Clinical trial results:
A randomized double-blind cross-over patient preference study of pazopanib vs. sunitinib in-treatment naïve locally advanced or metastatic renal cell carcinoma

Summary

EudraCT number	2009-014249-10
Trial protocol	FI DE IT GB
Global end of trial date	23 November 2015

Results information

Result version number	v1 (current)
This version publication date	09 December 2016
First version publication date	09 December 2016

Trial information

Trial identification

Sponsor protocol code	VEG113046

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01064310
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharmaceuticals
Sponsor organisation address	CH - 4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharmaceuticals, 41 613241111,
Scientific contact	Clinical Disclosure Office, Novartis Pharmaceuticals, 41 613241111,

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	23 November 2015
Is this the analysis of the primary completion data?	Yes
Primary completion date	23 November 2015
Global end of trial reached?	Yes
Global end of trial date	23 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of the study was to assess how the tolerability and safety differences between pazopanib and sunitinib translated into patient preference, defined by the patient's stated preference for which drug they prefered.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	17 May 2010
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	France: 61
Country: Number of subjects enrolled	Italy: 40
Country: Number of subjects enrolled	United Kingdom: 37
Country: Number of subjects enrolled	Germany: 16
Country: Number of subjects enrolled	Finland: 14
Worldwide total number of subjects	168
EEA total number of subjects	168

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)	0
From 65 to 84 years	168
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

There were169 participants randomized and one participant randomized in error with no data available. Eighty-four patients entered open label pazopinib follow up until withdrawal for toxicity (12), disease progression (51),physician decision (20), subject decision (1). No new patients were added.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Sunitinib 50 mg followed by pazopanib 800 mg

Arm description:

Period 1: Participants received 4 overencapsulated capsules of sunitinib, each containing 12.5 milligrams (mg) of sunitinib, once daily (OD) orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Period 1 was followed by a 2-week wash-out period in which no treatment was given. Period 2: Participants received 4 overencapsulated tablets of pazopanib, each containing 200 mg of pazopanib, OD orally for 10 weeks. Study drugs were taken without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drugs were taken remained relatively constant.

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

Dosage and administration details:

Participants received 4 overencapsulated capsules of sunitinib, each containing 12.5 milligrams (mg) of sunitinib, once daily (OD) orally for 4 weeks

Investigational medicinal product name	pazopanib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Pazopanib 800 mg followed by sunitinib 50 mg

Arm title	Pazopanib 800 mg followed by sunitinib 50 mg

Arm description:

Period 1: Participants received 4 overencapsulated tablets of pazopanib, each containing 200 mg of pazopanib, OD orally for 10 weeks. Period 1 was followed by a 2-week wash-out period in which no treatment was given. Period2: Participants received 4 overencapsulated capsules of sunitinib, each containing 12.5 mg of sunitinib, OD orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Study drugs were taken without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drugs were taken remained relatively constant.

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

Dosage and administration details:

Pazopanib 800 mg followed by sunitinib 50 mg

Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received 4 overencapsulated capsules of sunitinib, each containing 12.5 milligrams (mg) of sunitinib, once daily (OD) orally for 4 weeks

Number of subjects in period 1	Sunitinib 50 mg followed by pazopanib 800 mg	Pazopanib 800 mg followed by sunitinib 50 mg
Started	82	86
Completed	68	68
Not completed	14	18
Consent withdrawn by subject	2	2
Physician decision	1	-
Adverse event, non-fatal	7	10
Lack of efficacy	3	5
Entered Open-label Period	1	1

Period 2

Period 2 title	Period 2
Is this the baseline period?	No
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Carer, Data analyst, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Sunitinib 50 mg followed by pazopanib 800 mg

Arm description:

Period 1: Participants received 4 overencapsulated capsules of sunitinib, each containing 12.5 milligrams (mg) of sunitinib, once daily (OD) orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Period 1 was followed by a 2-week wash-out period in which no treatment was given. Period 2: Participants received 4 overencapsulated tablets of pazopanib, each containing 200 mg of pazopanib, OD orally for

10 weeks. Study drugs were taken without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drugs were taken remained relatively constant.

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

Dosage and administration details:

Pazopanib 800 mg followed by sunitinib 50 mg

Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received 4 overencapsulated capsules of sunitinib, each containing 12.5 milligrams (mg) of sunitinib, once daily (OD) orally for 4 weeks

Arm title	Pazopanib 800 mg followed by sunitinib 50 mg

Arm description:

Period 1: Participants received 4 overencapsulated tablets of pazopanib, each containing 200 mg of pazopanib, OD orally for 10 weeks. Period 1 was followed by a 2-week wash-out period in which no treatment was given. Period2: Participants received 4 overencapsulated capsules of sunitinib, each containing 12.5 mg of sunitinib, OD orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Study drugs were taken without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drugs were taken remained relatively constant.

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

Dosage and administration details:

Pazopanib 800 mg followed by sunitinib 50 mg

Investigational medicinal product name	Sunitinib
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

Participants received 4 overencapsulated capsules of sunitinib, each containing 12.5 milligrams (mg) of sunitinib, once daily (OD) orally for 4 weeks

Number of subjects in period 2	Sunitinib 50 mg followed by pazopanib 800 mg	Pazopanib 800 mg followed by sunitinib 50 mg
Started	68	68
Completed	64	62
Not completed	4	6
Physician decision	-	1
Adverse event, non-fatal	2	1
Lack of efficacy	1	4
Entered Open-label Period	1	-

Baseline characteristics

Reporting groups

Reporting group title	Sunitinib 50 mg followed by pazopanib 800 mg

Reporting group description:

Period 1: Participants received 4 overencapsulated capsules of sunitinib, each containing 12.5 milligrams (mg) of sunitinib, once daily (OD) orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Period 1 was followed by a 2-week wash-out period in which no treatment was given. Period 2: Participants received 4 overencapsulated tablets of pazopanib, each containing 200 mg of pazopanib, OD orally for 10 weeks. Study drugs were taken without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drugs were taken remained relatively constant.

Reporting group title	Pazopanib 800 mg followed by sunitinib 50 mg

Reporting group description:

Period 1: Participants received 4 overencapsulated tablets of pazopanib, each containing 200 mg of pazopanib, OD orally for 10 weeks. Period 1 was followed by a 2-week wash-out period in which no treatment was given. Period2: Participants received 4 overencapsulated capsules of sunitinib, each containing 12.5 mg of sunitinib, OD orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Study drugs were taken without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drugs were taken remained relatively constant.

Reporting group values	Sunitinib 50 mg followed by pazopanib 800 mg	Pazopanib 800 mg followed by sunitinib 50 mg	Total
Number of subjects	82	86	168
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	46	48	94
From 65-84 years	36	38	74
85 years and over	0	0	0
Age continuous Units: years			
arithmetic mean	62.1	62.2	
standard deviation	± 9.56	± 11.35	-
Gender categorical Units: Subjects			
Female	30	25	55
Male	52	61	113
RaceEthnicityOther Units: Subjects			
African American/African Heritage	1	0	1
Asian-Central/South Asian Heritage	1	0	1
White	74	83	157

Missing	6	3	9

End points

End points reporting groups

Reporting group title	Sunitinib 50 mg followed by pazopanib 800 mg

Reporting group description:

Period 1: Participants received 4 overencapsulated capsules of sunitinib, each containing 12.5 milligrams (mg) of sunitinib, once daily (OD) orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Period 1 was followed by a 2-week wash-out period in which no treatment was given. Period 2: Participants received 4 overencapsulated tablets of pazopanib, each containing 200 mg of pazopanib, OD orally for 10 weeks. Study drugs were taken without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drugs were taken remained relatively constant.

Reporting group title	Pazopanib 800 mg followed by sunitinib 50 mg

Reporting group description:

Period 1: Participants received 4 overencapsulated tablets of pazopanib, each containing 200 mg of pazopanib, OD orally for 10 weeks. Period 1 was followed by a 2-week wash-out period in which no treatment was given. Period2: Participants received 4 overencapsulated capsules of sunitinib, each containing 12.5 mg of sunitinib, OD orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Study drugs were taken without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drugs were taken remained relatively constant.

Reporting group title	Sunitinib 50 mg followed by pazopanib 800 mg

Reporting group description:

Period 1: Participants received 4 overencapsulated capsules of sunitinib, each containing 12.5 milligrams (mg) of sunitinib, once daily (OD) orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Period 1 was followed by a 2-week wash-out period in which no treatment was given. Period 2: Participants received 4 overencapsulated tablets of pazopanib, each containing 200 mg of pazopanib, OD orally for 10 weeks. Study drugs were taken without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drugs were taken remained relatively constant.

Reporting group title	Pazopanib 800 mg followed by sunitinib 50 mg

Reporting group description:

Period 1: Participants received 4 overencapsulated tablets of pazopanib, each containing 200 mg of pazopanib, OD orally for 10 weeks. Period 1 was followed by a 2-week wash-out period in which no treatment was given. Period2: Participants received 4 overencapsulated capsules of sunitinib, each containing 12.5 mg of sunitinib, OD orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Study drugs were taken without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drugs were taken remained relatively constant.

Subject analysis set title	Sunitinib
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received 4 overencapsulated capsules of sunitinib (either in Period 1 or Period 2), each containing 12.5 mg of sunitinib, OD orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Study drug was taken orally OD without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drug was taken remained relatively constant.

Subject analysis set title	Pazopanib
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received 4 overencapsulated tablets of pazopanib (either in Period 1 or Period 2), each containing 200 mg of pazopanib, OD orally for 10 weeks. Study drug was taken orally OD without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drug was taken remained relatively constant.

Subject analysis set title	Sunitinib

Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received 4 overencapsulated capsules of sunitinib (either in Period 1 or Period 2), each containing 12.5 mg of sunitinib, OD orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Study drug was taken orally OD without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drug was taken remained relatively constant.

Subject analysis set title	Pazopanib
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received 4 overencapsulated tablets of pazopanib (either in Period 1 or Period 2), each containing 200 mg of pazopanib, OD orally for 10 weeks. Study drug was taken orally OD without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drug was taken remained relatively constant.

Subject analysis set title	Sunitinib
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received 4 overencapsulated capsules of sunitinib (either in Period 1 or Period 2), each containing 12.5 mg of sunitinib, OD orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Study drug was taken orally OD without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drug was taken remained relatively constant.

Subject analysis set title	Pazopanib
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received 4 overencapsulated tablets of pazopanib (either in Period 1 or Period 2), each containing 200 mg of pazopanib, OD orally for 10 weeks. Study drug was taken orally OD without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drug was taken remained relatively constant.

Subject analysis set title	Sunitinib
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received 4 overencapsulated capsules of sunitinib (either in Period 1 or Period 2), each containing 12.5 mg of sunitinib, OD orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Study drug was taken orally OD without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drug was taken remained relatively constant.

Subject analysis set title	Pazopanib
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received 4 overencapsulated tablets of pazopanib (either in Period 1 or Period 2), each containing 200 mg of pazopanib, OD orally for 10 weeks. Study drug was taken orally OD without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drug was taken remained relatively constant.

Subject analysis set title	Sunitinib
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received 4 overencapsulated capsules of sunitinib (either in Period 1 or Period 2), each containing 12.5 mg of sunitinib, OD orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Study drug was taken orally OD without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drug was taken remained relatively constant.

Subject analysis set title	Pazopanib
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received 4 overencapsulated tablets of pazopanib (either in Period 1 or Period 2), each

containing 200 mg of pazopanib, OD orally for 10 weeks. Study drug was taken orally OD without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drug was taken remained relatively constant.

Subject analysis set title	Sunitinib
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received 4 overencapsulated capsules of sunitinib (either in Period 1 or Period 2), each containing 12.5 mg of sunitinib, OD orally for 4 weeks, followed by 2 weeks off treatment (matching placebo capsules to maintain blind), followed by 50 mg (4 x 12.5 mg) OD orally for 4 weeks. Study drug was taken orally OD without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drug was taken remained relatively constant.

Subject analysis set title	Pazopanib
Subject analysis set type	Sub-group analysis

Subject analysis set description:

Participants received 4 overencapsulated tablets of pazopanib (either in Period 1 or Period 2), each containing 200 mg of pazopanib, OD orally for 10 weeks. Study drug was taken orally OD without food at least one hour before or two hours after a meal. The capsules were swallowed whole and not crushed or broken. The time of day the study drug was taken remained relatively constant.

Primary: Number of participants with preference for pazopanib versus sunitinib as assessed by the patient preference questionnaire (PPQ)

End point title	Number of participants with preference for pazopanib versus sunitinib as assessed by the patient preference questionnaire (PPQ)

End point description:

The PPQ is used to measure participants' preference for pazopanib or sunitinib for renal cell carcinoma management and is used to determine a participant's preference for 1 of the 2 drugs given in the 2 double-blind treatment periods. Participants were asked to select 1 of the following: 1. prefer the drug taken as the first treatment; 2. prefer the drug taken as the second treatment; or 3, no preference. Those participants who indicated a preference were asked to select the factors that had an influence on their treatment preference, as well as the most important reason for their preference.

End point type	Primary

End point timeframe:

End of treatment of both study drugs (maximum of 22 weeks)

End point values	Sunitinib 50 mg followed by pazopanib 800 mg	Pazopanib 800 mg followed by sunitinib 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	60	54		
Units: participants				
Sunitinib	19	6		
Pazopanib	37	43		
No preference	4	5		

Statistical analyses

Statistical analysis title	difference in preference
Comparison groups	Sunitinib 50 mg followed by pazopanib 800 mg v Pazopanib 800 mg followed by sunitinib 50 mg

Number of subjects included in analysis	114
Analysis specification	Pre-specified
Analysis type	
P-value	< 0.001 [1]
Method	Prescotts test
Parameter estimate	Percentage of participants
Point estimate	49.26
Confidence interval	
level	90 %
sides	2-sided
lower limit	37
upper limit	61.5

Notes:

[1] - The p value indicates the difference in preference for pazopanib versus sunitinib treatment

Primary: Number of participants answering "yes," "no," or not applicable (N/A) to the question of whether the indicated factors influenced their preference for sunitinib or pazopanib treatment as assessed by the patient preference questionnaire

End point title	Number of participants answering "yes," "no," or not applicable (N/A) to the question of whether the indicated factors influenced their preference for sunitinib or pazopanib treatment as assessed by the patient preference questionnaire[2]

End point description:

The PPQ is used to measure participants' preference for pazopanib or sunitinib for renal cell carcinoma management and is used to determine a participant's preference for 1 of the 2 drugs given in the 2 double-blind treatment periods. Participants were asked to select 1 of the following: 1. prefer the drug taken as the first treatment; 2. prefer the drug taken as the second treatment; or 3, no preference. Those participants who indicated a preference were asked to select the factors that had an influence on their treatment preference, as well as the most important reason for their preference. No statistical analysis was performed for this endpoint.

End point type	Primary

End point timeframe:

End of treatment of both study drugs (maximum of 22 weeks)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No statistical analysis was performed for this endpoint.

End point values	Sunitinib	Pazopanib		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	25	80		
Units: participants				
Fatigue had less impact on life, Yes	12	47		
Fatigue had less impact on life, No	8	26		
Fatigue had less impact on life, not applicable (N	5	6		
Soreness in hands/feet had less impact, Yes	6	30		
Soreness in hands/feet had less impact, No	7	22		
Soreness in hands/feet had less impact, NA	12	28		
Soreness in mouth/throat had less impact, Yes	6	32		

Soreness in mouth/throat had less impact, No	8	25		
Soreness in mouth/throat had less impact, NA	11	23		
Loss of appetite had less impact, Yes	10	28		
Loss of appetite had less impact, No	8	28		
Loss of appetite had less impact, NA	7	22		
Change in hair color had less impact, Yes	5	9		
Change in hair color had less impact, No	11	51		
Change in hair color had less impact, NA	9	20		
Nausea/vomiting had less impact, Yes	11	32		
Nausea/vomiting had less impact, No	7	30		
Nausea/vomiting had less impact, NA	7	17		
Diarrhea had less impact, Yes	16	21		
Diarrhea had less impact, No	5	44		
Diarrhea had less impact, NA	4	15		
Pain in stomach area had less impact, Yes	9	23		
Pain in stomach area had less impact, No	4	30		
Pain in stomach area had less impact, NA	12	27		
Changes in food tastes had less impact, Yes	5	44		
Changes in food tastes had less impact, No	14	23		
Changes in food tastes had less impact, NA	6	12		
Quality of life better, Yes	15	65		
Quality of life better, No	6	12		
Quality of life better, NA	4	2		
Other, Yes	5	14		
Other, No	0	0		
Other, NA	20	66		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from Period Baseline (BL) in fatigue as assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) score

End point title	Change from Period Baseline (BL) in fatigue as assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue) score

End point description:

Change from period (P) BL is computed as participants' (par.) average post-BL fatigue score within each P minus their P-specific BL score. P 1 BL is the P 1 Pre-Dose assessment; P 2 BL is the wash-out assessment. Crossover analyses compared par. average scores on each treatment, adjusting for sequence. FACIT-Fatigue Scale: overall score (0 to 52)=the sum of scores for 13 questions. For each question, par. rated their condition for the past week on a 5-point scale: 0 (not at all) to 4 (very much). A high score indicates low fatigue. A negative change from BL represents a worsening of condition.

End point type	Secondary

End point timeframe:

Day 1 (Period [P] 1 Pre-dose); Weeks 2, 4, 6, 8, and 10 of P 1; during 2-week Wash-out Period (Study Weeks 11 and 12); Weeks 2, 4, 6, and 8 of P 2 (Study Weeks 14, 16, 18, 20, and 22, respectively); End of Study (Week 10 of P 2 [Study Week 22])

End point values	Sunitinib 50 mg followed by pazopanib 800 mg	Pazopanib 800 mg followed by sunitinib 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	77	79		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Period 1 Average; n=77, 79	-4.4 (± 7.73)	-4.6 (± 9.22)		
Period 2 Average; n=63, 65	-3.6 (± 7.11)	-7.3 (± 11.16)		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of life as assessed by the EuroQoL-5 Dimensions (EQ-5D) thermometer and utility scores

End point title	Quality of life as assessed by the EuroQoL-5 Dimensions (EQ-5D) thermometer and utility scores

End point description:

The EQ-5D is a participant-answered questionnaire measuring 5 dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. The EQ-5D has two separate components: utility score and thermometer score. The EQ-5D total utility score ranges from 0 (worst health state) to 1 (perfect health state); 1 reflects the best outcome. The thermometer score ranges from 0 (worst imaginable health state) to 100 (best imaginable health state).

End point type	Secondary

End point timeframe:

Day 1 (Period 1 Pre-dose); during 2-week Wash-out Period (Study Weeks 11 and 12); and End of Study (Week 10 of Period 2 [Study Week 22])

End point values	Sunitinib 50 mg followed by pazopanib 800 mg	Pazopanib 800 mg followed by sunitinib 50 mg		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	80	86		
Units: Scores on a scale				
arithmetic mean (standard deviation)				
Thermometer Score, Day 1; n=74, 79	75.7 (± 17.65)	74.8 (± 18.54)		
Thermometer Score, Washout; n=60, 63	74.4 (± 16.76)	69.8 (± 19.94)		
Thermometer Score, End of Study; n=51, 45	71.3 (± 16.19)	65.1 (± 22.55)		

Utility Score, Day 1; n=76, 81	0.7625 (± 0.25331)	0.7664 (± 0.22946)		
Utility Score, Washout; n=61, 67	0.8103 (± 0.20776)	0.7595 (± 0.26826)		
Utility Score, End of Study; n=52, 47	0.7487 (± 0.21324)	0.6325 (± 0.29635)		

Statistical analyses

No statistical analyses for this end point

Secondary: Time to dose modification

End point title	Time to dose modification

End point description:

For the subset of participants who had a dose modification, time to dose modification was defined as the time from the first dose in each period until the first reduction in dose within a period.

End point type	Secondary

End point timeframe:

End of second treatment period (maximum of 22 weeks)

End point values	Sunitinib	Pazopanib		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	20		
Units: weeks				
median (confidence interval 95%)	3.7 (2.7 to 5.9)	4 (2.1 to 6)		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated number of dose reductions

End point title	Number of participants with the indicated number of dose reductions

End point description:

Participants are recorded under the treatment they were receiving at the time the dose reduction was reported.

End point type	Secondary

End point timeframe:

End of second treatment period (maximum of 22 weeks)

End point values	Sunitinib	Pazopanib		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	20		
Units: participants				
1 dose reduction	16	8		
2 dose reductions	10	11		
3 or more dose reductions	4	1		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated reason for receiving a dose reduction

End point title	Number of participants with the indicated reason for receiving a dose reduction

End point description:

Dose reduction of study drug was a stepwise reduction of the dose of the study drug: one less capsule was received at each step reduction. Participants were monitored for approximately 10 to 14 days at each dose level. Participants are recorded under the treatment they were receiving at the time the dose reduction was reported.

End point type	Secondary

End point timeframe:

End of second treatment period (maximum of 22 weeks)

End point values	Sunitinib	Pazopanib		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	30	20		
Units: participants				
Adverse Event	46	33		
Other	3	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with Grade 1 to Grade 5 adverse events (AEs)

End point title	Number of participants with Grade 1 to Grade 5 adverse events (AEs)

End point description:

AEs were graded using the Common Toxicity Criteria from the Cancer Therapy Evaluation Program, Division of Cancer Therapy, National Cancer Institute. Grades: 0 = No AE or within normal limits; 1 = Mild AE; 2 = Moderate AE; 3 = Severe and undesirable AE; 4 = Life-threatening or disabling AE; 5 = Death related to AE.

End point type	Secondary

End point timeframe:

Baseline to end of study (maximum of 22 weeks)

End point values	Sunitinib	Pazopanib		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	148	153		
Units: participants				
Grade 0	0	0		
Grade 1	20	25		
Grade 2	57	63		
Grade 3	58	51		
Grade 4	11	8		
Grade 5	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of participants with the indicated AEs leading to permanent discontinuation of study treatment

End point title	Number of participants with the indicated AEs leading to permanent discontinuation of study treatment

End point description:

An AE is any untoward medical occurrence in a participant administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment. An AE that spans more than one period is considered to be an AE for each period during which the AE increased in grade. There is only one action with respect to study drug recorded for the whole event. As such, it is not always possible to determine in which study period treatment was discontinued due to the AE.

End point type	Secondary

End point timeframe:

Baseline to end of study (maximum of 22 weeks)

End point values	Sunitinib	Pazopanib		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	38	25		
Units: participants				
Fatigue	5	3		
Alanine aminotransferase increased	2	4		
Vomiting	1	3		
Aspartate aminotransferase increased	0	3		
Diarrhoea	1	2		
Thrombocytopenia	3	0		
Acute myocardial infarction	1	1		
Asthenia	2	0		

Back pain	1	1		
Dyspnoea	2	0		
Epistaxis	2	0		
Hypertension	2	0		
Nasal congestion	1	1		
Pleural effusion	2	0		
Transient ischaemic attack	0	2		
Atrial flutter	0	1		
Blood potassium decreased	1	0		
Cardiac disorder	0	1		
Cardiac failure	0	1		
Cough	1	0		
Decreased appetite	1	0		
Dizziness	0	1		
Dysgeusia	0	1		
Haematemesis	0	1		
Haematoma	1	0		
Haematuria	1	0		
Haemorrhage intracranial	1	0		
Headache	1	0		
Hepatic function abnormal	0	1		
Hepatotoxicity	0	1		
Infection	1	0		
Infectious peritonitis	0	1		
Influenza	1	0		
Influenza like illness	1	0		
Mucosal inflammation	1	0		
Myocardial ischaemia	0	1		
Nausea	0	1		
Neutropenic infection	1	0		
Ovarian cyst	1	0		
Pain in extremity	1	0		
Palmar-plantar erythrodysaesthesia syndrome	1	0		
Pancytopenia	1	0		
Proteinuria	0	1		
Pyrexia	1	0		
Rash	0	1		
Renal failure	1	0		
Respiratory failure	0	1		
Sinusitis	1	0		
Skin ulcer	0	1		
Spinal cord compression	0	1		
Stomatitis	1	0		
Tooth infection	1	0		
Transaminases increased	1	0		
Urine protein/creatinine ratio decreased	1	0		
Weight decreased	1	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline (BL) in systolic blood pressure (SBP) and diastolic BP (DBP)

End point title	Change from baseline (BL) in systolic blood pressure (SBP) and diastolic BP (DBP)

End point description:

When the heart beats, it contracts and pushes blood through the arteries to the rest of body. This force creates pressure on the arteries called SBP. DBP is the pressure in the arteries when the heart rests between beats. Normal levels: SBP (120 mmHg or less); DBP (80 mmHg or less). Mean change from BL for each assessment week was calculated as the average change from period BL at the specified visits (combining data across P 1 and 2 for Weeks 2 and 6). Study weeks are approximate; participants could have crossed over from P 1 to P 2 at earlier time points than specified in the protocol.

End point type	Secondary

End point timeframe:

Baseline of Period (P) 1 (Screening); Period 1 Weeks 2 and 6 (Study Weeks 2 and 6); Baseline of Period 2 (Washout=Study Week 12); Period 2 Weeks 2, 6, and 10 (Study Weeks 14, 18, and 22)

End point values	Sunitinib	Pazopanib		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	139	147		
Units: Millimeters of mercury (mmHg)				
arithmetic mean (standard deviation)				
SBP, Week 2; n=139, 147	6.3 (± 15.26)	7.5 (± 16.36)		
SBP, Week 6; n=109, 134	-0.4 (± 18.65)	7.5 (± 17.21)		
SBP, Week 10; n=61, 64	4.5 (± 18.43)	4.7 (± 20.45)		
DBP, Week 2; n=139, 147	6.5 (± 9.91)	6.5 (± 10.49)		
DBP, Week 6; n=109, 134	-0.4 (± 9.48)	6.9 (± 10.87)		
DBP, Week 10; n=61, 64	3.1 (± 10.69)	5.6 (± 11.44)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change from baseline (BL) in heart rate

End point title	Change from baseline (BL) in heart rate

End point description:

Heart rate (HR) is the number of heartbeats per unit of time, typically expressed as beats per minute. HR can vary as the body's need to absorb oxygen and excrete carbon dioxide changes, such as during exercise or sleep. A normal resting HR ranges from 60 to 100 beats per minute. Mean change from BL for each assessment week was calculated as the average change from period BL at the specified visits (combining data across P 1 and 2 for Weeks 2 and 6). Study weeks are approximate; participants could have crossed over from P 1 to P 2 at earlier time points than specified in the protocol.

End point type	Secondary

End point timeframe:

Baseline of Period (P) 1 (Screening); Period 1 Weeks 2 and 6 (Study Weeks 2 and 6); Baseline of Period 2 (Washout=Study Week 12); Period 2 Weeks 2, 6, and 10 (Study Weeks 14, 18, and 22)

End point values	Sunitinib	Pazopanib		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	137	145		
Units: Beats per minute				
arithmetic mean (standard deviation)				
Week 2, n=137, 145	-3.1 (± 12.39)	-2.7 (± 13.09)		
Week 6, n=106, 131	0.8 (± 11.43)	-3.3 (± 12.41)		
Week 10, n=60, 64	-3.8 (± 13.54)	-1.8 (± 13.84)		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events are collected from First Patient First Visit (FPFV) until Last Patient Last Visit (LPLV). All Adverse Events are reported in this record from First Patient First Treatment until Last Patient Last Visit.

Adverse event reporting additional description:

Consistent with EudraCT disclosure specifications, Novartis has reported under the Serious Adverse Events field "number of deaths resulting from adverse events" all those deaths, resulting from serious adverse events that are deemed to be causally related to treatment by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	19.0

Reporting groups

Reporting group title	Pazopanib

Reporting group description:

Pazopanib

Reporting group title	Sunitinib

Reporting group description:

Sunitinib

Reporting group title	Open Label Pazopanib

Reporting group description:

Open Label Pazopanib

Serious adverse events	Pazopanib	Sunitinib	Open Label Pazopanib
Total subjects affected by serious adverse events			
subjects affected / exposed	30 / 153 (19.61%)	35 / 148 (23.65%)	15 / 84 (17.86%)
number of deaths (all causes)	4	5	3
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastases to bone			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metastases to central nervous system			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Tumour haemorrhage			

subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Vascular disorders			
Haematoma			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Hypertension			
subjects affected / exposed	3 / 153 (1.96%)	2 / 148 (1.35%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	8 / 8	4 / 4	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 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Fatigue			
subjects affected / exposed	2 / 153 (1.31%)	3 / 148 (2.03%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	4 / 4	3 / 3	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General physical health deterioration			
subjects affected / exposed	0 / 153 (0.00%)	3 / 148 (2.03%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 4	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Mucosal inflammation			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Oedema			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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

Oedema peripheral			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Performance status decreased			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Pyrexia			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Respiratory, thoracic and mediastinal disorders			
Bronchial obstruction			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Dyspnoea			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Epistaxis			
subjects affected / exposed	0 / 153 (0.00%)	2 / 148 (1.35%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	3 / 3	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pleural effusion			

subjects affected / exposed	1 / 153 (0.65%)	2 / 148 (1.35%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pulmonary embolism			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Respiratory failure			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Psychiatric disorders			
Disorientation			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 153 (1.96%)	2 / 148 (1.35%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	5 / 5	4 / 4	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Aspartate aminotransferase increased			
subjects affected / exposed	2 / 153 (1.31%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	5 / 5	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood bilirubin increased			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 5	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gamma-glutamyltransferase increased			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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

Lipase abnormal			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Injury, poisoning and procedural complications			
Incisional hernia			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tibia fracture			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Tracheal obstruction			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Upper limb fracture			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Cardiac disorders			
Acute myocardial infarction			
subjects affected / exposed	1 / 153 (0.65%)	1 / 148 (0.68%)	0 / 84 (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
Angina pectoris			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Atrial flutter			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Cardiac failure			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Myocardial ischaemia			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Dysgeusia			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Epilepsy			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Haemorrhage intracranial			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Hemiparesis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Partial seizures			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sciatica			

subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Spinal cord compression			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Transient ischaemic attack			
subjects affected / exposed	2 / 153 (1.31%)	0 / 148 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	2 / 2	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	2 / 153 (1.31%)	3 / 148 (2.03%)	2 / 84 (2.38%)
occurrences causally related to treatment / all	1 / 2	0 / 4	1 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancytopenia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Thrombocytopenia			
subjects affected / exposed	0 / 153 (0.00%)	3 / 148 (2.03%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	7 / 7	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Retinal detachment			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Anal fissure			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Anal fistula			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Diarrhoea			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Hiatus hernia			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nausea			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Rectal haemorrhage			
subjects affected / exposed	0 / 153 (0.00%)	2 / 148 (1.35%)	0 / 84 (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
Stomatitis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Vomiting			
subjects affected / exposed	1 / 153 (0.65%)	1 / 148 (0.68%)	0 / 84 (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
Hepatobiliary disorders			
Cholelithiasis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatic function abnormal			

subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Hepatotoxicity			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Renal and urinary disorders			
Haematuria			
subjects affected / exposed	1 / 153 (0.65%)	2 / 148 (1.35%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 2	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Ureteric obstruction			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Urinary retention			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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			
Back pain			
subjects affected / exposed	1 / 153 (0.65%)	1 / 148 (0.68%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 1	1 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Bone pain			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal chest pain			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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

Osteoarthritis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pain in extremity			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Infections and infestations			
Abdominal abscess			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Biliary sepsis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Colonic abscess			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	2 / 2
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Infection			
subjects affected / exposed	0 / 153 (0.00%)	2 / 148 (1.35%)	0 / 84 (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
Lung infection			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Neutropenic infection			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Oral candidiasis			

subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	1 / 1	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Peritonitis			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (0.00%)
occurrences causally related to treatment / all	0 / 3	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pneumonia			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sepsis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	1 / 84 (1.19%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Sinusitis			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Urinary tract infection			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 153 (0.65%)	0 / 148 (0.00%)	0 / 84 (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
Hyponatraemia			
subjects affected / exposed	0 / 153 (0.00%)	1 / 148 (0.68%)	0 / 84 (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

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

Non-serious adverse events	Pazopanib	Sunitinib	Open Label Pazopanib
Total subjects affected by non-serious adverse events			
subjects affected / exposed	142 / 153 (92.81%)	143 / 148 (96.62%)	73 / 84 (86.90%)
Vascular disorders			
Hypertension			
subjects affected / exposed	32 / 153 (20.92%)	37 / 148 (25.00%)	13 / 84 (15.48%)
occurrences (all)	44	52	33
General disorders and administration site conditions			
Asthenia			
subjects affected / exposed	26 / 153 (16.99%)	35 / 148 (23.65%)	16 / 84 (19.05%)
occurrences (all)	34	51	23
Fatigue			
subjects affected / exposed	43 / 153 (28.10%)	42 / 148 (28.38%)	25 / 84 (29.76%)
occurrences (all)	71	69	62
Mucosal inflammation			
subjects affected / exposed	25 / 153 (16.34%)	32 / 148 (21.62%)	6 / 84 (7.14%)
occurrences (all)	27	51	8
Pyrexia			
subjects affected / exposed	5 / 153 (3.27%)	10 / 148 (6.76%)	1 / 84 (1.19%)
occurrences (all)	5	11	1
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	6 / 153 (3.92%)	10 / 148 (6.76%)	5 / 84 (5.95%)
occurrences (all)	6	11	5
Dysphonia			
subjects affected / exposed	7 / 153 (4.58%)	2 / 148 (1.35%)	6 / 84 (7.14%)
occurrences (all)	7	2	7
Dyspnoea			
subjects affected / exposed	12 / 153 (7.84%)	7 / 148 (4.73%)	6 / 84 (7.14%)
occurrences (all)	12	10	7
Epistaxis			
subjects affected / exposed	8 / 153 (5.23%)	15 / 148 (10.14%)	7 / 84 (8.33%)
occurrences (all)	11	19	9

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	9 / 153 (5.88%)	5 / 148 (3.38%)	7 / 84 (8.33%)
occurrences (all)	13	6	12
Blood creatinine increased			
subjects affected / exposed	2 / 153 (1.31%)	5 / 148 (3.38%)	5 / 84 (5.95%)
occurrences (all)	2	5	12
Blood thyroid stimulating hormone increased			
subjects affected / exposed	0 / 153 (0.00%)	2 / 148 (1.35%)	5 / 84 (5.95%)
occurrences (all)	0	2	6
Weight decreased			
subjects affected / exposed	9 / 153 (5.88%)	7 / 148 (4.73%)	9 / 84 (10.71%)
occurrences (all)	12	8	9
Nervous system disorders			
Dysgeusia			
subjects affected / exposed	25 / 153 (16.34%)	40 / 148 (27.03%)	12 / 84 (14.29%)
occurrences (all)	28	45	14
Headache			
subjects affected / exposed	22 / 153 (14.38%)	17 / 148 (11.49%)	7 / 84 (8.33%)
occurrences (all)	33	20	9
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	4 / 153 (2.61%)	5 / 148 (3.38%)	5 / 84 (5.95%)
occurrences (all)	4	8	5
Neutropenia			
subjects affected / exposed	6 / 153 (3.92%)	8 / 148 (5.41%)	4 / 84 (4.76%)
occurrences (all)	9	19	10
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	20 / 153 (13.07%)	16 / 148 (10.81%)	11 / 84 (13.10%)
occurrences (all)	25	19	17
Abdominal pain upper			
subjects affected / exposed	7 / 153 (4.58%)	19 / 148 (12.84%)	8 / 84 (9.52%)
occurrences (all)	10	19	8
Constipation			

subjects affected / exposed	13 / 153 (8.50%)	23 / 148 (15.54%)	10 / 84 (11.90%)
occurrences (all)	13	31	10
Diarrhoea			
subjects affected / exposed	63 / 153 (41.18%)	49 / 148 (33.11%)	45 / 84 (53.57%)
occurrences (all)	106	64	130
Dyspepsia			
subjects affected / exposed	17 / 153 (11.11%)	23 / 148 (15.54%)	6 / 84 (7.14%)
occurrences (all)	18	28	7
Flatulence			
subjects affected / exposed	10 / 153 (6.54%)	5 / 148 (3.38%)	5 / 84 (5.95%)
occurrences (all)	10	5	5
Haemorrhoids			
subjects affected / exposed	3 / 153 (1.96%)	10 / 148 (6.76%)	1 / 84 (1.19%)
occurrences (all)	4	14	1
Nausea			
subjects affected / exposed	50 / 153 (32.68%)	46 / 148 (31.08%)	26 / 84 (30.95%)
occurrences (all)	62	57	42
Stomatitis			
subjects affected / exposed	7 / 153 (4.58%)	22 / 148 (14.86%)	5 / 84 (5.95%)
occurrences (all)	7	31	8
Vomiting			
subjects affected / exposed	21 / 153 (13.73%)	26 / 148 (17.57%)	18 / 84 (21.43%)
occurrences (all)	30	31	38
Hepatobiliary disorders			
Jaundice			
subjects affected / exposed	0 / 153 (0.00%)	8 / 148 (5.41%)	0 / 84 (0.00%)
occurrences (all)	0	10	0
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	11 / 153 (7.19%)	6 / 148 (4.05%)	6 / 84 (7.14%)
occurrences (all)	11	7	6
Dry skin			
subjects affected / exposed	6 / 153 (3.92%)	14 / 148 (9.46%)	6 / 84 (7.14%)
occurrences (all)	6	15	6
Erythema			

subjects affected / exposed	8 / 153 (5.23%)	5 / 148 (3.38%)	3 / 84 (3.57%)
occurrences (all)	10	6	3
Hair colour changes			
subjects affected / exposed	26 / 153 (16.99%)	19 / 148 (12.84%)	9 / 84 (10.71%)
occurrences (all)	27	19	9
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	27 / 153 (17.65%)	39 / 148 (26.35%)	11 / 84 (13.10%)
occurrences (all)	36	65	22
Rash			
subjects affected / exposed	13 / 153 (8.50%)	17 / 148 (11.49%)	10 / 84 (11.90%)
occurrences (all)	16	18	14
Skin depigmentation			
subjects affected / exposed	8 / 153 (5.23%)	6 / 148 (4.05%)	1 / 84 (1.19%)
occurrences (all)	8	6	1
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	6 / 153 (3.92%)	6 / 148 (4.05%)	5 / 84 (5.95%)
occurrences (all)	6	6	5
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	11 / 153 (7.19%)	5 / 148 (3.38%)	6 / 84 (7.14%)
occurrences (all)	12	6	6
Back pain			
subjects affected / exposed	13 / 153 (8.50%)	9 / 148 (6.08%)	4 / 84 (4.76%)
occurrences (all)	15	10	4
Muscle spasms			
subjects affected / exposed	9 / 153 (5.88%)	6 / 148 (4.05%)	6 / 84 (7.14%)
occurrences (all)	11	7	9
Myalgia			
subjects affected / exposed	5 / 153 (3.27%)	5 / 148 (3.38%)	5 / 84 (5.95%)
occurrences (all)	6	5	7
Pain in extremity			
subjects affected / exposed	9 / 153 (5.88%)	10 / 148 (6.76%)	2 / 84 (2.38%)
occurrences (all)	10	11	2
Infections and infestations			

Bronchitis			
subjects affected / exposed	0 / 153 (0.00%)	0 / 148 (0.00%)	5 / 84 (5.95%)
occurrences (all)	0	0	7
Lower respiratory tract infection			
subjects affected / exposed	0 / 153 (0.00%)	2 / 148 (1.35%)	6 / 84 (7.14%)
occurrences (all)	0	2	7
Urinary tract infection			
subjects affected / exposed	5 / 153 (3.27%)	4 / 148 (2.70%)	5 / 84 (5.95%)
occurrences (all)	5	4	5
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	32 / 153 (20.92%)	30 / 148 (20.27%)	18 / 84 (21.43%)
occurrences (all)	36	35	26

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
14 March 2011	Updated Hepatotoxicity Management Guidelines and corrected minor errors in the protocol. Added text for clarification SAE reporting procedure, blood pressure measurement requirements, completion definition, dose modifications, drug supply storage, recommendations for patients who previously received or currently were receiving IV bisphosphonates, timing of study procedures and PK assessments. Declaration of Helsinski wording updated and definition of end of study added.
04 January 2013	This amendment permits continued access to clinical trial material for subjects ongoing at the time of implementation of this amendment with adjustment to the frequency of clinic visits, and labs. Subject treatment and disease management will be as indicated by local standard of medical care and local approved labeling (or the DCSI) for pazopanib. Investigators will be required to collect and report to the Sponsor all SAEs and pregnancies, AEs leading to IP discontinuation or other AEs the investigator deems important to report, and all other reasons leading to IP discontinuation. Collection of additional safety information will no longer be required by the Sponsor but will be at the discretion and judgment of the investigator in accordance with the local standard of medical care. Change 3 – Appropriate subjects may be withdrawn from Study VEG113046 and may continue pazopanib therapy via an alternative approved mechanism.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

The study remained open to allow subjects currently on treatment continued access to treatment with open label pazopanib.

Notes: