Clinical trial results:
A randomized discontinuation study of XL184 in subjects with advanced solid tumors

Summary

EudraCT number	2009-012964-14
Trial protocol	BE GB
Global end of trial date	23 June 2014

Results information

Result version number	v1 (current)
This version publication date	24 March 2022
First version publication date	24 March 2022

Trial information

Trial identification

Sponsor protocol code	XL184-203

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00940225
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Exelixis, Inc.
Sponsor organisation address	1851 Harbor Bay Parkway, Alameda, United States, 94502
Public contact	Medical Information, Exelixis Inc, +1 866939 4041,
Scientific contact	Medical Information, Exelixis Inc, +1 866939 4041,

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	30 May 2013
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 May 2013
Global end of trial reached?	Yes
Global end of trial date	23 June 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is:
- To evaluate the efficacy of XL184 in subjects with advanced solid tumors

Protection of trial subjects:

An independent data monitoring committee was in place to monitor safety during the randomized discontinuation portion of the study.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 September 2009
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 15
Country: Number of subjects enrolled	Belgium: 43
Country: Number of subjects enrolled	Israel: 49
Country: Number of subjects enrolled	Taiwan: 23
Country: Number of subjects enrolled	United States: 600
Worldwide total number of subjects	730
EEA total number of subjects	43

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)	403
From 65 to 84 years	314

85 years and over	13

Subject disposition

Recruitment

Recruitment details:

Enrollment into the Randomized Discontinuation Trial (RDT) Cohorts: September 2009 - July 2011. Enrollment into the Non Randomized Expansion (NRE) Cohorts: February 2011 - April 2012.

Pre-assignment

Screening details:

Screening evaluations were completed prior to enrollment to determine the eligibility of subjects per protocol inclusion/exclusion criteria.

Period 1

Period 1 title	Treatment Period (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	RDT Cohort - Castration Resistant Prostate Cancer

Arm description: -

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

Dosage and administration details:

Administered orally, once daily, at the assigned dose

Arm title	RDT Cohort - Melanoma

Arm description: -

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

Dosage and administration details:

Administered orally, once daily, at the assigned dose

Arm title	RDT Cohort - Non Small Cell Lung Cancer

Arm description: -

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

Dosage and administration details:

Administered orally, once daily, at the assigned dose

Arm title	RDT Cohort - Pancreatic Cancer

Arm description: -	
Arm type	Experimental
Investigational medicinal product name	cabozantinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details: Administered orally, once daily, at the assigned dose	
Arm title	RDT Cohort - Gastric/Gastroesophageal Cancer
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	cabozantinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details: Administered orally, once daily, at the assigned dose	
Arm title	RDT Cohort - Hepatocellular Carcinoma
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	cabozantinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details: Administered orally, once daily, at the assigned dose	
Arm title	RDT Cohort - Small Cell Lung Cancer
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	cabozantinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details: Administered orally, once daily, at the assigned dose	
Arm title	RDT Cohort - Ovarian Cancer
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	cabozantinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use
Dosage and administration details: Administered orally, once daily, at the assigned dose	
Arm title	RDT Cohort - Metastatic Breast Cancer

Arm description: -	
Arm type	Experimental
Investigational medicinal product name	cabozantinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Administered orally, once daily, at the assigned dose

Arm title	NRE Cohort - Castration Resistant Prostate Cancer (100 mg)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	cabozantinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Administered orally, once daily, at the assigned dose

Arm title	NRE Cohort - Castration Resistant Prostate Cancer (40 mg)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	cabozantinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Administered orally, once daily, at the assigned dose

Arm title	NRE Cohort - Ovarian Cancer
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	cabozantinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

Administered orally, once daily, at the assigned dose

Number of subjects in period 1	RDT Cohort - Castration Resistant Prostate Cancer	RDT Cohort - Melanoma	RDT Cohort - Non Small Cell Lung Cancer
Started	171	77	60
Completed	171	77	60

Number of subjects in period 1	RDT Cohort - Pancreatic Cancer	RDT Cohort - Gastric/Gastroesoph	RDT Cohort - Hepatocellular

		ageal Cancer	Carcinoma
Started	20	21	41
Completed	20	21	41

Number of subjects in period 1	RDT Cohort - Small Cell Lung Cancer	RDT Cohort - Ovarian Cancer	RDT Cohort - Metastatic Breast Cancer
Started	21	70	45
Completed	21	70	45

Number of subjects in period 1	NRE Cohort - Castration Resistant Prostate Cancer (100 mg)	NRE Cohort - Castration Resistant Prostate Cancer (40 mg)	NRE Cohort - Ovarian Cancer
Started	93	51	60
Completed	93	51	60

Baseline characteristics

Reporting groups	
Reporting group title	RDT Cohort - Castration Resistant Prostate Cancer
Reporting group description: -	
Reporting group title	RDT Cohort - Melanoma
Reporting group description: -	
Reporting group title	RDT Cohort - Non Small Cell Lung Cancer
Reporting group description: -	
Reporting group title	RDT Cohort - Pancreatic Cancer
Reporting group description: -	
Reporting group title	RDT Cohort - Gastric/Gastroesophageal Cancer
Reporting group description: -	
Reporting group title	RDT Cohort - Hepatocellular Carcinoma
Reporting group description: -	
Reporting group title	RDT Cohort - Small Cell Lung Cancer
Reporting group description: -	
Reporting group title	RDT Cohort - Ovarian Cancer
Reporting group description: -	
Reporting group title	RDT Cohort - Metastatic Breast Cancer
Reporting group description: -	
Reporting group title	NRE Cohort - Castration Resistant Prostate Cancer (100 mg)
Reporting group description: -	
Reporting group title	NRE Cohort - Castration Resistant Prostate Cancer (40 mg)
Reporting group description: -	
Reporting group title	NRE Cohort - Ovarian Cancer
Reporting group description: -	

Reporting group values	RDT Cohort - Castration Resistant Prostate Cancer	RDT Cohort - Melanoma	RDT Cohort - Non Small Cell Lung Cancer
Number of subjects	171	77	60
Age categorical Units: Subjects			
Adult (18 - 65 years)	64	39	27
Adult (over 65 years)	107	38	33
Age continuous Units: years			
median	68.0	65.0	66.0
full range (min-max)	47 to 88	30 to 90	36 to 87
Gender categorical Units: Subjects			
Female	171	35	27
Male	0	42	33

Reporting group values	RDT Cohort - Pancreatic Cancer	RDT Cohort - Gastric/Gastroesophageal Cancer	RDT Cohort - Hepatocellular Carcinoma
Number of subjects	20	21	41

Age categorical Units: Subjects			
Adult (18 - 65 years)	13	13	29
Adult (over 65 years)	7	8	12
Age continuous Units: years			
median	63.0	62.0	60.0
full range (min-max)	40 to 78	40 to 80	32 to 82
Gender categorical Units: Subjects			
Female	7	5	10
Male	13	16	31

Reporting group values	RDT Cohort - Small Cell Lung Cancer	RDT Cohort - Ovarian Cancer	RDT Cohort - Metastatic Breast Cancer
Number of subjects	21	70	45
Age categorical Units: Subjects			
Adult (18 - 65 years)	14	48	39
Adult (over 65 years)	7	22	6
Age continuous Units: years			
median	65.0	60.5	56.0
full range (min-max)	47 to 81	26 to 79	27 to 74
Gender categorical Units: Subjects			
Female	12	70	44
Male	9	0	1

Reporting group values	NRE Cohort - Castration Resistant Prostate Cancer (100 mg)	NRE Cohort - Castration Resistant Prostate Cancer (40 mg)	NRE Cohort - Ovarian Cancer
Number of subjects	93	51	60
Age categorical Units: Subjects			
Adult (18 - 65 years)	44	29	44
Adult (over 65 years)	49	22	16
Age continuous Units: years			
median	66.0	65.0	59.5
full range (min-max)	46 to 85	43 to 83	38 to 76
Gender categorical Units: Subjects			
Female	0	0	60
Male	93	51	0

Reporting group values	Total		
Number of subjects	730		
Age categorical Units: Subjects			
Adult (18 - 65 years)	403		

Adult (over 65 years)	327		

Age continuous Units: years median full range (min-max)	- 		
Gender categorical Units: Subjects			
Female	441		
Male	289		

End points

End points reporting groups

Reporting group title	RDT Cohort - Castration Resistant Prostate Cancer
Reporting group description: -	
Reporting group title	RDT Cohort - Melanoma
Reporting group description: -	
Reporting group title	RDT Cohort - Non Small Cell Lung Cancer
Reporting group description: -	
Reporting group title	RDT Cohort - Pancreatic Cancer
Reporting group description: -	
Reporting group title	RDT Cohort - Gastric/Gastroesophageal Cancer
Reporting group description: -	
Reporting group title	RDT Cohort - Hepatocellular Carcinoma
Reporting group description: -	
Reporting group title	RDT Cohort - Small Cell Lung Cancer
Reporting group description: -	
Reporting group title	RDT Cohort - Ovarian Cancer
Reporting group description: -	
Reporting group title	RDT Cohort - Metastatic Breast Cancer
Reporting group description: -	
Reporting group title	NRE Cohort - Castration Resistant Prostate Cancer (100 mg)
Reporting group description: -	
Reporting group title	NRE Cohort - Castration Resistant Prostate Cancer (40 mg)
Reporting group description: -	
Reporting group title	NRE Cohort - Ovarian Cancer
Reporting group description: -	

Primary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)[1][2]

End point description:

End point type	Primary

End point timeframe:

assessed every 6 weeks until radiographic disease progression, and analyzed at the time of the primary analysis

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive endpoint (single arm, no across-arm comparison)

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was only assessed for certain tumor types.

End point values	RDT Cohort - Castration Resistant Prostate Cancer	RDT Cohort - Melanoma	RDT Cohort - Non Small Cell Lung Cancer	RDT Cohort - Pancreatic Cancer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	171	77	60	20
Units: Percentage of subjects				
number (confidence interval 95%)	4.7 (2.0 to 8.7)	5.2 (1.8 to 12.4)	10.0 (4.4 to 20.3)	0 (0 to 15.4)

End point values	RDT Cohort - Gastric/Gastroesophageal Cancer	RDT Cohort - Hepatocellular Carcinoma	RDT Cohort - Small Cell Lung Cancer	RDT Cohort - Ovarian Cancer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	41	21	70
Units: Percentage of subjects				
number (confidence interval 95%)	4.8 (0.2 to 21.8)	4.9 (0.9 to 16.1)	4.8 (0.2 to 21.8)	21.7 (13.1 to 32.4)

End point values	RDT Cohort - Metastatic Breast Cancer	NRE Cohort - Ovarian Cancer		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	45	60		
Units: Percentage of subjects				
number (confidence interval 95%)	10.0 (6.0 to 25.7)	10.0 (3.3 to 21.8)		

Statistical analyses

No statistical analyses for this end point

Primary: Bone scan response

End point title	Bone scan response[3][4]

End point description:

End point type	Primary

End point timeframe:

Assessed approximately every 6 weeks using MRI, CT, and/or bone scans

Notes:

[3] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive endpoint (single arm, no across-arm comparison)

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: End point was only appropriate for prostate cancer, and was only prospectively measured in the two NRE cohorts.

End point values	NRE Cohort - Castration Resistant Prostate Cancer (100 mg)	NRE Cohort - Castration Resistant Prostate Cancer (40 mg)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	93	51		
Units: Percentage of subjects				
number (confidence interval 95%)	74.2 (64.1 to 82.7)	47.1 (32.9 to 61.5)		

Statistical analyses

No statistical analyses for this end point

Primary: Progression Free Survival

End point title	Progression Free Survival[5][6]

End point description:

End point type	Primary

End point timeframe:

Assessed approximately every 6 weeks using MRI/CT until progressive disease

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Descriptive endpoint (single arm, no across-arm comparison)

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Endpoint was only assessed for certain tumor types.

End point values	RDT Cohort - Castration Resistant Prostate Cancer	RDT Cohort - Melanoma	RDT Cohort - Non Small Cell Lung Cancer	RDT Cohort - Pancreatic Cancer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	171	77	60	20
Units: months				
median (confidence interval 95%)	6.8 (3.9 to 9.7)	2.8 (1.4 to 6.9)	4.0 (1.4 to 5.7)	2.7 (1.3 to 5.5)

End point values	RDT Cohort - Gastric/Gastroesophageal Cancer	RDT Cohort - Hepatocellular Carcinoma	RDT Cohort - Small Cell Lung Cancer	RDT Cohort - Ovarian Cancer
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	21	41	21	70
Units: months				
median (confidence interval 95%)	1.4 (1.3 to 1.4)	5.2 (3.6 to 9.3)	3.4 (1.4 to 8.2)	5.5 (2.7 to 11.0)

End point values	RDT Cohort - Metastatic Breast Cancer			
Subject group type	Reporting group			
Number of subjects analysed	45			
Units: months				
median (confidence interval 95%)	4.3 (1.4 to 8.1)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Assessed at regular study visits from baseline until discontinuation from study, through to the date of the primary analysis.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	RDT - All Cohorts

Reporting group description:

Includes subjects in all 9 of the RDT cohorts.

Reporting group title	NRE Cohort - CRPC 100 mg

Reporting group description: -

Reporting group title	NRE Cohort - CRPC 40 mg

Reporting group description: -

Reporting group title	NRE Cohort - Ovarian Cancer

Reporting group description: -

Serious adverse events	RDT - All Cohorts	NRE Cohort - CRPC 100 mg	NRE Cohort - CRPC 40 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	223 / 526 (42.40%)	53 / 93 (56.99%)	30 / 51 (58.82%)
number of deaths (all causes)	54	12	12
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Cancer pain			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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 pleural effusion			
subjects affected / exposed	4 / 526 (0.76%)	0 / 93 (0.00%)	0 / 51 (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
metastases to the central nervous system			
subjects affected / exposed	1 / 526 (0.19%)	1 / 93 (1.08%)	0 / 51 (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
metastatic pain			
subjects affected / exposed	2 / 526 (0.38%)	1 / 93 (1.08%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Non-small cell lung cancer			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
Ovarian cancer			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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
Prostate cancer			
subjects affected / exposed	0 / 526 (0.00%)	3 / 93 (3.23%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Squamous cell carcinoma of the oral cavity			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Vascular disorders			
Bleeding varicose vein			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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

Deep vein thrombosis			
subjects affected / exposed	12 / 526 (2.28%)	1 / 93 (1.08%)	2 / 51 (3.92%)
occurrences causally related to treatment / all	5 / 12	0 / 1	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematoma			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Haemorrhage			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Hypertension			
subjects affected / exposed	3 / 526 (0.57%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	5 / 526 (0.95%)	1 / 93 (1.08%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypovolaemic shock			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Lymphoedema			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Orthostatic hypotension			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Pelvic venous thrombosis			

subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Venous stenosis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Venous thrombosis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Venous thrombosis limb			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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			
Acute hepatic failure			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Asthenia			
subjects affected / exposed	9 / 526 (1.71%)	1 / 93 (1.08%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	2 / 9	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chest pain			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Death			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Drug withdrawal syndrome			

subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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	2 / 526 (0.38%)	5 / 93 (5.38%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	2 / 2	4 / 5	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	5 / 526 (0.95%)	0 / 93 (0.00%)	0 / 51 (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
Malaise			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
multi-organ failure			
subjects affected / exposed	4 / 526 (0.76%)	1 / 93 (1.08%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Non-cardiac chest pain			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
Oedema peripheral			
subjects affected / exposed	3 / 526 (0.57%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain			
subjects affected / exposed	2 / 526 (0.38%)	1 / 93 (1.08%)	0 / 51 (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
Performance status decreased			

subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyrexia			
subjects affected / exposed	5 / 526 (0.95%)	2 / 93 (2.15%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Drug hypersensitivity			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Reproductive system and breast disorders			
Vaginal haemorrhage			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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
Respiratory, thoracic and mediastinal disorders			
Acute respiratory failure			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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
Atelectasis			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Bronchopleural fistula			

subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Chronic obstructive pulmonary disease			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Dyspnoea			
subjects affected / exposed	8 / 526 (1.52%)	4 / 93 (4.30%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 8	2 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Epistaxis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Hypoxia			
subjects affected / exposed	1 / 526 (0.19%)	2 / 93 (2.15%)	0 / 51 (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
Pleural effusion			
subjects affected / exposed	6 / 526 (1.14%)	1 / 93 (1.08%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 6	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonitis			
subjects affected / exposed	2 / 526 (0.38%)	1 / 93 (1.08%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	3 / 526 (0.57%)	1 / 93 (1.08%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 3	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary alveolar haemorrhage			

subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Pulmonary embolism			
subjects affected / exposed	23 / 526 (4.37%)	7 / 93 (7.53%)	8 / 51 (15.69%)
occurrences causally related to treatment / all	16 / 23	6 / 7	7 / 8
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary thrombosis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory distress			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory failure			
subjects affected / exposed	7 / 526 (1.33%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 7	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Confusional state			
subjects affected / exposed	6 / 526 (1.14%)	2 / 93 (2.15%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	2 / 6	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mental status changes			
subjects affected / exposed	9 / 526 (1.71%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 9	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Alanine aminotransferase increased			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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
Amylase increased			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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 sodium decreased			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood uric acid increased			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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 / 526 (0.19%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Liver function test abnormal			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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
Platelet count decreased			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Transaminases increased			

subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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
Injury, poisoning and procedural complications			
Clavicle fracture			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Hip fracture			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
laceration			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Radiation pneumonitis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Rib fracture			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Spinal compression fracture			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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
Subdural haematoma			
subjects affected / exposed	1 / 526 (0.19%)	1 / 93 (1.08%)	0 / 51 (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
Wound dehiscence			

subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
Wrist fracture			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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
Cardiac disorders			
Supraventricular tachycardia			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
tachycardia			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Anaemia			
subjects affected / exposed	8 / 526 (1.52%)	4 / 93 (4.30%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 8	1 / 4	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute myocardial infarction			
subjects affected / exposed	4 / 526 (0.76%)	0 / 93 (0.00%)	0 / 51 (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
Angina pectoris			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
Atrial fibrillation			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	1 / 51 (1.96%)
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			

subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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 arrest			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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 tamponade			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Coronary artery stenosis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Palpitations			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Sinus bradycardia			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
6th nerve paralysis			

subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Cerebral haemorrhage			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Cerebrovascular accident			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
convulsion			
subjects affected / exposed	3 / 526 (0.57%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depressed level of consciousness			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Encephalopathy			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Headache			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
Haemorrhage intracranial			

subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic encephalopathy			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
Occipital neuralgia			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Presyncope			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Sciatica			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Speech disorder			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Spinal cord compression			
subjects affected / exposed	1 / 526 (0.19%)	1 / 93 (1.08%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subdural effusion			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Syncope			

subjects affected / exposed	3 / 526 (0.57%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient ischaemic attack			
subjects affected / exposed	3 / 526 (0.57%)	1 / 93 (1.08%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	3 / 3	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Disseminated intravascular coagulation			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
idiopathic thrombocytopenia purpura			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Eye disorders			
Cataract			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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
Corneal epithelium defect			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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

Macular oedema			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Parophthalmia			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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 distension			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal hernia			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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
Abdominal pain			
subjects affected / exposed	9 / 526 (1.71%)	2 / 93 (2.15%)	2 / 51 (3.92%)
occurrences causally related to treatment / all	0 / 9	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal pain upper			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Anal fissure			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Anal fistula			

subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Anal ulcer			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Ascites			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
Colitis			
subjects affected / exposed	0 / 526 (0.00%)	2 / 93 (2.15%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Constipation			
subjects affected / exposed	4 / 526 (0.76%)	1 / 93 (1.08%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	2 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	15 / 526 (2.85%)	2 / 93 (2.15%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	11 / 15	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticular perforation			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
Duodenal ulcer haemorrhage			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Dyspepsia			

subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Dysphagia			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Enterocutaneous fistula			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Enterovesical fistula			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Gastric ulcer			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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 haemorrhage			
subjects affected / exposed	5 / 526 (0.95%)	0 / 93 (0.00%)	0 / 51 (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
Haematemesis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Haemorrhoids			

subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Ileus paralytic			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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
Inflammatory bowel disease			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Inguinal hernia			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Intestinal obstruction			
subjects affected / exposed	3 / 526 (0.57%)	0 / 93 (0.00%)	0 / 51 (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
Intestinal perforation			
subjects affected / exposed	4 / 526 (0.76%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	3 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Melaena			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Nausea			

subjects affected / exposed	12 / 526 (2.28%)	9 / 93 (9.68%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	10 / 12	6 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstruction gastric			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Oesophagitis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Pancreatitis			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis acute			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
peritoneal haemorrhage			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Pneumoperitoneum			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Proctalgia			
subjects affected / exposed	1 / 526 (0.19%)	1 / 93 (1.08%)	0 / 51 (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
Rectal haemorrhage			

subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal obstruction			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal stenosis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Retroperitoneal haematoma			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Small intestinal obstruction			
subjects affected / exposed	5 / 526 (0.95%)	0 / 93 (0.00%)	0 / 51 (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
Upper gastrointestinal haemorrhage			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Vomiting			
subjects affected / exposed	15 / 526 (2.85%)	7 / 93 (7.53%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	10 / 15	3 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice cholestatic			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
bile duct obstruction			

subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	2 / 51 (3.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholangitis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Cholecystitis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Cholestasis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Hepatic failure			
subjects affected / exposed	5 / 526 (0.95%)	1 / 93 (1.08%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Hyperbilirubinaemia			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
Portal vein thrombosis			
subjects affected / exposed	1 / 526 (0.19%)	2 / 93 (2.15%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 1	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Decubitus ulcer			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Palmar-plantar erythrodysaesthesia syndrome			

subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Psoriasis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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 pruritic			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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 prerenal failure			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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	3 / 526 (0.57%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemorrhage urinary tract			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Hydronephrosis			
subjects affected / exposed	3 / 526 (0.57%)	1 / 93 (1.08%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 3	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal failure			

subjects affected / exposed	5 / 526 (0.95%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
renal failure acute			
subjects affected / exposed	11 / 526 (2.09%)	4 / 93 (4.30%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 11	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric obstruction			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urethral obstruction			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Urinary tract obstruction			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Endocrine disorders			
Adrenal insufficiency			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Hypopituitarism			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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 and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Back pain			
subjects affected / exposed	5 / 526 (0.95%)	5 / 93 (5.38%)	4 / 51 (7.84%)
occurrences causally related to treatment / all	0 / 5	0 / 5	0 / 4
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	0 / 526 (0.00%)	6 / 93 (6.45%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 6	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Flank pain			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Groin pain			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Intervertebral disc protrusion			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Muscle haemorrhage			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Muscular weakness			
subjects affected / exposed	3 / 526 (0.57%)	1 / 93 (1.08%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 3	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Neck pain			

subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteonecrosis of jaw			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	1 / 526 (0.19%)	2 / 93 (2.15%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pathological fracture			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
Rhabdomyolysis			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malignant melanoma			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Infections and infestations			
Abscess limb			
subjects affected / exposed	1 / 526 (0.19%)	1 / 93 (1.08%)	0 / 51 (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
Bacterial sepsis			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Bronchitis			

subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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 / 526 (0.00%)	2 / 93 (2.15%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Clostridium difficile colitis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Clostridium difficile infection			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Cystitis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Device related infection			
subjects affected / exposed	1 / 526 (0.19%)	1 / 93 (1.08%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic foot infection			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Diverticulitis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Douglas' abscess			

subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Empyema			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Escherichia bacteraemia			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Gastroenteritis viral			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Herpes oesophagitis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Klebsiella bacteraemia			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Osteomyelitis			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Otitis media			

subjects affected / exposed	1 / 526 (0.19%)	1 / 93 (1.08%)	0 / 51 (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
Pelvic abscess			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Perirectal abscess			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Peritonitis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Pneumonia			
subjects affected / exposed	16 / 526 (3.04%)	3 / 93 (3.23%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 16	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 1	0 / 1	0 / 0
Pneumonia fungal			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (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
Rectal abscess			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Sepsis			
subjects affected / exposed	5 / 526 (0.95%)	0 / 93 (0.00%)	0 / 51 (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
Septic shock			

subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
Staphylococcal infection			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Staphylococcal sepsis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Tooth infection			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary tract infection			
subjects affected / exposed	7 / 526 (1.33%)	5 / 93 (5.38%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 7	0 / 5	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Wound infection			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
Wound sepsis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences causally related to treatment / all	0 / 2	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	17 / 526 (3.23%)	6 / 93 (6.45%)	2 / 51 (3.92%)
occurrences causally related to treatment / all	7 / 17	4 / 6	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetic ketoacidosis			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Failure to thrive			
subjects affected / exposed	3 / 526 (0.57%)	2 / 93 (2.15%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 3	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gout			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Hypercalcaemia			
subjects affected / exposed	2 / 526 (0.38%)	0 / 93 (0.00%)	0 / 51 (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
Hyperglycaemia			
subjects affected / exposed	1 / 526 (0.19%)	0 / 93 (0.00%)	0 / 51 (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
Hyperkalaemia			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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
Hypoglycaemia			

subjects affected / exposed	5 / 526 (0.95%)	0 / 93 (0.00%)	0 / 51 (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
Hypokalaemia			
subjects affected / exposed	3 / 526 (0.57%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	7 / 526 (1.33%)	2 / 93 (2.15%)	0 / 51 (0.00%)
occurrences causally related to treatment / all	4 / 7	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malnutrition			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (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

Serious adverse events	NRE Cohort - Ovarian Cancer		
Total subjects affected by serious adverse events			
subjects affected / exposed	34 / 60 (56.67%)		
number of deaths (all causes)	11		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast cancer			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cancer pain			
subjects affected / exposed	0 / 60 (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 / 60 (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 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
metastases to the central nervous system				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
metastatic pain				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Non-small cell lung cancer				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian cancer				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Prostate cancer				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous cell carcinoma of the oral cavity				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Bleeding varicose vein				
subjects affected / exposed	0 / 60 (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 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematoma				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypovolaemic shock				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphoedema				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Orthostatic hypotension				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic venous thrombosis				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Venous stenosis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Venous thrombosis limb				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Acute hepatic failure				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Asthenia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest pain				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Death				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug withdrawal syndrome				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 1			
Malaise				
subjects affected / exposed	0 / 60 (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 / 60 (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 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oedema peripheral				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pain				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Performance status decreased				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	4 / 60 (6.67%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Anaphylactic reaction				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Drug hypersensitivity				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Vaginal haemorrhage				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Acute respiratory failure				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Atelectasis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchopleural fistula				

subjects affected / exposed	0 / 60 (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 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoxia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural effusion				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary alveolar haemorrhage				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary embolism				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pulmonary thrombosis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory distress				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory failure				
subjects affected / exposed	0 / 60 (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 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Confusional state				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Mental status changes				
subjects affected / exposed	0 / 60 (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	1 / 60 (1.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Amylase increased				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Aspartate aminotransferase increased				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood sodium decreased				
subjects affected / exposed	0 / 60 (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 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lipase increased				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Liver function test abnormal				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Platelet count decreased				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transaminases increased				

subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Clavicle fracture				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
laceration				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Radiation pneumonitis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rib fracture				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound dehiscence				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wrist fracture				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Supraventricular tachycardia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
tachycardia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anaemia				
subjects affected / exposed	0 / 60 (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 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial fibrillation				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrioventricular block				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac arrest				
subjects affected / exposed	0 / 60 (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 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac tamponade				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Palpitations				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
pericardial effusion				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sinus bradycardia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
6th nerve paralysis				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral haemorrhage				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular accident				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
convulsion				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depressed level of consciousness				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Encephalopathy				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage intracranial				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic encephalopathy				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Occipital neuralgia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Presyncope				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sciatica				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Speech disorder				
subjects affected / exposed	0 / 60 (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 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subdural effusion				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Disseminated intravascular coagulation				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
idiopathic thrombocytopenia purpura				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ear and labyrinth disorders				
Vertigo				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Cataract				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Corneal epithelium defect				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			

Macular oedema				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Parophthalmia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Abdominal discomfort				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal distension				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal hernia				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	7 / 60 (11.67%)			
occurrences causally related to treatment / all	1 / 7			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal fissure				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal fistula				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Anal ulcer				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ascites				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Colitis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Constipation				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	0 / 0			
Diverticular perforation				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer haemorrhage				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspepsia				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterocutaneous fistula				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Enterovesical fistula				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				
subjects affected / exposed	0 / 60 (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 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematemesis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhoids				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus paralytic				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Inflammatory bowel disease				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Inguinal hernia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	4 / 60 (6.67%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Intestinal perforation				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower gastrointestinal haemorrhage				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Melaena				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				

subjects affected / exposed	8 / 60 (13.33%)			
occurrences causally related to treatment / all	0 / 8			
deaths causally related to treatment / all	0 / 0			
Obstruction gastric				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Oesophagitis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis acute				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
peritoneal haemorrhage				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumoperitoneum				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Proctalgia				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Rectal haemorrhage				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal obstruction				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal stenosis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retroperitoneal haematoma				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small intestinal obstruction				
subjects affected / exposed	5 / 60 (8.33%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Upper gastrointestinal haemorrhage				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	11 / 60 (18.33%)			
occurrences causally related to treatment / all	0 / 11			
deaths causally related to treatment / all	0 / 0			
Jaundice cholestatic				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
bile duct obstruction				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholangitis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cholestasis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic failure				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Hyperbilirubinaemia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Portal vein thrombosis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Skin and subcutaneous tissue disorders				
Decubitus ulcer				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Palmar-plantar erythrodysaesthesia syndrome				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Psoriasis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rash pruritic				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal and urinary disorders				
acute prerenal failure				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematuria				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemorrhage urinary tract				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hydronephrosis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal failure				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
renal failure acute				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ureteric obstruction				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urethral obstruction				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary tract obstruction				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Adrenal insufficiency				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypopituitarism				
subjects affected / exposed	0 / 60 (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	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Back pain				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone pain				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Flank pain				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Groin pain				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intervertebral disc protrusion				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscle haemorrhage				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Muscular weakness				
subjects affected / exposed	0 / 60 (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 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neck pain				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteonecrosis of jaw				
subjects affected / exposed	0 / 60 (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 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pathological fracture				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rhabdomyolysis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malignant melanoma				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abscess limb				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bacterial sepsis				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	1 / 1			
Bronchitis				

subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cellulitis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile colitis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Clostridium difficile infection				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cystitis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device related infection				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic foot infection				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Douglas' abscess				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Empyema				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Escherichia bacteraemia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis viral				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes oesophagitis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Klebsiella bacteraemia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
lung infection				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteomyelitis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Otitis media				

subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pelvic abscess				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Perirectal abscess				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia fungal				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal abscess				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Septic shock				

subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Staphylococcal infection				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal sepsis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tooth infection				
subjects affected / exposed	0 / 60 (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 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound infection				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound sepsis				
subjects affected / exposed	0 / 60 (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	2 / 60 (3.33%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetic ketoacidosis				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Failure to thrive				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gout				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperglycaemia				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyperkalaemia				
subjects affected / exposed	1 / 60 (1.67%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				

subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypokalaemia			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Malnutrition			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	RDT - All Cohorts	NRE Cohort - CRPC 100 mg	NRE Cohort - CRPC 40 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	524 / 526 (99.62%)	93 / 93 (100.00%)	51 / 51 (100.00%)
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	0 / 526 (0.00%)	6 / 93 (6.45%)	4 / 51 (7.84%)
occurrences (all)	0	6	4
Hot flush			
subjects affected / exposed	0 / 526 (0.00%)	5 / 93 (5.38%)	0 / 51 (0.00%)
occurrences (all)	0	5	0
Hypertension			
subjects affected / exposed	127 / 526 (24.14%)	25 / 93 (26.88%)	10 / 51 (19.61%)
occurrences (all)	127	25	10
Hypotension			
subjects affected / exposed	0 / 526 (0.00%)	11 / 93 (11.83%)	2 / 51 (3.92%)
occurrences (all)	0	11	2
Pallor			

subjects affected / exposed	0 / 526 (0.00%)	7 / 93 (7.53%)	1 / 51 (1.96%)
occurrences (all)	0	7	1
Thrombosis			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	118 / 526 (22.43%)	18 / 93 (19.35%)	7 / 51 (13.73%)
occurrences (all)	118	18	7
Chest discomfort			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	3 / 51 (5.88%)
occurrences (all)	0	1	3
Chills			
subjects affected / exposed	0 / 526 (0.00%)	5 / 93 (5.38%)	0 / 51 (0.00%)
occurrences (all)	0	5	0
Oedema peripheral			
subjects affected / exposed	78 / 526 (14.83%)	13 / 93 (13.98%)	11 / 51 (21.57%)
occurrences (all)	78	13	11
Fatigue			
subjects affected / exposed	345 / 526 (65.59%)	77 / 93 (82.80%)	32 / 51 (62.75%)
occurrences (all)	345	77	32
Mucosal inflammation			
subjects affected / exposed	84 / 526 (15.97%)	14 / 93 (15.05%)	8 / 51 (15.69%)
occurrences (all)	84	14	8
Pain			
subjects affected / exposed	38 / 526 (7.22%)	6 / 93 (6.45%)	6 / 51 (11.76%)
occurrences (all)	38	6	6
Pyrexia			
subjects affected / exposed	50 / 526 (9.51%)	7 / 93 (7.53%)	1 / 51 (1.96%)
occurrences (all)	50	7	1
Spinal pain			
subjects affected / exposed	0 / 526 (0.00%)	5 / 93 (5.38%)	2 / 51 (3.92%)
occurrences (all)	0	5	2
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	88 / 526 (16.73%)	14 / 93 (15.05%)	3 / 51 (5.88%)
occurrences (all)	88	14	3
Dysphonia			
subjects affected / exposed	142 / 526 (27.00%)	34 / 93 (36.56%)	9 / 51 (17.65%)
occurrences (all)	142	34	9
Dyspnoea			
subjects affected / exposed	109 / 526 (20.72%)	30 / 93 (32.26%)	13 / 51 (25.49%)
occurrences (all)	109	30	13
Dyspnoea exertional			
subjects affected / exposed	0 / 526 (0.00%)	5 / 93 (5.38%)	3 / 51 (5.88%)
occurrences (all)	0	5	3
Epistaxis			
subjects affected / exposed	36 / 526 (6.84%)	7 / 93 (7.53%)	1 / 51 (1.96%)
occurrences (all)	36	7	1
Hypoxia			
subjects affected / exposed	0 / 526 (0.00%)	5 / 93 (5.38%)	0 / 51 (0.00%)
occurrences (all)	0	5	0
Oropharyngeal pain			
subjects affected / exposed	60 / 526 (11.41%)	3 / 93 (3.23%)	4 / 51 (7.84%)
occurrences (all)	60	3	4
Pleural effusion			
subjects affected / exposed	28 / 526 (5.32%)	8 / 93 (8.60%)	1 / 51 (1.96%)
occurrences (all)	28	8	1
Productive cough			
subjects affected / exposed	0 / 526 (0.00%)	3 / 93 (3.23%)	0 / 51 (0.00%)
occurrences (all)	0	3	0
Pulmonary embolism			
subjects affected / exposed	29 / 526 (5.51%)	8 / 93 (8.60%)	9 / 51 (17.65%)
occurrences (all)	29	8	9
Psychiatric disorders			
Anxiety			
subjects affected / exposed	34 / 526 (6.46%)	3 / 93 (3.23%)	1 / 51 (1.96%)
occurrences (all)	34	3	1
Confusional state			

subjects affected / exposed	38 / 526 (7.22%)	8 / 93 (8.60%)	0 / 51 (0.00%)
occurrences (all)	38	8	0
Depression			
subjects affected / exposed	38 / 526 (7.22%)	4 / 93 (4.30%)	2 / 51 (3.92%)
occurrences (all)	38	4	2
Insomnia			
subjects affected / exposed	44 / 526 (8.37%)	7 / 93 (7.53%)	2 / 51 (3.92%)
occurrences (all)	44	7	2
Sleep disorder			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	71 / 526 (13.50%)	7 / 93 (7.53%)	3 / 51 (5.88%)
occurrences (all)	71	7	3
Aspartate aminotransferase increased			
subjects affected / exposed	94 / 526 (17.87%)	10 / 93 (10.75%)	5 / 51 (9.80%)
occurrences (all)	94	10	5
Blood albumin decreased			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Blood alkaline phosphatase increased			
subjects affected / exposed	0 / 526 (0.00%)	2 / 93 (2.15%)	3 / 51 (5.88%)
occurrences (all)	0	2	3
Blood creatinine increased			
subjects affected / exposed	0 / 526 (0.00%)	2 / 93 (2.15%)	3 / 51 (5.88%)
occurrences (all)	0	2	3
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	0 / 51 (0.00%)
occurrences (all)	0	1	0
Gamma-glutamyltransferase increased			
subjects affected / exposed	0 / 526 (0.00%)	2 / 93 (2.15%)	1 / 51 (1.96%)
occurrences (all)	0	2	1
Haemoglobin decreased			

subjects affected / exposed	0 / 526 (0.00%)	5 / 93 (5.38%)	2 / 51 (3.92%)
occurrences (all)	0	5	2
Lipase increased			
subjects affected / exposed	35 / 526 (6.65%)	2 / 93 (2.15%)	1 / 51 (1.96%)
occurrences (all)	35	2	1
Platelet count decreased			
subjects affected / exposed	0 / 526 (0.00%)	6 / 93 (6.45%)	0 / 51 (0.00%)
occurrences (all)	0	6	0
Transaminases increased			
subjects affected / exposed	0 / 526 (0.00%)	3 / 93 (3.23%)	0 / 51 (0.00%)
occurrences (all)	0	3	0
Weight decreased			
subjects affected / exposed	165 / 526 (31.37%)	42 / 93 (45.16%)	19 / 51 (37.25%)
occurrences (all)	165	42	19
Cardiac disorders			
Tachycardia			
subjects affected / exposed	0 / 526 (0.00%)	2 / 93 (2.15%)	1 / 51 (1.96%)
occurrences (all)	0	2	1
Nervous system disorders			
Cognitive disorder			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	2 / 51 (3.92%)
occurrences (all)	0	1	2
Dizziness			
subjects affected / exposed	87 / 526 (16.54%)	15 / 93 (16.13%)	7 / 51 (13.73%)
occurrences (all)	87	15	7
Dysgeusia			
subjects affected / exposed	156 / 526 (29.66%)	35 / 93 (37.63%)	14 / 51 (27.45%)
occurrences (all)	156	35	14
Headache			
subjects affected / exposed	80 / 526 (15.21%)	13 / 93 (13.98%)	8 / 51 (15.69%)
occurrences (all)	80	13	8
Hypoaesthesia			
subjects affected / exposed	0 / 526 (0.00%)	3 / 93 (3.23%)	5 / 51 (9.80%)
occurrences (all)	0	3	5
Neuropathy peripheral			

subjects affected / exposed	38 / 526 (7.22%)	7 / 93 (7.53%)	0 / 51 (0.00%)
occurrences (all)	38	7	0
Peripheral sensory neuropathy			
subjects affected / exposed	0 / 526 (0.00%)	5 / 93 (5.38%)	2 / 51 (3.92%)
occurrences (all)	0	5	2
Syncope			
subjects affected / exposed	0 / 526 (0.00%)	2 / 93 (2.15%)	1 / 51 (1.96%)
occurrences (all)	0	2	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	66 / 526 (12.55%)	30 / 93 (32.26%)	6 / 51 (11.76%)
occurrences (all)	66	30	6
Leukopenia			
subjects affected / exposed	27 / 526 (5.13%)	7 / 93 (7.53%)	3 / 51 (5.88%)
occurrences (all)	27	7	3
Neutropenia			
subjects affected / exposed	35 / 526 (6.65%)	8 / 93 (8.60%)	3 / 51 (5.88%)
occurrences (all)	35	8	3
Thrombocytopenia			
subjects affected / exposed	58 / 526 (11.03%)	10 / 93 (10.75%)	4 / 51 (7.84%)
occurrences (all)	58	10	4
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	1 / 51 (1.96%)
occurrences (all)	0	1	1
Vision blurred			
subjects affected / exposed	0 / 526 (0.00%)	2 / 93 (2.15%)	4 / 51 (7.84%)
occurrences (all)	0	2	4
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Abdominal distension			
subjects affected / exposed	31 / 526 (5.89%)	4 / 93 (4.30%)	3 / 51 (5.88%)
occurrences (all)	31	4	3
Abdominal pain			

subjects affected / exposed	126 / 526 (23.95%)	18 / 93 (19.35%)	9 / 51 (17.65%)
occurrences (all)	126	18	9
Abdominal pain upper			
subjects affected / exposed	52 / 526 (9.89%)	6 / 93 (6.45%)	3 / 51 (5.88%)
occurrences (all)	52	6	3
Ascites			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Chest pain			
subjects affected / exposed	0 / 526 (0.00%)	8 / 93 (8.60%)	3 / 51 (5.88%)
occurrences (all)	0	8	3
Constipation			
subjects affected / exposed	171 / 526 (32.51%)	33 / 93 (35.48%)	16 / 51 (31.37%)
occurrences (all)	171	33	16
Diarrhoea			
subjects affected / exposed	317 / 526 (60.27%)	66 / 93 (70.97%)	23 / 51 (45.10%)
occurrences (all)	317	66	23
Dry mouth			
subjects affected / exposed	87 / 526 (16.54%)	9 / 93 (9.68%)	4 / 51 (7.84%)
occurrences (all)	87	9	4
Dyspepsia			
subjects affected / exposed	64 / 526 (12.17%)	12 / 93 (12.90%)	7 / 51 (13.73%)
occurrences (all)	64	12	7
Dysphagia			
subjects affected / exposed	38 / 526 (7.22%)	6 / 93 (6.45%)	0 / 51 (0.00%)
occurrences (all)	38	6	0
Early satiety			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1
Oesophagitis			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	1 / 51 (1.96%)
occurrences (all)	0	1	1
Flatulence			
subjects affected / exposed	33 / 526 (6.27%)	8 / 93 (8.60%)	3 / 51 (5.88%)
occurrences (all)	33	8	3
Gastrooesophageal reflux disease			

subjects affected / exposed	46 / 526 (8.75%)	6 / 93 (6.45%)	5 / 51 (9.80%)
occurrences (all)	46	6	5
Glossodynia			
subjects affected / exposed	42 / 526 (7.98%)	2 / 93 (2.15%)	3 / 51 (5.88%)
occurrences (all)	42	2	3
Haemorrhoids			
subjects affected / exposed	0 / 526 (0.00%)	2 / 93 (2.15%)	2 / 51 (3.92%)
occurrences (all)	0	2	2
Hypoaesthesia oral			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	3 / 51 (5.88%)
occurrences (all)	0	1	3
Intestinal obstruction			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	273 / 526 (51.90%)	66 / 93 (70.97%)	30 / 51 (58.82%)
occurrences (all)	273	66	30
Proctalgia			
subjects affected / exposed	0 / 526 (0.00%)	6 / 93 (6.45%)	1 / 51 (1.96%)
occurrences (all)	0	6	1
Small intestinal obstruction			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Stomatitis			
subjects affected / exposed	99 / 526 (18.82%)	15 / 93 (16.13%)	5 / 51 (9.80%)
occurrences (all)	99	15	5
Toothache			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	1 / 51 (1.96%)
occurrences (all)	0	1	1
Vomiting			
subjects affected / exposed	196 / 526 (37.26%)	39 / 93 (41.94%)	19 / 51 (37.25%)
occurrences (all)	196	39	19
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	43 / 526 (8.17%)	1 / 93 (1.08%)	0 / 51 (0.00%)
occurrences (all)	43	1	0

Dry skin			
subjects affected / exposed	54 / 526 (10.27%)	6 / 93 (6.45%)	4 / 51 (7.84%)
occurrences (all)	54	6	4
Hair colour changes			
subjects affected / exposed	53 / 526 (10.08%)	4 / 93 (4.30%)	0 / 51 (0.00%)
occurrences (all)	53	4	0
Hyperhidrosis			
subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	2 / 51 (3.92%)
occurrences (all)	0	1	2
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	179 / 526 (34.03%)	24 / 93 (25.81%)	7 / 51 (13.73%)
occurrences (all)	179	24	7
Pruritus			
subjects affected / exposed	0 / 526 (0.00%)	4 / 93 (4.30%)	1 / 51 (1.96%)
occurrences (all)	0	4	1
Rash			
subjects affected / exposed	102 / 526 (19.39%)	19 / 93 (20.43%)	6 / 51 (11.76%)
occurrences (all)	102	19	6
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	27 / 526 (5.13%)	3 / 93 (3.23%)	4 / 51 (7.84%)
occurrences (all)	27	3	4
Haematuria			
subjects affected / exposed	0 / 526 (0.00%)	3 / 93 (3.23%)	6 / 51 (11.76%)
occurrences (all)	0	3	6
Micturition urgency			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	3 / 51 (5.88%)
occurrences (all)	0	0	3
Pollakiuria			
subjects affected / exposed	0 / 526 (0.00%)	6 / 93 (6.45%)	3 / 51 (5.88%)
occurrences (all)	0	6	3
Proteinuria			
subjects affected / exposed	34 / 526 (6.46%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences (all)	34	0	0
renal failure acute			

subjects affected / exposed	0 / 526 (0.00%)	5 / 93 (5.38%)	1 / 51 (1.96%)
occurrences (all)	0	5	1
Urinary incontinence			
subjects affected / exposed	0 / 526 (0.00%)	3 / 93 (3.23%)	4 / 51 (7.84%)
occurrences (all)	0	3	4
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	66 / 526 (12.55%)	30 / 93 (32.26%)	4 / 51 (7.84%)
occurrences (all)	66	30	4
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	39 / 526 (7.41%)	29 / 93 (31.18%)	6 / 51 (11.76%)
occurrences (all)	39	29	6
Back pain			
subjects affected / exposed	79 / 526 (15.02%)	30 / 93 (32.26%)	15 / 51 (29.41%)
occurrences (all)	79	30	15
Bone pain			
subjects affected / exposed	0 / 526 (0.00%)	16 / 93 (17.20%)	7 / 51 (13.73%)
occurrences (all)	0	16	7
Flank pain			
subjects affected / exposed	0 / 526 (0.00%)	5 / 93 (5.38%)	1 / 51 (1.96%)
occurrences (all)	0	5	1
Groin pain			
subjects affected / exposed	0 / 526 (0.00%)	2 / 93 (2.15%)	3 / 51 (5.88%)
occurrences (all)	0	2	3
Muscle spasms			
subjects affected / exposed	56 / 526 (10.65%)	10 / 93 (10.75%)	9 / 51 (17.65%)
occurrences (all)	56	10	9
Muscular weakness			
subjects affected / exposed	0 / 526 (0.00%)	13 / 93 (13.98%)	7 / 51 (13.73%)
occurrences (all)	0	13	7
Musculoskeletal chest pain			
subjects affected / exposed	27 / 526 (5.13%)	13 / 93 (13.98%)	4 / 51 (7.84%)
occurrences (all)	27	13	4
Musculoskeletal pain			

subjects affected / exposed	34 / 526 (6.46%)	21 / 93 (22.58%)	7 / 51 (13.73%)
occurrences (all)	34	21	7
Myalgia			
subjects affected / exposed	36 / 526 (6.84%)	9 / 93 (9.68%)	1 / 51 (1.96%)
occurrences (all)	36	9	1
Neck pain			
subjects affected / exposed	0 / 526 (0.00%)	4 / 93 (4.30%)	4 / 51 (7.84%)
occurrences (all)	0	4	4
Pain in extremity			
subjects affected / exposed	90 / 526 (17.11%)	29 / 93 (31.18%)	12 / 51 (23.53%)
occurrences (all)	90	29	12
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	0 / 51 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 526 (0.00%)	6 / 93 (6.45%)	1 / 51 (1.96%)
occurrences (all)	0	6	1
Upper respiratory tract infection			
subjects affected / exposed	0 / 526 (0.00%)	4 / 93 (4.30%)	3 / 51 (5.88%)
occurrences (all)	0	4	3
Urinary tract infection			
subjects affected / exposed	64 / 526 (12.17%)	9 / 93 (9.68%)	4 / 51 (7.84%)
occurrences (all)	64	9	4
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	271 / 526 (51.52%)	70 / 93 (75.27%)	23 / 51 (45.10%)
occurrences (all)	271	70	23
Dehydration			
subjects affected / exposed	84 / 526 (15.97%)	22 / 93 (23.66%)	5 / 51 (9.80%)
occurrences (all)	84	22	5
Hyperglycaemia			
subjects affected / exposed	0 / 526 (0.00%)	3 / 93 (3.23%)	1 / 51 (1.96%)
occurrences (all)	0	3	1
Hypoalbuminaemia			

subjects affected / exposed	0 / 526 (0.00%)	1 / 93 (1.08%)	1 / 51 (1.96%)
occurrences (all)	0	1	1
Hypocalcaemia			
subjects affected / exposed	0 / 526 (0.00%)	6 / 93 (6.45%)	2 / 51 (3.92%)
occurrences (all)	0	6	2
Hypokalaemia			
subjects affected / exposed	64 / 526 (12.17%)	14 / 93 (15.05%)	6 / 51 (11.76%)
occurrences (all)	64	14	6
Hypomagnesaemia			
subjects affected / exposed	70 / 526 (13.31%)	6 / 93 (6.45%)	3 / 51 (5.88%)
occurrences (all)	70	6	3
Hyponatraemia			
subjects affected / exposed	30 / 526 (5.70%)	7 / 93 (7.53%)	3 / 51 (5.88%)
occurrences (all)	30	7	3
Hypophosphataemia			
subjects affected / exposed	41 / 526 (7.79%)	5 / 93 (5.38%)	3 / 51 (5.88%)
occurrences (all)	41	5	3
Malnutrition			
subjects affected / exposed	0 / 526 (0.00%)	0 / 93 (0.00%)	1 / 51 (1.96%)
occurrences (all)	0	0	1

Non-serious adverse events	NRE Cohort - Ovarian Cancer		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	60 / 60 (100.00%)		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Hot flush			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Hypertension			
subjects affected / exposed	19 / 60 (31.67%)		
occurrences (all)	19		
Hypotension			

subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Pallor			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Thrombosis			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	10		
Chest discomfort			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Chills			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		
Oedema peripheral			
subjects affected / exposed	7 / 60 (11.67%)		
occurrences (all)	7		
Fatigue			
subjects affected / exposed	47 / 60 (78.33%)		
occurrences (all)	47		
Mucosal inflammation			
subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	10		
Pain			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Pyrexia			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	6		
Spinal pain			

subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	11 / 60 (18.33%)		
occurrences (all)	11		
Dysphonia			
subjects affected / exposed	16 / 60 (26.67%)		
occurrences (all)	16		
Dyspnoea			
subjects affected / exposed	11 / 60 (18.33%)		
occurrences (all)	11		
Dyspnoea exertional			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Epistaxis			
subjects affected / exposed	7 / 60 (11.67%)		
occurrences (all)	7		
Hypoxia			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Oropharyngeal pain			
subjects affected / exposed	11 / 60 (18.33%)		
occurrences (all)	11		
Pleural effusion			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Productive cough			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Pulmonary embolism			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Psychiatric disorders			

Anxiety			
subjects affected / exposed	8 / 60 (13.33%)		
occurrences (all)	8		
Confusional state			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Depression			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Insomnia			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Sleep disorder			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	16 / 60 (26.67%)		
occurrences (all)	16		
Aspartate aminotransferase increased			
subjects affected / exposed	21 / 60 (35.00%)		
occurrences (all)	21		
Blood albumin decreased			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Blood alkaline phosphatase increased			
subjects affected / exposed	11 / 60 (18.33%)		
occurrences (all)	11		
Blood creatinine increased			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Blood thyroid stimulating hormone increased			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Gamma-glutamyltransferase increased			

subjects affected / exposed	7 / 60 (11.67%)			
occurrences (all)	7			
Haemoglobin decreased				
subjects affected / exposed	0 / 60 (0.00%)			
occurrences (all)	0			
Lipase increased				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences (all)	3			
Platelet count decreased				
subjects affected / exposed	2 / 60 (3.33%)			
occurrences (all)	2			
Transaminases increased				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences (all)	3			
Weight decreased				
subjects affected / exposed	18 / 60 (30.00%)			
occurrences (all)	18			
Cardiac disorders				
Tachycardia				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences (all)	3			
Nervous system disorders				
Cognitive disorder				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences (all)	3			
Dizziness				
subjects affected / exposed	18 / 60 (30.00%)			
occurrences (all)	18			
Dysgeusia				
subjects affected / exposed	21 / 60 (35.00%)			
occurrences (all)	21			
Headache				
subjects affected / exposed	17 / 60 (28.33%)			
occurrences (all)	17			
Hypoaesthesia				

subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Neuropathy peripheral			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	6		
Peripheral sensory neuropathy			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Syncope			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	10		
Leukopenia			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		
Neutropenia			
subjects affected / exposed	7 / 60 (11.67%)		
occurrences (all)	7		
Thrombocytopenia			
subjects affected / exposed	9 / 60 (15.00%)		
occurrences (all)	9		
Eye disorders			
Dry eye			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Vision blurred			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Abdominal distension			

subjects affected / exposed	10 / 60 (16.67%)			
occurrences (all)	10			
Abdominal pain				
subjects affected / exposed	28 / 60 (46.67%)			
occurrences (all)	28			
Abdominal pain upper				
subjects affected / exposed	7 / 60 (11.67%)			
occurrences (all)	7			
Ascites				
subjects affected / exposed	6 / 60 (10.00%)			
occurrences (all)	6			
Chest pain				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences (all)	3			
Constipation				
subjects affected / exposed	22 / 60 (36.67%)			
occurrences (all)	22			
Diarrhoea				
subjects affected / exposed	47 / 60 (78.33%)			
occurrences (all)	47			
Dry mouth				
subjects affected / exposed	12 / 60 (20.00%)			
occurrences (all)	12			
Dyspepsia				
subjects affected / exposed	15 / 60 (25.00%)			
occurrences (all)	15			
Dysphagia				
subjects affected / exposed	8 / 60 (13.33%)			
occurrences (all)	8			
Early satiety				
subjects affected / exposed	3 / 60 (5.00%)			
occurrences (all)	3			
Oesophagitis				
subjects affected / exposed	4 / 60 (6.67%)			
occurrences (all)	4			
Flatulence				

subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		
Gastrooesophageal reflux disease			
subjects affected / exposed	9 / 60 (15.00%)		
occurrences (all)	9		
Glossodynia			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Haemorrhoids			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Hypoaesthesia oral			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Intestinal obstruction			
subjects affected / exposed	6 / 60 (10.00%)		
occurrences (all)	6		
Nausea			
subjects affected / exposed	39 / 60 (65.00%)		
occurrences (all)	39		
Proctalgia			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Small intestinal obstruction			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		
Stomatitis			
subjects affected / exposed	17 / 60 (28.33%)		
occurrences (all)	17		
Toothache			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Vomiting			
subjects affected / exposed	30 / 60 (50.00%)		
occurrences (all)	30		
Skin and subcutaneous tissue disorders			

Alopecia			
subjects affected / exposed	8 / 60 (13.33%)		
occurrences (all)	8		
Dry skin			
subjects affected / exposed	7 / 60 (11.67%)		
occurrences (all)	7		
Hair colour changes			
subjects affected / exposed	8 / 60 (13.33%)		
occurrences (all)	8		
Hyperhidrosis			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	20 / 60 (33.33%)		
occurrences (all)	20		
Pruritus			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		
Rash			
subjects affected / exposed	12 / 60 (20.00%)		
occurrences (all)	12		
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Haematuria			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Micturition urgency			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Pollakiuria			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Proteinuria			

subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
renal failure acute			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Urinary incontinence			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	15 / 60 (25.00%)		
occurrences (all)	15		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		
Back pain			
subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	10		
Bone pain			
subjects affected / exposed	1 / 60 (1.67%)		
occurrences (all)	1		
Flank pain			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Groin pain			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Muscle spasms			
subjects affected / exposed	13 / 60 (21.67%)		
occurrences (all)	13		
Muscular weakness			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Musculoskeletal chest pain			

subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Musculoskeletal pain			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Myalgia			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Neck pain			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Pain in extremity			
subjects affected / exposed	9 / 60 (15.00%)		
occurrences (all)	9		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		
Pneumonia			
subjects affected / exposed	0 / 60 (0.00%)		
occurrences (all)	0		
Upper respiratory tract infection			
subjects affected / exposed	2 / 60 (3.33%)		
occurrences (all)	2		
Urinary tract infection			
subjects affected / exposed	11 / 60 (18.33%)		
occurrences (all)	11		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	31 / 60 (51.67%)		
occurrences (all)	31		
Dehydration			
subjects affected / exposed	9 / 60 (15.00%)		
occurrences (all)	9		
Hyperglycaemia			

subjects affected / exposed	10 / 60 (16.67%)		
occurrences (all)	10		
Hypoalbuminaemia			
subjects affected / exposed	7 / 60 (11.67%)		
occurrences (all)	7		
Hypocalcaemia			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		
Hypokalaemia			
subjects affected / exposed	9 / 60 (15.00%)		
occurrences (all)	9		
Hypomagnesaemia			
subjects affected / exposed	12 / 60 (20.00%)		
occurrences (all)	12		
Hyponatraemia			
subjects affected / exposed	4 / 60 (6.67%)		
occurrences (all)	4		
Hypophosphataemia			
subjects affected / exposed	5 / 60 (8.33%)		
occurrences (all)	5		
Malnutrition			
subjects affected / exposed	3 / 60 (5.00%)		
occurrences (all)	3		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
22 October 2010	Suspended randomization stage and specified that all randomized subjects would undergo unblinding. Added new non-randomized cohorts ("NRE") for prostate cancer and ovarian cancer, with specific inclusion/exclusion criteria and endpoints. Updates to safety management guidelines.
22 August 2011	A second non-randomized cohort at a lower dose was added for prostate cancer. Inclusion/exclusion criteria for the non-randomized cohorts (prostate cancer and ovarian cancer) were revised. Updated safety management guidelines, including potential drug interactions. Added clarifications on dose modifications.
13 August 2012	Decreased some study procedures for subjects on study longer than 12 months.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28426123

http://www.ncbi.nlm.nih.gov/pubmed/30528315

http://www.ncbi.nlm.nih.gov/pubmed/27714541

http://www.ncbi.nlm.nih.gov/pubmed/23169517

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