Clinical trial results:
A Randomized, Double-blind, Placebo-controlled, Multi-center Phase III Study to Evaluate the Efficacy and Safety of Pazopanib (GW786034) Compared to Placebo in Patients with Locally Advanced and/or Metastatic Renal Cell Carcinoma Who Have Progressed Following Cytokine-based First-line Treatment

Summary

EudraCT number	2005-004078-25
Trial protocol	GB IE SK LT EE AT CZ IT GR HU LV
Global end of trial date	29 December 2014

Results information

Result version number	v1 (current)
This version publication date	26 May 2016
First version publication date	26 May 2016

Trial information

Trial identification

Sponsor protocol code	VEG105192

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	GlaxoSmithKline
Sponsor organisation address	980 Great West Road, Brentford, Middlesex, United Kingdom,
Public contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,
Scientific contact	GSK Response Center, GlaxoSmithKline, 1 866-435-7343,

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	05 June 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	29 December 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate and compare Progression Free Survival (PFS) of patients treated with pazopanib to those treated with placebo.

Protection of trial subjects:

Not applicable

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	12 April 2006
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Poland: 108
Country: Number of subjects enrolled	Russian Federation: 32
Country: Number of subjects enrolled	France: 22
Country: Number of subjects enrolled	Slovakia: 18
Country: Number of subjects enrolled	United Kingdom: 28
Country: Number of subjects enrolled	Austria: 12
Country: Number of subjects enrolled	Czech Republic: 14
Country: Number of subjects enrolled	Estonia: 9
Country: Number of subjects enrolled	Ireland: 1
Country: Number of subjects enrolled	Italy: 16
Country: Number of subjects enrolled	Lithuania: 19
Country: Number of subjects enrolled	Chile: 21
Country: Number of subjects enrolled	India: 13
Country: Number of subjects enrolled	Korea, Republic of: 22
Country: Number of subjects enrolled	Argentina: 25
Country: Number of subjects enrolled	Brazil: 11
Country: Number of subjects enrolled	China: 6
Country: Number of subjects enrolled	New Zealand: 12
Country: Number of subjects enrolled	Pakistan: 15
Country: Number of subjects enrolled	Australia: 13
Country: Number of subjects enrolled	Ukraine: 13
Country: Number of subjects enrolled	Hong Kong: 3

Country: Number of subjects enrolled	Latvia: 2
Worldwide total number of subjects	435
EEA total number of subjects	249

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)	281
From 65 to 84 years	153
85 years and over	1

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Participants with advanced renal cell carcinoma who were either treatment naïve, or had received one prior cytokine-based systemic treatment for advanced renal cell carcinoma (RCC) (cytokine pretreated) were enrolled.

Period 1

Period 1 title	Overall Study (overall period)
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	Pazopanib 800 mg

Arm description:

Pazopanib 800 mg (tablets) administered orally once a day

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

Dosage and administration details:

800 mg (2 x 400 mg tablets) once daily. 200 and 400 mg tablets were available to sites, to allow for dose modifications (typically 600 mg).

Arm title	Placebo

Arm description:

Matching Placebo administered orally once a day

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

Dosage and administration details:

800 mg (2 x 400 mg placebo tablets) once daily. 200 and 400 mg tablets were available to sites, to allow for dose modifications (typically 600 mg).

Number of subjects in period 1	Pazopanib 800 mg	Placebo
Started	290	145
Completed	68	37
Not completed	222	108
Consent withdrawn by subject	17	3
Death	194	100
Lost to follow-up	11	5

Baseline characteristics

Reporting groups	
Reporting group title	Pazopanib 800 mg
Reporting group description:	
Pazopanib 800 mg (tablets) administered orally once a day	
Reporting group title	Placebo
Reporting group description:	
Matching Placebo administered orally once a day	

Reporting group values	Pazopanib 800 mg	Placebo	Total
Number of subjects	290	145	435
Age categorical Units: Subjects			
Age continuous Units: years			
arithmetic mean	59.1	59.6	
standard deviation	± 10.06	± 11.04	-
Gender categorical Units: Subjects			
Female	92	36	128
Male	198	109	307
Race, Customized Units: Subjects			
White	252	122	374
Asian	36	23	59
African American/African Heritage	1	0	1
Native Hawaiian or other Pacific Islander	1	0	1

End points

End points reporting groups

Reporting group title	Pazopanib 800 mg
Reporting group description:	
Pazopanib 800 mg (tablets) administered orally once a day	
Reporting group title	Placebo
Reporting group description:	
Matching Placebo administered orally once a day	

Primary: Progression-free survival

End point title	Progression-free survival
End point description:	
Progression-free survival (PFS) is defined as the interval between the date of randomization and the earliest date of disease progression or death due to any cause. Assessments of progression and non-progression were made by an independent imaging review committee (IRC) for the primary analysis.	
End point type	Primary
End point timeframe:	
Randomization until progression (up to 2 years)	

End point values	Pazopanib 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290[1]	145[2]		
Units: months				
median (confidence interval 95%)	9.2 (7.4 to 12.9)	4.2 (2.8 to 5.6)		

Notes:

[1] - Intent-to-Treat (ITT) Population: all randomized participants

[2] - Intent-to-Treat (ITT) Population: all randomized participants

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Pazopanib 800 mg v Placebo
Number of subjects included in analysis	435
Analysis specification	Pre-specified
Analysis type	superiority[3]
P-value	= 1E-7 [4]
Method	Logrank
Parameter estimate	Hazard ratio (HR)
Point estimate	0.46
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.34
upper limit	0.62

Notes:

[3] - The estimated value is the hazard ratio comparing pazopanib to placebo.

[4] - stratified log-rank test

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival is defined as the time from randomization until death. The length of this interval was estimated as the date of death minus the date of randomization plus 1 day. Participants who were still alive at the time of analysis were censored.

End point type	Secondary

End point timeframe:

Randomization until death (up to 2 years)

End point values	Pazopanib 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290[5]	145[6]		
Units: Months				
median (confidence interval 95%)	22.9 (19.9 to 25.4)	20.5 (15.6 to 27.6)		

Notes:

[5] - ITT Population

[6] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Response

End point title	Overall Response

End point description:

Overall response is the number of participants who had a complete response (CR) or a partial response (PR). Per Response Evaluation Criteria In Solid Tumors (RECIST): CR, all detectable tumor has disappeared; PR, a >=30% decrease in the sum of the longest dimensions of the target lesions (TLs) taking as a reference the Baseline sum, no worsening of non-TLs, and no new lesions; Progressive disease (PD), a >=20% increase in TLs, clearly worsening of non-TLs, or emergence of new lesions; Stable Disease, small changes that do not meet previously given criteria. IRC, independent review committee.

End point type	Secondary

End point timeframe:

Baseline until either response or progression (up to 2 years)

End point values	Pazopanib 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290[7]	145[8]		
Units: participants				
Complete Response, IRC assessed	1	0		
Partial Response, IRC assessed	87	5		
Stable Disease, IRC assessed	110	59		
Progressive Disease, IRC assessed	51	58		
Unknown, IRC assessed	41	23		
Complete Response, Investigator assessed	4	0		
Partial Response, Investigator assessed	99	9		
Stable Disease, Investigator assessed	118	62		
Progressive Disease, Investigator assessed	46	65		
Unknown, Investigator assessed	23	9		

Notes:

[7] - ITT Population

[8] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Participants with complete response, partial response, or 6 months of stable disease

End point title	Participants with complete response, partial response, or 6 months of stable disease

End point description:

This is similar to overall response rate, but also includes participants who had stable disease for at least 6 months. Per Response Evaluation Criteria In Solid Tumors (RECIST): CR, all detectable tumor has disappeared; PR, a >=30% decrease in the sum of the longest dimensions of the target lesions taking as a reference the Baseline sum; Stable Disease, small changes that do not meet previously given criteria; Progressive Disease, a >=20% increase in target lesions. IRC, independent review committee.

End point type	Secondary

End point timeframe:

Baseline until 6 months post-Baseline or progressive disease

End point values	Pazopanib 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	290[9]	145[10]		
Units: participants				
Complete Response, IRC assessed	1	0		
Partial Response, IRC assessed	87	5		
6-months Stable Disease, IRC assessed	48	17		
Progressive Disease, IRC assessed	92	84		
Unknown, IRC assessed	62	39		

Notes:

[9] - ITT Population

[10] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of response

End point title	Duration of response[11]

End point description:

Duration of response is defined as the time from first observation of response until progression of disease or death.

End point type	Secondary

End point timeframe:

Time from response until progression (up to 2 years)

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: There are no statistical data to report.

End point values	Pazopanib 800 mg			
Subject group type	Reporting group			
Number of subjects analysed	290[12]			
Units: weeks				
median (confidence interval 95%)	58.7 (52.1 to 68.1)			

Notes:

[12] - ITT Population. Only results for pazopanib are given because there were too few placebo responders.

Statistical analyses

No statistical analyses for this end point

Secondary: Time to response as assessed by an Independent Review Committee (IRC) and the Investigator

End point title	Time to response as assessed by an Independent Review Committee (IRC) and the Investigator[13]

End point description:

Time to response is defined as the time from randomization until the first documented evidence of complete reponse (all detectable tumor has disappeared) or partial response (a >=30% decrease in the sum of the longest dimensions of the target lesions taking as a reference the Baseline sum) (whichever status was recorded first). Only results for pazopanib are given because there were not enough placebo responders. The different number of participants analyzed is due to differences in clinical judgement, measurement, and the selection of target lesions.

End point type	Secondary

End point timeframe:

Randomization until CR or PR (assessed for up to 2 years)

Notes:

[13] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical data to report.

End point values	Pazopanib 800 mg			
Subject group type	Reporting group			
Number of subjects analysed	103[14]			
Units: weeks				
median (confidence interval 95%)				
IRC assessed, n=88	11.9 (9.4 to 12.3)			
Investigator assessed, n=103	12 (11.6 to 12.3)			

Notes:

[14] - ITT Population. Only participants with a complete or partial response were analyzed.

Statistical analyses

No statistical analyses for this end point

Secondary: Adjusted Mean change from Baseline (BL) in the European Organization for Research and Treatment of Cancer Quality of Life (QOL) Questionnaire Core 30 (EORTC QLQ C-30) score at Weeks 6, 12, 18, 24, and 48

End point title	Adjusted Mean change from Baseline (BL) in the European Organization for Research and Treatment of Cancer Quality of Life (QOL) Questionnaire Core 30 (EORTC QLQ C-30) score at Weeks 6, 12, 18, 24, and 48

End point description:

The EORTC QLQ-C30 is a questionnaire developed to assess the quality of life of cancer participants. The analyses for EORTC QLQ-C30 were focused on global health status/Health-Related Quality of Life (HRQOL) scores on the questionnaire. The scores (from 1 [very poor quality of life] to 7 [excellent quality of life]) for these two questions were averaged and then transformed to a 0 - 100 scale (based on published methods) prior to analysis of change from Baseline. Only participants who were on treatment at the given time point were asked to complete the questionnaire, and only those who completed the questionnaire could be analyzed for each individual time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 6, 12, 18, 24, and 48

End point values	Pazopanib 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	246[15]	111[16]		
Units: points on a scale				
arithmetic mean (standard deviation)				
Week 6, n=243, 110	-3.2 (± 19.66)	-2.6 (± 19.18)		
Week 12, n=219, 81	-3.6 (± 20.16)	-0.5 (± 17.55)		
Week 18, n=191, 61	-2.5 (± 21.7)	-0.3 (± 18.13)		
Week 24, n=164, 49	0.1 (± 19.81)	-0.5 (± 18.67)		
Week 48, n=96, 24	-0.3 (± 18.36)	0.3 (± 15.63)		

Notes:

[15] - ITT Population participants who completed HRQOL assessments at BL and had >=1 post-BL assessment
[16] - ITT Population participants who completed HRQOL assessments at BL and had >=1 post-BL assessment

Statistical analyses

No statistical analyses for this end point

Secondary: Adjusted Mean change from Baseline in the Index Score of the EQ-5D (EuroQoL [Quality of Life]-5D) Questionnaire at Weeks 6, 12, 18, 24, and 48

End point title	Adjusted Mean change from Baseline in the Index Score of the EQ-5D (EuroQoL [Quality of Life]-5D) Questionnaire at Weeks 6, 12, 18, 24, and 48

End point description:

The EQ-5D is comprised of a 5-item health status measure and a visual analogue rating scale, and measures mobility, self-care, usual activities, pain, discomfort, and anxiety/depression. Responses to each of the 5 health states are measured on a 3-point scale (no, moderate, and extreme problems). Scoring of the EQ-5D yields an index-based summary score (Index), through application of societal weights, and a VAS score (VAS). Index is interpreted on a continuum from 1.0 (best possible health) to 0 (represents dead), to some health sates being worse than dead (<0). Only participants who were on treatment at the given time point were asked to complete the questionnaire, and only those who completed the questionnaire could be analyzed for each individual time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 6, 12, 18, 24, and 48

End point values	Pazopanib 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	253[17]	125[18]		
Units: points on a scale				
arithmetic mean (standard deviation)				
Week 6, n=253, 125	-0.014 (± 0.2203)	-0.029 (± 0.2674)		
Week 12, n=219, 86	-0.04 (± 0.2148)	0.007 (± 0.1969)		
Week 18, n=196, 62	-0.023 (± 0.2305)	-0.006 (± 0.1466)		
Week 24, n=166, 51	-0.025 (± 0.242)	-0.001 (± 0.2411)		
Week 36, n=98, 24	0.03 (± 0.1961)	-0.005 (± 0.2015)		

Notes:

[17] - ITT Population participants who completed HRQOL assessments at BL and had >=1 post-BL assessment
[18] - ITT Population participants who completed HRQOL assessments at BL and had >=1 post-BL assessment

Statistical analyses

No statistical analyses for this end point

Secondary: Adjusted Mean change from Baseline in the Visual Analog Scale (VAS) Score of the EQ-5D (EuroQoL [Quality of Life]-5D) Questionnaire at Weeks 6, 12, 18, 24, and 48

End point title	Adjusted Mean change from Baseline in the Visual Analog Scale (VAS) Score of the EQ-5D (EuroQoL [Quality of Life]-5D) Questionnaire at Weeks 6, 12, 18, 24, and 48

End point description:

The EQ-5D is comprised of a 5-item health status measure and a visual analogue rating scale, and measures mobility, self-care, usual activities, pain, discomfort, and anxiety/depression. Responses to each of the 5 health states are measured on a 3-point scale (no, moderate, and extreme problems). Scoring of the EQ-5D yields an index-based summary score (Index) and a VAS score (VAS), obtained from participant's self-reports of their health on a VAS thermometer scale. The EQ-5D VAS ranges from 0% (worst imaginable health state) to 100% (best imaginable health state). Only participants who were on treatment at the given time point were asked to complete the questionnaire, and only those who completed the questionnaire could be analyzed for each individual time point.

End point type	Secondary

End point timeframe:

Baseline and Weeks 6, 12, 18, 24, and 48

End point values	Pazopanib 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	239[19]	111[20]		
Units: points on a scale				
arithmetic mean (standard deviation)				
Week 6, n=239, 111	-0.9 (± 21.07)	-3.6 (± 23.04)		
Week 12, n=212, 80	0.4 (± 22.55)	0.2 (± 25.35)		
Week 18, n=189, 60	0.1 (± 23.2)	0.1 (± 19.35)		
Week 24, n=161, 49	2.6 (± 22.16)	5.4 (± 21.27)		
Week 36, n=95, 23	2.4 (± 24.21)	8.8 (± 23.96)		

Notes:

[19] - ITT Population participants who completed HRQOL assessments at BL and had >=1 post-BL assessment

[20] - ITT Population participants who completed HRQOL assessments at BL and had >=1 post-BL assessment

Statistical analyses

No statistical analyses for this end point

Secondary: Plasma pazopanib concentrations before dosing and at 2, 4, and 8 hours after dosing on Day 1 and Week 3

End point title	Plasma pazopanib concentrations before dosing and at 2, 4, and 8 hours after dosing on Day 1 and Week 3[21]

End point description:

Subgroup of enrolled participants who agreed to have blood samples collected for analysis of pazopanib in plasma. Data were missing or not collected at Week 3 for 8 participants for whom data were available on Day 1. No samples were collected at Week 3 from 2 participants.

End point type	Secondary

End point timeframe:

Day 1 and Week 3

Notes:

[21] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.

Justification: There are no statistical data to report.

End point values	Pazopanib 800 mg			
Subject group type	Reporting group			
Number of subjects analysed	57[22]			
Units: nanograms per milliliter				
median (full range (min-max))				
Day 1, before dosing, n=57	0 (0 to 846)			
Week 3, before dosing, n=48	31851 (2634 to 61720)			
Day 1, 2 hours after dosing, n=57	17270 (0 to 107454)			
Week 3, 2 hours after dosing, n=49	42205 (4282 to 79977)			
Day 1, 4 hours after dosing, n=57	24360 (2371 to 74606)			
Week 3, 4 hours after dosing, n=49	42637 (3532 to 107972)			
Day 1, 8 hours after dosing, n=57	19925 (3273 to 60974)			
Week 3, 8 hours after dosing, n=48	40117.5 (3760 to 96548)			

Notes:

[22] - Enrolled participants who agreed to have blood samples collected for analysis of pazopanib in plasma

Statistical analyses

No statistical analyses for this end point

Secondary: Baseline expression levels of the indicated target proteins in pazopanib- and placebo-treated participants

End point title	Baseline expression levels of the indicated target proteins in pazopanib- and placebo-treated participants

End point description:

Baseline plasma samples were obtained from participants and were tested for the indicated cytokine and angiogenesis factors. Protein levels were determined using the Searchlight multiplex system based on chemiluminescence.

End point type	Secondary

End point timeframe:

Baseline

End point values	Pazopanib 800 mg	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	225[23]	119[24]		
Units: picograms per milliliter				
arithmetic mean (standard deviation)				
Interleukin-6	31.003 (± 65.247)	24.145 (± 31.708)		
Interleukin-8	35.429 (± 164.12)	27.755 (± 66.129)		
Vascular endothelial growth factor	308.61 (± 365.19)	273.15 (± 350.91)		
Hepatocyte growth factor	383.55 (± 308.89)	522.94 (± 1003.8)		
Tissue inhibitor of metalloproteinase 1	847464 (± 690744)	735915 (± 423493)		
e-Selectin	41649.28 (± 22389.04)	41231.45 (± 19825.7)		
Osteopotin	444343 (± 707005)	369317 (± 490931)		

Notes:

[23] - Subgroup of enrolled participants who agreed to have plasma samples collected for biomarker analyses

[24] - Subgroup of enrolled participants who agreed to have plasma samples collected for biomarker analyses

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
On treatment	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups	
Reporting group title	Pazopanib 800 mg
Reporting group description:	
Pazopanib 800 mg (tablets) administered orally once a day	
Reporting group title	Placebo
Reporting group description:	
Matching Placebo administered orally once a day	

Serious adverse events	Pazopanib 800 mg	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	79 / 290 (27.24%)	28 / 145 (19.31%)	
number of deaths (all causes)	14	4	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric cancer			
subjects affected / exposed	2 / 290 (0.69%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Neoplasm			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Squamous cell carcinoma			

subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 290 (0.69%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	2 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypertensive crisis			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Deep vein thrombosis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	0 / 290 (0.00%)	2 / 145 (1.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 1	
Chest pain			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fatigue			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hernia			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pain			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pyrexia			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Sudden death			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Immune system disorders			
Anaphylactic reaction			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Reproductive system and breast disorders			
Pelvic pain			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute pulmonary oedema			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Cough			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dyspnoea			

subjects affected / exposed	6 / 290 (2.07%)	3 / 145 (2.07%)	
occurrences causally related to treatment / all	0 / 6	0 / 3	
deaths causally related to treatment / all	0 / 1	0 / 0	
Epistaxis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoptysis			
subjects affected / exposed	4 / 290 (1.38%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	2 / 4	1 / 1	
deaths causally related to treatment / all	0 / 2	0 / 0	
Pleural effusion			
subjects affected / exposed	3 / 290 (1.03%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 4	0 / 1	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pleurisy			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumothorax			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	2 / 290 (0.69%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary haemorrhage			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Confusional state			

subjects affected / exposed	2 / 290 (0.69%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	2 / 290 (0.69%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotranserase increased			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood bilirubin increased			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	2 / 290 (0.69%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	1 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood urea increased			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Electrocardiogram QT prolonged			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Haemoglobin decreased			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutrophil count decreased			

subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Femur fracture			
subjects affected / exposed	0 / 290 (0.00%)	2 / 145 (1.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Contusion			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin graft failure			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower limb fracture			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	2 / 290 (0.69%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bradycardia			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Cardiac arrest			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac failure			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Myocardial infarction			
subjects affected / exposed	3 / 290 (1.03%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Myocardial ischaemia			
subjects affected / exposed	2 / 290 (0.69%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Nervous system disorders			
Coordination abnormal			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dizziness			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Paraplegia			
subjects affected / exposed	1 / 290 (0.34%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seizure			
subjects affected / exposed	1 / 290 (0.34%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Speech disorder			

subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transient ischaemic			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebrovascular insufficiency			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ischaemic stroke			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	6 / 290 (2.07%)	4 / 145 (2.76%)	
occurrences causally related to treatment / all	7 / 9	1 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Leukopenia			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Abdominal pain			
subjects affected / exposed	2 / 290 (0.69%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain upper			
subjects affected / exposed	2 / 290 (0.69%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 3	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	6 / 290 (2.07%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	5 / 6	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Gastritis			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal obstruction			
subjects affected / exposed	2 / 290 (0.69%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Irritable bowel syndrome			

subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nausea			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Oesophageal haemorrhage			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Rectal haemorrhage			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Retroperitoneal haemorrhage			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	4 / 290 (1.38%)	2 / 145 (1.38%)	
occurrences causally related to treatment / all	2 / 4	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Enterocutaneous fistula			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anorectal varices haemorrhage			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatic function abnormal			

subjects affected / exposed	2 / 290 (0.69%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	2 / 2	0 / 1	
deaths causally related to treatment / all	2 / 2	0 / 0	
Hepatotoxicity			
subjects affected / exposed	3 / 290 (1.03%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperbilirubinaemia			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	1 / 290 (0.34%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin lesion			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal haemorrhage			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal vein thrombosis			

subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary retention			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute kidney injury			
subjects affected / exposed	0 / 290 (0.00%)	2 / 145 (1.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal pain			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pathological fracture			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Appendicitis			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Bronchopneumonia			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ear infection			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Herpes zoster			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lower respiratory tract infection			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Myelitis			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Peritonitis			
subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 290 (0.69%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 3	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Septic shock			

subjects affected / exposed	1 / 290 (0.34%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Upper respiratory tract infection			
subjects affected / exposed	0 / 290 (0.00%)	2 / 145 (1.38%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Cachexia			
subjects affected / exposed	0 / 290 (0.00%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dehydration			
subjects affected / exposed	2 / 290 (0.69%)	2 / 145 (1.38%)	
occurrences causally related to treatment / all	0 / 2	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hyperkalaemia			
subjects affected / exposed	2 / 290 (0.69%)	0 / 145 (0.00%)	
occurrences causally related to treatment / all	1 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Decreased appetite			
subjects affected / exposed	1 / 290 (0.34%)	1 / 145 (0.69%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

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

Non-serious adverse events	Pazopanib 800 mg	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	258 / 290 (88.97%)	87 / 145 (60.00%)	
Vascular disorders			
Hypertension			
subjects affected / exposed	115 / 290 (39.66%)	16 / 145 (11.03%)	
occurrences (all)	146	21	
General disorders and administration			

site conditions			
Asthenia			
subjects affected / exposed	44 / 290 (15.17%)	13 / 145 (8.97%)	
occurrences (all)	62	14	
Chest pain			
subjects affected / exposed	16 / 290 (5.52%)	2 / 145 (1.38%)	
occurrences (all)	18	2	
Fatigue			
subjects affected / exposed	58 / 290 (20.00%)	13 / 145 (8.97%)	
occurrences (all)	78	14	
Pyrexia			
subjects affected / exposed	14 / 290 (4.83%)	9 / 145 (6.21%)	
occurrences (all)	17	10	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	25 / 290 (8.62%)	14 / 145 (9.66%)	
occurrences (all)	34	14	
Dyspnoea			
subjects affected / exposed	19 / 290 (6.55%)	8 / 145 (5.52%)	
occurrences (all)	20	8	
Psychiatric disorders			
Insomnia			
subjects affected / exposed	16 / 290 (5.52%)	10 / 145 (6.90%)	
occurrences (all)	17	11	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	54 / 290 (18.62%)	4 / 145 (2.76%)	
occurrences (all)	90	4	
Aspartate aminotransferase increased			
subjects affected / exposed	46 / 290 (15.86%)	5 / 145 (3.45%)	
occurrences (all)	77	5	
Weight decreased			
subjects affected / exposed	31 / 290 (10.69%)	6 / 145 (4.14%)	
occurrences (all)	44	6	
Nervous system disorders			

Dysgeusia			
subjects affected / exposed	25 / 290 (8.62%)	1 / 145 (0.69%)	
occurrences (all)	30	1	
Headache			
subjects affected / exposed	31 / 290 (10.69%)	8 / 145 (5.52%)	
occurrences (all)	49	15	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	19 / 290 (6.55%)	7 / 145 (4.83%)	
occurrences (all)	19	11	
Neutropenia			
subjects affected / exposed	15 / 290 (5.17%)	0 / 145 (0.00%)	
occurrences (all)	22	0	
Thrombocytopenia			
subjects affected / exposed	22 / 290 (7.59%)	2 / 145 (1.38%)	
occurrences (all)	26	2	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	32 / 290 (11.03%)	2 / 145 (1.38%)	
occurrences (all)	52	2	
Abdominal pain upper			
subjects affected / exposed	24 / 290 (8.28%)	8 / 145 (5.52%)	
occurrences (all)	28	13	
Constipation			
subjects affected / exposed	20 / 290 (6.90%)	9 / 145 (6.21%)	
occurrences (all)	24	9	
Diarrhoea			
subjects affected / exposed	149 / 290 (51.38%)	13 / 145 (8.97%)	
occurrences (all)	321	15	
Dyspepsia			
subjects affected / exposed	16 / 290 (5.52%)	1 / 145 (0.69%)	
occurrences (all)	18	1	
Nausea			
subjects affected / exposed	75 / 290 (25.86%)	13 / 145 (8.97%)	
occurrences (all)	98	16	
Vomiting			

subjects affected / exposed	59 / 290 (20.34%)	12 / 145 (8.28%)	
occurrences (all)	122	13	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	24 / 290 (8.28%)	1 / 145 (0.69%)	
occurrences (all)	25	1	
Hair colour changes			
subjects affected / exposed	109 / 290 (37.59%)	5 / 145 (3.45%)	
occurrences (all)	111	5	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	17 / 290 (5.86%)	1 / 145 (0.69%)	
occurrences (all)	20	1	
Rash			
subjects affected / exposed	24 / 290 (8.28%)	4 / 145 (2.76%)	
occurrences (all)	31	6	
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	30 / 290 (10.34%)	0 / 145 (0.00%)	
occurrences (all)	47	0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	20 / 290 (6.90%)	0 / 145 (0.00%)	
occurrences (all)	22	0	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	25 / 290 (8.62%)	14 / 145 (9.66%)	
occurrences (all)	32	15	
Back pain			
subjects affected / exposed	23 / 290 (7.93%)	17 / 145 (11.72%)	
occurrences (all)	27	30	
Pain in extremity			
subjects affected / exposed	20 / 290 (6.90%)	9 / 145 (6.21%)	
occurrences (all)	24	11	
Metabolism and nutrition disorders			
Decreased appetite			

subjects affected / exposed occurrences (all)	70 / 290 (24.14%) 93	17 / 145 (11.72%) 17	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
31 January 2006	Am 01: To clarify determination on objective disease progression and to provide other minor clarifications to the protocol.
22 March 2006	Am 02: Minor changes in clinical visit schedules and other minor clarifications to the protocol.
09 May 2006	Am 03: Major changes include: expansion of subject population, inclusion of pazopanib as a post-progression treatment option, revisions to the interim analysis.
07 August 2006	Am 04: Revision in inclusion criteria #5 for subject population
23 May 2007	Am 05: Addition of new medical monitors for the study. Update on pazopanib safety and efficacy. Addition of detailed instruction for dose modification for liver toxicity and minor revision on sensitivity analysis.
01 May 2012	Am 06: Study has reported primary and key secondary objectives. Discontinue collection of many study-specific assessments while allowing subjects on treatment with pazopanib to have continued access until occurrence of unacceptable toxicity, disease progression, or other reason for withdrawal from treatment. Data collected will include serious adverse events, pregnancies, adverse events (AEs) leading to discontinuation of investigational product, and other significant AEs.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported