Clinical trial results:
An International, Randomised, Double-Blind, Two-Arm Study to Evaluate the Safety and Efficacy of Vandetanib 150 and 300 mg/day in Patients with Unresectable Locally Advanced or Metastatic Medullary Thyroid Carcinoma with Progressive or Symptomatic Disease

Summary

EudraCT number	2011-004701-24
Trial protocol	CZ NL IT PL GB
Global end of trial date	11 July 2024

Results information

Result version number	v1 (current)
This version publication date	23 October 2025
First version publication date	23 October 2025

Trial information

Trial identification

Sponsor protocol code	D4200C00097

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01496313
WHO universal trial number (UTN)	-
Other trial identifiers	Sanofi-Genzyme : LPS14809

Notes:

Sponsors

Sponsor organisation name	Genzyme Corporation
Sponsor organisation address	500 Kendall 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	03 March 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 July 2024
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study was to assess the objective response rate for 2 starting doses of vandetanib, 150 milligrams (mg) and 300 mg, in participants with unresectable locally advanced or metastatic medullary thyroid carcinoma having progressive or symptomatic disease.

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	08 June 2012
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	Czechia: 2
Country: Number of subjects enrolled	India: 2
Country: Number of subjects enrolled	Israel: 9
Country: Number of subjects enrolled	Italy: 33
Country: Number of subjects enrolled	Netherlands: 5
Country: Number of subjects enrolled	Poland: 17
Country: Number of subjects enrolled	Russian Federation: 1
Country: Number of subjects enrolled	United Kingdom: 9
Country: Number of subjects enrolled	United States: 3
Worldwide total number of subjects	81
EEA total number of subjects	57

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)	60
From 65 to 84 years	20
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

From 8 June 2012 to 2 April 2014, 93 participants were screened; 81 participants were randomized. The study consisted of a double-blind randomized period and an open-label period.

Pre-assignment

Screening details:

Participants with objective disease progression within 14 months on blinded treatment were given option to continue to receive vandetanib in open-label period for up to 2 years from time of study entry. They were followed for efficacy during randomized period only. No further efficacy data was collected in open-label period.

Period 1

Period 1 title	Randomized Period: up to 14 Months
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Randomized Period: Vandetanib 150 mg

Arm description:

Oral blinded tablet, taken once daily

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg, oral tablet

Arm title	Randomized Period: Vandetanib 300 mg

Arm description:

Oral blinded tablet, taken once daily

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg, oral tablet

Number of subjects in period 1	Randomized Period: Vandetanib 150 mg	Randomized Period: Vandetanib 300 mg
Started	40	41
Completed	35	26
Not completed	5	15
Adverse event, serious fatal	-	2
Participant decision	1	3
Adverse event, non-fatal	1	3
Condition under investigation worsened	2	3
Unspecified	1	2
Study-specific discontinuation criteria	-	2

Period 2

Period 2 title	Open-Label Period (Month 14 to 2 Years)
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Are arms mutually exclusive?	Yes
Arm title	Open-Label Period: Vandetanib 100 mg

Arm description:

Participants who received vandetanib 150 mg orally once daily but the dose was reduced to vandetanib 100 mg orally once daily for an adverse event (AE) or QT prolongation in randomized period continued receiving the reduced dose of vandetanib 100 mg orally once daily in open-label period as per the Investigator for a maximum of 2 years from study entry.

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

100 mg, oral tablet

Arm title	Open-Label Period: Vandetanib 150 mg

Arm description:

Participants who received vandetanib 150 mg orally once daily without any dose reduction for an AE or QT prolongation in randomized period were given an option to stay on vandetanib 150 mg orally once daily in open-label period for a maximum of 2 years from study entry.

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

150 mg, oral tablet

Arm title	Open-Label Period: Vandetanib 200 mg

Arm description:

Participants who received vandetanib 300 mg orally once daily but the dose was reduced to vandetanib 200 mg orally once daily for an AE or QT prolongation in randomized period continued receiving the reduced dose of vandetanib 200 mg orally once daily in open-label period as per the Investigator for a maximum of 2 years from study entry.

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

200 mg, oral tablet

Arm title	Open-Label Period: Vandetanib 300 mg

Arm description:

Participants who received vandetanib 150 mg or 300 mg orally once daily without any dose reduction for an AE or QT prolongation in randomized period were given an option to increase or continue vandetanib 300 mg orally once daily in open-label period respectively for a maximum of 2 years from study entry.

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300 mg, oral tablet

Number of subjects in period 2	Open-Label Period: Vandetanib 100 mg	Open-Label Period: Vandetanib 150 mg	Open-Label Period: Vandetanib 200 mg
Started	5	9	8
Completed	3	7	7
Not completed	2	2	1
Participant decision	-	-	-
Unspecified	2	2	1
Study-specific withdrawal criteria	-	-	-

Number of subjects in period 2	Open-Label Period: Vandetanib 300 mg
Started	39
Completed	28
Not completed	11
Participant decision	3

Unspecified	7
Study-specific withdrawal criteria	1

Baseline characteristics

Reporting groups	
Reporting group title	Randomized Period: Vandetanib 150 mg
Reporting group description: Oral blinded tablet, taken once daily	
Reporting group title	Randomized Period: Vandetanib 300 mg
Reporting group description: Oral blinded tablet, taken once daily	

Reporting group values	Randomized Period: Vandetanib 150 mg	Randomized Period: Vandetanib 300 mg	Total
Number of subjects	40	41	81
Age categorical Units: Subjects			
Age Continuous | Units: Years			
arithmetic mean	52.2	52.7	
standard deviation	± 15.24	± 15.42	-
Gender, Male/Female Units: Participants			
Female	15	12	27
Male	25	29	54
Age, Customized Units: Subjects			
>=18 to <40 years	9	9	18
>=40 to <65 years	22	20	42
>=65 to <75 years	7	10	17
>=75 years	2	2	4
Race/Ethnicity, Customized Units: Subjects			
Asian	1	2	3
Black or African American	0	1	1
White	39	37	76
Other	0	1	1

End points

End points reporting groups

Reporting group title	Randomized Period: Vandetanib 150 mg
Reporting group description:	
Oral blinded tablet, taken once daily	
Reporting group title	Randomized Period: Vandetanib 300 mg
Reporting group description:	
Oral blinded tablet, taken once daily	
Reporting group title	Open-Label Period: Vandetanib 100 mg
Reporting group description:	
Participants who received vandetanib 150 mg orally once daily but the dose was reduced to vandetanib 100 mg orally once daily for an adverse event (AE) or QT prolongation in randomized period continued receiving the reduced dose of vandetanib 100 mg orally once daily in open-label period as per the Investigator for a maximum of 2 years from study entry.	
Reporting group title	Open-Label Period: Vandetanib 150 mg
Reporting group description:	
Participants who received vandetanib 150 mg orally once daily without any dose reduction for an AE or QT prolongation in randomized period were given an option to stay on vandetanib 150 mg orally once daily in open-label period for a maximum of 2 years from study entry.	
Reporting group title	Open-Label Period: Vandetanib 200 mg
Reporting group description:	
Participants who received vandetanib 300 mg orally once daily but the dose was reduced to vandetanib 200 mg orally once daily for an AE or QT prolongation in randomized period continued receiving the reduced dose of vandetanib 200 mg orally once daily in open-label period as per the Investigator for a maximum of 2 years from study entry.	
Reporting group title	Open-Label Period: Vandetanib 300 mg
Reporting group description:	
Participants who received vandetanib 150 mg or 300 mg orally once daily without any dose reduction for an AE or QT prolongation in randomized period were given an option to increase or continue vandetanib 300 mg orally once daily in open-label period respectively for a maximum of 2 years from study entry.	

Primary: Overall Response Rate (ORR) for Vandetanib 150 and 300 mg With Responses Determined by the Investigator

End point title	Overall Response Rate (ORR) for Vandetanib 150 and 300 mg With Responses Determined by the Investigator[1]
End point description:	
ORR=proportion of patients with a best response of complete or partial response as per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1. Per Response Evaluation Criteria in Solid Tumors Criteria (RECIST v1.1) for target lesions and assessed by MRI: Complete Response (CR), disappearance of all target lesions; Partial response (PR), at least a 30% decrease in the sum of diameters of target lesions; ORR = CR + PR.	
End point type	Primary
End point timeframe:	
Randomisation to week 60 (maximum)	

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 Period: Vandetanib 150 mg	Randomized Period: Vandetanib 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	41		
Units: Proportion of participants				
number (confidence interval 95%)	0.2 (0.105 to 0.348)	0.29 (0.176 to 0.445)		

Statistical analyses

No statistical analyses for this end point

Secondary: Best Objective Response

End point title	Best Objective Response

End point description:

Per RECIST v1.1 for target lesions: CR, disappearance of all target lesions; PR, at least a 30% decrease in the sum of diameters of target lesions; Progressive disease (PD), at least 20% increase in the sum of diameters of target lesions; Stable disease (SD), neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD.

End point type	Secondary

End point timeframe:

Randomisation to week 60 (maximum)

End point values	Randomized Period: Vandetanib 150 mg	Randomized Period: Vandetanib 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	41		
Units: Participants				
Complete response	0	1		
Partial response	8	11		
Stable disease	21	23		
Progressive disease	9	2		
Non-evaluable	2	4		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of Objective Response (RECIST 1.1) by Treatment arm

End point title	Duration of Objective Response (RECIST 1.1) by Treatment arm

End point description:

Per RECIST v1.1 for target lesions: CR, disappearance of all target lesions; PR, at least a 30% decrease

in the sum of diameters of target lesions; Progressive disease (PD), at least 20% increase in the sum of diameters of target lesions; Stable disease (SD), neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD.

End point type	Secondary

End point timeframe:

Randomization to Week 60 (maximum)

End point values	Randomized Period: Vandetanib 150 mg	Randomized Period: Vandetanib 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	12		
Units: Months				
median (confidence interval 95%)	9.8 (2.8 to 11.2)	8.4 (3 to 11.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to Objective Response (RECIST 1.1) by Treatment arm

End point title	Time to Objective Response (RECIST 1.1) by Treatment arm

End point description:

Per RECIST v1.1 for target lesions: CR, disappearance of all target lesions; PR, at least a 30% decrease in the sum of diameters of target lesions; Progressive disease (PD), at least 20% increase in the sum of diameters of target lesions; Stable disease (SD), neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD.

End point type	Secondary

End point timeframe:

Randomization to Week 60 (maximum)

End point values	Randomized Period: Vandetanib 150 mg	Randomized Period: Vandetanib 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	8	12		
Units: Months				
median (confidence interval 95%)	4.2 (2.8 to 11.2)	4.4 (2.8 to 11.1)		

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage Change From Baseline in Target Lesion Size (RECIST 1.1) by Treatment arm

End point title	Percentage Change From Baseline in Target Lesion Size (RECIST 1.1) by Treatment arm

End point description:

Per RECIST v1.1 for target lesions: CR, disappearance of all target lesions; PR, at least a 30% decrease in the sum of diameters of target lesions; Progressive disease (PD), at least 20% increase in the sum of diameters of target lesions; Stable disease (SD), neither sufficient shrinkage to qualify for PR nor sufficient increase to qualify for PD.

End point type	Secondary

End point timeframe:

Randomization to Week 60 (maximum)

End point values	Randomized Period: Vandetanib 150 mg	Randomized Period: Vandetanib 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	41		
Units: % change				
arithmetic mean (standard deviation)				
Week 12	-3.8 (± 29.24)	-17.5 (± 18.24)		
Week 24	-13 (± 19.51)	-24.9 (± 22.11)		
Week 36	-16.7 (± 24.33)	-29.1 (± 22.96)		
Week 48	-20.7 (± 23.56)	-30.6 (± 25.31)		
Follow-up RECIST assessment	-51 (± 0)	-11.4 (± 67.05)		
Disc. of blinded vandetanib	-11.9 (± 27.98)	-27.3 (± 29.58)		

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma Concentration of Vandetanib in the Bloodstream (Cmax) for Patients by Treatment arm

End point title	Plasma Concentration of Vandetanib in the Bloodstream (Cmax) for Patients by Treatment arm

End point description:

All patients who received at least 1 dose of vandetanib and for whom quantifiable plasma concentration data were available.

End point type	Secondary

End point timeframe:

Week 3 to week 60 (maximum)

End point values	Randomized Period: Vandetanib 150 mg	Randomized Period: Vandetanib 300 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	40	41		
Units: ng/ml				
arithmetic mean (standard deviation)				
Week 3 (Day 21)	428.6 (± 140.71)	786.2 (± 243.15)		
Week 8 (Day 56)	510.5 (± 206.50)	941.0 (± 249.4)		
Week 12 (Day 84)	561.4 (± 215.66)	969.9 (± 396.18)		
Week 24 (Day 168)	549.7 (± 189.62)	1017.7 (± 330.89)		
Discontinuation of blinded vandetanib	536.8 (± 225.34)	964.0 (± 357.30)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Serious adverse events (SAEs) and all-cause mortality (deaths) were collected from randomization (Day 1) up to end of follow-up, approximately 12 years. Other (non-serious) AEs were reported from randomization (Day 1) up to Week 108 (final analysis visit)

Adverse event reporting additional description:

Analysis was performed on the safety population which included all participants who received at least 1 dose of randomized study drug (vandetanib) and for whom any post-dose data were available.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	12.0-25.1

Reporting groups

Reporting group title	Randomized Period: Vandetanib 150 mg

Reporting group description:

Oral blinded tablet, taken once daily

Reporting group title	Randomized Period: Vandetanib 300 mg

Reporting group description:

Oral blinded tablet, taken once daily

Reporting group title	Open-label Period: Vandetanib 100 mg

Reporting group description:

Participants who received vandetanib 150 mg orally once daily but the dose was reduced to vandetanib 100 mg orally once daily for an AE or QT prolongation in randomized period continued receiving the reduced dose of vandetanib 100 mg orally once daily in open-label period as per the Investigator for a maximum of 2 years from study entry.

Reporting group title	Open-label Period: Vandetanib 150 mg

Reporting group description:

Participants who received vandetanib 150 mg orally once daily without any dose reduction for an AE or QT prolongation in randomized period were given an option to stay on vandetanib 150 mg orally once daily in open-label period for a maximum of 2 years from study entry.

Reporting group title	Open-label Period: Vandetanib 200 mg

Reporting group description:

Participants who received vandetanib 300 mg orally once daily but the dose was reduced to vandetanib 200 mg orally once daily for an AE or QT prolongation in randomized period continued receiving the reduced dose of vandetanib 200 mg orally once daily in open-label period as per the Investigator for a maximum of 2 years from study entry.

Reporting group title	Open-label Period: Vandetanib 300 mg

Reporting group description:

Participants who received vandetanib 150 mg or 300 mg orally once daily without any dose reduction for an AE or QT prolongation in randomized period were given an option to increase or continue vandetanib 300 mg orally once daily in open-label period respectively for a maximum of 2 years from study entry.

Serious adverse events	Randomized Period: Vandetanib 150 mg	Randomized Period: Vandetanib 300 mg	Open-label Period: Vandetanib 100 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 40 (22.50%)	9 / 41 (21.95%)	0 / 5 (0.00%)
number of deaths (all causes)	1	6	0
number of deaths resulting from adverse events	0	2	0

Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast Cancer			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Benign Laryngeal Neoplasm			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Adenocarcinoma Pancreas			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Vascular disorders			
Deep Vein Thrombosis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (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			
Drug Interaction			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (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
Sudden Death			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Malaise			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General Physical Health Deterioration			

subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal Haemorrhage			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Laryngeal Obstruction			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Laryngeal Oedema			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (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
Pulmonary Embolism			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (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
Injury, poisoning and procedural complications			
Post Procedural Fistula			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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 Haemorrhage			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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 Haematoma			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute Myocardial Infarction			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Failure Acute			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Angina Pectoris			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (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
Myocardial Infarction			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Miller Fisher Syndrome			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (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
Hemiparesis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Epilepsy			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (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

Cerebrovascular Accident			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (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
Paraesthesia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (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
Peripheral Motor Neuropathy			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (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
Spinal Cord Compression			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (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
Tremor			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Gastritis Erosive			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Oesophageal Obstruction			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Colitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Pain Upper			

subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Duodenal Ulcer Perforation			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Pancreatitis			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (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
Cholecystitis Acute			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (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
Bile Duct Stone			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (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 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Skin and subcutaneous tissue disorders			
Skin Ulcer			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			

Urinary Retention			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Calculus Ureteric			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (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			
Hypothyroidism			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (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			
Soft Tissue Necrosis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Back Pain			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (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
Infections and infestations			
Diverticulitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Abscess			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Neurocysticercosis			

subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Aspiration			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (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
Urinary Tract Infection			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Viral Infection			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (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
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	1 / 40 (2.50%)	1 / 41 (2.44%)	0 / 5 (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
Dehydration			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Hyponatraemia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (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
Hypomagnesaemia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (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

Serious adverse events	Open-label Period:	Open-label Period:	Open-label Period:

	Vandetanib 150 mg	Vandetanib 200 mg	Vandetanib 300 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	4 / 9 (44.44%)	2 / 8 (25.00%)	11 / 39 (28.21%)
number of deaths (all causes)	0	1	10
number of deaths resulting from adverse events	0	1	4
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast Cancer			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (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
Benign Laryngeal Neoplasm			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Adenocarcinoma Pancreas			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
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			
Deep Vein Thrombosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Drug Interaction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Sudden Death			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Malaise			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General Physical Health Deterioration			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (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
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal Haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Laryngeal Obstruction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Laryngeal Oedema			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Pulmonary Embolism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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			
Post Procedural Fistula			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Post Procedural Haemorrhage			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Post Procedural Haematoma			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute Myocardial Infarction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Failure Acute			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Angina Pectoris			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Myocardial Infarction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Nervous system disorders			
Miller Fisher Syndrome			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Hemiparesis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Epilepsy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Cerebrovascular Accident			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Paraesthesia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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 Motor Neuropathy			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Spinal Cord Compression			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Tremor			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Gastrointestinal disorders			
Gastritis Erosive			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (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
Oesophageal Obstruction			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colitis			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Abdominal Pain Upper			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (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
Duodenal Ulcer Perforation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Cholecystitis Acute			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Bile Duct Stone			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Cholelithiasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Skin and subcutaneous tissue disorders			

Skin Ulcer			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Urinary Retention			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Calculus Ureteric			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Musculoskeletal and connective tissue disorders			
Soft Tissue Necrosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Back Pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Infections and infestations			
Diverticulitis			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (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
Abscess			

subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (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
Neurocysticercosis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia Aspiration			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (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
Urinary Tract Infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Viral Infection			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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
Metabolism and nutrition disorders			
Hypocalcaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (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
Dehydration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyponatraemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypomagnesaemia			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (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

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

Non-serious adverse events	Randomized Period: Vandetanib 150 mg	Randomized Period: Vandetanib 300 mg	Open-label Period: Vandetanib 100 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 40 (95.00%)	40 / 41 (97.56%)	5 / 5 (100.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases To Bone			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	8 / 40 (20.00%)	11 / 41 (26.83%)	1 / 5 (20.00%)
occurrences (all)	10	14	1
Surgical and medical procedures			
Cataract Operation			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	2
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Oedema Peripheral			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 40 (0.00%)	4 / 41 (9.76%)	0 / 5 (0.00%)
occurrences (all)	0	4	0
Fatigue			
subjects affected / exposed	8 / 40 (20.00%)	7 / 41 (17.07%)	0 / 5 (0.00%)
occurrences (all)	8	7	0
Asthenia			

subjects affected / exposed	5 / 40 (12.50%)	7 / 41 (17.07%)	1 / 5 (20.00%)
occurrences (all)	6	7	1
Respiratory, thoracic and mediastinal disorders			
Lower Respiratory Tract Inflammation			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Dyspnoea			
subjects affected / exposed	2 / 40 (5.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Dysphonia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Dysaesthesia Pharynx			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Pulmonary Hypertension			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cough			
subjects affected / exposed	2 / 40 (5.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 40 (5.00%)	6 / 41 (14.63%)	0 / 5 (0.00%)
occurrences (all)	2	6	0
Depression			
subjects affected / exposed	2 / 40 (5.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	2	0	0
Depressed Mood			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Anxiety			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Investigations			

Blood Alkaline Phosphatase Increased			
subjects affected / exposed	1 / 40 (2.50%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Aspartate Aminotransferase Increased			
subjects affected / exposed	3 / 40 (7.50%)	6 / 41 (14.63%)	1 / 5 (20.00%)
occurrences (all)	3	6	1
Alanine Aminotransferase Increased			
subjects affected / exposed	5 / 40 (12.50%)	7 / 41 (17.07%)	0 / 5 (0.00%)
occurrences (all)	5	7	0
Electrocardiogram Qt Prolonged			
subjects affected / exposed	5 / 40 (12.50%)	14 / 41 (34.15%)	1 / 5 (20.00%)
occurrences (all)	5	15	1
Blood Thyroid Stimulating Hormone Increased			
subjects affected / exposed	12 / 40 (30.00%)	9 / 41 (21.95%)	0 / 5 (0.00%)
occurrences (all)	12	11	0
Blood Creatinine Increased			
subjects affected / exposed	5 / 40 (12.50%)	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	6	2	0
Blood Glucose Increased			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Blood Thyroid Stimulating Hormone Decreased			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Blood Bilirubin Increased			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	2 / 40 (5.00%)	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	3	2	0
Ejection Fraction Decreased			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
White Blood Cell Count Decreased			

subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	1 / 5 (20.00%)
occurrences (all)	0	1	1
Weight Decreased			
subjects affected / exposed	2 / 40 (5.00%)	5 / 41 (12.20%)	0 / 5 (0.00%)
occurrences (all)	2	6	0
Platelet Count Decreased			
subjects affected / exposed	1 / 40 (2.50%)	2 / 41 (4.88%)	1 / 5 (20.00%)
occurrences (all)	1	2	1
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	1 / 40 (2.50%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Arthropod Bite			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Corneal Abrasion			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Cardiac disorders			
Sinus Tachycardia			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Nervous system disorders			
Head Titubation			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	1 / 5 (20.00%)
occurrences (all)	1	0	1
Dysgeusia			
subjects affected / exposed	1 / 40 (2.50%)	3 / 41 (7.32%)	0 / 5 (0.00%)
occurrences (all)	2	3	0
Disturbance In Attention			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Headache			

subjects affected / exposed	1 / 40 (2.50%)	2 / 41 (4.88%)	1 / 5 (20.00%)
occurrences (all)	1	2	1
Transient Ischaemic Attack			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Neuropathy Peripheral			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tremor			
subjects affected / exposed	0 / 40 (0.00%)	3 / 41 (7.32%)	1 / 5 (20.00%)
occurrences (all)	0	4	1
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 40 (0.00%)	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Corneal Opacity			
subjects affected / exposed	2 / 40 (5.00%)	4 / 41 (9.76%)	0 / 5 (0.00%)
occurrences (all)	2	5	0
Keratopathy			
subjects affected / exposed	6 / 40 (15.00%)	14 / 41 (34.15%)	2 / 5 (40.00%)
occurrences (all)	6	17	3
Keratitis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye Pain			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Dry Mouth			
subjects affected / exposed	4 / 40 (10.00%)	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	4	2	0
Diarrhoea			

subjects affected / exposed	15 / 40 (37.50%)	18 / 41 (43.90%)	0 / 5 (0.00%)
occurrences (all)	17	21	0
Constipation			
subjects affected / exposed	2 / 40 (5.00%)	3 / 41 (7.32%)	0 / 5 (0.00%)
occurrences (all)	2	3	0
Anal Fissure			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Abdominal Pain Upper			
subjects affected / exposed	1 / 40 (2.50%)	3 / 41 (7.32%)	0 / 5 (0.00%)
occurrences (all)	1	4	0
Vomiting			
subjects affected / exposed	0 / 40 (0.00%)	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Nausea			
subjects affected / exposed	4 / 40 (10.00%)	5 / 41 (12.20%)	0 / 5 (0.00%)
occurrences (all)	5	6	0
Dysphagia			
subjects affected / exposed	2 / 40 (5.00%)	4 / 41 (9.76%)	1 / 5 (20.00%)
occurrences (all)	2	4	1
Dyspepsia			
subjects affected / exposed	0 / 40 (0.00%)	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	0	3	0
Skin and subcutaneous tissue disorders			
Acne			
subjects affected / exposed	2 / 40 (5.00%)	3 / 41 (7.32%)	0 / 5 (0.00%)
occurrences (all)	2	3	0
Alopecia			
subjects affected / exposed	3 / 40 (7.50%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	3	1	0
Dermatitis Acneiform			
subjects affected / exposed	6 / 40 (15.00%)	6 / 41 (14.63%)	1 / 5 (20.00%)
occurrences (all)	7	8	1
Dry Skin			
subjects affected / exposed	5 / 40 (12.50%)	5 / 41 (12.20%)	0 / 5 (0.00%)
occurrences (all)	5	5	0

Erythema			
subjects affected / exposed	1 / 40 (2.50%)	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	1	2	0
Onychoclasis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Palmar-Plantar Erythrodysaesthesia Syndrome			
subjects affected / exposed	1 / 40 (2.50%)	4 / 41 (9.76%)	0 / 5 (0.00%)
occurrences (all)	1	5	0
Photosensitivity Reaction			
subjects affected / exposed	2 / 40 (5.00%)	3 / 41 (7.32%)	0 / 5 (0.00%)
occurrences (all)	2	4	0
Pruritus			
subjects affected / exposed	2 / 40 (5.00%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Psoriasis			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash			
subjects affected / exposed	8 / 40 (20.00%)	13 / 41 (31.71%)	0 / 5 (0.00%)
occurrences (all)	9	19	0
Rash Erythematous			
subjects affected / exposed	1 / 40 (2.50%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Proteinuria			
subjects affected / exposed	6 / 40 (15.00%)	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	7	4	0
Nephrolithiasis			
subjects affected / exposed	3 / 40 (7.50%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	3	1	0
Micturition Urgency			

subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Renal Pain			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Haematuria			
subjects affected / exposed	4 / 40 (10.00%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	6	1	0
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	3 / 40 (7.50%)	5 / 41 (12.20%)	0 / 5 (0.00%)
occurrences (all)	3	6	0
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Muscular Weakness			
subjects affected / exposed	1 / 40 (2.50%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Muscle Spasms			
subjects affected / exposed	3 / 40 (7.50%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	5	0	0
Back Pain			
subjects affected / exposed	1 / 40 (2.50%)	3 / 41 (7.32%)	0 / 5 (0.00%)
occurrences (all)	1	3	0
Pain In Extremity			
subjects affected / exposed	3 / 40 (7.50%)	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	3	2	0
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Paronychia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Lower Respiratory Tract Infection Bacterial			

subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Influenza			
subjects affected / exposed	0 / 40 (0.00%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Conjunctivitis			
subjects affected / exposed	2 / 40 (5.00%)	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	2	3	0
Pneumonia Staphylococcal			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Rash Pustular			
subjects affected / exposed	2 / 40 (5.00%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	2	1	0
Urinary Tract Infection			
subjects affected / exposed	0 / 40 (0.00%)	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Vulval Abscess			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed	1 / 40 (2.50%)	1 / 41 (2.44%)	0 / 5 (0.00%)
occurrences (all)	1	1	0
Hypercalcaemia			
subjects affected / exposed	0 / 40 (0.00%)	2 / 41 (4.88%)	0 / 5 (0.00%)
occurrences (all)	0	2	0
Dehydration			
subjects affected / exposed	0 / 40 (0.00%)	2 / 41 (4.88%)	1 / 5 (20.00%)
occurrences (all)	0	2	1
Decreased Appetite			
subjects affected / exposed	2 / 40 (5.00%)	7 / 41 (17.07%)	1 / 5 (20.00%)
occurrences (all)	2	8	1
Hypocalcaemia			
subjects affected / exposed	7 / 40 (17.50%)	10 / 41 (24.39%)	2 / 5 (40.00%)
occurrences (all)	8	11	3

Iron Deficiency			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypophosphataemia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Hyponatraemia			
subjects affected / exposed	0 / 40 (0.00%)	0 / 41 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Hypomagnesaemia			
subjects affected / exposed	4 / 40 (10.00%)	6 / 41 (14.63%)	2 / 5 (40.00%)
occurrences (all)	5	9	2
Hypokalaemia			
subjects affected / exposed	2 / 40 (5.00%)	7 / 41 (17.07%)	2 / 5 (40.00%)
occurrences (all)	3	8	3

Non-serious adverse events	Open-label Period: Vandetanib 150 mg	Open-label Period: Vandetanib 200 mg	Open-label Period: Vandetanib 300 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	7 / 9 (77.78%)	7 / 8 (87.50%)	31 / 39 (79.49%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases To Bone			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 39 (2.56%)
occurrences (all)	0	1	1
Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	6 / 39 (15.38%)
occurrences (all)	1	0	7
Surgical and medical procedures			
Cataract Operation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Oedema Peripheral			

subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Non-Cardiac Chest Pain			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
Fatigue			
subjects affected / exposed	0 / 9 (0.00%)	2 / 8 (25.00%)	3 / 39 (7.69%)
occurrences (all)	0	2	3
Asthenia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	8 / 39 (20.51%)
occurrences (all)	1	0	10
Respiratory, thoracic and mediastinal disorders			
Lower Respiratory Tract Inflammation			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Dyspnoea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 39 (7.69%)
occurrences (all)	0	0	3
Dysphonia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Dysaesthesia Pharynx			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Pulmonary Hypertension			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Cough			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	3 / 39 (7.69%)
occurrences (all)	0	1	3
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
Depression			

subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Depressed Mood			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Anxiety			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	1 / 39 (2.56%)
occurrences (all)	0	1	1
Investigations			
Blood Alkaline Phosphatase Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	6 / 39 (15.38%)
occurrences (all)	0	0	7
Alanine Aminotransferase Increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	6 / 39 (15.38%)
occurrences (all)	1	0	7
Electrocardiogram Qt Prolonged			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	7 / 39 (17.95%)
occurrences (all)	0	1	8
Blood Thyroid Stimulating Hormone Increased			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	5 / 39 (12.82%)
occurrences (all)	0	1	8
Blood Creatinine Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 39 (7.69%)
occurrences (all)	0	0	4
Blood Glucose Increased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Blood Thyroid Stimulating Hormone Decreased			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Blood Bilirubin Increased			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
Blood Creatine Phosphokinase Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Ejection Fraction Decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
White Blood Cell Count Decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Weight Decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	4 / 39 (10.26%)
occurrences (all)	0	0	4
Platelet Count Decreased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
Gamma-Glutamyltransferase Increased			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Arthropod Bite			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Corneal Abrasion			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Sinus Tachycardia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Nervous system disorders			

Head Titubation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Dysgeusia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Disturbance In Attention			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Headache			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 39 (7.69%)
occurrences (all)	0	0	4
Transient Ischaemic Attack			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Neuropathy Peripheral			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Tremor			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Eye disorders			
Corneal Opacity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
Keratopathy			
subjects affected / exposed	2 / 9 (22.22%)	0 / 8 (0.00%)	6 / 39 (15.38%)
occurrences (all)	2	0	7
Keratitis			

subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Eye Pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Dry Mouth			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Diarrhoea			
subjects affected / exposed	1 / 9 (11.11%)	2 / 8 (25.00%)	7 / 39 (17.95%)
occurrences (all)	1	3	7
Constipation			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Anal Fissure			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Abdominal Pain Upper			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Vomiting			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 39 (7.69%)
occurrences (all)	0	0	3
Nausea			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	5 / 39 (12.82%)
occurrences (all)	0	0	5
Dysphagia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Dyspepsia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Skin and subcutaneous tissue disorders			
Acne			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Alopecia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	2
Dermatitis Acneiform			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
Dry Skin			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 39 (7.69%)
occurrences (all)	0	0	3
Erythema			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Onychoclasis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Palmar-Plantar Erythrodysaesthesia Syndrome			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Photosensitivity Reaction			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	2 / 39 (5.13%)
occurrences (all)	2	0	2
Pruritus			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 39 (7.69%)
occurrences (all)	0	0	3
Psoriasis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Rash			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	5 / 39 (12.82%)
occurrences (all)	0	2	5
Rash Erythematous			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	2	0

Renal and urinary disorders			
Pollakiuria			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Proteinuria			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Nephrolithiasis			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Micturition Urgency			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Renal Pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Haematuria			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	2 / 39 (5.13%)
occurrences (all)	1	1	2
Musculoskeletal and connective tissue disorders			
Myalgia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Muscular Weakness			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Muscle Spasms			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
Back Pain			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	2 / 39 (5.13%)
occurrences (all)	0	1	2

Pain In Extremity			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	0	0	1
Infections and infestations			
Pneumonia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Paronychia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Lower Respiratory Tract Infection Bacterial			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Influenza			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	1	0	0
Conjunctivitis			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Pneumonia Staphylococcal			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Rash Pustular			
subjects affected / exposed	2 / 9 (22.22%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	2	0	1
Urinary Tract Infection			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Vulval Abscess			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Metabolism and nutrition disorders			
Hypoalbuminaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	2	0
Hypercalcaemia			

subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	2 / 39 (5.13%)
occurrences (all)	0	0	2
Dehydration			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	0 / 39 (0.00%)
occurrences (all)	0	0	0
Decreased Appetite			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Hypocalcaemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	8 / 39 (20.51%)
occurrences (all)	0	0	9
Iron Deficiency			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	0 / 39 (0.00%)
occurrences (all)	0	1	0
Hypophosphataemia			
subjects affected / exposed	1 / 9 (11.11%)	0 / 8 (0.00%)	1 / 39 (2.56%)
occurrences (all)	1	0	1
Hyponatraemia			
subjects affected / exposed	0 / 9 (0.00%)	0 / 8 (0.00%)	3 / 39 (7.69%)
occurrences (all)	0	0	3
Hypomagnesaemia			
subjects affected / exposed	0 / 9 (0.00%)	1 / 8 (12.50%)	5 / 39 (12.82%)
occurrences (all)	0	2	6
Hypokalaemia			
subjects affected / exposed	1 / 9 (11.11%)	1 / 8 (12.50%)	6 / 39 (15.38%)
occurrences (all)	1	1	8

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 August 2012	Updates made due to new safety information, adding consistency with current label claims and clarification of wording where previously there was the potential for misinterpretation.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported