Clinical trial results:
A randomized phase II trial comparing pazopanib with doxorubicin as first line treatment in elderly patients with metastatic or advanced soft tissue sarcoma

Summary

EudraCT number	2011-004168-30
Trial protocol	DE BE
Global end of trial date	28 February 2017

Results information

Result version number	v1 (current)
This version publication date	13 May 2022
First version publication date	13 May 2022

Trial information

Trial identification

Sponsor protocol code	STS001

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01861951
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Hannover Medical School
Sponsor organisation address	Carl-Neuberg-Str. 1, Hannover, Germany, 30625
Public contact	Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.de
Scientific contact	Zentrum für Klinische Studien, Hannover Medical School, EudraCT@mh-hannover.de

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	08 March 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	28 February 2017
Global end of trial reached?	Yes
Global end of trial date	28 February 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Primary objective:
To show that progression-free survival (PFS) in the pazopanib group is not inferior to that in the doxorubicin group

Key secondary objectives:
- To show that the proportion of patients with neutrophil granulocytopenia grade 4 is smaller in the pazopanib group than in the doxorubicin group
- To show that the proportion of patients with febrile neutropenia is smaller in the pazopanib group than in the doxorubicin group

Protection of trial subjects:

The clinical trial was conducted in accordance with the ethical principles that have their origins in the Declaration of Helsinki and with the standards of International Conference on Harmonisation (ICH) Good Clinical Practice (GCP).
A continuous risk assessment was performed during the study.

Background therapy:

Use of concomitant medication with doxorubicin and pazopanib were handled according to the summary of product characteristics (SmPC)/investigator's brochure (IB).
Patients have received full supportive care during the study, including transfusion of blood and blood products, and treatment with antibiotics, analgesics, erythropoietin, or bisphosphonates, when appropriate. Anti-emetics (such as prochlorperazine, lorazepam, ondansetron, or other 5-HT antagonists) were administered prophylactically in the event of nausea. Anti-diarrheals such as loperamide were administered as needed in the event of diarrhea. Although acetaminophen at doses of ≤2 g/day was permitted, it should have been used with caution in subjects with impaired liver function.

Evidence for comparator:

As a result of the heterogeneity of soft tissue sarcomas (STS), finding an effective anti-tumor agent has been difficult. For decades, doxorubicin has formed the backbone of systemic treatment of a wide range of cancers including hematological malignancies, many types of carcinoma, and unresectable or metastatic STS. Hematological toxicity is frequently associated with doxorubicin treatment. Due to its aggressiveness it is usually not suited for elderly patients. Finding a drug with similar efficacy, but less adverse effects is particularly important for this patient group.
The aim of the clinical trial was to compare pazopanib with doxorubicin in elderly patients with metastatic or advanced STS. We tested the hypothesis whether pazopanib treatment has comparable efficacy to doxorubicin treatment while offering better tolerability in elderly patients with metastatic or advanced STS.

Actual start date of recruitment	12 October 2012
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	Belgium: 12
Country: Number of subjects enrolled	Germany: 108
Worldwide total number of subjects	120
EEA total number of subjects	120

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)	22
From 65 to 84 years	96
85 years and over	2

Subject disposition

Recruitment

Recruitment details:

Subjects were enrolled at a total of 14 study sites in Germany and Belgium (Germany: 13 study sites, Belgium: 1 study site).

First patient first visit: 12-Oct-2012
Last patient first visit: 18-Mar-2016
Last patient last visit: 28-Feb-2017

Pre-assignment

Screening details:

A total of 120 patients were randomized. 39 patients were randomized to Doxorubicin (Arm A) and 81 patients to Pazopanib (Arm B). 118 patients received at least one dose of study drug. Two patients in Arm A did not receive any study drug (one patient withdrew consent and one patient were excluded by investigator's decision).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Doxorubicin (Arm A)

Arm description:

Participants randomized to receive Doxorubicin 75 mg/m² body surface area (BSA), intravenous (i.v.), day 1 (d1), every 3 weeks (q3wk). Participants received a maximum of 6 cycles of study treatment. The duration of the study intervention was 18 weeks or until disease progression, treatment failure, or death due to any cause, whichever occurred first.

Arm type	Active comparator
Investigational medicinal product name	Doxorubicin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Doxorubicin 75 mg/m² BSA, d1, q3wk, maximum of 6 cycles
Duration of the study intervention: 18 weeks or until disease progression, treatment failure, or death due to any cause, whichever occurred first

Arm title	Pazopanib (Arm B)

Arm description:

Participants randomized to receive Pazopanib 800 mg, per oral (p.o.), daily. Participants received Pazopanib continuously until disease progression, treatment failure, or death due to any cause, whichever occurred first.

Arm type	Experimental
Investigational medicinal product name	Pazopanib
Investigational medicinal product code	
Other name	Votrient®
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Pazopanib 800 mg (2 x 400 mg or 4 x 200 mg), p.o., daily
Duration of the study intervention: Participants received Pazopanib continuously until disease

progression, treatment failure, or death due to any cause, whichever occurred first.

Number of subjects in period 1	Doxorubicin (Arm A)	Pazopanib (Arm B)
Started	39	81
Completed	15	3
Not completed	24	78
Adverse event, serious fatal	-	1
Physician decision	2	2
Consent withdrawn by subject	5	2
Adverse event, non-fatal	3	18
Unknown	2	4
Progressive disease	12	51

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	120	120	
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	71		
full range (min-max)	60 to 88	-	
Gender categorical Units: Subjects			
Female	59	59	
Male	61	61	

End points

End points reporting groups

Reporting group title	Doxorubicin (Arm A)

Reporting group description:

Participants randomized to receive Doxorubicin 75 mg/m² body surface area (BSA), intravenous (i.v.), day 1 (d1), every 3 weeks (q3wk). Participants received a maximum of 6 cycles of study treatment. The duration of the study intervention was 18 weeks or until disease progression, treatment failure, or death due to any cause, whichever occurred first.

Reporting group title	Pazopanib (Arm B)

Reporting group description:

Participants randomized to receive Pazopanib 800 mg, per oral (p.o.), daily. Participants received Pazopanib continuously until disease progression, treatment failure, or death due to any cause, whichever occurred first.

Subject analysis set title	progression free survival rate (PFR) PP
Subject analysis set type	Per protocol

Subject analysis set description:

The primary analysis will be performed on the PP population and, as a sensitivity analysis, on the ITT population. Consistency between results in the ITT analysis and PP analysis is needed to draw any conclusion regarding differences in progression-free survival. For progression-free survival a Cox-regression model will be used to calculate the hazard ratio of pazopanib and doxorubicin (pazopanib/doxorubicin) and the respective two-sided 95% CI.If the upper limit of the two-sided 95% CI in the PP-population is smaller than 1.8, non-inferiority will be concluded. Additionally, Kaplan-Meier curves will be drawn.

Primary: Progression-free survival PP population

End point title	Progression-free survival PP population

End point description:

inter-quartile range (Q1-Q3) was not available in the primary study report

End point type	Primary

End point timeframe:

time from date of randomization until the date of first objective documentation of disease progression, treatment failure, or death due to any cause, whichever occurs first

End point values	Doxorubicin (Arm A)	Pazopanib (Arm B)	progression free survival rate (PFR) PP	
Subject group type	Reporting group	Reporting group	Subject analysis set	
Number of subjects analysed	39	81	120	
Units: month				
median (confidence interval 95%)	5.3 (1.7 to 8.2)	4.4 (2.7 to 6.0)	4.4 (1.7 to 8.2)	

Statistical analyses

Statistical analysis title	Primary analysis
Comparison groups	Doxorubicin (Arm A) v Pazopanib (Arm B)

Number of subjects included in analysis	120
Analysis specification	Pre-specified
Analysis type	non-inferiority[1]
Method	Regression, Cox
Parameter estimate	Hazard ratio (HR)
Point estimate	1
Confidence interval	
level	95 %
sides	2-sided
lower limit	0.65
upper limit	1.53
Variability estimate	Standard deviation

Notes:

[1] - The upper limit of the 95%-CI was lower than the predefined non-inferiority margin of 1.8. Thus, non-inferiority of Pazopanib regarding PFS could be concluded.

Secondary: Neutrophil granulocytopenia grade 4

End point title	Neutrophil granulocytopenia grade 4

End point description:

Key secondary analysis was performed in the ITT population. Descriptive results for neutropenia grade 4 and febrile neutropenia during the study indicated a strong difference between Doxorubicin and Pazopanib. Some events have been observed prior to randomization (excluded from analysis) or after progression (excluded from analysis in case of occurrence of neutropenia after start of another anticancer agent). Considering events during the study, neutropenia grade 4 and febrile neutropenia were only observed in the Doxorubicin group. A total of 28 neutropenia of CTC grade 4 occurred in 22 Doxorubicin patients (56.4%), and a total of 4 febrile neutropenia in 4 Doxorubicin patients (10.3%). Most patients experienced only one event. Neutropenia predominantly occurred 2 weeks after start of treatment. Superiority testing with chi-square tests showed significant results for the first key-secondary endpoint neutropenia grade 4 ($p<0.0001$) as well as for febrile neutropenia ($p=0.003$).

End point type	Secondary

End point timeframe:

during study; from randomization until progression/ death

End point values	Doxorubicin (Arm A)	Pazopanib (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	81		
Units: number	22	0		

Statistical analyses

No statistical analyses for this end point

Secondary: Febrile neutropenia

End point title	Febrile neutropenia

End point description:

Key secondary analysis was performed in the ITT population. Descriptive results for neutropenia grade 4 and febrile neutropenia during the study indicated a strong difference between Doxorubicin and Pazopanib. Some events have been observed prior to randomization (excluded from analysis) or after progression (excluded from analysis in case of occurrence of neutropenia after start of another

anticancer agent). Considering events during the study, neutropenia grade 4 and febrile neutropenia were only observed in the Doxorubicin group. A total of 28 neutropenia of CTC grade 4 occurred in 22 Doxorubicin patients (56.4%), and a total of 4 febrile neutropenia in 4 Doxorubicin patients (10.3%). Most patients experienced only one event. Neutropenia predominantly occurred 2 weeks after start of treatment. Superiority testing with chi-square tests showed significant results for the first key-secondary endpoint neutropenia grade 4 ($p<0.0001$) as well as for febrile neutropenia ($p=0.003$).

End point type	Secondary

End point timeframe:

during study; from randomization until progression/ death

End point values	Doxorubicin (Arm A)	Pazopanib (Arm B)		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	39	81		
Units: number	4	0		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The AE documentation period for this trial begins upon first administration of the IMP(s) and ends 28 days after the last application of the IMP.

Adverse event reporting additional description:

Numbers in the non-serious adverse events section reflect all adverse events occurring during the study (non-serious and serious).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	20.0

Reporting groups

Reporting group title	Pazopanib (Arm B)

Reporting group description: -

Reporting group title	Doxorubicin (Arm A)

Reporting group description: -

Serious adverse events	Pazopanib (Arm B)	Doxorubicin (Arm A)	
Total subjects affected by serious adverse events			
subjects affected / exposed	45 / 81 (55.56%)	13 / 37 (35.14%)	
number of deaths (all causes)	10	1	
number of deaths resulting from adverse events			
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 3	0 / 0	
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Lymphoedema			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Shock haemorrhagic			

subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgical and medical procedures			
Catheter management			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Surgery			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
General physical health deterioration			
subjects affected / exposed	7 / 81 (8.64%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	3 / 7	1 / 1	
deaths causally related to treatment / all	0 / 3	0 / 0	
Impaired healing			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Pyrexia			
subjects affected / exposed	2 / 81 (2.47%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 2	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	1 / 1	
Haemothorax			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Obliterative bronchiolitis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Pneumothorax			
subjects affected / exposed	3 / 81 (3.70%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	3 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia aspiration			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	4 / 81 (4.94%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood creatinine increased			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatic enzyme increased			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Transaminases increased			
subjects affected / exposed	3 / 81 (3.70%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	4 / 4	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Cervical vertebral fracture			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Seroma			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Acute myocardial infarction			

subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Atrial fibrillation			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cerebellar syndrome			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	0 / 81 (0.00%)	2 / 37 (5.41%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			

Macular hole			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Duodenal ulcer perforation			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastric haemorrhage			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Intestinal perforation			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Stomatitis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Subileus			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	2 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Hypertransaminasaemia			
subjects affected / exposed	3 / 81 (3.70%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	3 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Acute kidney injury			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Spinal column stenosis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Clostridium difficile infection			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Erysipelas			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Device related infection			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			

subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Infected seroma			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neutropenic sepsis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	3 / 81 (3.70%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	2 / 3	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Sepsis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urosepsis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 81 (1.23%)	2 / 37 (5.41%)	
occurrences causally related to treatment / all	0 / 1	1 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Wound infection			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Hyponatraemia			

subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hypokalaemia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Pazopanib (Arm B)	Doxorubicin (Arm A)	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	80 / 81 (98.77%)	37 / 37 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Neoplasm progression			
subjects affected / exposed	3 / 81 (3.70%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
Tumour pain			
subjects affected / exposed	3 / 81 (3.70%)	0 / 37 (0.00%)	
occurrences (all)	4	0	
Vascular disorders			
Hypertensive crisis			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Hypotension			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Lymphoedema			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Haematoma			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Hypertension			

subjects affected / exposed	30 / 81 (37.04%)	3 / 37 (8.11%)	
occurrences (all)	38	3	
Thrombophlebitis superficial			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Shock haemorrhagic			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Thrombosis			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Surgical and medical procedures			
Catheter management			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Surgery			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Disease progression			
subjects affected / exposed	3 / 81 (3.70%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
Chills			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Chest pain			
subjects affected / exposed	1 / 81 (1.23%)	2 / 37 (5.41%)	
occurrences (all)	1	2	
Chest discomfort			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Asthenia			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Influenza like illness			

subjects affected / exposed	1 / 81 (1.23%)	2 / 37 (5.41%)	
occurrences (all)	1	2	
Impaired healing			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
General physical health deterioration			
subjects affected / exposed	11 / 81 (13.58%)	1 / 37 (2.70%)	
occurrences (all)	12	1	
Gait disturbance			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Fatigue			
subjects affected / exposed	47 / 81 (58.02%)	24 / 37 (64.86%)	
occurrences (all)	59	29	
Drug intolerance			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Localised oedema			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Oedema peripheral			
subjects affected / exposed	5 / 81 (6.17%)	3 / 37 (8.11%)	
occurrences (all)	8	3	
Mucosal inflammation			
subjects affected / exposed	10 / 81 (12.35%)	9 / 37 (24.32%)	
occurrences (all)	10	10	
Pain			
subjects affected / exposed	10 / 81 (12.35%)	1 / 37 (2.70%)	
occurrences (all)	10	1	
Temperature intolerance			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Sensation of blood flow			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Pyrexia			

subjects affected / exposed	3 / 81 (3.70%)	2 / 37 (5.41%)	
occurrences (all)	3	5	
Peripheral swelling			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Reproductive system and breast disorders			
Balanoposthitis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
Pelvic pain			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Acute respiratory distress syndrome			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Dyspnoea			
subjects affected / exposed	8 / 81 (9.88%)	3 / 37 (8.11%)	
occurrences (all)	8	4	
Dysphonia			
subjects affected / exposed	7 / 81 (8.64%)	0 / 37 (0.00%)	
occurrences (all)	7	0	
Cough			
subjects affected / exposed	11 / 81 (13.58%)	3 / 37 (8.11%)	
occurrences (all)	12	3	
Dyspnoea exertional			
subjects affected / exposed	3 / 81 (3.70%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
Haemothorax			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Haemoptysis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Epistaxis			

subjects affected / exposed	5 / 81 (6.17%)	0 / 37 (0.00%)	
occurrences (all)	5	0	
Pneumonia aspiration			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Pleural effusion			
subjects affected / exposed	1 / 81 (1.23%)	2 / 37 (5.41%)	
occurrences (all)	1	3	
Oropharyngeal pain			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Pneumothorax			
subjects affected / exposed	3 / 81 (3.70%)	0 / 37 (0.00%)	
occurrences (all)	4	0	
Hiccups			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Obliterative bronchiolitis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Pulmonary embolism			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Psychiatric disorders			
Agitation			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Anxiety			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Depressed mood			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Depression			
subjects affected / exposed	3 / 81 (3.70%)	1 / 37 (2.70%)	
occurrences (all)	3	1	

Insomnia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Mental disorder			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	4 / 81 (4.94%)	2 / 37 (5.41%)	
occurrences (all)	4	2	
Product issues			
Device fastener issue			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	9 / 81 (11.11%)	1 / 37 (2.70%)	
occurrences (all)	9	1	
Amylase increased			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Blood bilirubin increased			
subjects affected / exposed	4 / 81 (4.94%)	0 / 37 (0.00%)	
occurrences (all)	6	0	
Blood creatinine increased			
subjects affected / exposed	4 / 81 (4.94%)	0 / 37 (0.00%)	
occurrences (all)	4	0	
Blood urea increased			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Blood alkaline phosphatase increased			
subjects affected / exposed	4 / 81 (4.94%)	0 / 37 (0.00%)	
occurrences (all)	4	0	
Aspartate aminotransferase increased			
subjects affected / exposed	8 / 81 (9.88%)	0 / 37 (0.00%)	
occurrences (all)	8	0	
Breath sounds abnormal			

subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
C-reactive protein increased			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Hepatic enzyme increased			
subjects affected / exposed	3 / 81 (3.70%)	1 / 37 (2.70%)	
occurrences (all)	3	1	
Lipase increased			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Lymphocyte count decreased			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Neutrophil count decreased			
subjects affected / exposed	0 / 81 (0.00%)	5 / 37 (13.51%)	
occurrences (all)	0	7	
Platelet count decreased			
subjects affected / exposed	4 / 81 (4.94%)	0 / 37 (0.00%)	
occurrences (all)	4	0	
Respiratory sinus arrhythmia magnitude			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Transaminases increased			
subjects affected / exposed	3 / 81 (3.70%)	0 / 37 (0.00%)	
occurrences (all)	5	0	
White blood cell count decreased			
subjects affected / exposed	1 / 81 (1.23%)	2 / 37 (5.41%)	
occurrences (all)	1	3	
Weight decreased			
subjects affected / exposed	10 / 81 (12.35%)	2 / 37 (5.41%)	
occurrences (all)	10	2	
Injury, poisoning and procedural complications			

Wound dehiscence			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Wound complication			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Seroma			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
Rib fracture			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Incisional hernia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Cervical vertebral fracture			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Atrial fibrillation			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Aortic valve stenosis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Acute myocardial infarction			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Bradycardia			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Cardiac failure			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Cardiovascular disorder			

subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Ventricular arrhythmia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Tachyarrhythmia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Nervous system disorders			
Dizziness			
subjects affected / exposed	4 / 81 (4.94%)	1 / 37 (2.70%)	
occurrences (all)	5	1	
Disturbance in attention			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Cerebrovascular accident			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Cerebellar syndrome			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Ageusia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Hemiparesis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Headache			
subjects affected / exposed	9 / 81 (11.11%)	1 / 37 (2.70%)	
occurrences (all)	9	1	
Head discomfort			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Facial paralysis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	

Dysgeusia			
subjects affected / exposed	14 / 81 (17.28%)	3 / 37 (8.11%)	
occurrences (all)	14	3	
Hypoaesthesia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Dysarthria			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Neuralgia			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Syncope			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Polyneuropathy			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Phantom pain			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Peroneal nerve palsy			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Paraesthesia			
subjects affected / exposed	4 / 81 (4.94%)	0 / 37 (0.00%)	
occurrences (all)	5	0	
Orthostatic intolerance			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	7 / 81 (8.64%)	8 / 37 (21.62%)	
occurrences (all)	15	11	
Febrile neutropenia			

subjects affected / exposed	0 / 81 (0.00%)	3 / 37 (8.11%)	
occurrences (all)	0	3	
Anaemia			
subjects affected / exposed	8 / 81 (9.88%)	9 / 37 (24.32%)	
occurrences (all)	10	13	
Lymphopenia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Neutropenia			
subjects affected / exposed	8 / 81 (9.88%)	11 / 37 (29.73%)	
occurrences (all)	13	20	
Thrombocytopenia			
subjects affected / exposed	11 / 81 (13.58%)	3 / 37 (8.11%)	
occurrences (all)	19	3	
Ear and labyrinth disorders			
Hypoacusis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Vertigo			
subjects affected / exposed	2 / 81 (2.47%)	2 / 37 (5.41%)	
occurrences (all)	2	2	
Eye disorders			
Eye haemorrhage			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Visual acuity reduced			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Macular hole			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Lacrimation increased			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Visual impairment			

subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Gastrointestinal disorders			
Diarrhoea			
subjects affected / exposed	35 / 81 (43.21%)	5 / 37 (13.51%)	
occurrences (all)	41	5	
Abdominal distension			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Abdominal pain			
subjects affected / exposed	7 / 81 (8.64%)	0 / 37 (0.00%)	
occurrences (all)	8	0	
Abdominal pain upper			
subjects affected / exposed	5 / 81 (6.17%)	0 / 37 (0.00%)	
occurrences (all)	5	0	
Abdominal wall haemorrhage			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Anal fissure			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Anorectal discomfort			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Constipation			
subjects affected / exposed	7 / 81 (8.64%)	5 / 37 (13.51%)	
occurrences (all)	8	5	
Dry mouth			
subjects affected / exposed	2 / 81 (2.47%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Duodenal ulcer perforation			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Dyspepsia			
subjects affected / exposed	1 / 81 (1.23%)	2 / 37 (5.41%)	
occurrences (all)	1	2	

Dysphagia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Epulis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Eructation			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Flatulence			
subjects affected / exposed	3 / 81 (3.70%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
Gastric haemorrhage			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Gastritis			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 81 (1.23%)	2 / 37 (5.41%)	
occurrences (all)	1	2	
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Intestinal perforation			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Nausea			
subjects affected / exposed	35 / 81 (43.21%)	18 / 37 (48.65%)	
occurrences (all)	40	25	
Oesophagitis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	

Vomiting			
subjects affected / exposed	16 / 81 (19.75%)	7 / 37 (18.92%)	
occurrences (all)	18	9	
Subileus			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	2	
Stomatitis			
subjects affected / exposed	3 / 81 (3.70%)	7 / 37 (18.92%)	
occurrences (all)	3	13	
Retroperitoneal haematoma			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Regurgitation			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Hypertransaminasaemia			
subjects affected / exposed	3 / 81 (3.70%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
Jaundice			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 81 (2.47%)	20 / 37 (54.05%)	
occurrences (all)	2	21	
Decubitus ulcer			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Dry skin			
subjects affected / exposed	3 / 81 (3.70%)	0 / 37 (0.00%)	
occurrences (all)	3	0	
Erythema			

subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Hair colour changes			
subjects affected / exposed	5 / 81 (6.17%)	0 / 37 (0.00%)	
occurrences (all)	5	0	
Intertrigo			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Nail dystrophy			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Night sweats			
subjects affected / exposed	2 / 81 (2.47%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Rash			
subjects affected / exposed	5 / 81 (6.17%)	1 / 37 (2.70%)	
occurrences (all)	5	1	
Xeroderma			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Skin lesion			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Skin hypopigmentation			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Skin fissures			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Skin exfoliation			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences (all)	2	0	

Scar pain			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Bladder discomfort			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Acute kidney injury			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Urinary retention			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Polyuria			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Nocturia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Leukocyturia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Haematuria			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Dysuria			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Endocrine disorders			
Hyperthyroidism			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Hypothyroidism			
subjects affected / exposed	11 / 81 (13.58%)	0 / 37 (0.00%)	
occurrences (all)	11	0	
Musculoskeletal and connective tissue disorders			

Flank pain			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Coccydynia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Clubbing			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Bone pain			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Back pain			
subjects affected / exposed	5 / 81 (6.17%)	0 / 37 (0.00%)	
occurrences (all)	6	0	
Groin pain			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Arthralgia			
subjects affected / exposed	2 / 81 (2.47%)	2 / 37 (5.41%)	
occurrences (all)	2	2	
Muscular weakness			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal chest pain			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal pain			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Muscle tightness			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Muscle spasms			
subjects affected / exposed	5 / 81 (6.17%)	0 / 37 (0.00%)	
occurrences (all)	5	0	

Limb discomfort			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Myalgia			
subjects affected / exposed	2 / 81 (2.47%)	1 / 37 (2.70%)	
occurrences (all)	2	1	
Pain in extremity			
subjects affected / exposed	10 / 81 (12.35%)	2 / 37 (5.41%)	
occurrences (all)	12	3	
Spinal pain			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Spinal column stenosis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Clostridium difficile infection			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Candida infection			
subjects affected / exposed	0 / 81 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Bronchitis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Acinetobacter infection			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Abscess			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Cystitis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Infection			

subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Infected seroma			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Herpes virus infection			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Gastroenteritis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Erysipelas			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Device related infection			
subjects affected / exposed	0 / 81 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Pneumonia staphylococcal			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Pneumonia			
subjects affected / exposed	4 / 81 (4.94%)	1 / 37 (2.70%)	
occurrences (all)	4	1	
Pharyngitis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Oral candidiasis			
subjects affected / exposed	0 / 81 (0.00%)	2 / 37 (5.41%)	
occurrences (all)	0	2	
Oesophageal candidiasis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Respiratory tract infection			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Neutropenic sepsis			

subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Sepsis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Streptococcal infection			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Urosepsis			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Urinary tract infection			
subjects affected / exposed	4 / 81 (4.94%)	4 / 37 (10.81%)	
occurrences (all)	5	4	
Upper respiratory tract infection			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Tonsillitis			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Subcutaneous abscess			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Wound infection			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
Hypercalcaemia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Fluid retention			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	2	

Dehydration			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Decreased appetite			
subjects affected / exposed	28 / 81 (34.57%)	10 / 37 (27.03%)	
occurrences (all)	32	12	
Hyperglycaemia			
subjects affected / exposed	1 / 81 (1.23%)	1 / 37 (2.70%)	
occurrences (all)	1	1	
Hypoalbuminaemia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Hyponatraemia			
subjects affected / exposed	2 / 81 (2.47%)	0 / 37 (0.00%)	
occurrences (all)	2	0	
Hypomagnesaemia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Hypokalaemia			
subjects affected / exposed	3 / 81 (3.70%)	2 / 37 (5.41%)	
occurrences (all)	3	3	
Hypocalcaemia			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	
Hypophosphataemia			
subjects affected / exposed	0 / 81 (0.00%)	1 / 37 (2.70%)	
occurrences (all)	0	1	
Magnesium deficiency			
subjects affected / exposed	1 / 81 (1.23%)	0 / 37 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
23 August 2012	SA No. 1 covered the following major changes: additional assessment of vital signs after week 2, 3, 6, 9, 12, 15, 19, 26, and every 6 weeks as part of the extension study; adjustment of tumor imaging methods
27 September 2013	SA No. 2 covered the following major changes: changes due to update of Investigator's Brochure of pazopanib
27 March 2015	SA No. 3 covered the following major changes: clarification of study duration and end
09 November 2015	SA No. 4 covered the following major changes: 6-months prolongation of recruiting time

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.

None reported

Notes:

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27387325

http://www.ncbi.nlm.nih.gov/pubmed/32840417