Clinical trial results:
A randomized, double-blind, placebo-controlled Phase II-III multi-centre study to evaluate the effect of adjuvant pazopanib (GW786034) versus placebo on post-surgical disease-free survival in patients with stage I non small cell lung cancer and tumor size equal or inferior to 7 cm.

Summary

EudraCT number	2008-004897-41
Trial protocol	FR
Global end of trial date	01 April 2016

Results information

Result version number	v1 (current)
This version publication date	10 February 2023
First version publication date	10 February 2023

Trial information

Trial identification

Sponsor protocol code	IFCT-0703

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00775307
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	IFCT
Sponsor organisation address	10 rue de la Grange Batelière , Paris, France, 75009
Public contact	Contact, IFCT, +33 156811045, contact@ifct.fr
Scientific contact	Contact, IFCT, +33 156811045, contact@ifct.fr

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	01 October 2013
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	01 April 2016
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

To evaluate 'feasibility of regimen' by measuring compliance in patients with once-daily (QD) pazopanib, or placebo, dosed according to protocol, based on the proportion (%) of patients that receive pazopanib, or placebo, for at least 12 weeks within 24 weeks of randomization.

Protection of trial subjects:

Algorithms for management of adverse events were provided in the protocol.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	11 March 2009
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	France: 142
Worldwide total number of subjects	142
EEA total number of subjects	142

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)	114
From 65 to 84 years	28
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between March 2009 and August 2012, 143 patients were randomly assigned, 72 to pazopanib and 71 to placebo, in 29 centers. One patient (pazopanib arm) was ineligible being randomized without consent (and did not receive any treatment) and was excluded from all analyses.

Pre-assignment

Screening details:

Patients (18 to 70 years) with completely resected stage I NSCLC (7th TNM edition), an ECOG performance status of 0 or 1, and adequate hematologic, hepatic, renal, and blood coagulation function were eligible.

Pre-assignment period milestones

Number of subjects started	142
Number of subjects completed	142

Period 1

Period 1 title	Overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor

Blinding implementation details:

This double-blind, multicenter, phase II/III study assigned by central randomization (1:1, block method)

Arms

Are arms mutually exclusive?	Yes
Arm title	Pazopanib

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Pazopanib
Investigational medicinal product code	
Other name	GW786034
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Pazopanib was administered at 800 or 400 mg once a day.
After 64 patients were included (interim analysis), the independent data monitoring committee (IDMC) recommended reducing the pazopanib dose to 400 mg/day given insufficient compliance.

Arm title	Placebo

Arm description: -

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:

Placebo was administered at 800 or 400 mg once a day.

After 64 patients were included (interim analysis), the independent data monitoring committee (IDMC) recommended reducing the dose to 400 mg/day given insufficient compliance.

Number of subjects in period 1	Pazopanib	Placebo
Started	71	71
Completed	69	69
Not completed	2	2
Physician decision	1	1
Consent withdrawn by subject	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Pazopanib
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Reporting group values	Pazopanib	Placebo	Total
Number of subjects	71	71	142
Age categorical Units: Subjects			
In utero			0
Preterm newborn infants (gestational age < 37 wks)			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 65-84 years			0
85 years and over			0
Age continuous Units: years			
median	57	61	
full range (min-max)	33 to 70	44 to 71	-
Gender categorical Units: Subjects			
Female	30	26	56
Male	41	45	86
ECOG performance status Units: Subjects			
PS 0	47	58	105
PS 1	24	13	37
Ethnicity Units: Subjects			
Caucasian	69	69	138
Other	2	2	4
Smoking status Units: Subjects			
Never	6	6	12
Current	13	12	25
Former	52	52	104
Missing	0	1	1
Stage Units: Subjects			
IA	54	59	113
IB	16	12	28

Missing	1	0	1
Histology Units: Subjects			
Adenocarcinoma	51	56	107
Squamous cell carcinoma	12	11	23
Other	8	4	12

End points

End points reporting groups

Reporting group title	Pazopanib
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Primary: Compliance rate by planned dose and treatment arm

End point title	Compliance rate by planned dose and treatment arm[1]

End point description:

To evaluate 'feasibility of regimen' by measuring compliance in patients with once-daily (QD) pazopanib, or placebo, dosed according to protocol, based on the proportion (%) of patients that receive pazopanib, or placebo, for at least 12 weeks within 24 weeks of randomization.

End point type	Primary

End point timeframe:

Within 24 weeks of randomization.

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: Not available

End point values	Pazopanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: % of patients				
number (confidence interval 95%)				
800 mg/day	38 (23 to 55)	88 (73 to 96)		
400 mg/day	69 (50 to 84)	93 (77 to 99)		

Statistical analyses

No statistical analyses for this end point

Secondary: Duration of treatment

End point title	Duration of treatment

End point description:

End point type	Secondary

End point timeframe:

Within 24 weeks of randomization

End point values	Pazopanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: weeks				
median (full range (min-max))				
800 mg/day	7.2 (0.3 to 26.0)	24.1 (0.3 to 26.4)		
400 mg/day	22.6 (0.7 to 26.6)	24.3 (0.3 to 26.3)		

Statistical analyses

No statistical analyses for this end point

Secondary: Dose modification

End point title	Dose modification

End point description:

End point type	Secondary

End point timeframe:

Within 24 weeks of randomization

End point values	Pazopanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: Number of patients				
800 mg/day	16	2		
400 mg/day	12	2		

Statistical analyses

No statistical analyses for this end point

Secondary: Number of dose modification

End point title	Number of dose modification

End point description:

End point type	Secondary

End point timeframe:

Within 24 weeks from randomization

End point values	Pazopanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: Number of patients				
800 mg/day : 1 dose reduction	13	12		
800 mg/day : 2 dose reductions	3	2		
400 mg/day : 1 dose reduction	2	0		
400 mg/day :2 dose reductions	0	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Quality of life

End point title	Quality of life

End point description:

End point type	Secondary

End point timeframe:

Within 24 weeks from randomization

End point values	Pazopanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: Pourcentage				
arithmetic mean (standard error)				
Global Health Status : baseline	64.9 (± 17.4)	67.8 (± 20.5)		
Global Health Status : W12	63.2 (± 20.3)	72.7 (± 18.1)		
Global Health Status : W24	64.1 (± 20.1)	68.6 (± 23.1)		
Physical functioning : baseline	84.4 (± 12.8)	83.2 (± 15.0)		
Physical functioning : W12	81.0 (± 15.6)	84.4 (± 14.5)		
Physical functioning : W24	86.4 (± 13.4)	86.1 (± 12.0)		
Fatigue : baseline	31.3 (± 22.8)	32.4 (± 23.8)		
Fatigue : W12	32.3 (± 23.2)	27.1 (± 25.6)		
Fatigue : W24	31.6 (± 25.9)	23.8 (± 21.9)		
Nausea and vomiting : baseline	3.5 (± 9.6)	5.4 (± 11.8)		
Nausea and vomiting : W12	7.0 (± 16.7)	8.2 (± 15.3)		
Nausea and vomiting : W24	9.6 (± 17.1)	4.3 (± 12.3)		
Dyspnoea : baseline	24.2 (± 18.5)	25.5 (± 20.7)		
Dyspnoea : W12	24.2 (± 22.9)	23.6 (± 21.2)		
Dyspnoea : W24	26.4 (± 22.7)	25.4 (± 20.8)		
Pain in chest : baseline	18.8 (± 27.4)	20.6 (± 23.8)		
Pain in chest : W12	17.1 (± 24.9)	20.8 (± 24.5)		
Pain in chest : W24	14.7 (± 21.7)	14.6 (± 19.3)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Quality of blinding - Treatment guess by patient

End point title	Quality of blinding - Treatment guess by patient

End point description:

End point type	Post-hoc

End point timeframe:

Up to 47 months

End point values	Pazopanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	69		
Units: Number of patients				
Placebo	3	32		
Pazopanib	61	29		
Missing	5	8		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Quality of blinding - Treatment guess by investigator

End point title	Quality of blinding - Treatment guess by investigator

End point description:

End point type	Post-hoc

End point timeframe:

Up to 47 months

End point values	Pazopanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	69		
Units: Number of patients				
Placebo	5	48		
Pazopanib	62	15		
Missing	2	6		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Quality of blinding - Concordance between patients' and clinicians' guess of treatment

End point title	Quality of blinding - Concordance between patients' and clinicians' guess of treatment

End point description:

End point type	Post-hoc

End point timeframe:

Up to 47 weeks

End point values	Pazopanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	64	56		
Units: Number of patients				
Yes	5	17		
No	59	39		

Statistical analyses

No statistical analyses for this end point

Post-hoc: 5-year overall survival

End point title	5-year overall survival

End point description:

End point type	Post-hoc

End point timeframe:

Up to 47 months

End point values	Pazopanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: % of patients				
number (confidence interval 95%)	83 (72 to 94)	94 (88 to 100)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Three-year Recurrence-Free Survival

End point title	Three-year Recurrence-Free Survival

End point description:

End point type	Post-hoc

End point timeframe:

Up to 47 months

End point values	Pazopanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: % of patients				
number (confidence interval 95%)	76 (65 to 86)	83 (74 to 92)		

Statistical analyses

No statistical analyses for this end point

Post-hoc: Second primary cancers

End point title	Second primary cancers

End point description:

End point type	Post-hoc

End point timeframe:

Up to 47 patients

End point values	Pazopanib	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	71	71		
Units: Number of patients				
800 mg/day	8	3		
400 mg/day	0	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected for a patient from the date of signature of inform consent form, during treatment period and until 30 days after the last dose of study treatment. Deaths were collected until data analysis.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	18.0

Reporting groups

Reporting group title	Safety population - Pazopanib 800 mg
Reporting group description: -	
Reporting group title	Safety population - Placebo 800 mg
Reporting group description: -	
Reporting group title	Safety population - Pazopanib 400 mg
Reporting group description: -	
Reporting group title	Safety population - Placebo 400 mg
Reporting group description: -	

Serious adverse events	Safety population - Pazopanib 800 mg	Safety population - Placebo 800 mg	Safety population - Pazopanib 400 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 39 (7.69%)	2 / 41 (4.88%)	4 / 32 (12.50%)
number of deaths (all causes)	6	1	1
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Frature			
subjects affected / exposed	0 / 39 (0.00%)	0 / 41 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fall			
subjects affected / exposed	0 / 39 (0.00%)	0 / 41 (0.00%)	1 / 32 (3.13%)
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			
Cardiac disorder			

subjects affected / exposed	1 / 39 (2.56%)	0 / 41 (0.00%)	0 / 32 (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
Pericardial effusion			
subjects affected / exposed	0 / 39 (0.00%)	1 / 41 (2.44%)	0 / 32 (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
Pericarditis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 41 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Loss of consciousness			
subjects affected / exposed	0 / 39 (0.00%)	1 / 41 (2.44%)	0 / 32 (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
Convulsion			
subjects affected / exposed	0 / 39 (0.00%)	0 / 41 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	0 / 39 (0.00%)	1 / 41 (2.44%)	0 / 32 (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
Reduced general condition			
subjects affected / exposed	0 / 39 (0.00%)	0 / 41 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Fever			
subjects affected / exposed	0 / 39 (0.00%)	0 / 41 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Social circumstances			
Pregnancy of partner			
subjects affected / exposed	0 / 39 (0.00%)	0 / 41 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 41 (0.00%)	0 / 32 (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
Vomiting			
subjects affected / exposed	1 / 39 (2.56%)	0 / 41 (0.00%)	0 / 32 (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
Bloody diarrhea			
subjects affected / exposed	0 / 39 (0.00%)	0 / 41 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 39 (0.00%)	1 / 41 (2.44%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Dyspnoea			
subjects affected / exposed	0 / 39 (0.00%)	0 / 41 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 41 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	1 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Renal and urinary disorders			
Proteinuria			

subjects affected / exposed	0 / 39 (0.00%)	0 / 41 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	1 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 39 (2.56%)	0 / 41 (0.00%)	0 / 32 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 39 (0.00%)	0 / 41 (0.00%)	1 / 32 (3.13%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Safety population - Placebo 400 mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 30 (10.00%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events			
Injury, poisoning and procedural complications			
Frature			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Fall			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac disorder			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Pericardial effusion			

subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Pericarditis				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Loss of consciousness				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Convulsion				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Malaise				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Reduced general condition				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Fever				
subjects affected / exposed	1 / 30 (3.33%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Social circumstances				
Pregnancy of partner				
subjects affected / exposed	0 / 30 (0.00%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			

Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Bloody diarrhea			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Pleural effusion			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic cytolysis			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Proteinuria			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Back pain			

subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Anorexia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences causally related to treatment / all	0 / 0		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Safety population - Pazopanib 800 mg	Safety population - Placebo 800 mg	Safety population - Pazopanib 400 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	38 / 39 (97.44%)	39 / 41 (95.12%)	31 / 32 (96.88%)
Vascular disorders			
Hypertension			
subjects affected / exposed	21 / 39 (53.85%)	11 / 41 (26.83%)	16 / 32 (50.00%)
occurrences (all)	21	11	16
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	23 / 39 (58.97%)	19 / 41 (46.34%)	26 / 32 (81.25%)
occurrences (all)	23	19	26
Fever			
subjects affected / exposed	1 / 39 (2.56%)	4 / 41 (9.76%)	4 / 32 (12.50%)
occurrences (all)	1	4	4
Pain			
subjects affected / exposed	22 / 39 (56.41%)	19 / 41 (46.34%)	24 / 32 (75.00%)
occurrences (all)	22	19	24
Respiratory, thoracic and mediastinal disorders			
Haemorrhage nose			
subjects affected / exposed	5 / 39 (12.82%)	1 / 41 (2.44%)	2 / 32 (6.25%)
occurrences (all)	5	1	2
Cough			
subjects affected / exposed	13 / 39 (33.33%)	16 / 41 (39.02%)	10 / 32 (31.25%)
occurrences (all)	13	16	10

Dyspnea			
subjects affected / exposed	12 / 39 (30.77%)	19 / 41 (46.34%)	15 / 32 (46.88%)
occurrences (all)	12	19	15
Voice change			
subjects affected / exposed	3 / 39 (7.69%)	2 / 41 (4.88%)	2 / 32 (6.25%)
occurrences (all)	3	2	2
Psychiatric disorders			
Insomnia			
subjects affected / exposed	2 / 39 (5.13%)	9 / 41 (21.95%)	5 / 32 (15.63%)
occurrences (all)	2	9	5
Mood altered			
subjects affected / exposed	5 / 39 (12.82%)	4 / 41 (9.76%)	6 / 32 (18.75%)
occurrences (all)	5	4	6
Irritability			
subjects affected / exposed	0 / 39 (0.00%)	0 / 41 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Investigations			
Weight loss			
subjects affected / exposed	3 / 39 (7.69%)	0 / 41 (0.00%)	1 / 32 (3.13%)
occurrences (all)	3	0	1
Alanine aminotransferase			
subjects affected / exposed	17 / 39 (43.59%)	12 / 41 (29.27%)	17 / 32 (53.13%)
occurrences (all)	17	12	17
Aspartate aminotransferase			
subjects affected / exposed	18 / 39 (46.15%)	14 / 41 (34.15%)	10 / 32 (31.25%)
occurrences (all)	18	14	10
Alkaline phosphatase			
subjects affected / exposed	6 / 39 (15.38%)	7 / 41 (17.07%)	5 / 32 (15.63%)
occurrences (all)	6	7	5
Bicarbonate serum-low			
subjects affected / exposed	1 / 39 (2.56%)	3 / 41 (7.32%)	0 / 32 (0.00%)
occurrences (all)	1	3	0
Bilirubin			
subjects affected / exposed	9 / 39 (23.08%)	7 / 41 (17.07%)	6 / 32 (18.75%)
occurrences (all)	9	7	6
Cholesterol			

subjects affected / exposed	9 / 39 (23.08%)	15 / 41 (36.59%)	13 / 32 (40.63%)
occurrences (all)	9	15	13
Creatinine			
subjects affected / exposed	0 / 39 (0.00%)	4 / 41 (9.76%)	2 / 32 (6.25%)
occurrences (all)	0	4	2
Gamma-glutamyltransferase			
subjects affected / exposed	15 / 39 (38.46%)	16 / 41 (39.02%)	12 / 32 (37.50%)
occurrences (all)	15	16	12
Nervous system disorders			
Dizziness			
subjects affected / exposed	1 / 39 (2.56%)	6 / 41 (14.63%)	1 / 32 (3.13%)
occurrences (all)	1	6	1
Headache			
subjects affected / exposed	11 / 39 (28.21%)	6 / 41 (14.63%)	11 / 32 (34.38%)
occurrences (all)	11	6	11
Memory impairment			
subjects affected / exposed	1 / 39 (2.56%)	2 / 41 (4.88%)	0 / 32 (0.00%)
occurrences (all)	1	2	0
Neuropathy-sensory			
subjects affected / exposed	0 / 39 (0.00%)	4 / 41 (9.76%)	1 / 32 (3.13%)
occurrences (all)	0	4	1
Blood and lymphatic system disorders			
Haemoglobin			
subjects affected / exposed	7 / 39 (17.95%)	9 / 41 (21.95%)	5 / 32 (15.63%)
occurrences (all)	7	9	5
Leukocyte			
subjects affected / exposed	3 / 39 (7.69%)	0 / 41 (0.00%)	3 / 32 (9.38%)
occurrences (all)	3	0	3
Lymphopenia			
subjects affected / exposed	3 / 39 (7.69%)	3 / 41 (7.32%)	2 / 32 (6.25%)
occurrences (all)	3	3	2
Neutrophil			
subjects affected / exposed	5 / 39 (12.82%)	4 / 41 (9.76%)	9 / 32 (28.13%)
occurrences (all)	5	4	9
Platelet			

subjects affected / exposed	3 / 39 (7.69%)	1 / 41 (2.44%)	7 / 32 (21.88%)
occurrences (all)	3	1	7
Eye disorders			
Blurred vision			
subjects affected / exposed	2 / 39 (5.13%)	0 / 41 (0.00%)	4 / 32 (12.50%)
occurrences (all)	2	0	4
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	15 / 39 (38.46%)	5 / 41 (12.20%)	10 / 32 (31.25%)
occurrences (all)	15	5	10
Anorexia			
subjects affected / exposed	16 / 39 (41.03%)	5 / 41 (12.20%)	8 / 32 (25.00%)
occurrences (all)	16	5	8
Constipation			
subjects affected / exposed	4 / 39 (10.26%)	5 / 41 (12.20%)	2 / 32 (6.25%)
occurrences (all)	4	5	2
Diarrhoea			
subjects affected / exposed	24 / 39 (61.54%)	11 / 41 (26.83%)	21 / 32 (65.63%)
occurrences (all)	24	1	21
Dysguesia			
subjects affected / exposed	9 / 39 (23.08%)	2 / 41 (4.88%)	3 / 32 (9.38%)
occurrences (all)	9	2	3
Flatulence			
subjects affected / exposed	3 / 39 (7.69%)	1 / 41 (2.44%)	0 / 32 (0.00%)
occurrences (all)	3	1	0
Gastritis			
subjects affected / exposed	1 / 39 (2.56%)	0 / 41 (0.00%)	0 / 32 (0.00%)
occurrences (all)	1	0	0
Mucositis stomatitis			
subjects affected / exposed	5 / 39 (12.82%)	2 / 41 (4.88%)	3 / 32 (9.38%)
occurrences (all)	5	2	3
Nausea			
subjects affected / exposed	18 / 39 (46.15%)	5 / 41 (12.20%)	14 / 32 (43.75%)
occurrences (all)	18	5	14
Vomiting			

subjects affected / exposed	10 / 39 (25.64%)	7 / 41 (17.07%)	9 / 32 (28.13%)
occurrences (all)	10	7	9
Gastrointestinal haemorrhage			
subjects affected / exposed	0 / 39 (0.00%)	0 / 41 (0.00%)	1 / 32 (3.13%)
occurrences (all)	0	0	1
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	5 / 39 (12.82%)	1 / 41 (2.44%)	9 / 32 (28.13%)
occurrences (all)	5	1	9
Dry skin			
subjects affected / exposed	5 / 39 (12.82%)	1 / 41 (2.44%)	1 / 32 (3.13%)
occurrences (all)	5	1	1
Erythema multiforme			
subjects affected / exposed	2 / 39 (5.13%)	1 / 41 (2.44%)	1 / 32 (3.13%)
occurrences (all)	2	1	1
Hand foot skin reaction			
subjects affected / exposed	4 / 39 (10.26%)	0 / 41 (0.00%)	2 / 32 (6.25%)
occurrences (all)	4	0	2
Hyperpigmentation			
subjects affected / exposed	1 / 39 (2.56%)	2 / 41 (4.88%)	0 / 32 (0.00%)
occurrences (all)	1	2	0
Hypopigmentation			
subjects affected / exposed	13 / 39 (33.33%)	2 / 41 (4.88%)	19 / 32 (59.38%)
occurrences (all)	13	2	19
Pruritus			
subjects affected / exposed	2 / 39 (5.13%)	3 / 41 (7.32%)	2 / 32 (6.25%)
occurrences (all)	2	3	2
Rash			
subjects affected / exposed	8 / 39 (20.51%)	6 / 41 (14.63%)	5 / 32 (15.63%)
occurrences (all)	8	6	5
Ulceration			
subjects affected / exposed	2 / 39 (5.13%)	3 / 41 (7.32%)	2 / 32 (6.25%)
occurrences (all)	2	3	2
Dermatitis			
subjects affected / exposed	0 / 39 (0.00%)	0 / 41 (0.00%)	2 / 32 (6.25%)
occurrences (all)	0	0	2

Renal and urinary disorders			
Haemoglobinuria			
subjects affected / exposed	3 / 39 (7.69%)	1 / 41 (2.44%)	0 / 32 (0.00%)
occurrences (all)	3	1	0
Hypercalcaemia			
subjects affected / exposed	3 / 39 (7.69%)	2 / 41 (4.88%)	2 / 32 (6.25%)
occurrences (all)	3	2	2
Proteinuria			
subjects affected / exposed	19 / 39 (48.72%)	16 / 41 (39.02%)	10 / 32 (31.25%)
occurrences (all)	19	16	10
Endocrine disorders			
Hot flashes			
subjects affected / exposed	1 / 39 (2.56%)	3 / 41 (7.32%)	0 / 32 (0.00%)
occurrences (all)	1	3	0
Hyperthyroidism			
subjects affected / exposed	2 / 39 (5.13%)	2 / 41 (4.88%)	0 / 32 (0.00%)
occurrences (all)	2	2	0
Hypothyroidism			
subjects affected / exposed	1 / 39 (2.56%)	2 / 41 (4.88%)	1 / 32 (3.13%)
occurrences (all)	1	2	1
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	5 / 39 (12.82%)	1 / 41 (2.44%)	3 / 32 (9.38%)
occurrences (all)	5	1	3
Metabolism and nutrition disorders			
Hyperglycaemia			
subjects affected / exposed	12 / 39 (30.77%)	18 / 41 (43.90%)	10 / 32 (31.25%)
occurrences (all)	12	18	10
Hyperkalaemia			
subjects affected / exposed	2 / 39 (5.13%)	5 / 41 (12.20%)	4 / 32 (12.50%)
occurrences (all)	2	5	4
Hypertriglyceridemia			
subjects affected / exposed	14 / 39 (35.90%)	21 / 41 (51.22%)	22 / 32 (68.75%)
occurrences (all)	14	21	22
Hyperuricemia			

subjects affected / exposed	3 / 39 (7.69%)	3 / 41 (7.32%)	8 / 32 (25.00%)
occurrences (all)	3	3	8
Hypoalbuminemia			
subjects affected / exposed	3 / 39 (7.69%)	3 / 41 (7.32%)	0 / 32 (0.00%)
occurrences (all)	3	3	0
Hypocalcemia			
subjects affected / exposed	4 / 39 (10.26%)	3 / 41 (7.32%)	3 / 32 (9.38%)
occurrences (all)	4	3	3
Hypoglycemia			
subjects affected / exposed	1 / 39 (2.56%)	3 / 41 (7.32%)	1 / 32 (3.13%)
occurrences (all)	1	3	1
Hyponatremia			
subjects affected / exposed	2 / 39 (5.13%)	2 / 41 (4.88%)	3 / 32 (9.38%)
occurrences (all)	2	2	3
Hypophosphatemia			
subjects affected / exposed	0 / 39 (0.00%)	3 / 41 (7.32%)	1 / 32 (3.13%)
occurrences (all)	0	3	1

Non-serious adverse events	Safety population - Placebo 400 mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	29 / 30 (96.67%)		
Vascular disorders			
Hypertension			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	15 / 30 (50.00%)		
occurrences (all)	15		
Fever			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Pain			
subjects affected / exposed	22 / 30 (73.33%)		
occurrences (all)	22		
Respiratory, thoracic and mediastinal disorders			

Haemorrhage nose subjects affected / exposed occurrences (all)	2 / 30 (6.67%) 2		
Cough subjects affected / exposed occurrences (all)	14 / 30 (46.67%) 14		
Dyspnea subjects affected / exposed occurrences (all)	10 / 30 (33.33%) 10		
Voice change subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1		
Psychiatric disorders Insomnia subjects affected / exposed occurrences (all)	5 / 30 (16.67%) 5		
Mood altered subjects affected / exposed occurrences (all)	5 / 30 (16.67%) 5		
Irritability subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 3		
Investigations Weight loss subjects affected / exposed occurrences (all)	0 / 30 (0.00%) 0		
Alanine aminotransferase subjects affected / exposed occurrences (all)	4 / 30 (13.33%) 4		
Aspartate aminotransferase subjects affected / exposed occurrences (all)	5 / 30 (16.67%) 5		
Alkaline phosphatase subjects affected / exposed occurrences (all)	3 / 30 (10.00%) 3		
Bicarbonate serum-low			

subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Bilirubin			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Cholesterol			
subjects affected / exposed	15 / 30 (50.00%)		
occurrences (all)	15		
Creatinine			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Gamma-glutamyltransferase			
subjects affected / exposed	11 / 30 (36.67%)		
occurrences (all)	11		
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	4		
Headache			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	5		
Memory impairment			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Neuropathy-sensory			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Blood and lymphatic system disorders			
Haemoglobin			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	5		
Leukocyte			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Lymphopenia			

subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Neutrophil			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Platelet			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Eye disorders			
Blurred vision			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Anorexia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Constipation			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Diarrhoea			
subjects affected / exposed	8 / 30 (26.67%)		
occurrences (all)	8		
Dysguesia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Flatulence			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Gastritis			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Mucositis stomatitis			

subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Nausea			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Vomiting			
subjects affected / exposed	5 / 30 (16.67%)		
occurrences (all)	5		
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Dry skin			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Erythema multiforme			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Hand foot skin reaction			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hyperpigmentation			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		
Hypopigmentation			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	4		
Pruritus			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Rash			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		

Ulceration subjects affected / exposed occurrences (all) Dermatitis subjects affected / exposed occurrences (all)	1 / 30 (3.33%) 1 2 / 30 (6.67%) 2		
Renal and urinary disorders Haemoglobinuria subjects affected / exposed occurrences (all) Hypercalcaemia subjects affected / exposed occurrences (all) Proteinuria subjects affected / exposed occurrences (all)	 0 / 30 (0.00%) 0 2 / 30 (6.67%) 2 3 / 30 (10.00%) 3		
Endocrine disorders Hot flashes subjects affected / exposed occurrences (all) Hyperthyroidism subjects affected / exposed occurrences (all) Hypothyroidism subjects affected / exposed occurrences (all)	 0 / 30 (0.00%) 0 2 / 30 (6.67%) 2 2 / 30 (6.67%) 2		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all)	 1 / 30 (3.33%) 1		
Metabolism and nutrition disorders Hyperglycaemia subjects affected / exposed occurrences (all) Hyperkalaemia	 9 / 30 (30.00%) 9		

subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	4		
Hypertriglyceridemia			
subjects affected / exposed	16 / 30 (53.33%)		
occurrences (all)	16		
Hyperuricemia			
subjects affected / exposed	7 / 30 (23.33%)		
occurrences (all)	7		
Hypoalbuminemia			
subjects affected / exposed	3 / 30 (10.00%)		
occurrences (all)	3		
Hypocalcemia			
subjects affected / exposed	2 / 30 (6.67%)		
occurrences (all)	2		
Hypoglycemia			
subjects affected / exposed	4 / 30 (13.33%)		
occurrences (all)	4		
Hyponatremia			
subjects affected / exposed	1 / 30 (3.33%)		
occurrences (all)	1		
Hypophosphatemia			
subjects affected / exposed	0 / 30 (0.00%)		
occurrences (all)	0		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 November 2008	Clarify recurrence or second cancer.
23 March 2009	Make minor correction to the protocol and update according to the new investigator brochure.
19 October 2009	Update IFCT address.
10 March 2010	Make minor correction to the protocol and update according to the new investigator brochure.
22 October 2010	Update statistical section following recommendations of the independent data monitoring committee (IDMC) to perform ITT analyses.
29 December 2010	Reduce the pazopanib dose to 400 mg/day given insufficient compliance as recommended by IDMC and increase the number of inclusions as the recruitment of 31 additional patients in each arm is necessary to evaluate compliance.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/28327934