



Clinical trial results:

A Randomized, International, Open-Label, Multi-Centre, Phase III Study to Assess the Effect of a Patient Outreach Program on the Percentage of Time Patients with Locally Advanced or Metastatic Medullary Thyroid Cancer Experience Grade 2 or Higher Adverse Events during the First 12 Months of Treatment with Vandetanib

Summary

EudraCT number	2010-023428-26
Trial protocol	DE BE IT AT GB SE FI GR DK PL NO
Global end of trial date	13 March 2025

Results information

Result version number	v1 (current)
This version publication date	28 March 2026
First version publication date	28 March 2026

Trial information

Trial identification

Sponsor protocol code	D4200C00088
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Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01298323
WHO universal trial number (UTN)	-
Other trial identifiers	Sanofi-Genzyme Code: LPS14815

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	13 March 2025
Is this the analysis of the primary completion data?	No
Global end of trial reached?	Yes
Global end of trial date	13 March 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To demonstrate a decrease in the percentage of time patients with locally advanced or metastatic medullary thyroid cancer experience adverse events of Common Terminology Criteria for Adverse Event (CTCAE) grade 2 or higher in the first 12 months of receiving vandetanib with the use of a patient outreach program.

Protection of trial subjects:

Patients 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 patient and considering the local culture. During the course of the trial, patients were provided with individual patient cards indicating the nature of the trial the patient 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	25 February 2011
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Australia: 3
Country: Number of subjects enrolled	Austria: 2
Country: Number of subjects enrolled	Belgium: 4
Country: Number of subjects enrolled	Brazil: 18
Country: Number of subjects enrolled	Bulgaria: 2
Country: Number of subjects enrolled	Canada: 8
Country: Number of subjects enrolled	China: 16
Country: Number of subjects enrolled	Czechia: 4
Country: Number of subjects enrolled	Denmark: 4
Country: Number of subjects enrolled	Finland: 1
Country: Number of subjects enrolled	Germany: 28
Country: Number of subjects enrolled	Greece: 4
Country: Number of subjects enrolled	India: 12
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Italy: 33
Country: Number of subjects enrolled	Korea, Republic of: 6

Country: Number of subjects enrolled	Poland: 19
Country: Number of subjects enrolled	Russian Federation: 19
Country: Number of subjects enrolled	Sweden: 4
Country: Number of subjects enrolled	United Kingdom: 12
Worldwide total number of subjects	205
EEA total number of subjects	105

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)	161
From 65 to 84 years	44
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

From 25 February 2011 to 27 April 2012, 205 patients were randomized by 33 centers in global 20 countries.

Pre-assignment

Screening details:

217 patients were screened; 205 patients were randomized in a 1:1 ratio to either Vandetanib 300 mg or Vandetanib 300 mg + Outreach Program arm in randomized treatment period for 12 months. Post completion of randomized treatment period, eligible patients entered continuing treatment period.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Vandetanib 300 mg

Arm description:

Patients received vandetanib (3 x 100 milligram [mg] tablet form) orally, once daily for 12 months in the randomized treatment period.

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	ZACTIMA™, 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	Vandetanib 300 mg + Outreach Program
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Arm description:

Patients received vandetanib (3 x 100 mg tablet form) orally, once daily for 12 months in the randomized treatment period.

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	ZACTIMA™, 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 1	Vandetanib 300 mg	Vandetanib 300 mg + Outreach Program
Started	102	103
Completed	77	78
Not completed	25	25
Severe non-compliance to protocol	1	-
Consent withdrawn by subject	2	2
Adverse event, non-fatal	1	6
Condition under investigation worsened	16	11
Unspecified	4	6
Lost to follow-up	1	-

Period 2

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Vandetanib 300 mg

Arm description:

After completion of randomized treatment period, eligible patients entered the continuing treatment period and had the option to either permanently discontinue the study or continue taking vandetanib (3 x 100 mg tablet form) orally, once daily unless they met any criteria for discontinuation.

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	ZACTIMA™, 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	Vandetanib 300 mg + Outreach Program
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Arm description:

After completion of randomized treatment period, eligible patients entered the continuing treatment period and had the option to either permanently discontinue the study or continue taking vandetanib (3 x 100 mg tablet form) orally, once daily unless they met any criteria for discontinuation.

Arm type	Experimental
Investigational medicinal product name	Vandetanib
Investigational medicinal product code	ZD6474
Other name	ZACTIMA™, 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^[1]	Vandetanib 300 mg	Vandetanib 300 mg + Outreach Program
Started	55	55
Completed	55	55

Notes:

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

Justification: Patients who completed the randomized treatment and continued with vandetanib in the continuing treatment period.

Baseline characteristics

Reporting groups

Reporting group title	Vandetanib 300 mg
Reporting group description: Patients received vandetanib (3 x 100 milligram [mg] tablet form) orally, once daily for 12 months in the randomized treatment period.	
Reporting group title	Vandetanib 300 mg + Outreach Program
Reporting group description: Patients received vandetanib (3 x 100 mg tablet form) orally, once daily for 12 months in the randomized treatment period.	

Reporting group values	Vandetanib 300 mg	Vandetanib 300 mg + Outreach Program	Total
Number of subjects	102	103	205
Age categorical			
Units: Subjects			
>=18 - <40 Years	21	23	44
>=40 - <65 Years	65	52	117
>=65 - <75 Years	15	22	37
>=75 Years	1	6	7
Age continuous			
Units: years			
arithmetic mean	50.8	53.0	
standard deviation	± 13.47	± 14.34	-
Gender categorical			
Units: Subjects			
Female	38	37	75
Male	64	66	130
Race/Ethnicity, Customized			
Units: Subjects			
Asian	15	19	34
White	87	84	171

End points

End points reporting groups

Reporting group title	Vandetanib 300 mg
Reporting group description: Patients received vandetanib (3 x 100 milligram [mg] tablet form) orally, once daily for 12 months in the randomized treatment period.	
Reporting group title	Vandetanib 300 mg + Outreach Program
Reporting group description: Patients received vandetanib (3 x 100 mg tablet form) orally, once daily for 12 months in the randomized treatment period.	
Reporting group title	Vandetanib 300 mg
Reporting group description: After completion of randomized treatment period, eligible patients entered the continuing treatment period and had the option to either permanently discontinue the study or continue taking vandetanib (3 x 100 mg tablet form) orally, once daily unless they met any criteria for discontinuation.	
Reporting group title	Vandetanib 300 mg + Outreach Program
Reporting group description: After completion of randomized treatment period, eligible patients entered the continuing treatment period and had the option to either permanently discontinue the study or continue taking vandetanib (3 x 100 mg tablet form) orally, once daily unless they met any criteria for discontinuation.	
Subject analysis set title	Vandetanib 300 mg + Outreach Program
Subject analysis set type	Per protocol
Subject analysis set description: Patients on this arm will be contacted by site personnel at week 1 and then every 2 weeks during the first 52 weeks on the study (or prior discontinuation) to detect and possibly treat adverse events sooner than they might have been without the patient outreach, and at a time of lesser CTCAE grade.	
Subject analysis set title	Vandetanib 300 mg
Subject analysis set type	Per protocol
Subject analysis set description: Patients on this arm will get a standard AE monitoring schedule, similar to that used on previous studies. Patients will be asked about any AEs at scheduled visits and will have the option to contact the investigator at any time if experiencing any AE or symptoms and discuss the best treatment options.	

Primary: Percentage of Time a Patient Experienced at Least 1 AE of CTCAE Grade ≥ 2 in First 12 Months of Receiving Vandetanib in Patients Who Participated in Patient Outreach Program

End point title	Percentage of Time a Patient Experienced at Least 1 AE of CTCAE Grade ≥ 2 in First 12 Months of Receiving Vandetanib in Patients Who Participated in Patient Outreach Program
End point description: The primary endpoint is the percentage of time a patient experienced at least one AE of CTCAE grade 2 or higher in the first 12 months of treatment with vandetanib. If the patient discontinues treatment with vandetanib prior to the 12-month time point for any reason, this endpoint will be the time a patient experienced at least one AE of CTCAE grade 2 or higher as a percentage of the time the patient was receiving vandetanib. Number of Months Analyzed is the cumulative sum of number of months that all the participants were present in the study.	
End point type	Primary
End point timeframe: 12 months	

End point values	Vandetanib 300 mg + Outreach Program	Vandetanib 300 mg		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	102 ^[1]	103 ^[2]		
Units: Percentage of days				
arithmetic mean (standard deviation)	51.65 (± 35.548)	45.19 (± 36.347)		

Notes:

[1] - Type of Units Analyzed: months= 1513

[2] - Type of Units Analyzed: months= 1480

Statistical analyses

Statistical analysis title	Vandetanib 300mg+Outreach Program,Vandetanib 300mg
Comparison groups	Vandetanib 300 mg + Outreach Program v Vandetanib 300 mg
Number of subjects included in analysis	205
Analysis specification	Pre-specified
Analysis type	superiority ^[3]
P-value	= 0.199 ^[4]
Method	t-test, 2-sided
Parameter estimate	t-Statistic
Point estimate	1.29
Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.44
upper limit	16.37

Notes:

[3] - Superiority or Other (legacy)

[4] - Statistical significance threshold at this analysis was 10%.

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events (AEs) and all-cause mortality (deaths) were collected from randomization (Day 1) up to end of follow-up for each patient, approximately 168 months. Non-serious AEs were not collected during the continuing treatment period.

Adverse event reporting additional description:

Analysis was performed on Safety analysis set. Of 103 patients randomized to Vandetanib 300 mg + Outreach arm, all except 1 patient took part in outreach program. This patient was withdrawn due to eligibility criteria failure and could not be contacted successfully. Hence the results have been summarized under Vandetanib 300 mg for safety summaries.

Assessment type	Systematic
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Dictionary used

Dictionary name	MedDRA
Dictionary version	10.1-25.1

Reporting groups

Reporting group title	Randomized Treatment Period:Vandetanib 300mg+Outreach Program
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Reporting group description:

Patients received vandetanib (3 x 100 mg tablet form) orally, once daily for 12 months in the randomized treatment period.

Reporting group title	Randomized Treatment Period: Vandetanib 300 mg
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Reporting group description:

Patients received vandetanib (3 x 100 mg tablet form) orally, once daily for 12 months in the randomized treatment period.

Reporting group title	Continuing Treatment Period:Vandetanib 300mg+Outreach Program
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Reporting group description:

After completion of randomized treatment period, eligible patients entered the continuing treatment period and had the option to either permanently discontinue the study or continue taking vandetanib (3 x 100 mg tablet form) orally, once daily unless they met any criteria for discontinuation.

Reporting group title	Continuing Treatment Period: Vandetanib 300 mg
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Reporting group description:

After completion of randomized treatment period, eligible patients entered the continuing treatment period and had the option to either permanently discontinue the study or continue taking vandetanib (3 x 100 mg tablet form) orally, once daily unless they met any criteria for discontinuation.

	Randomized Treatment Period:Vandetanib 300mg+Outreach Program	Randomized Treatment Period: Vandetanib 300 mg	Continuing Treatment Period:Vandetanib 300mg+Outreach Program
Serious adverse events			
Total subjects affected by serious adverse events			
subjects affected / exposed	27 / 102 (26.47%)	31 / 103 (30.10%)	18 / 55 (32.73%)
number of deaths (all causes)	16	11	7
number of deaths resulting from adverse events	4	2	5
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant Neoplasm Progression			

subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastasis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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
Metastases To Bone			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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
Metastatic Pain			
subjects affected / exposed	1 / 102 (0.98%)	1 / 103 (0.97%)	0 / 55 (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
Prostate Cancer			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Vascular disorders			
Aortic Dissection			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertension			
subjects affected / exposed	2 / 102 (1.96%)	2 / 103 (1.94%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	3 / 3	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypertensive Crisis			
subjects affected / exposed	1 / 102 (0.98%)	1 / 103 (0.97%)	0 / 55 (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
Hypotension			

subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Venous Insufficiency			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Ischaemia			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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
Surgical and medical procedures			
Leg Amputation			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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
Angioplasty			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Catheter Site Pain			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Chest Pain			
subjects affected / exposed	0 / 102 (0.00%)	2 / 103 (1.94%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	2 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Death			
subjects affected / exposed	0 / 102 (0.00%)	2 / 103 (1.94%)	2 / 55 (3.64%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	2 / 2	2 / 2
Multiple Organ Dysfunction Syndrome			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Disease Progression			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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, thoracic and mediastinal disorders			
Laryngeal Dyspnoea			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Haemoptysis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	1 / 102 (0.98%)	1 / 103 (0.97%)	3 / 55 (5.45%)
occurrences causally related to treatment / all	0 / 1	0 / 1	0 / 5
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Productive Cough			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Pulmonary Embolism			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory Failure			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	1 / 1
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Fear			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood Creatinine Increased			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Haematocrit Increased			
subjects affected / exposed	1 / 102 (0.98%)	1 / 103 (0.97%)	0 / 55 (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

Injury, poisoning and procedural complications			
Femur Fracture			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Joint Dislocation			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Radius Fracture			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Cardiac disorders			
Acute Myocardial Infarction			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac Arrest			
subjects affected / exposed	2 / 102 (1.96%)	0 / 103 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	2 / 2	0 / 0	0 / 0
Atrial Fibrillation			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Coronary Artery Disease			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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	2 / 102 (1.96%)	1 / 103 (0.97%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Carotid Arteriosclerosis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Mental Impairment			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Sciatica			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Migraine With Aura			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Vocal Cord Paralysis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Sensorimotor Disorder			

subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Ear and labyrinth disorders			
Deafness Neurosensory			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Abdominal Pain			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Anal Fistula			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Crohn's Disease			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Enteritis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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	3 / 102 (2.94%)	0 / 103 (0.00%)	0 / 55 (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
Gastric Ulcer			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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
Ileus Paralytic			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Haematemesis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Jejunal Perforation			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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
Large Intestinal Ulcer			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Large Intestine Perforation			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Nausea			

subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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	0 / 102 (0.00%)	2 / 103 (1.94%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatitis Acute			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Toothache			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Rectal Haemorrhage			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Vomiting			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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	1 / 102 (0.98%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 1	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Jaundice			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cholecystitis Acute			

subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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			
Dermatitis Acneiform			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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
Photosensitivity Reaction			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Skin Necrosis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bladder Disorder			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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
Glomerulonephritis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Nephrolithiasis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Renal Failure			

subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	1 / 1	0 / 0	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Endocrine disorders			
Ectopic Acth Syndrome			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Musculoskeletal and connective tissue disorders			
Muscle Haemorrhage			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Neck Pain			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Pathological Fracture			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Scoliosis			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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			
Enterocolitis Bacterial			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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
Appendicitis			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Anal Abscess			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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 Limb			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Gastroenteritis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastroenteritis Caliciviral			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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			
subjects affected / exposed	0 / 102 (0.00%)	2 / 103 (1.94%)	2 / 55 (3.64%)
occurrences causally related to treatment / all	0 / 0	0 / 2	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	2 / 2
Lung Infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Herpes Zoster			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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
Postoperative Wound Infection			

subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Subcutaneous Abscess			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pyelonephritis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
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 Tuberculosis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	0 / 55 (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
Urinary Tract Infection			
subjects affected / exposed	1 / 102 (0.98%)	1 / 103 (0.97%)	0 / 55 (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
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Tracheobronchitis			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Hypoglycaemia			

subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hypocalcaemia			
subjects affected / exposed	0 / 102 (0.00%)	2 / 103 (1.94%)	0 / 55 (0.00%)
occurrences causally related to treatment / all	0 / 0	1 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hyperglycaemia			
subjects affected / exposed	0 / 102 (0.00%)	1 / 103 (0.97%)	0 / 55 (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
Hypercalcaemia			
subjects affected / exposed	1 / 102 (0.98%)	1 / 103 (0.97%)	0 / 55 (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
Dehydration			
subjects affected / exposed	1 / 102 (0.98%)	0 / 103 (0.00%)	0 / 55 (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
Hyponatraemia			
subjects affected / exposed	0 / 102 (0.00%)	0 / 103 (0.00%)	1 / 55 (1.82%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Continuing Treatment Period: Vandetanib 300 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	21 / 55 (38.18%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	7		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Malignant Neoplasm Progression			

subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metastasis			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastases To Bone			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastatic Pain			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Prostate Cancer			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Aortic Dissection			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypertension			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertensive Crisis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypotension			

subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Venous Insufficiency			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ischaemia			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Leg Amputation			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angioplasty			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Catheter Site Pain			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Chest Pain			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Death				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Multiple Organ Dysfunction Syndrome				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Disease Progression				
subjects affected / exposed	3 / 55 (5.45%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	3 / 3			
Sudden Death				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Respiratory, thoracic and mediastinal disorders				
Laryngeal Dyspnoea				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	2 / 55 (3.64%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Productive Cough				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Pulmonary Embolism			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Respiratory Failure			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Depression			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fear			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Investigations			
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 55 (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 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Haematocrit Increased			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Injury, poisoning and procedural complications			
Femur Fracture			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Joint Dislocation			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Radius Fracture			
subjects affected / exposed	0 / 55 (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	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Angina Pectoris			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac Arrest			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Atrial Fibrillation			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Coronary Artery Disease			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Myocardial Infarction			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Carotid Arteriosclerosis			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebrovascular Accident			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Mental Impairment			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sciatica			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Migraine With Aura			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vocal Cord Paralysis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Sensorimotor Disorder			

subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Neutropenia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Deafness Neurosensory			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal Pain Upper			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Abdominal Pain			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Anal Fistula			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Crohn's Disease			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Enteritis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

Diarrhoea				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric Ulcer				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ileus Paralytic				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Haematemesis				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Intestinal Obstruction				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Jejunal Perforation				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Large Intestinal Ulcer				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Large Intestine Perforation				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Nausea				

subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pancreatitis			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	1 / 1		
Pancreatitis Acute			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Toothache			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Rectal Haemorrhage			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Jaundice			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cholecystitis Acute			

subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis Acneiform			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Photosensitivity Reaction			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Skin Necrosis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Azotaemia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bladder Disorder			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Glomerulonephritis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal Failure			

subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Endocrine disorders			
Ectopic Acth Syndrome			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscle Haemorrhage			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Neck Pain			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pathological Fracture			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Scoliosis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Enterocolitis Bacterial			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Appendicitis			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Anal Abscess				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Abscess Limb				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis Caliciviral				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis Viral				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pneumonia				
subjects affected / exposed	6 / 55 (10.91%)			
occurrences causally related to treatment / all	0 / 6			
deaths causally related to treatment / all	3 / 3			
Lung Infection				
subjects affected / exposed	0 / 55 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Herpes Zoster				
subjects affected / exposed	1 / 55 (1.82%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Postoperative Wound Infection				

subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Subcutaneous Abscess			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pyelonephritis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pulmonary Tuberculosis			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary Tract Infection			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Upper Respiratory Tract Infection			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Tracheobronchitis			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			

subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypocalcaemia			
subjects affected / exposed	1 / 55 (1.82%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hypercalcaemia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	0 / 55 (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 300mg+Outreach Program	Randomized Treatment Period: Vandetanib 300 mg	Continuing Treatment Period:Vandetanib 300mg+Outreach Program
Total subjects affected by non-serious adverse events			
subjects affected / exposed	96 / 102 (94.12%)	89 / 103 (86.41%)	0 / 55 (0.00%)
Investigations			
Electrocardiogram Qt Prolonged			

subjects affected / exposed occurrences (all)	9 / 102 (8.82%) 13	7 / 103 (6.80%) 12	0 / 55 (0.00%) 0
Blood Creatinine Increased subjects affected / exposed occurrences (all)	5 / 102 (4.90%) 5	8 / 103 (7.77%) 9	0 / 55 (0.00%) 0
Aspartate Aminotransferase Increased subjects affected / exposed occurrences (all)	5 / 102 (4.90%) 6	8 / 103 (7.77%) 8	0 / 55 (0.00%) 0
Weight Decreased subjects affected / exposed occurrences (all)	12 / 102 (11.76%) 12	11 / 103 (10.68%) 11	0 / 55 (0.00%) 0
Alanine Aminotransferase Increased subjects affected / exposed occurrences (all)	9 / 102 (8.82%) 9	10 / 103 (9.71%) 10	0 / 55 (0.00%) 0
Vascular disorders Hypertension subjects affected / exposed occurrences (all)	35 / 102 (34.31%) 40	29 / 103 (28.16%) 33	0 / 55 (0.00%) 0
Nervous system disorders Dysgeusia subjects affected / exposed occurrences (all)	0 / 102 (0.00%) 0	6 / 103 (5.83%) 6	0 / 55 (0.00%) 0
Dizziness subjects affected / exposed occurrences (all)	7 / 102 (6.86%) 8	3 / 103 (2.91%) 4	0 / 55 (0.00%) 0
Headache subjects affected / exposed occurrences (all)	12 / 102 (11.76%) 16	8 / 103 (7.77%) 9	0 / 55 (0.00%) 0
General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all)	18 / 102 (17.65%) 19	17 / 103 (16.50%) 17	0 / 55 (0.00%) 0
Asthenia subjects affected / exposed occurrences (all)	12 / 102 (11.76%) 14	12 / 103 (11.65%) 13	0 / 55 (0.00%) 0
Gastrointestinal disorders			

Constipation subjects affected / exposed occurrences (all)	8 / 102 (7.84%) 9	5 / 103 (4.85%) 5	0 / 55 (0.00%) 0
Diarrhoea subjects affected / exposed occurrences (all)	55 / 102 (53.92%) 85	48 / 103 (46.60%) 63	0 / 55 (0.00%) 0
Dry Mouth subjects affected / exposed occurrences (all)	7 / 102 (6.86%) 7	4 / 103 (3.88%) 4	0 / 55 (0.00%) 0
Nausea subjects affected / exposed occurrences (all)	26 / 102 (25.49%) 34	18 / 103 (17.48%) 20	0 / 55 (0.00%) 0
Vomiting subjects affected / exposed occurrences (all)	8 / 102 (7.84%) 8	11 / 103 (10.68%) 13	0 / 55 (0.00%) 0
Respiratory, thoracic and mediastinal disorders Oropharyngeal Pain subjects affected / exposed occurrences (all)	6 / 102 (5.88%) 6	1 / 103 (0.97%) 1	0 / 55 (0.00%) 0
Skin and subcutaneous tissue disorders Dry Skin subjects affected / exposed occurrences (all)	7 / 102 (6.86%) 8	12 / 103 (11.65%) 12	0 / 55 (0.00%) 0
Dermatitis Acneiform subjects affected / exposed occurrences (all)	22 / 102 (21.57%) 24	22 / 103 (21.36%) 23	0 / 55 (0.00%) 0
Alopecia subjects affected / exposed occurrences (all)	2 / 102 (1.96%) 2	8 / 103 (7.77%) 8	0 / 55 (0.00%) 0
Acne subjects affected / exposed occurrences (all)	7 / 102 (6.86%) 9	10 / 103 (9.71%) 11	0 / 55 (0.00%) 0
Photosensitivity Reaction subjects affected / exposed occurrences (all)	13 / 102 (12.75%) 18	7 / 103 (6.80%) 8	0 / 55 (0.00%) 0
Rash			

subjects affected / exposed occurrences (all)	26 / 102 (25.49%) 28	25 / 103 (24.27%) 31	0 / 55 (0.00%) 0
Rash Maculo-Papular subjects affected / exposed occurrences (all)	4 / 102 (3.92%) 4	7 / 103 (6.80%) 7	0 / 55 (0.00%) 0
Erythema subjects affected / exposed occurrences (all)	6 / 102 (5.88%) 6	2 / 103 (1.94%) 2	0 / 55 (0.00%) 0
Palmar-Plantar Erythrodysaesthesia Syndrome subjects affected / exposed occurrences (all)	5 / 102 (4.90%) 5	6 / 103 (5.83%) 6	0 / 55 (0.00%) 0
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	11 / 102 (10.78%) 15	8 / 103 (7.77%) 8	0 / 55 (0.00%) 0
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	8 / 102 (7.84%) 10	9 / 103 (8.74%) 9	0 / 55 (0.00%) 0
Anxiety subjects affected / exposed occurrences (all)	4 / 102 (3.92%) 4	7 / 103 (6.80%) 7	0 / 55 (0.00%) 0
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	15 / 102 (14.71%) 16	15 / 103 (14.56%) 16	0 / 55 (0.00%) 0
Musculoskeletal and connective tissue disorders Myalgia subjects affected / exposed occurrences (all)	9 / 102 (8.82%) 11	4 / 103 (3.88%) 4	0 / 55 (0.00%) 0
Metabolism and nutrition disorders Hypocalcaemia subjects affected / exposed occurrences (all)	13 / 102 (12.75%) 14	14 / 103 (13.59%) 18	0 / 55 (0.00%) 0
Decreased Appetite			

subjects affected / exposed	13 / 102 (12.75%)	19 / 103 (18.45%)	0 / 55 (0.00%)
occurrences (all)	15	20	0

Non-serious adverse events	Continuing Treatment Period: Vandetanib 300 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 55 (0.00%)		
Investigations			
Electrocardiogram Qt Prolonged			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Blood Creatinine Increased			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Aspartate Aminotransferase Increased			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Weight Decreased			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Alanine Aminotransferase Increased			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Dizziness			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Headache			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		

General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Asthenia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Constipation			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Diarrhoea			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Dry Mouth			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Vomiting			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal Pain			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Skin and subcutaneous tissue disorders			
Dry Skin			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Dermatitis Acneiform			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Alopecia			

subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Acne			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Photosensitivity Reaction			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Rash			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Rash Maculo-Papular			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Erythema			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Palmar-Plantar Erythrodysaesthesia Syndrome			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Anxiety			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	0 / 55 (0.00%)		
occurrences (all)	0		
Musculoskeletal and connective tissue disorders			

Myalgia subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0		
Metabolism and nutrition disorders Hypocalcaemia subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0		
Decreased Appetite subjects affected / exposed occurrences (all)	0 / 55 (0.00%) 0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 March 2011	Clarified and corrected the management of vandetanib treatment in patients who developed hypertension adverse events of CTCAE grade 4 found in the clinical study protocol (CSP). Investigators that had already recruited patients in the study had been informed about this change and this guideline had been already implemented for patient safety reasons.
19 August 2011	Number of patients were increased. Dose reduction for patients with moderate renal impairment was added. CSP Appendix E was updated. Administrative changes to ensure the text was consistent or to provide clarification and correct typing errors.
29 February 2016	Genzyme assumption of responsibility for trial from AstraZeneca in cover page, header, appendices and all sections of the protocol. The Sanofi-Genzyme study code LPS14815 was added. Sections regarding investigational medicinal product and pharmacovigilance were updated to reflect the Genzyme environment. Minor typographical errors or inconsistencies were corrected.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported