 / 85 (5.88%)
occurrences (all)	20	0	5
Electrocardiogram QT prolonged			
subjects affected / exposed	27 / 261 (10.34%)	2 / 131 (1.53%)	9 / 85 (10.59%)
occurrences (all)	53	3	26
Lipase increased			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	4 / 85 (4.71%)
occurrences (all)	0	0	7
Ejection fraction decreased			
subjects affected / exposed	18 / 261 (6.90%)	1 / 131 (0.76%)	7 / 85 (8.24%)
occurrences (all)	31	1	9
Platelet count decreased			
subjects affected / exposed	17 / 261 (6.51%)	0 / 131 (0.00%)	2 / 85 (2.35%)
occurrences (all)	108	0	2
Weight decreased			
subjects affected / exposed	142 / 261 (54.41%)	20 / 131 (15.27%)	44 / 85 (51.76%)
occurrences (all)	450	22	101
White blood cell count decreased			
subjects affected / exposed	14 / 261 (5.36%)	4 / 131 (3.05%)	0 / 85 (0.00%)
occurrences (all)	47	4	0
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	48 / 261 (18.39%)	4 / 131 (3.05%)	10 / 85 (11.76%)
occurrences (all)	70	4	13
Dizziness			
subjects affected / exposed	45 / 261 (17.24%)	13 / 131 (9.92%)	15 / 85 (17.65%)
occurrences (all)	77	14	19
Hyperaesthesia			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	105 / 261 (40.23%)	15 / 131 (11.45%)	19 / 85 (22.35%)
occurrences (all)	223	21	28
Paraesthesia			
subjects affected / exposed	14 / 261 (5.36%)	4 / 131 (3.05%)	2 / 85 (2.35%)
occurrences (all)	18	8	2

Sciatica			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	2
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	31 / 261 (11.88%)	6 / 131 (4.58%)	7 / 85 (8.24%)
occurrences (all)	60	13	11
Leukopenia			
subjects affected / exposed	15 / 261 (5.75%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences (all)	47	1	0
Lymphopenia			
subjects affected / exposed	20 / 261 (7.66%)	2 / 131 (1.53%)	0 / 85 (0.00%)
occurrences (all)	60	2	0
Thrombocytopenia			
subjects affected / exposed	25 / 261 (9.58%)	3 / 131 (2.29%)	7 / 85 (8.24%)
occurrences (all)	83	4	84
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	50 / 261 (19.16%)	5 / 131 (3.82%)	20 / 85 (23.53%)
occurrences (all)	109	10	34
Abdominal distension			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences (all)	0	0	0
Abdominal pain upper			
subjects affected / exposed	46 / 261 (17.62%)	11 / 131 (8.40%)	11 / 85 (12.94%)
occurrences (all)	85	11	13
Cheilitis			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	5 / 85 (5.88%)
occurrences (all)	0	0	5
Constipation			
subjects affected / exposed	83 / 261 (31.80%)	20 / 131 (15.27%)	25 / 85 (29.41%)
occurrences (all)	113	26	32
Diarrhoea			
subjects affected / exposed	182 / 261 (69.73%)	22 / 131 (16.79%)	55 / 85 (64.71%)
occurrences (all)	740	27	263
Dyspepsia			

subjects affected / exposed	38 / 261 (14.56%)	6 / 131 (4.58%)	11 / 85 (12.94%)
occurrences (all)	66	6	14
Dry mouth			
subjects affected / exposed	46 / 261 (17.62%)	11 / 131 (8.40%)	11 / 85 (12.94%)
occurrences (all)	58	13	12
Flatulence			
subjects affected / exposed	15 / 261 (5.75%)	1 / 131 (0.76%)	3 / 85 (3.53%)
occurrences (all)	18	1	4
Dysphagia			
subjects affected / exposed	34 / 261 (13.03%)	9 / 131 (6.87%)	15 / 85 (17.65%)
occurrences (all)	47	10	15
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	2 / 85 (2.35%)
occurrences (all)	0	0	2
Gingival pain			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	2 / 85 (2.35%)
occurrences (all)	0	0	3
Glossodynia			
subjects affected / exposed	18 / 261 (6.90%)	0 / 131 (0.00%)	9 / 85 (10.59%)
occurrences (all)	32	0	12
Haemorrhoids			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	6 / 85 (7.06%)
occurrences (all)	0	0	6
Nausea			
subjects affected / exposed	127 / 261 (48.66%)	34 / 131 (25.95%)	34 / 85 (40.00%)
occurrences (all)	295	48	67
Oral pain			
subjects affected / exposed	26 / 261 (9.96%)	1 / 131 (0.76%)	5 / 85 (5.88%)
occurrences (all)	44	3	9
Stomatitis			
subjects affected / exposed	100 / 261 (38.31%)	9 / 131 (6.87%)	28 / 85 (32.94%)
occurrences (all)	246	10	50
Toothache			
subjects affected / exposed	18 / 261 (6.90%)	5 / 131 (3.82%)	7 / 85 (8.24%)
occurrences (all)	22	5	8
Vomiting			

subjects affected / exposed	100 / 261 (38.31%)	19 / 131 (14.50%)	36 / 85 (42.35%)
occurrences (all)	217	24	67
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	34 / 261 (13.03%)	7 / 131 (5.34%)	9 / 85 (10.59%)
occurrences (all)	39	7	14
Dermatitis acneiform			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	4 / 85 (4.71%)
occurrences (all)	0	0	5
Decubitus ulcer			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	5 / 85 (5.88%)
occurrences (all)	0	0	6
Dry skin			
subjects affected / exposed	32 / 261 (12.26%)	8 / 131 (6.11%)	10 / 85 (11.76%)
occurrences (all)	35	8	11
Hyperkeratosis			
subjects affected / exposed	19 / 261 (7.28%)	2 / 131 (1.53%)	0 / 85 (0.00%)
occurrences (all)	36	3	0
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	86 / 261 (32.95%)	1 / 131 (0.76%)	24 / 85 (28.24%)
occurrences (all)	268	1	85
Hyperhidrosis			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	2 / 85 (2.35%)
occurrences (all)	0	0	2
Pruritus			
subjects affected / exposed	19 / 261 (7.28%)	6 / 131 (4.58%)	0 / 85 (0.00%)
occurrences (all)	25	6	0
Skin fissures			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	1 / 85 (1.18%)
occurrences (all)	0	0	1
Rash			
subjects affected / exposed	55 / 261 (21.07%)	2 / 131 (1.53%)	14 / 85 (16.47%)
occurrences (all)	81	4	16
Renal and urinary disorders			

Dysuria			
subjects affected / exposed	15 / 261 (5.75%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences (all)	17	1	0
Proteinuria			
subjects affected / exposed	99 / 261 (37.93%)	4 / 131 (3.05%)	26 / 85 (30.59%)
occurrences (all)	604	5	126
Haematuria			
subjects affected / exposed	18 / 261 (6.90%)	3 / 131 (2.29%)	6 / 85 (7.06%)
occurrences (all)	22	4	9
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	14 / 261 (5.36%)	0 / 131 (0.00%)	7 / 85 (8.24%)
occurrences (all)	26	0	7
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	52 / 261 (19.92%)	12 / 131 (9.16%)	18 / 85 (21.18%)
occurrences (all)	81	14	29
Arthralgia			
subjects affected / exposed	85 / 261 (32.57%)	9 / 131 (6.87%)	19 / 85 (22.35%)
occurrences (all)	148	15	39
Flank pain			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	3 / 85 (3.53%)
occurrences (all)	0	0	3
Muscle spasms			
subjects affected / exposed	22 / 261 (8.43%)	5 / 131 (3.82%)	11 / 85 (12.94%)
occurrences (all)	31	5	15
Joint swelling			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	2 / 85 (2.35%)
occurrences (all)	0	0	2
Muscular weakness			
subjects affected / exposed	20 / 261 (7.66%)	3 / 131 (2.29%)	5 / 85 (5.88%)
occurrences (all)	23	3	8
Musculoskeletal pain			
subjects affected / exposed	46 / 261 (17.62%)	11 / 131 (8.40%)	14 / 85 (16.47%)
occurrences (all)	60	13	27
Musculoskeletal chest pain			

subjects affected / exposed	32 / 261 (12.26%)	13 / 131 (9.92%)	11 / 85 (12.94%)
occurrences (all)	40	14	14
Myalgia			
subjects affected / exposed	51 / 261 (19.54%)	6 / 131 (4.58%)	12 / 85 (14.12%)
occurrences (all)	95	9	16
Pain in extremity			
subjects affected / exposed	48 / 261 (18.39%)	9 / 131 (6.87%)	12 / 85 (14.12%)
occurrences (all)	73	13	27
Neck pain			
subjects affected / exposed	23 / 261 (8.81%)	15 / 131 (11.45%)	6 / 85 (7.06%)
occurrences (all)	33	19	8
Infections and infestations			
Bronchitis			
subjects affected / exposed	17 / 261 (6.51%)	2 / 131 (1.53%)	5 / 85 (5.88%)
occurrences (all)	24	2	13
Influenza			
subjects affected / exposed	16 / 261 (6.13%)	1 / 131 (0.76%)	0 / 85 (0.00%)
occurrences (all)	17	1	0
Gastrointestinal infection			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	6 / 85 (7.06%)
occurrences (all)	0	0	11
Nasopharyngitis			
subjects affected / exposed	28 / 261 (10.73%)	8 / 131 (6.11%)	6 / 85 (7.06%)
occurrences (all)	54	8	7
Upper respiratory tract infection			
subjects affected / exposed	26 / 261 (9.96%)	7 / 131 (5.34%)	5 / 85 (5.88%)
occurrences (all)	40	9	10
Sinusitis			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	6 / 85 (7.06%)
occurrences (all)	0	0	11
Urinary tract infection			
subjects affected / exposed	30 / 261 (11.49%)	7 / 131 (5.34%)	6 / 85 (7.06%)
occurrences (all)	54	9	8

Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	148 / 261 (56.70%)	24 / 131 (18.32%)	43 / 85 (50.59%)
occurrences (all)	352	31	86
Dehydration			
subjects affected / exposed	24 / 261 (9.20%)	3 / 131 (2.29%)	0 / 85 (0.00%)
occurrences (all)	29	3	0
Hyperglycaemia			
subjects affected / exposed	15 / 261 (5.75%)	6 / 131 (4.58%)	5 / 85 (5.88%)
occurrences (all)	22	7	5
Hypoalbuminaemia			
subjects affected / exposed	27 / 261 (10.34%)	2 / 131 (1.53%)	12 / 85 (14.12%)
occurrences (all)	50	2	17
Hypokalaemia			
subjects affected / exposed	41 / 261 (15.71%)	5 / 131 (3.82%)	0 / 85 (0.00%)
occurrences (all)	78	5	0
Hypocalcaemia			
subjects affected / exposed	38 / 261 (14.56%)	0 / 131 (0.00%)	11 / 85 (12.94%)
occurrences (all)	74	0	23
Hypomagnesaemia			
subjects affected / exposed	20 / 261 (7.66%)	2 / 131 (1.53%)	6 / 85 (7.06%)
occurrences (all)	28	2	13
Vitamin D deficiency			
subjects affected / exposed	0 / 261 (0.00%)	0 / 131 (0.00%)	0 / 85 (0.00%)
occurrences (all)	0	0	0
Hyponatraemia			
subjects affected / exposed	17 / 261 (6.51%)	3 / 131 (2.29%)	5 / 85 (5.88%)
occurrences (all)	25	6	11

Non-serious adverse events	OOL, Treatment Period: Lenvatinib 20 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 30 (96.67%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	21 / 30 (70.00%)		
occurrences (all)	69		

Hypotension			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	5		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	13 / 30 (43.33%)		
occurrences (all)	28		
Asthenia			
subjects affected / exposed	10 / 30 (33.33%)		
occurrences (all)	26		
Influenza like illness			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Malaise			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
General physical health deterioration			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Non-cardiac chest pain			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Pain			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Oedema peripheral			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	8		
Pyrexia			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	8		
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	4		
Respiratory, thoracic and mediastinal			

disorders			
Cough			
subjects affected / exposed	8 / 30 (26.67%)		
occurrences (all)	13		
Dysphonia			
subjects affected / exposed	10 / 30 (33.33%)		
occurrences (all)	13		
Dyspnoea			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	5		
Dyspnoea exertional			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	5		
Haemoptysis			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	4		
Epistaxis			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	6		
Oropharyngeal pain			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	4		
Productive cough			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	3		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Insomnia			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Depression			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Investigations			

Alanine aminotransferase increased				
subjects affected / exposed	2 / 30 (6.67%)			
occurrences (all)	2			
Aspartate aminotransferase increased				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences (all)	0			
Blood alkaline phosphatase increased				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences (all)	0			
Blood cholesterol increased				
subjects affected / exposed	2 / 30 (6.67%)			
occurrences (all)	2			
Blood creatinine increased				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences (all)	2			
Blood thyroid stimulating hormone increased				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences (all)	0			
Electrocardiogram QT prolonged				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences (all)	5			
Lipase increased				
subjects affected / exposed	2 / 30 (6.67%)			
occurrences (all)	5			
Ejection fraction decreased				
subjects affected / exposed	2 / 30 (6.67%)			
occurrences (all)	2			
Platelet count decreased				
subjects affected / exposed	5 / 30 (16.67%)			
occurrences (all)	7			
Weight decreased				
subjects affected / exposed	18 / 30 (60.00%)			
occurrences (all)	49			
White blood cell count decreased				

subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	9		
Dizziness			
subjects affected / exposed	8 / 30 (26.67%)		
occurrences (all)	12		
Hyperaesthesia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Headache			
subjects affected / exposed	10 / 30 (33.33%)		
occurrences (all)	35		
Paraesthesia			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	4		
Sciatica			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	11		
Leukopenia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Lymphopenia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Thrombocytopenia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Gastrointestinal disorders			

Abdominal pain subjects affected / exposed occurrences (all)	8 / 30 (26.67%) 15			
Abdominal distension subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2			
Abdominal pain upper subjects affected / exposed occurrences (all)	9 / 30 (30.00%) 11			
Cheilitis subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0			
Constipation subjects affected / exposed occurrences (all)	5 / 30 (16.67%) 8			
Diarrhoea subjects affected / exposed occurrences (all)	21 / 30 (70.00%) 66			
Dyspepsia subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 10			
Dry mouth subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1			
Flatulence subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 6			
Dysphagia subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 5			
Gastrooesophageal reflux disease subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2			
Gingival pain subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2			

Glossodynia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Haemorrhoids			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	12 / 30 (40.00%)		
occurrences (all)	31		
Oral pain			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Stomatitis			
subjects affected / exposed	13 / 30 (43.33%)		
occurrences (all)	22		
Toothache			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	3		
Vomiting			
subjects affected / exposed	9 / 30 (30.00%)		
occurrences (all)	19		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	8		
Dermatitis acneiform			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	4		
Decubitus ulcer			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Dry skin			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	3		
Hyperkeratosis			

subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	9 / 30 (30.00%)		
occurrences (all)	44		
Hyperhidrosis			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Pruritus			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Skin fissures			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	8		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Proteinuria			
subjects affected / exposed	12 / 30 (40.00%)		
occurrences (all)	24		
Haematuria			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	7		
Arthralgia			

subjects affected / exposed	12 / 30 (40.00%)		
occurrences (all)	25		
Flank pain			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Muscle spasms			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	13		
Joint swelling			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Muscular weakness			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Musculoskeletal pain			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	6		
Musculoskeletal chest pain			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	5		
Myalgia			
subjects affected / exposed	9 / 30 (30.00%)		
occurrences (all)	16		
Pain in extremity			
subjects affected / exposed	7 / 30 (23.33%)		
occurrences (all)	9		
Neck pain			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	3		
Influenza			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		

Gastrointestinal infection			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Pneumonia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Nasopharyngitis			
subjects affected / exposed	6 / 30 (20.00%)		
occurrences (all)	6		
Upper respiratory tract infection			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	4		
Sinusitis			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	5		
Urinary tract infection			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	4		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	11 / 30 (36.67%)		
occurrences (all)	24		
Dehydration			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Hyperglycaemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	3		
Hypoalbuminaemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	3		
Hypokalaemia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Hypocalcaemia			

subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	6		
Hypomagnesaemia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Vitamin D deficiency			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Hyponatraemia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 June 2011	Amendment 1: The purpose of this amendment is to address a specific requirement from the EU-VHP assessment to add an inclusion criterion specifying that eligibility must exclude possible curative surgery.
07 July 2011	Amendment 02: the purpose of this amendment is to comply with local regulatory and health authority (PMDA and MHLW) requirements in Japan.
10 April 2012	Amendment 03: the purpose of this amendment is to update the protocol with the study name 'SELECT' and the approved generic name for E7080 (lenvatinib).
20 February 2013	Amendment 04: the purpose of this amendment is to comply with Data Monitoring Committee (DMC) recommendations.
19 February 2014	Amendment 05: the purpose of this amendment is to include guidance on management of hepatotoxicity and thromboembolic events under section headings, as per the agreement with Voluntary Harmonisation Procedure (VHP).
06 October 2014	Amendment 06: The purpose of this amendment is to 1. Clarified that when the study becomes a postmarketing study in Japan, study drug for individual subjects in Japan may be switched to postmarketing-labeled study drug until lenvatinib is commercially available for individual subjects, at which time the subjects in Japan may be switched to commercial lenvatinib. 2. Clarified that overall survival data collection and source verification will continue during the postmarketing study in Japan. 3. Increased the time window for performing some assessments (tumor assessments [CT/MRI], echocardiograms, etc) in the Open Label Lenvatinib Treatment Period. 4. Noted that, as of this amendment, clinical laboratory assessments will be performed by local laboratory only.
29 October 2014	Amendment 07: the purpose of this amendment is addition of a new section (Section 8.4.2.5) on the management of posterior reversible encephalopathy syndrome in agreement with the Voluntary Harmonisation Procedure (VHP).
10 August 2015	Amendment 08: the purpose of this amendment is 1. clarified that following approval of lenvatinib in Japan, all subjects treated in Japan will be discontinued from the study and transitioned to commercial lenvatinib, and will be followed under the postmarketing program in Japan. 2. Frequency of study visits and assessments in the OOL Lenvatinib Treatment Period of the Extension Phase of the study revised to once every 12 weeks. 3. Revised frequency of tumor assessments in the OOL Lenvatinib Treatment Period of the Extension Phase to no more frequently than once every 12 weeks and no less frequently than once every 24 weeks (±2 weeks) or sooner if clinically indicated, until documentation of disease progression. 4. Addition of a new section (Section 8.4.2.6) on the management of hypocalcemia in compliance with the Voluntary Harmonisation Procedure (VHP) assessment report.
26 January 2016	Amendment 09: the purpose of this amendment is to revised to change the frequency of echocardiograms from every 12 weeks to every 24 weeks in the Extension Phase of the study.
22 September 2017	Amendment 10: the purpose of this amendment is to update Synopsis, to clarify that subjects will continue to receive study treatment until disease progression, development of unacceptable toxicity, or withdrawal of consent.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported