Clinical trial results:
An International, Phase III, Randomized, Double-Blinded, Placebo-Controlled, Multi-Center Study to Assess the Efficacy of ZD6474 versus Placebo in Subjects with Unresectable Locally Advanced or Metastatic Medullary Thyroid Cancer

Summary

EudraCT number	2005-005077-29
Trial protocol	DE NL FR BE HU PT SE DK AT IT GB CZ ES
Global end of trial date	26 July 2024

Results information

Result version number	v2 (current)
This version publication date	03 December 2025
First version publication date	09 August 2025
Version creation reason	• Correction of full data set Correction of data.

Trial information

Trial identification

Sponsor protocol code	D4200C00058

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00410761
WHO universal trial number (UTN)	-
Other trial identifiers	Sanofi-Genzyme Code: LPS14811

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	50 Binney Street, Cambridge, Massachusetts, United States, 02142
Public contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com
Scientific contact	Trial Transparency Team, Sanofi aventis recherche & développement, Contact-US@sanofi.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	26 July 2024
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	26 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate an improvement in progression-free survival (PFS) with vandetanib as compared to placebo in participants with unresectable locally advanced or metastatic medullary thyroid carcinoma.

Protection of trial subjects:

Participants were fully informed of all pertinent aspects of the clinical trial as well as the possibility to discontinue at any time in language and terms appropriate for the participant and considering the local culture. During the course of the trial, participants were provided with individual participant cards indicating the nature of the trial the participant is participating, contact details and any information needed in the event of a medical emergency.
Collected personal data and human biological samples were processed in compliance with the Sanofi-Aventis Group Personal Data Protection Charter ensuring that the Group abides by the laws governing personal data protection in force in all countries in which it operates.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	23 November 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Austria: 4
Country: Number of subjects enrolled	Belgium: 9
Country: Number of subjects enrolled	Brazil: 6
Country: Number of subjects enrolled	Canada: 12
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	Denmark: 5
Country: Number of subjects enrolled	France: 45
Country: Number of subjects enrolled	Germany: 28
Country: Number of subjects enrolled	Hungary: 4
Country: Number of subjects enrolled	India: 6
Country: Number of subjects enrolled	Italy: 38
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Netherlands: 13
Country: Number of subjects enrolled	Poland: 32
Country: Number of subjects enrolled	Portugal: 7
Country: Number of subjects enrolled	Romania: 4

Country: Number of subjects enrolled	Russian Federation: 8
Country: Number of subjects enrolled	Serbia: 7
Country: Number of subjects enrolled	Spain: 4
Country: Number of subjects enrolled	Sweden: 2
Country: Number of subjects enrolled	Switzerland: 7
Country: Number of subjects enrolled	United States: 73
Worldwide total number of subjects	331
EEA total number of subjects	199

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)	262
From 65 to 84 years	69
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 331 participants were enrolled in the study. The study was conducted at 60 study sites in 23 countries.

Pre-assignment

Screening details:

First participant enrolled 23 November 2006, last participant enrolled 19 October 2007.

Period 1

Period 1 title	Randomized Treatment Period
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Randomized Treatment Period: Vandetanib 300 mg

Arm description:

Participants received vandetanib 300 mg orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period.

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	SAR390530
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Vandetanib 300 mg oral tablet was administered once daily.

Arm title	Randomized Treatment Period: Placebo

Arm description:

Participants received placebo matched to vandetanib orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo matched to vandetanib oral tablet was administered once daily.

Number of subjects in period 1	Randomized Treatment Period: Vandetanib 300 mg	Randomized Treatment Period: Placebo
Started	231	100
Received Randomized Treatment	231	99
Completed	14	1
Not completed	217	99
Consent withdrawn by subject	11	6
Objective disease progression	103	68
Randomized but did not receive treatment	-	1
Adverse event, non-fatal	34	3
Unspecified	69	21

Period 2

Period 2 title	Open-Label Treatment Period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	No
Arm title	Vandetanib 300 mg/Vandetanib 300 mg

Arm description:

Participants who received vandetanib 300 mg during the blinded randomized treatment period and who were unblinded due to disease progression or as a result of protocol amendment 6 were given the option to continue to receive vandetanib 300 mg orally once daily in the open-label treatment period for as long as they still benefitted of it per investigator judgement or until they were given another anti-cancer therapy.

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	SAR390530
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Vandetanib 300 mg oral tablet was administered once daily.

Arm title	Placebo/Vandetanib 300 mg

Arm description:

Participants who received placebo matched to vandetanib during the blinded randomized treatment period and who were unblinded due to disease progression or as a result of protocol amendment 6 were given the option to receive vandetanib 300 mg orally once daily in the open-label treatment period for as long as they still benefitted of it per investigator judgement or until they were given another anti-cancer therapy.

Arm type	Placebo

Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	SAR390530
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Vandetanib 300 mg oral tablet was administered once daily.

Number of subjects in period 2	Vandetanib 300 mg/Vandetanib 300 mg	Placebo/Vandetanib 300 mg
Started	109	79
Completed	28	21
Not completed	81	58
Consent withdrawn by subject	8	7
Objective disease progression	42	27
Adverse event, non-fatal	13	15
Unspecified	18	9

Baseline characteristics

Reporting groups	
Reporting group title	Randomized Treatment Period: Vandetanib 300 mg
Reporting group description:	
Participants received vandetanib 300 mg orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period.	
Reporting group title	Randomized Treatment Period: Placebo
Reporting group description:	
Participants received placebo matched to vandetanib orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period.	

Reporting group values	Randomized Treatment Period: Vandetanib 300 mg	Randomized Treatment Period: Placebo	Total
Number of subjects	231	100	331
Age categorical			
Units: Subjects			
Age continuous			
Units: years			
arithmetic mean	50.7	53.4	
full range (min-max)	18 to 83	26 to 84	-
Gender categorical			
Units: Subjects			
Female	97	44	141
Male	134	56	190

End points

End points reporting groups

Reporting group title	Randomized Treatment Period: Vandetanib 300 mg
Reporting group description:	
Participants received vandetanib 300 mg orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period.	
Reporting group title	Randomized Treatment Period: Placebo
Reporting group description:	
Participants received placebo matched to vandetanib orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period.	
Reporting group title	Vandetanib 300 mg/Vandetanib 300 mg
Reporting group description:	
Participants who received vandetanib 300 mg during the blinded randomized treatment period and who were unblinded due to disease progression or as a result of protocol amendment 6 were given the option to continue to receive vandetanib 300 mg orally once daily in the open-label treatment period for as long as they still benefitted of it per investigator judgement or until they were given another anti-cancer therapy.	
Reporting group title	Placebo/Vandetanib 300 mg
Reporting group description:	
Participants who received placebo matched to vandetanib during the blinded randomized treatment period and who were unblinded due to disease progression or as a result of protocol amendment 6 were given the option to receive vandetanib 300 mg orally once daily in the open-label treatment period for as long as they still benefitted of it per investigator judgement or until they were given another anti-cancer therapy.	

Primary: Progression-Free Survival

End point title	Progression-Free Survival[1]
End point description:	
Median time to progression (months) from randomisation until objective disease progression (determined by RECIST assessments) or death (by any cause in the absence of objective progression) provided death is within 3 months from the last evaluable RECIST assessment. Values here are estimated (from a Weibull model) as the medians were not met. -99999/99999 indicates that PFS is a time to event endpoint and because the medians were not met in this study there is no appropriate measure of dispersion of the median.	
End point type	Primary
End point timeframe:	
RECIST tumour assessments were performed at screening (within 3 weeks before date of randomisation), then once every 12 weeks up to and including discontinuation of blinded study treatment, unless patients had withdrawn consent.	

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: As the endpoint is descriptive in nature, no statistical analysis is provided.

End point values	Randomized Treatment Period: Vandetanib 300 mg	Randomized Treatment Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	100		
Units: Months				

median (confidence interval 95%)	30.5 (-99999 to 99999)	19.2 (-99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Objective Response Rate (ORR)

End point title	Objective Response Rate (ORR)

End point description:

The ORR is the number of patients that are responders i.e. those patients with a confirmed best objective response of complete response (CR) or partial response (PR) as defined by RECIST criteria. The categories for best objective response are CR, PR, stable disease (SD) >= 12 weeks, progressive disease (PD) or NE.

End point type	Secondary

End point timeframe:

RECIST assessments performed at screening (within 3 weeks before randomisation), then every 12 weeks. For patients with objective response of CR or PR, an additional confirmatory scan was performed ≥4 weeks following the date of first response.

End point values	Randomized Treatment Period: Vandetanib 300 mg	Randomized Treatment Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	100		
Units: Participants				
number (not applicable)	104	13		

Statistical analyses

No statistical analyses for this end point

Secondary: Disease Control Rate (DCR)

End point title	Disease Control Rate (DCR)

End point description:

Disease control rate is defined as the number of patients who achieved disease control at 8 weeks following randomisation. Disease control at 8 weeks is defined as a best objective response of complete response (CR), partial response (PR) or stable disease (SD) >= 12 weeks.

End point type	Secondary

End point timeframe:

RECIST tumour assessments were performed at screening (within 3 weeks before date of randomisation), then once every 12 weeks up to and including discontinuation of blinded study treatment, unless patients had withdrawn consent

End point values	Randomized Treatment Period: Vandetanib 300 mg	Randomized Treatment Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	100		
Units: Participants				
number (not applicable)	200	71		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Response (DoR)

End point title	Duration of Response (DoR)

End point description:

Response is defined as a confirmed best objective response of CR or PR. Duration of response is defined as time from the date of first documented response until date of documented progression or death in the absence of disease progression (provided death is within 3 months of last RECIST assessment). Values are estimated as the medians weren't met. -99999/99999 indicates that DoR is a time to event endpoint and because the medians were not met in this study there is no appropriate measure of dispersion of the median.

End point type	Secondary

End point timeframe:

RECIST tumour assessments were performed at screening (within 3 weeks before date of randomisation), then once every 12 weeks up to and including discontinuation of blinded study treatment, unless patients had withdrawn consent

End point values	Randomized Treatment Period: Vandetanib 300 mg	Randomized Treatment Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	104	13		
Units: Months				
median (confidence interval 95%)	22.2 (-99999 to 99999)	16.3 (-99999 to 99999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival (OS)

End point title	Overall Survival (OS)

End point description:

OS is defined as the time from the date of randomization until death. "9999" indicates that the upper limit of confidence interval was not estimable due to insufficient number of participants with events.

End point type	Secondary

End point timeframe:

From date of randomization until death, up to approximately 105 months

End point values	Randomized Treatment Period: Vandetanib 300 mg	Randomized Treatment Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	100		
Units: Months				
median (confidence interval 95%)	81.6 (64.6 to 98.5)	80.4 (52.5 to 9999)		

Statistical analyses

No statistical analyses for this end point

Secondary: Biochemical Response Calcitonin (CTN)

End point title	Biochemical Response Calcitonin (CTN)

End point description:

Best biochemical response was calculated from assessments at baseline and during treatment. Responders were those patients with a best biochemical response of CR or PR, confirmed by repeat assessments, which were to be performed no less than 4 weeks after the criteria for PR or CR were first met. CR and PR being defined according to level of CTN.

End point type	Secondary

End point timeframe:

Blood samples Blood samples for analysis of CTN were taken at screening baseline (average of 0, 1, 4 and 8 hours), then every 4 weeks until discontinuation and 60 day follow up

End point values	Randomized Treatment Period: Vandetanib 300 mg	Randomized Treatment Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	100		
Units: Participants				
number (not applicable)	160	3		

Statistical analyses

No statistical analyses for this end point

Secondary: Biochemical Response Carcinoembryonic Antigen (CEA)

End point title	Biochemical Response Carcinoembryonic Antigen (CEA)

End point description:

Best biochemical response was calculated from assessments at baseline and during treatment. Responders were those patients with a best biochemical response of CR or PR, confirmed by repeat assessments, which were to be performed no less than 4 weeks after the criteria for PR or CR were first met. CR and PR being defined according to level of CEA.

End point type	Secondary

End point timeframe:

Blood samples for analysis of CEA were taken at screening baseline (average of 0, 1, 4 and 8 hours), then every 4 weeks until discontinuation and 60 day follow up

End point values	Randomized Treatment Period: Vandetanib 300 mg	Randomized Treatment Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	100		
Units: Participants				
number (not applicable)	119	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Worsening of Pain (TWP)

End point title	Time to Worsening of Pain (TWP)

End point description:

TWP was derived using the worst pain score from brief pain inventory (BPI) and patient reported opioid analgesic use. BPI uses 0 to 10 numeric rating scales asking subjects to rate their pain. TWP results are presented.

End point type	Secondary

End point timeframe:

During the last week of the screening period (Day -7 to Day 0), the brief pain inventory (BPI) and opioid analgesic use were self-reported once a day for 4 days to establish baseline, then every week during blinded study treatment, up to discontinuation.

End point values	Randomized Treatment Period: Vandetanib 300 mg	Randomized Treatment Period: Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	231	100		
Units: Months				
median (confidence interval 95%)	7.85 (5.39 to 12.16)	3.25 (1.87 to 5.26)		

Statistical analyses

No statistical analyses for this end point

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and deaths: From randomization (Day 1) up to end of follow-up, approximately 212 months. Non-serious adverse events: From randomization (Day 1) up to data cut-off date of 01-Jun-2010, approximately 42 months.

Adverse event reporting additional description:

The safety population included all participants who received at least 1 dose of vandetanib/placebo. AEs and SAEs were collected from Day 1 to cut-off date 01-Jun-2010 and were presented in clinical database. After this cut-off date, SAEs were reported in pharmacovigilance database, but no non-serious AEs were reported.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	13 - 25.1

Reporting groups

Reporting group title	Randomized Treatment Period: Vandetanib 300 mg

Reporting group description:

Participants received vandetanib 300 mg orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period.

Reporting group title	Open-Label Treatment Period: Placebo/Vandetanib 300 mg

Reporting group description:

Participants who received placebo matched to vandetanib during the blinded randomized treatment period and who were unblinded due to disease progression or as a result of protocol amendment 6 were given the option to receive vandetanib 300 mg orally once daily in the open-label treatment period for as long as they still benefitted of it per investigator judgement or until they were given another anti-cancer therapy.

Reporting group title	Open-Label Treatment Period: Vandetanib 300 mg/Vandetanib 300

Reporting group description:

Participants who received vandetanib 300 mg during the blinded randomized treatment period and who were unblinded due to disease progression or as a result of protocol amendment 6 were given the option to continue to receive vandetanib 300 mg orally once daily in the open-label treatment period for as long as they still benefitted of it per investigator judgement or until they were given another anti-cancer therapy.

Reporting group title	Randomized Treatment Period: Placebo

Reporting group description:

Participants received placebo matched to vandetanib orally once daily until objective disease progression, any other withdrawal criteria was met or at the investigator's discretion, the approval and implementation of protocol amendment 6 during the blinded randomized treatment period.

Serious adverse events	Randomized Treatment Period: Vandetanib 300 mg	Open-Label Treatment Period: Placebo/Vandetanib 300 mg	Open-Label Treatment Period: Vandetanib 300 mg/Vandetanib 300
Total subjects affected by serious adverse events			
subjects affected / exposed	92 / 231 (39.83%)	36 / 79 (45.57%)	53 / 109 (48.62%)
number of deaths (all causes)	66	41	52
number of deaths resulting from adverse events	10	3	7

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast Cancer Female			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Basal Cell Carcinoma			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 9	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Chronic Myeloid Leukaemia			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colorectal Adenoma			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Neoplasm Malignant			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases To Bone			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Germ Cell Cancer			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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 Cancer Metastatic			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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

Pancreatic Neoplasm			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Prostate Cancer			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Phaeochromocytoma			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	0 / 109 (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
Squamous Cell Carcinoma			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Cell Carcinoma			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Squamous Cell Carcinoma Of Skin			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Testicular Seminoma (Pure)			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Accelerated Hypertension			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Deep Vein Thrombosis			

subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive Crisis			
subjects affected / exposed	4 / 231 (1.73%)	0 / 79 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	3 / 231 (1.30%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	3 / 4	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypotension			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Jugular Vein Thrombosis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	0 / 109 (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
Vena Cava Thrombosis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Pregnancy, puerperium and perinatal conditions			
Abortion Spontaneous			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
General disorders and administration site conditions			

Asthenia			
subjects affected / exposed	2 / 231 (0.87%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Device Occlusion			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Chest Pain			
subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	2 / 109 (1.83%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fatigue			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
General Physical Health Deterioration			
subjects affected / exposed	1 / 231 (0.43%)	2 / 79 (2.53%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Malaise			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Mucosal Inflammation			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Pyrexia			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sudden Death			

subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Swelling			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Immune system disorders			
Iodine Allergy			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	0 / 109 (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
Reproductive system and breast disorders			
Intermenstrual Bleeding			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ovarian Cyst Ruptured			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Asthmatic Crisis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Acute Respiratory Distress Syndrome			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bronchospasm			

subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Chylothorax			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Epistaxis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 2	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Cough			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haemoptysis			
subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	0 / 109 (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
Interstitial Lung Disease			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Disorder			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Infiltration			

subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural Effusion			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Pneumonia Aspiration			
subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Pneumonitis			
subjects affected / exposed	2 / 231 (0.87%)	1 / 79 (1.27%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 3	0 / 3	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumothorax			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Embolism			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Oedema			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary Thrombosis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	0 / 109 (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 Arrest			

subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Respiratory Failure			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Psychiatric disorders			
Anxiety			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bipolar Disorder			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Depression			
subjects affected / exposed	3 / 231 (1.30%)	0 / 79 (0.00%)	2 / 109 (1.83%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Confusional State			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Completed Suicide			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Suicide Attempt			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Investigations			

Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Blood Creatinine Increased			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
C-Reactive Protein Increased			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Electrocardiogram Qt Prolonged			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic Enzyme Increased			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
International Normalised Ratio Increased			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Prostatic Specific Antigen Increased			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	0 / 109 (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			
Compression Fracture			

subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Exposure During Pregnancy			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Jaw Fracture			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	0 / 109 (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
Joint Injury			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Overdose			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	0 / 109 (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
Post Procedural Complication			
subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	0 / 109 (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
Post Procedural Haematuria			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Road Traffic Accident			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Seroma			

subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal Fracture			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Tibia Fracture			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venomous Bite			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Wound Dehiscence			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Wound Necrosis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Congenital, familial and genetic disorders			
Patent Ductus Arteriosus			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			

Acute Myocardial Infarction			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	4 / 109 (3.67%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	2 / 2
Arrhythmia			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Atrial Fibrillation			
subjects affected / exposed	2 / 231 (0.87%)	0 / 79 (0.00%)	0 / 109 (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
Bradycardia			
subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	0 / 109 (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
Cardiac Failure Acute			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Cardiac Failure Congestive			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardio-Respiratory Arrest			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Cardiovascular Insufficiency			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Myocardial Infarction			

subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Pericardial Effusion			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	0 / 109 (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
Pericardial Haemorrhage			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	0 / 109 (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
Pericarditis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Stress Cardiomyopathy			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Brain Oedema			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Carotid Artery Stenosis			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Cerebellar Syndrome			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebral Ischaemia			

subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cerebrovascular Accident			
subjects affected / exposed	0 / 231 (0.00%)	2 / 79 (2.53%)	3 / 109 (2.75%)
occurrences causally related to treatment / all	0 / 0	0 / 2	1 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Convulsion			
subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	0 / 109 (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
Depressed Level Of Consciousness			
subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dizziness			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Epilepsy			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	3 / 109 (2.75%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hemiparesis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	0 / 109 (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
Internal Capsule Infarction			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Loss Of Consciousness			

subjects affected / exposed	3 / 231 (1.30%)	0 / 79 (0.00%)	0 / 109 (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
Neuralgia			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	0 / 109 (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
Peripheral Sensorimotor Neuropathy			
subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Somnolence			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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 Cord Compression			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Subarachnoid Haemorrhage			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Syncope			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Transient Ischaemic Attack			
subjects affected / exposed	2 / 231 (0.87%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	1 / 3	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Disseminated Intravascular Coagulation			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Lymphadenopathy			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
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 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Glaucoma			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Retinal Artery Occlusion			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Retinal Detachment			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vision Blurred			

subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	4 / 231 (1.73%)	0 / 79 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	2 / 4	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Diarrhoea			
subjects affected / exposed	6 / 231 (2.60%)	2 / 79 (2.53%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	4 / 6	1 / 2	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dry Mouth			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Dysphagia			
subjects affected / exposed	2 / 231 (0.87%)	0 / 79 (0.00%)	0 / 109 (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
Faecaloma			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Gastritis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal Haemorrhage			

subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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 Inflammation			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ileus			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Intestinal Perforation			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mechanical Ileus			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive Pancreatitis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis Acute			

subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	3 / 109 (2.75%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Pancreatitis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis Chronic			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis Haemorrhagic			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Peritonitis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Pneumatosis Intestinalis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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 Haemorrhage			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Reflux Gastritis			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Small Intestinal Perforation			

subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Subileus			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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	2 / 231 (0.87%)	2 / 79 (2.53%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 2	2 / 2	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Biliary Colic			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	2 / 109 (1.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis			
subjects affected / exposed	2 / 231 (0.87%)	1 / 79 (1.27%)	0 / 109 (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
Cholecystitis Acute			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholelithiasis			
subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	0 / 109 (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
Cholestasis			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Jaundice			

subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis Acneiform			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Photosensitivity Reaction			
subjects affected / exposed	2 / 231 (0.87%)	0 / 79 (0.00%)	0 / 109 (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
Pruritus			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Skin Exfoliation			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin Ulcer			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Anuria			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Calculus Ureteric			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Calculus Urinary			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Chronic Kidney Disease			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Hydronephrosis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Obstructive Uropathy			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Nephrolithiasis			
subjects affected / exposed	3 / 231 (1.30%)	3 / 79 (3.80%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 4	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Colic			
subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	0 / 109 (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
Renal Failure			

subjects affected / exposed	1 / 231 (0.43%)	2 / 79 (2.53%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal Failure Acute			
subjects affected / exposed	1 / 231 (0.43%)	2 / 79 (2.53%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	1 / 1	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tubulointerstitial Nephritis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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			
Cushing's Syndrome			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Arthritis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back Pain			
subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	2 / 109 (1.83%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone Pain			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Flank Pain			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Musculoskeletal Chest Pain			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Myopathy			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Neck Pain			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Osteoarthritis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infections and infestations			
Abdominal Abscess			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Abdominal Wall Abscess			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Appendicitis			
subjects affected / exposed	3 / 231 (1.30%)	2 / 79 (2.53%)	3 / 109 (2.75%)
occurrences causally related to treatment / all	0 / 3	0 / 2	0 / 3
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Appendicitis Perforated			

subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bartholin's Abscess			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Biliary Sepsis			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Bronchitis			
subjects affected / exposed	2 / 231 (0.87%)	0 / 79 (0.00%)	0 / 109 (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
Bronchitis Bacterial			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Covid-19			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dermatitis Infected			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diverticulitis			
subjects affected / exposed	2 / 231 (0.87%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	1 / 2	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Folliculitis			

subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	2 / 109 (1.83%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis Bacterial			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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 Infection			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Infected Bites			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Infection			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Influenza			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngitis			

subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Lower Respiratory Tract Infection			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lung Infection			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Meningitis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Meningitis Bacterial			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peridiverticular Abscess			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	7 / 231 (3.03%)	1 / 79 (1.27%)	3 / 109 (2.75%)
occurrences causally related to treatment / all	0 / 9	0 / 1	1 / 5
deaths causally related to treatment / all	1 / 1	0 / 0	1 / 1
Postoperative Wound Infection			

subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Pyelonephritis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Tract Infection			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	1 / 1	0 / 0
Staphylococcal Infection			
subjects affected / exposed	1 / 231 (0.43%)	1 / 79 (1.27%)	0 / 109 (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
Sepsis			
subjects affected / exposed	4 / 231 (1.73%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 4	0 / 0	0 / 1
deaths causally related to treatment / all	1 / 1	0 / 0	0 / 0
Staphylococcal Sepsis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Streptococcal Sepsis			
subjects affected / exposed	0 / 231 (0.00%)	1 / 79 (1.27%)	0 / 109 (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
Tracheitis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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 Infection			

subjects affected / exposed	3 / 231 (1.30%)	0 / 79 (0.00%)	2 / 109 (1.83%)
occurrences causally related to treatment / all	0 / 6	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary Tract Infection Pseudomonal			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urosepsis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	2 / 109 (1.83%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Acidosis			
subjects affected / exposed	0 / 231 (0.00%)	0 / 79 (0.00%)	1 / 109 (0.92%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Decreased Appetite			
subjects affected / exposed	4 / 231 (1.73%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	1 / 4	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dehydration			
subjects affected / exposed	3 / 231 (1.30%)	3 / 79 (3.80%)	0 / 109 (0.00%)
occurrences causally related to treatment / all	0 / 3	1 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diabetes Mellitus			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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	3 / 231 (1.30%)	0 / 79 (0.00%)	0 / 109 (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
Hypocalcaemia			

subjects affected / exposed	2 / 231 (0.87%)	0 / 79 (0.00%)	2 / 109 (1.83%)
occurrences causally related to treatment / all	1 / 2	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypoglycaemia			
subjects affected / exposed	2 / 231 (0.87%)	0 / 79 (0.00%)	0 / 109 (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
Hypokalaemia			
subjects affected / exposed	2 / 231 (0.87%)	1 / 79 (1.27%)	0 / 109 (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
Hyponatraemia			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Ketoacidosis			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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
Malnutrition			
subjects affected / exposed	1 / 231 (0.43%)	0 / 79 (0.00%)	0 / 109 (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

Serious adverse events	Randomized Treatment Period: Placebo		
Total subjects affected by serious adverse events			
subjects affected / exposed	16 / 99 (16.16%)		
number of deaths (all causes)	10		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast Cancer Female			

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Basal Cell Carcinoma				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic Myeloid Leukaemia				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Colorectal Adenoma				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung Neoplasm Malignant				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metastases To Bone				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Germ Cell Cancer				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic Cancer Metastatic				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatic Neoplasm				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostate Cancer				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Phaeochromocytoma				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Squamous Cell Carcinoma				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal Cell Carcinoma				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Squamous Cell Carcinoma Of Skin				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Testicular Seminoma (Pure)				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vascular disorders				
Accelerated Hypertension				
subjects affected / exposed	0 / 99 (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 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertensive Crisis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypertension				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypotension				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Jugular Vein Thrombosis				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Vena Cava Thrombosis				
subjects affected / exposed	0 / 99 (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 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pregnancy, puerperium and perinatal conditions				
Abortion Spontaneous				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				

Asthenia				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Device Occlusion				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chest Pain				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fatigue				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General Physical Health Deterioration				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Malaise				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mucosal Inflammation				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sudden Death				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Swelling				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Immune system disorders				
Iodine Allergy				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Reproductive system and breast disorders				
Intermenstrual Bleeding				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ovarian Cyst Ruptured				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Asthmatic Crisis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Acute Respiratory Distress Syndrome				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchospasm				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chylothorax				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cough				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Interstitial Lung Disease				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung Disorder				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung Infiltration				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pleural Effusion				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia Aspiration				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonitis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumothorax				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary Embolism				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary Oedema				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pulmonary Thrombosis				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory Arrest				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory Failure				
subjects affected / exposed	0 / 99 (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 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bipolar Disorder				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Confusional State				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Completed Suicide				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Suicide Attempt				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Investigations				

Blood Creatine Phosphokinase Increased				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood Creatinine Increased				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
C-Reactive Protein Increased				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Electrocardiogram Qt Prolonged				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatic Enzyme Increased				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
International Normalised Ratio Increased				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Prostatic Specific Antigen Increased				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				
Compression Fracture				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Exposure During Pregnancy				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Jaw Fracture				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Joint Injury				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Overdose				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Post Procedural Complication				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Post Procedural Haematuria				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Road Traffic Accident				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Seroma				

subjects affected / exposed	0 / 99 (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 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal Fracture				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tibia Fracture				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Venomous Bite				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound Dehiscence				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Wound Necrosis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Patent Ductus Arteriosus				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				

Acute Myocardial Infarction				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arrhythmia				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Atrial Fibrillation				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bradycardia				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiac Failure Acute				
subjects affected / exposed	0 / 99 (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 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardio-Respiratory Arrest				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cardiovascular Insufficiency				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myocardial Infarction				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericardial Effusion				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pericardial Haemorrhage				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Stress Cardiomyopathy				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Brain Oedema				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Carotid Artery Stenosis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebellar Syndrome				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebral Ischaemia				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cerebrovascular Accident				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Convulsion				
subjects affected / exposed	0 / 99 (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	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Epilepsy				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Internal Capsule Infarction				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Loss Of Consciousness				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neuralgia				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral Sensorimotor Neuropathy				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Somnolence				
subjects affected / exposed	0 / 99 (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 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subarachnoid Haemorrhage				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Syncope				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient Ischaemic Attack				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Anaemia				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disseminated Intravascular Coagulation				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lymphadenopathy				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Thrombocytopenia				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Cataract				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Glaucoma				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retinal Artery Occlusion				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Retinal Detachment				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vision Blurred				

subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Colitis			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Diarrhoea			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dry Mouth			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dysphagia			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Faecaloma			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastritis			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal Haemorrhage			

subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	1 / 1			
Gastrointestinal Inflammation				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ileus				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal Obstruction				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal Perforation				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Mechanical Ileus				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Obstructive Pancreatitis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis Acute				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis Chronic				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pancreatitis Haemorrhagic				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumatosis Intestinalis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Rectal Haemorrhage				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reflux Gastritis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Small Intestinal Perforation				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hepatobiliary disorders				
Biliary Colic				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholecystitis Acute				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholelithiasis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Cholestasis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Jaundice				

subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dermatitis Acneiform			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Photosensitivity Reaction			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pruritus			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rash			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin Exfoliation			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin Ulcer			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			

Anuria				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Calculus Ureteric				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Calculus Urinary				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Chronic Kidney Disease				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hydronephrosis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Obstructive Uropathy				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nephrolithiasis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal Colic				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal Failure				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Renal Failure Acute				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tubulointerstitial Nephritis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Endocrine disorders				
Cushing's Syndrome				
subjects affected / exposed	0 / 99 (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 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Arthritis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Back Pain				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bone Pain				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Flank Pain				
subjects affected / exposed	0 / 99 (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 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Myopathy				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Neck Pain				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Osteoarthritis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infections and infestations				
Abdominal Abscess				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abdominal Wall Abscess				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Appendicitis Perforated				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bartholin's Abscess				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Biliary Sepsis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Bronchitis				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchitis Bacterial				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Covid-19				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dermatitis Infected				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diverticulitis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Folliculitis				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	1 / 1			
Gastroenteritis Bacterial				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis Viral				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal Infection				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infected Bites				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Infection				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Influenza				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Laryngitis				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lower Respiratory Tract Infection				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Lung Infection				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Meningitis Bacterial				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peridiverticular Abscess				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Postoperative Wound Infection				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory Tract Infection				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal Infection				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Staphylococcal Sepsis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Streptococcal Sepsis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Tracheitis				
subjects affected / exposed	0 / 99 (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 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urinary Tract Infection Pseudomonal				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Urosepsis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Acidosis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Decreased Appetite				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dehydration				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Diabetes Mellitus				
subjects affected / exposed	1 / 99 (1.01%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypercalcaemia				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypocalcaemia				

subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypoglycaemia				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hypokalaemia				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Hyponatraemia				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Ketoacidosis				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Malnutrition				
subjects affected / exposed	0 / 99 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

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

Non-serious adverse events	Randomized Treatment Period: Vandetanib 300 mg	Open-Label Treatment Period: Placebo/Vandetanib 300 mg	Open-Label Treatment Period: Vandetanib 300 mg/Vandetanib 300
Total subjects affected by non-serious adverse events			
subjects affected / exposed	226 / 231 (97.84%)	70 / 79 (88.61%)	32 / 109 (29.36%)
Vascular disorders			
Hypertension			
subjects affected / exposed	71 / 231 (30.74%)	15 / 79 (18.99%)	2 / 109 (1.83%)
occurrences (all)	79	18	2

General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	34 / 231 (14.72%)	12 / 79 (15.19%)	0 / 109 (0.00%)
occurrences (all)	39	13	0
Fatigue			
subjects affected / exposed	54 / 231 (23.38%)	13 / 79 (16.46%)	3 / 109 (2.75%)
occurrences (all)	64	16	3
Pyrexia			
subjects affected / exposed	18 / 231 (7.79%)	0 / 79 (0.00%)	3 / 109 (2.75%)
occurrences (all)	20	0	3
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	28 / 231 (12.12%)	3 / 79 (3.80%)	3 / 109 (2.75%)
occurrences (all)	31	4	3
Dysphonia			
subjects affected / exposed	17 / 231 (7.36%)	4 / 79 (5.06%)	1 / 109 (0.92%)
occurrences (all)	18	4	1
Dyspnoea			
subjects affected / exposed	16 / 231 (6.93%)	11 / 79 (13.92%)	3 / 109 (2.75%)
occurrences (all)	17	11	4
Dyspnoea Exertional			
subjects affected / exposed	3 / 231 (1.30%)	0 / 79 (0.00%)	0 / 109 (0.00%)
occurrences (all)	3	0	0
Epistaxis			
subjects affected / exposed	18 / 231 (7.79%)	3 / 79 (3.80%)	0 / 109 (0.00%)
occurrences (all)	20	4	0
Haemoptysis			
subjects affected / exposed	6 / 231 (2.60%)	4 / 79 (5.06%)	0 / 109 (0.00%)
occurrences (all)	6	4	0
Oropharyngeal Pain			
subjects affected / exposed	20 / 231 (8.66%)	3 / 79 (3.80%)	1 / 109 (0.92%)
occurrences (all)	32	3	1
Psychiatric disorders			
Anxiety			
subjects affected / exposed	12 / 231 (5.19%)	2 / 79 (2.53%)	0 / 109 (0.00%)
occurrences (all)	13	2	0

Depression			
subjects affected / exposed	22 / 231 (9.52%)	4 / 79 (5.06%)	1 / 109 (0.92%)
occurrences (all)	25	4	1
Insomnia			
subjects affected / exposed	32 / 231 (13.85%)	6 / 79 (7.59%)	1 / 109 (0.92%)
occurrences (all)	36	6	1
Investigations			
Electrocardiogram Qt Prolonged			
subjects affected / exposed	32 / 231 (13.85%)	7 / 79 (8.86%)	3 / 109 (2.75%)
occurrences (all)	46	8	3
Weight Increased			
subjects affected / exposed	6 / 231 (2.60%)	4 / 79 (5.06%)	0 / 109 (0.00%)
occurrences (all)	6	4	0
Weight Decreased			
subjects affected / exposed	27 / 231 (11.69%)	5 / 79 (6.33%)	2 / 109 (1.83%)
occurrences (all)	28	5	2
Nervous system disorders			
Dizziness			
subjects affected / exposed	21 / 231 (9.09%)	7 / 79 (8.86%)	1 / 109 (0.92%)
occurrences (all)	24	7	1
Dysgeusia			
subjects affected / exposed	20 / 231 (8.66%)	3 / 79 (3.80%)	0 / 109 (0.00%)
occurrences (all)	22	3	0
Headache			
subjects affected / exposed	62 / 231 (26.84%)	5 / 79 (6.33%)	4 / 109 (3.67%)
occurrences (all)	138	5	6
Paraesthesia			
subjects affected / exposed	13 / 231 (5.63%)	4 / 79 (5.06%)	2 / 109 (1.83%)
occurrences (all)	15	5	4
Tremor			
subjects affected / exposed	7 / 231 (3.03%)	4 / 79 (5.06%)	1 / 109 (0.92%)
occurrences (all)	7	4	1
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	10 / 231 (4.33%)	5 / 79 (6.33%)	1 / 109 (0.92%)
occurrences (all)	12	5	1
Eye disorders			

Corneal Opacity			
subjects affected / exposed	11 / 231 (4.76%)	4 / 79 (5.06%)	0 / 109 (0.00%)
occurrences (all)	11	4	0
Vision Blurred			
subjects affected / exposed	19 / 231 (8.23%)	5 / 79 (6.33%)	1 / 109 (0.92%)
occurrences (all)	23	5	1
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	33 / 231 (14.29%)	5 / 79 (6.33%)	2 / 109 (1.83%)
occurrences (all)	50	6	2
Abdominal Pain Upper			
subjects affected / exposed	23 / 231 (9.96%)	5 / 79 (6.33%)	1 / 109 (0.92%)
occurrences (all)	33	5	1
Constipation			
subjects affected / exposed	14 / 231 (6.06%)	9 / 79 (11.39%)	3 / 109 (2.75%)
occurrences (all)	21	9	3
Diarrhoea			
subjects affected / exposed	123 / 231 (53.25%)	32 / 79 (40.51%)	4 / 109 (3.67%)
occurrences (all)	180	39	5
Dry Mouth			
subjects affected / exposed	22 / 231 (9.52%)	7 / 79 (8.86%)	0 / 109 (0.00%)
occurrences (all)	22	7	0
Toothache			
subjects affected / exposed	7 / 231 (3.03%)	0 / 79 (0.00%)	2 / 109 (1.83%)
occurrences (all)	7	0	2
Nausea			
subjects affected / exposed	74 / 231 (32.03%)	18 / 79 (22.78%)	5 / 109 (4.59%)
occurrences (all)	97	24	5
Dyspepsia			
subjects affected / exposed	28 / 231 (12.12%)	4 / 79 (5.06%)	1 / 109 (0.92%)
occurrences (all)	33	4	1
Vomiting			
subjects affected / exposed	33 / 231 (14.29%)	9 / 79 (11.39%)	3 / 109 (2.75%)
occurrences (all)	45	9	5
Skin and subcutaneous tissue disorders			

Acne			
subjects affected / exposed	47 / 231 (20.35%)	21 / 79 (26.58%)	0 / 109 (0.00%)
occurrences (all)	66	25	0
Alopecia			
subjects affected / exposed	18 / 231 (7.79%)	4 / 79 (5.06%)	2 / 109 (1.83%)
occurrences (all)	19	4	2
Dermatitis Acneiform			
subjects affected / exposed	35 / 231 (15.15%)	4 / 79 (5.06%)	0 / 109 (0.00%)
occurrences (all)	45	6	0
Dry Skin			
subjects affected / exposed	36 / 231 (15.58%)	11 / 79 (13.92%)	0 / 109 (0.00%)
occurrences (all)	41	14	0
Erythema			
subjects affected / exposed	22 / 231 (9.52%)	6 / 79 (7.59%)	0 / 109 (0.00%)
occurrences (all)	22	8	0
Rash			
subjects affected / exposed	105 / 231 (45.45%)	25 / 79 (31.65%)	4 / 109 (3.67%)
occurrences (all)	158	40	4
Pruritus			
subjects affected / exposed	26 / 231 (11.26%)	4 / 79 (5.06%)	0 / 109 (0.00%)
occurrences (all)	31	6	0
Photosensitivity Reaction			
subjects affected / exposed	29 / 231 (12.55%)	11 / 79 (13.92%)	0 / 109 (0.00%)
occurrences (all)	33	14	0
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	23 / 231 (9.96%)	7 / 79 (8.86%)	1 / 109 (0.92%)
occurrences (all)	26	7	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	16 / 231 (6.93%)	1 / 79 (1.27%)	1 / 109 (0.92%)
occurrences (all)	19	1	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	19 / 231 (8.23%)	4 / 79 (5.06%)	2 / 109 (1.83%)
occurrences (all)	24	4	2

Back Pain			
subjects affected / exposed	23 / 231 (9.96%)	3 / 79 (3.80%)	6 / 109 (5.50%)
occurrences (all)	37	3	9
Bone Pain			
subjects affected / exposed	10 / 231 (4.33%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences (all)	10	1	0
Myalgia			
subjects affected / exposed	10 / 231 (4.33%)	4 / 79 (5.06%)	2 / 109 (1.83%)
occurrences (all)	11	4	2
Musculoskeletal Pain			
subjects affected / exposed	12 / 231 (5.19%)	6 / 79 (7.59%)	3 / 109 (2.75%)
occurrences (all)	20	6	3
Musculoskeletal Chest Pain			
subjects affected / exposed	18 / 231 (7.79%)	2 / 79 (2.53%)	2 / 109 (1.83%)
occurrences (all)	24	3	2
Muscle Spasms			
subjects affected / exposed	14 / 231 (6.06%)	4 / 79 (5.06%)	0 / 109 (0.00%)
occurrences (all)	16	5	0
Neck Pain			
subjects affected / exposed	17 / 231 (7.36%)	1 / 79 (1.27%)	0 / 109 (0.00%)
occurrences (all)	20	1	0
Pain In Extremity			
subjects affected / exposed	17 / 231 (7.36%)	6 / 79 (7.59%)	3 / 109 (2.75%)
occurrences (all)	24	6	3
Infections and infestations			
Bronchitis			
subjects affected / exposed	11 / 231 (4.76%)	2 / 79 (2.53%)	0 / 109 (0.00%)
occurrences (all)	11	2	0
Upper Respiratory Tract Infection			
subjects affected / exposed	19 / 231 (8.23%)	8 / 79 (10.13%)	2 / 109 (1.83%)
occurrences (all)	27	13	2
Nasopharyngitis			
subjects affected / exposed	29 / 231 (12.55%)	4 / 79 (5.06%)	2 / 109 (1.83%)
occurrences (all)	43	6	4
Influenza			

subjects affected / exposed	16 / 231 (6.93%)	3 / 79 (3.80%)	2 / 109 (1.83%)
occurrences (all)	16	4	2
Folliculitis			
subjects affected / exposed	8 / 231 (3.46%)	5 / 79 (6.33%)	0 / 109 (0.00%)
occurrences (all)	9	5	0
Urinary Tract Infection			
subjects affected / exposed	16 / 231 (6.93%)	5 / 79 (6.33%)	1 / 109 (0.92%)
occurrences (all)	27	6	3
Metabolism and nutrition disorders			
Decreased Appetite			
subjects affected / exposed	42 / 231 (18.18%)	17 / 79 (21.52%)	2 / 109 (1.83%)
occurrences (all)	53	19	3
Hypocalcaemia			
subjects affected / exposed	22 / 231 (9.52%)	7 / 79 (8.86%)	3 / 109 (2.75%)
occurrences (all)	27	9	3

Non-serious adverse events	Randomized Treatment Period: Placebo		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	87 / 99 (87.88%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	6 / 99 (6.06%)		
occurrences (all)	6		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	12 / 99 (12.12%)		
occurrences (all)	12		
Fatigue			
subjects affected / exposed	23 / 99 (23.23%)		
occurrences (all)	27		
Pyrexia			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			

Cough			
subjects affected / exposed	10 / 99 (10.10%)		
occurrences (all)	15		
Dysphonia			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Dyspnoea			
subjects affected / exposed	10 / 99 (10.10%)		
occurrences (all)	14		
Dyspnoea Exertional			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	5		
Epistaxis			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	6		
Haemoptysis			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Oropharyngeal Pain			
subjects affected / exposed	6 / 99 (6.06%)		
occurrences (all)	14		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	5		
Depression			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Insomnia			
subjects affected / exposed	12 / 99 (12.12%)		
occurrences (all)	12		
Investigations			
Electrocardiogram Qt Prolonged			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Weight Increased			

subjects affected / exposed	0 / 99 (0.00%)		
occurrences (all)	0		
Weight Decreased			
subjects affected / exposed	10 / 99 (10.10%)		
occurrences (all)	10		
Nervous system disorders			
Dizziness			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	5		
Dysgeusia			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Headache			
subjects affected / exposed	9 / 99 (9.09%)		
occurrences (all)	13		
Paraesthesia			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Tremor			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences (all)	0		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Eye disorders			
Corneal Opacity			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences (all)	0		
Vision Blurred			
subjects affected / exposed	1 / 99 (1.01%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal Pain			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	6		
Abdominal Pain Upper			

subjects affected / exposed	7 / 99 (7.07%)		
occurrences (all)	7		
Constipation			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	5		
Diarrhoea			
subjects affected / exposed	27 / 99 (27.27%)		
occurrences (all)	36		
Dry Mouth			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Toothache			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	17		
Nausea			
subjects affected / exposed	16 / 99 (16.16%)		
occurrences (all)	16		
Dyspepsia			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences (all)	5		
Vomiting			
subjects affected / exposed	7 / 99 (7.07%)		
occurrences (all)	7		
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	5		
Alopecia			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences (all)	0		
Dermatitis Acneiform			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	4		
Dry Skin			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	5		

Erythema			
subjects affected / exposed	3 / 99 (3.03%)		
occurrences (all)	3		
Rash			
subjects affected / exposed	11 / 99 (11.11%)		
occurrences (all)	12		
Pruritus			
subjects affected / exposed	4 / 99 (4.04%)		
occurrences (all)	5		
Photosensitivity Reaction			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	3		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 99 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	10 / 99 (10.10%)		
occurrences (all)	13		
Back Pain			
subjects affected / exposed	20 / 99 (20.20%)		
occurrences (all)	41		
Bone Pain			
subjects affected / exposed	5 / 99 (5.05%)		
occurrences (all)	5		
Myalgia			
subjects affected / exposed	2 / 99 (2.02%)		
occurrences (all)	2		
Musculoskeletal Pain			
subjects affected / exposed	10 / 99 (10.10%)		
occurrences (all)	14		

Musculoskeletal Chest Pain subjects affected / exposed occurrences (all)	6 / 99 (6.06%) 7		
Muscle Spasms subjects affected / exposed occurrences (all)	1 / 99 (1.01%) 2		
Neck Pain subjects affected / exposed occurrences (all)	9 / 99 (9.09%) 10		
Pain In Extremity subjects affected / exposed occurrences (all)	14 / 99 (14.14%) 17		
Infections and infestations Bronchitis subjects affected / exposed occurrences (all)	6 / 99 (6.06%) 8		
Upper Respiratory Tract Infection subjects affected / exposed occurrences (all)	3 / 99 (3.03%) 5		
Nasopharyngitis subjects affected / exposed occurrences (all)	9 / 99 (9.09%) 12		
Influenza subjects affected / exposed occurrences (all)	3 / 99 (3.03%) 3		
Folliculitis subjects affected / exposed occurrences (all)	1 / 99 (1.01%) 1		
Urinary Tract Infection subjects affected / exposed occurrences (all)	6 / 99 (6.06%) 7		
Metabolism and nutrition disorders Decreased Appetite subjects affected / exposed occurrences (all)	13 / 99 (13.13%) 13		
Hypocalcaemia			

subjects affected / exposed occurrences (all)	3 / 99 (3.03%) 4		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
29 June 2006	Clarified the procedures and requirements for participants who entered post-progression treatment with vandetanib, the secondary objectives of the study and section 5.1 was updated to be in accord with regulatory guidance.
30 May 2007	Ophthalmologic examinations were added to the study plan, inclusion and exclusion criteria were updated.
15 May 2008	The study was redefined as a Phase 3 study, language was updated for consistency with other vandetanib studies in the thyroid cancer program.
18 May 2009	The objectives for the patient reported outcome (PRO) variables were amended, PRO variables and statistical methods for PRO variables were also revised for consistency with changes to study objectives, participant weight was changed from a secondary to an exploratory objective, the co-primary analysis population of participants with a known rearranged during transfection (proto-oncogene) [RET] mutation was removed from the study, further clarification on determination of RET mutation status was provided.
13 January 2010	The study plan was updated to provide investigators with the option to unblind participants remaining on blinded, randomised therapy.
06 April 2010	Exploratory objectives and outcome variables were added, Sections 4.6.15 Histopathology, 4.6.16 CTN and CEA expression in tumor tissue, 4.6.17 Analysis of cell signaling pathways, and 4.6.18 Mutation status of oncogenes were newly created.
06 April 2011	Incorporated procedures for the management of participants who were still receiving study treatment following final planned data analyses and to update the estimated last subject out date.
03 November 2011	Provided clarification on unblinding participants once the OS endpoint was met, ZD6474 was approved by the Food and Drug Administration for the treatment of symptomatic or progressive medullary thyroid cancer in participants with unresectable locally advanced or metastatic disease, incorporated procedures for the management of participants who were still receiving study treatment following OS analysis, clarified the recording of adverse events for participants who switched from clinical supplies to marketed vandetanib prior to completing the 60 day follow up assessment, provided additional instruction regarding discontinuing participants from therapy once the OS analysis was completed, provided instruction for survival status contact to be completed within 1 week of the data cut-off for the OS analysis, provided clarification on management of participants who were still receiving blinded therapy at the time of OS analysis and on the timing for OS follow up contact once data-off for the OS analysis had occurred, clarified the process for reporting serious adverse events once the OS endpoint was met and the clinical study database was closed to new data, provided information about updated Appendix E and clarification on the use of drugs that were previously found on the Table 1 or Table 2 in Appendix E, version 3 and were no longer listed in Appendix E, version 4, added an unplanned safety analysis in order to update the vandetanib Risk Management Plan as requested by the European Committee for Medicinal Products for Human Use.

29 February 2016	The AstraZeneca logo and reference to AstraZeneca within the confidentiality statement were deleted from the title page, throughout all sections of the protocol including header and appendices, AstraZeneca was changed to "Genzyme" or "Sponsor.", the Sanofi-Genzyme study code LPS14811 was added to the AstraZeneca study code D4200C00058, the AstraZeneca study drug code ZD6474 was updated to the generic drug name vandetanib, references to ZACTIMA™ were deleted as the name is obsolete, sections regarding pharmacovigilance were updated to reflect the Genzyme environment, correction of minor typographical errors or inconsistencies were made.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported