Clinical trial results:
Multi-center, open-label, non-randomised phase II study to evaluate the activity and tolerability of GW786034 in patients with advanced and/or metastatic soft tissue sarcoma who have relapsed following standard therapies or for whom no standard therapy exists.

Summary

EudraCT number	2004-004378-10
Trial protocol	GB HU BE
Global end of trial date	11 February 2014

Results information

Result version number	v1 (current)
This version publication date	27 April 2016
First version publication date	13 May 2015

Trial information

Trial identification

Sponsor protocol code	EORTC 62043

Additional study identifiers

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

Notes:

Sponsors

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

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	30 June 2014
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	11 February 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The principal objective of the trial is to evaluate the therapeutic activity, safety and tolerability of GW786034 in participants with advanced and/or metastatic soft tissue sarcoma who have relapsed following standard therapies or for whom no standard therapy exists.

Protection of trial subjects:

In case toxicity occurred and treatment needed to be interrupted, a paticipant was allowed to remain on study without study drug intake for a maximum period of two weeks. If in this two-week period the toxicity was not resolved to Grade 1 or minimal toxicity and study treatment could not be restarted at a lower dose, study treatment had to be discontinued and the participant followed by clinical examination 28 days after last administration of the pazopanib and thereafter every 3 months for survival.

There was allowed use of more than 2 antihypertensive medications.

Cardiac monitoring had to be performed every 12 weeks.
-Left ventricular ejection fraction (LVEF) was checked by Echocardiogram (ECHO)/Multi gated acquisition scan (MUGA) (whichever method was preferred at site)
-In case of LVEF drop compared to baseline, investigator had to contact study physician at European Organization for Research and Treatment of Cancer (EORTC) for instructions

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	14 November 2005
Long term follow-up planned	Yes
Long term follow-up rationale	Efficacy
Long term follow-up duration	6 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United Kingdom: 26
Country: Number of subjects enrolled	Belgium: 14
Country: Number of subjects enrolled	France: 65
Country: Number of subjects enrolled	Hungary: 25
Country: Number of subjects enrolled	Netherlands: 12
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)	109
From 65 to 84 years	33
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The number of participants that died in this study (132) are reported as the number of completers due to a system constraint which does not allow the number of completers to equal 0.

Pre-assignment

Screening details:

The study included a Screening/Baseline Period, an open-label Treatment Period, and a post-treatment Follow-up period. After verification of the eligibility criteria, participants were stratified to 1 of 4 strata according to the WHO classification of STS based on local histopathology at study entry.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Pazopanib 800 mg

Arm description:

Pazopanib 800 milligram (mg) (tablets) administered orally once a day.

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

Dosage and administration details:

- pazopanib (GW786034) tablets were administered orally, once daily during Treatment Period of the study
- tablets were administered 1 hour before or 2 hours after breakfast
- tablets had to be taken with exactly 240 mL water on PK days and on other days with a full glass of water

Number of subjects in period 1	Pazopanib 800 mg
Started	142
Completed	132
Not completed	10
Disease Progression, Relapse, Death	8
Toxicity (or Toxic Death)	1
Missing	1

Baseline characteristics

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

Reporting group values	Pazopanib 800 mg	Total	
Number of subjects	142	142	
Age categorical Units: Subjects			
Age continuous Units: years median full range (min-max)	 51 18 to 79	 -	
Gender categorical Units: Subjects			
Female	71	71	
Male	71	71	

End points

End points reporting groups

Reporting group title	Pazopanib 800 mg
Reporting group description: Pazopanib 800 milligram (mg) (tablets) administered orally once a day.	
Subject analysis set title	Pazopanib 800 mg - Adipocytic tumors
Subject analysis set type	Sub-group analysis
Subject analysis set description: Pazopanib 800 mg (tablets) administered orally once a day	
Subject analysis set title	Pazopanib 800 mg - Leiomyosarcoma
Subject analysis set type	Sub-group analysis
Subject analysis set description: Pazopanib 800 mg (tablets) administered orally once a day	
Subject analysis set title	Pazopanib 800 mg - Synovial sarcoma
Subject analysis set type	Sub-group analysis
Subject analysis set description: Pazopanib 800 mg (tablets) administered orally once a day	
Subject analysis set title	Pazopanib 800 mg - Other Soft Tissue Sarcoma
Subject analysis set type	Sub-group analysis
Subject analysis set description: Pazopanib 800 mg (tablets) administered orally once a day	

Primary: Progression Free Survival at week 12

End point title	Progression Free Survival at week 12[1]

End point description:

Progression free survival at week 12 is the number of participants who had a complete response (CR, all detectable tumor had disappeared) or a partial response (PR, a >=30% decrease in the sum of the longest dimensions of the target lesions taking as a reference the baseline sum) or stable disease (SD, no change) 12 weeks from start of therapy, per response evaluation criteria in solid tumors (RECIST v1.0). Clinical progression is progression of disease without documented radiological evidence. Progressive disease (PD), a >=20% increase in target lesions. Intent-to-Treat (ITT) Population: All eligible participants entered into the study and who had taken >=1 dose of investigational product. Four participants were considered not evaluable for efficacy by the study coordinator for one of the following reasons: absence of target lesions, documented progression at trial entry, or ineligible histology.

End point type	Primary

End point timeframe:

Week 12

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: No Statistical analysis have been provided due to the system not accepting statisticial analysis data for 1 arm studies.

End point values	Pazopanib 800 mg - Adipocytic tumors	Pazopanib 800 mg - Leiomyosarcoma	Pazopanib 800 mg - Synovial sarcoma	Pazopanib 800 mg - Other Soft Tissue Sarcoma
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19[2]	41[3]	37[4]	41[5]
Units: participants				
Complete response	0	0	0	0
Partial response	0	1	4	1
Stable disease	5	16	14	16

Progressive disease	13	19	15	21
Unknown	0	2	0	1
Missing	1	3	4	2
CR+PR+SD	5	17	18	17

Notes:

[2] - ITT Population: all participants in the study who had taken >=1 dose of investigational product

[3] - ITT Population: all participants in the study who had taken >=1 dose of investigational product

[4] - ITT Population: all participants in the study who had taken >=1 dose of investigational product

[5] - ITT Population: all participants in the study who had taken >=1 dose of investigational product

Statistical analyses

No statistical analyses for this end point

Secondary: Overall Survival

End point title	Overall Survival

End point description:

Overall survival is defined as the time from start of therapy until death. Participants who were still alive at the time of analysis were censored. Four participants were considered not evaluable for efficacy by the study coordinator for one of the following reasons: absence of target lesions, documented progression at trial entry, or ineligible histology.

End point type	Secondary

End point timeframe:

Start of therapy until death (up to approximately 5 years)

End point values	Pazopanib 800 mg - Adipocytic tumors	Pazopanib 800 mg - Leiomyosarcoma	Pazopanib 800 mg - Synovial sarcoma	Pazopanib 800 mg - Other Soft Tissue Sarcoma
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19[6]	41[7]	37[8]	41[9]
Units: weeks				
median (confidence interval 90%)	28.1 (18.3 to 84)	50.9 (46.1 to 76.4)	44.6 (33 to 57.6)	42.6 (33.1 to 49.3)

Notes:

[6] - ITT Population

[7] - ITT Population

[8] - ITT Population

[9] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Progression Free Survival

End point title	Progression Free Survival

End point description:

Progression free survival is defined as the interval between the start of treatment and the earliest date of disease progression or death due to any cause. Assessments of progression were made by the investigator. Four participants were considered not evaluable for efficacy by the study coordinator for

one of the following reasons: absence of target lesions, documented progression at trial entry, or ineligible histology.

End point type	Secondary

End point timeframe:

Start of therapy until progression (up to approximately 5 years)

End point values	Pazopanib 800 mg - Adipocytic tumors	Pazopanib 800 mg - Leiomyosarcoma	Pazopanib 800 mg - Synovial sarcoma	Pazopanib 800 mg - Other Soft Tissue Sarcoma
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19[10]	41[11]	37[12]	41[13]
Units: weeks				
median (confidence interval 90%)	11.1 (7.1 to 11.9)	17.2 (12 to 24.1)	23.4 (11.7 to 29.3)	14 (12 to 36.3)

Notes:

[10] - ITT Population

[11] - ITT Population

[12] - ITT Population

[13] - ITT Population

Statistical analyses

No statistical analyses for this end point

Secondary: Overall response

End point title	Overall response

End point description:

Overall response is the number of participants who had a best outcome of a complete response (CR, all detectable tumor had disappeared) or a partial response (PR, a >=30% decrease in the sum of the longest dimensions of the target lesions taking as a reference the baseline sum) per response evaluation criteria in solid tumors (RECIST v1.0) at some point during the study. Progressive disease (PD), a >=20% increase in target lesions. Clinical progression is progression of disease without documented radiological evidence. Four participants were considered not evaluable for efficacy by the study coordinator for one of the following reasons: absence of target lesions, documented progression at trial entry, or ineligible histology.

End point type	Secondary

End point timeframe:

Baseline until either response or progression (up to approximately 5 years)

End point values	Pazopanib 800 mg - Adipocytic tumors	Pazopanib 800 mg - Leiomyosarcoma	Pazopanib 800 mg - Synovial sarcoma	Pazopanib 800 mg - Other Soft Tissue Sarcoma
Subject group type	Subject analysis set	Subject analysis set	Subject analysis set	Subject analysis set
Number of subjects analysed	19[14]	41[15]	37[16]	41[17]
Units: participants				
Complete response	0	0	0	0
Partial response	0	1	4	3
Stable disease	5	17	14	14

Progressive disease	13	19	13	21
Unknown	1	4	6	3
Missing	0	0	0	0

Notes:

[14] - ITT Population

[15] - ITT Population

[16] - ITT Population

[17] - ITT Population

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Entire Study (average of 8.24 years).

Adverse event reporting additional description:

Individual AEs of pneumonia, disease progression, fatigue, general physical health deterioration, hepatic function abnormal, petechiae, tumor pain, and vision blurred were not reported as serious, but are included because the outcome for these AEs was reported as "death" by the investigator.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	17.0

Reporting groups

Reporting group title	Pazopanib 800mg

Reporting group description:

Pazopanib 800mg (tablets) administered orally once a day

Serious adverse events	Pazopanib 800mg		
Total subjects affected by serious adverse events			
subjects affected / exposed	39 / 142 (27.46%)		
number of deaths (all causes)	132		
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	2 / 142 (1.41%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 1		
Vascular disorders			
Hypertension			
subjects affected / exposed	3 / 142 (2.11%)		
occurrences causally related to treatment / all	3 / 3		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	2 / 142 (1.41%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Fatigue			

subjects affected / exposed	3 / 142 (2.11%)			
occurrences causally related to treatment / all	2 / 3			
deaths causally related to treatment / all	1 / 1			
Oedema				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyrexia				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
General physical health deterioration				
subjects affected / exposed	3 / 142 (2.11%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 1			
Ill-defined disorder				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Lower respiratory tract infection				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	1 / 1			
Disease progression				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Social circumstances				
Pneumonia				

subjects affected / exposed	3 / 142 (2.11%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	1 / 2		
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pleuritic pain			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	5 / 142 (3.52%)		
occurrences causally related to treatment / all	5 / 10		
deaths causally related to treatment / all	0 / 0		
Pulmonary embolism			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pulmonary haemorrhage			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Embolism			
subjects affected / exposed	5 / 142 (3.52%)		
occurrences causally related to treatment / all	5 / 6		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			

Depression				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Injury, poisoning and procedural complications				
Fall				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Laceration				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple fractures				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Coronary artery disease				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Somnolence				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Syncope				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Disseminated intravascular coagulation				

subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	1 / 1			
Haemolysis				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Vision blurred				
subjects affected / exposed	2 / 142 (1.41%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	1 / 1			
Gastrointestinal disorders				
Abdominal distension				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Abdominal pain upper				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	3 / 142 (2.11%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Duodenal ulcer				
subjects affected / exposed	1 / 142 (0.70%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal haemorrhage				

subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ileal perforation			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal perforation			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Vomiting			
subjects affected / exposed	3 / 142 (2.11%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Skin and subcutaneous tissue disorders			
Petechiae			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	1 / 1		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 142 (1.41%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal pain			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Infections and infestations			
Gingivitis			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 142 (0.70%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Pazopanib 800mg		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	136 / 142 (95.77%)		
Investigations			
Weight decreased			
subjects affected / exposed	45 / 142 (31.69%)		
occurrences (all)	61		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	51 / 142 (35.92%)		
occurrences (all)	85		
Vascular disorders			
Hypertension			
subjects affected / exposed	57 / 142 (40.14%)		
occurrences (all)	93		
Nervous system disorders			
Dizziness			
subjects affected / exposed	12 / 142 (8.45%)		
occurrences (all)	24		

Dysgeusia			
subjects affected / exposed	13 / 142 (9.15%)		
occurrences (all)	16		
Headache			
subjects affected / exposed	30 / 142 (21.13%)		
occurrences (all)	42		
Peripheral sensory neuropathy			
subjects affected / exposed	9 / 142 (6.34%)		
occurrences (all)	12		
General disorders and administration site conditions			
Diarrhoea			
subjects affected / exposed	62 / 142 (43.66%)		
occurrences (all)	147		
Chest pain			
subjects affected / exposed	17 / 142 (11.97%)		
occurrences (all)	26		
Fatigue			
subjects affected / exposed	84 / 142 (59.15%)		
occurrences (all)	150		
Oedema			
subjects affected / exposed	21 / 142 (14.79%)		
occurrences (all)	26		
Pyrexia			
subjects affected / exposed	17 / 142 (11.97%)		
occurrences (all)	22		
Social circumstances			
Dry skin			
subjects affected / exposed	10 / 142 (7.04%)		
occurrences (all)	11		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	12 / 142 (8.45%)		
occurrences (all)	26		
Abdominal pain			
subjects affected / exposed	27 / 142 (19.01%)		
occurrences (all)	45		

Abdominal pain upper subjects affected / exposed occurrences (all)	14 / 142 (9.86%) 15		
Constipation subjects affected / exposed occurrences (all)	33 / 142 (23.24%) 44		
Nausea subjects affected / exposed occurrences (all)	60 / 142 (42.25%) 99		
Stomatitis subjects affected / exposed occurrences (all)	18 / 142 (12.68%) 23		
Vomiting subjects affected / exposed occurrences (all)	48 / 142 (33.80%) 76		
Respiratory, thoracic and mediastinal disorders			
Cough subjects affected / exposed occurrences (all)	33 / 142 (23.24%) 40		
Dyspnoea subjects affected / exposed occurrences (all)	31 / 142 (21.83%) 50		
Epistaxis subjects affected / exposed occurrences (all)	8 / 142 (5.63%) 14		
Skin and subcutaneous tissue disorders			
Alopecia subjects affected / exposed occurrences (all)	9 / 142 (6.34%) 9		
Hyperhidrosis subjects affected / exposed occurrences (all)	9 / 142 (6.34%) 11		
Skin hypopigmentation subjects affected / exposed occurrences (all)	53 / 142 (37.32%) 66		
Exfoliative rash			

subjects affected / exposed	23 / 142 (16.20%)		
occurrences (all)	28		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	13 / 142 (9.15%)		
occurrences (all)	19		
Insomnia			
subjects affected / exposed	11 / 142 (7.75%)		
occurrences (all)	12		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	9 / 142 (6.34%)		
occurrences (all)	13		
Back pain			
subjects affected / exposed	15 / 142 (10.56%)		
occurrences (all)	21		
Musculoskeletal pain			
subjects affected / exposed	32 / 142 (22.54%)		
occurrences (all)	54		
Pain in extremity			
subjects affected / exposed	8 / 142 (5.63%)		
occurrences (all)	8		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	45 / 142 (31.69%)		
occurrences (all)	57		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
28 July 2006	Clarified eligible/ineligible tumor types: •Revised leiomyosarcoma subtype in the WHO classification list: •Original text leiomyosarcoma (excluding skin and uterus); revised text leiomyosarcoma (excluding skin) •Removed neuroblastoma from the list of ineligible tumors as it is not on the WHO classification list. Defined the recovery period as 2 weeks. Allowed use of more than 2 antihypertensive medications. Updated participant information sheet with information on emerging toxicities.
05 September 2006	Participant information sheet amended to include information on a chemical identified in GW786034 that has the potential to impact the overall risk/benefit profile of pazopanib.
15 July 2008	Updated protocol in section 5 (Description of foreseeable risks and discomforts) with safety information. Updated participant information sheet with information.
30 April 2009	Updated participant information sheet with new safety information from Investigator's Brochure.
26 March 2010	Updated participant information sheet with information regarding potential cardio toxicity.
09 August 2010	Updated participant information sheet and protocol with potential risk of cardiac toxicity and information regarding cardiac monitoring.
08 December 2010	Updated participant information sheet and protocol regarding tablet strength changes.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported