Clinical trial results:
Phase II randomized clinical trial of Pazopanib alone and Pazopanib plus Gemcitabine in relapsed or metastatic soft tissue sarcoma

Summary

EudraCT number	2009-017261-32
Trial protocol	DE
Global end of trial date	10 May 2016

Results information

Result version number	v1 (current)
This version publication date	21 August 2025
First version publication date	21 August 2025
Summary attachment (see zip file)	PAPAGEMO Final Study Report (Ergebnisbericht_PAPAGEMO_final_Unterschriften.pdf)

Trial information

Trial identification

Sponsor protocol code	KKSH077

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	-
WHO universal trial number (UTN)	-
Other trial identifiers	AIO: AIO-STS-009, German Clinical Trials Register: DRKS00003139

Notes:

Sponsors

Sponsor organisation name	Martin-Luther-Universität Halle-Wittenberg
Sponsor organisation address	Magdeburger Str. 8, Halle (Saale), Germany, 06112
Public contact	Koordinierungszentrum für klinische Studien Halle/S., Koordinierungszentrum für klinische Studien Halle/S., +49 03455574903, info@kks-halle.de
Scientific contact	Koordinierungszentrum für klinische Studien Halle/S., Koordinierungszentrum für klinische Studien Halle/S., +49 03455574903, info@kks-halle.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	15 June 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	10 May 2016
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this phase II trial is to assess the efficacy and toxicity of pazopanib alone or pazopanib plus gemcitabine in patients with refractory or relapsed metastatic soft tissue sarcoma (STS).

Protection of trial subjects:

The responsible investigator will ensure that this study is conducted in agreement with either the Declaration of Helsinki (from June 1964, Tokyo October 1975, Venice October 1983, Hong Kong September 1989, Somerset West October 1996 and Edinburgh amendments from 2000) or the laws and regulations. The protocol has been written, and the study will be conducted according to the ICH Harmonized Tripartite Guideline for Good Clinical Practice (reference: http://www.ifpma.org/pdfifpma/e6.pdf). The protocol will be approved by Independent Ethics

Background therapy:

Subjects received full supportive care during the study, including transfusion of blood and blood products, and treatment with antibiotics, analgesics, erythropoietin, or bisphosphonates, when appropriate. Due to the low emetogen potential of either Pazopanib and gemcitabine no standard antiemetic medication was recommended. In case of vomiting or emesis procedures according to institutional guidelines had to be used. In patients with diarrhoea and neutropenia, even in the absence of fever, empiric use of antibiotics as prophylaxis against bowel sepsis was to be considered. The use of a quinolone was not recommended in this setting due to the potential for QT prolongation. Haematopoietic growth factors (i.e., G- or GM-CSF) may be used according to institutional guidelines to treat febrile neutropenia, and as primary or secondary prophylaxis in case of delayed haematologic recovery during the priory cycle of treatment in Arm A. Growth factors had to be discontinued at least 48 hours prior to initiation of the next treatment of chemotherapy.

Evidence for comparator:

An evidence based therapy regime cannot be recommended. New therapy options are awaited eagerly. The superior activity of pazopanib monotherapy, in the patients collective included in this trial, compared to placebo has been proven. Compared to historical data patients profit remarkable good by a pazopanib monotherpy.

Actual start date of recruitment	01 July 2011
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	Germany: 90
Worldwide total number of subjects	90
EEA total number of subjects	90

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)	66
From 65 to 84 years	24
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Between September 2011 and June 2014, the planned number of 90 patients were recruited at 14 trial sites, all of them in Germany. The last patient completed study treatment in September 2015 and study follow-up in May 2016. For the individual patient, study treatment was scheduled until progression or intolerable toxicity.

Pre-assignment

Screening details:

Patients eligable for this clinical trial will ultimately die of the disease and live expectancy in mean is short. Therefore all patients with relapsed or metastatic soft tissue sarcoma presenting at the participating trial sites with an indication for therapy were screened for selection criteria. There was no selection based on other criteria.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Pazopanib+GEM

Arm description:

Pazopanib 800 mg administered orally once a day, until disease progression. Gemcitabine administered intravenously over 30min at a dose of 1000 mg/m2 (day 1, 8,
repeated after 21 days), until disease progression

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

Dosage and administration details:

Pazopanib tablets were provided as 200 mg and 400 mg tablets, which contain pazopanib monohydrochloride salt equivalent to 200 mg and 400 mg of the free base, respectively. It was suggested to applicate 2x400 mg tablets to approach the initial dose level of 800 mg. 200 mg tablets were only be used in case of dose deescalation. Patients received pazopanib orally, 800 mg once daily until disease progression. In this study, a 3 week interval of dosing was considered as a "treatment period" or "cycle of therapy".

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	Gemcitabine
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine at a dose of 1000 mg/sqm i.v. over 30min (day 1, 8, repeated after 21days), until disease progression.

Arm title	Pazopanib

Arm description:

Pazopanib 800 mg administered orally once a day, until disease progression

Arm type	Active comparator

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

Dosage and administration details:

Pazopanib tablets were provided as 200 mg and 400 mg tablets, which contain pazopanib monohydrochloride salt equivalent to 200 mg and 400 mg of the free base, respectively. It was suggested to applicate 2x400 mg tablets to approach the initial dose level of 800 mg. 200 mg tablets were only be used in case of dose deescalation. Patients received pazopanib orally, 800 mg once daily until disease progression. In this study, a 3 week interval of dosing was considered as a "treatment period" or "cycle of therapy".

Investigational medicinal product name	Gemcitabine
Investigational medicinal product code	Gemcitabine
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Gemcitabine at a dose of 1000 mg/sqm i.v. over 30min (day 1, 8, repeated after 21days), until disease progression.

Number of subjects in period 1	Pazopanib+GEM	Pazopanib
Started	44	46
Completed	43	43
Not completed	1	3
Consent withdrawn by subject	-	1
Progress/relapse after one or two prior CTx	-	1
Did not received one dose of study medication	-	1
Failed inclusion crit.: Adequate organ fuction	1	-

Baseline characteristics

Reporting groups	
Reporting group title	Pazopanib+GEM
Reporting group description:	
Pazopanib 800 mg administered orally once a day, until disease progression. Gemcitabine administered intravenously over 30min at a dose of 1000 mg/m2 (day 1, 8, repeated after 21 days), until disease progression	
Reporting group title	Pazopanib
Reporting group description:	
Pazopanib 800 mg administered orally once a day, until disease progression	

Reporting group values	Pazopanib+GEM	Pazopanib	Total
Number of subjects	44	46	90
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			
ITT n=86			
Units: years			
median	57	59	
full range (min-max)	23 to 84	22 to 81	-
Gender categorical			
ITT n=86			
Units: Subjects			
Female	23	23	46
Male	20	20	40
not determined	1	3	4
ECOG performance status			
ITT n=86			
Units: Subjects			
Missing	2	5	7
ECOG 0	21	15	36
ECOG 1	17	24	41
ECOG 2	4	2	6
Liposarcoma			
ITT n=86			
Units: Subjects			
No	34	36	70
Yes	9	7	16

Not determined	1	3	4
WHO histological classification at initial diagnosis			
ITT n=86			
Units: Subjects			
Angiosarcoma	2	2	4
Fibrosarcoma	0	0	0
Haemangioendothelioma	0	0	0
Leiomyosarcoma	14	8	22
Liposarcoma	9	7	16
Malignant glomus tumour	0	0	0
Malignant peripheral nerve sheath tumour	1	3	4
Malignant tenosynovial giant cell tumour	0	0	0
Malignant fibrous histiocytoma (MFH)	1	1	2
Malignant haemangiopericytoma	0	0	0
Malignant mesenchymoma	1	0	1
Malignant paraganglioma	0	0	0
Mesothelioma	0	0	0
Rhabdomyosarcoma	0	3	3
Other	16	22	38
Grading at initial diagnosis			
ITT n=86			
Units: Subjects			
Missing	8	13	21
G0	0	0	0
G1	2	2	4
G1/2	1	2	3
G2	13	10	23
G2/3	2	2	4
G3	15	14	29
G3/4	2	0	2
G4	0	3	3
GX	1	0	1
Location at initial diagnosis, Upper extremity Units: Subjects			
No	42	39	81
Yes	1	4	5
Not determined	1	3	4
Location at initial diagnosis, Lower extremity			
ITT n=86			
Units: Subjects			
No	34	25	59
Yes	9	18	27
Not determined	1	3	4
Location at initial diagnosis - head, face and neck			
ITT n=86			
Units: Subjects			
No	41	41	82

Yes	2	2	4
Not determined	1	3	4
Location at initial diagnosis, Thorax			
ITT n=86			
Units: Subjects			
No	30	36	66
Yes	13	7	20
Not determined	1	3	4
Location at initial diagnosis, Abdomen			
ITT n=86			
Units: Subjects			
No	26	34	60
Yes	17	9	26
Not determined	1	3	4
Location at initial diagnosis, Pelvis			
ITT n=86			
Units: Subjects			
No	34	34	68
Yes	9	9	18
Not determined	1	3	4
Clinical stage at initial diagnosis - T-status			
ITT n=86			
Units: Subjects			
T0	0	1	1
T1	6	3	9
T2	20	17	37
T3	3	3	6
T4	3	0	3
Tis/Ta	0	0	0
TX	8	13	21
Missing	4	9	13
Clinical stage at initial diagnosis - N-status			
ITT n=86			
Units: Subjects			
N0	19	13	32
N1	5	1	6
N2	0	2	2
N3	0	1	1
NX	13	19	32
Missing	7	10	17
Clinical stage at initial diagnosis - M-status			
ITT n=86			
Units: Subjects			
M0	9	13	22
M1	29	18	47
MX	3	9	12
Missing	3	6	9
Clinical stage at initial diagnosis - Stage			
ITT n=86			

Units: Subjects			
0.	0	1	1
IA	1	1	2
IB	3	2	5
IIA	0	4	4
IIB	3	5	8
IIC	0	0	0
III	7	4	11
IV	26	20	46
Missing	4	9	13
Weight			
ITT n=86			
Units: kilogram(s)			
median	72.0	73.7	
full range (min-max)	49.0 to 108.0	46.0 to 115.0	-
Height			
ITT n=86			
Units: cm			
median	170	170	
full range (min-max)	152 to 195	151 to 193	-
BMI			
ITT n=86			
Units: kg/sqm			
median	24.91	24.79	
full range (min-max)	17.0 to 32.8	17.0 to 39.8	-
Alanine aminotransferase (ALT)			
ITT n=86			
Units: micromole(s)/litre*s			
arithmetic mean	0.451	0.437	
standard deviation	± 0.223	± 0.298	-
Aspartate aminotransferase (AST)			
ITT n=86			
Units: micromole(s)/litre*s			
arithmetic mean	0.434	0.470	
standard deviation	± 0.178	± 0.239	-
Alkaline phosphatase (ALP)			
ITT n=86			
Units: micromole(s)/litre*s			
arithmetic mean	1.985	1.646	
standard deviation	± 0.969	± 0.927	-
Gamma-glutamyl-transferase (GGT)			
ITT n=86			
Units: micromole(s)/litre*s			
arithmetic mean	1.783	1.222	
standard deviation	± 2.266	± 1.520	-
Total bilirubin			
ITT n=86			
Units: micromole(s)/litre			
arithmetic mean	8.4	8.8	
standard deviation	± 3.9	± 4.6	-

End points

End points reporting groups

Reporting group title	Pazopanib+GEM
Reporting group description:	
Pazopanib 800 mg administered orally once a day, until disease progression. Gemcitabine administered intravenously over 30min at a dose of 1000 mg/m2 (day 1, 8, repeated after 21 days), until disease progression	
Reporting group title	Pazopanib
Reporting group description:	
Pazopanib 800 mg administered orally once a day, until disease progression	

Primary: progression-free survival (PFS) 12 weeks after randomisation

End point title	progression-free survival (PFS) 12 weeks after randomisation
End point description:	
End point type	Primary
End point timeframe:	
12 weeks after randomisation	

End point values	Pazopanib+GEM	Pazopanib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	42	43		
Units: N	31	20		

Statistical analyses

Statistical analysis title	one-sided Cochran-Mantel-Haenszel (CMH) test
Comparison groups	Pazopanib+GEM v Pazopanib
Number of subjects included in analysis	85
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.006
Method	Cochran-Mantel-Haenszel

Secondary: overall survival (OS) after randomisation

End point title	overall survival (OS) after randomisation
End point description:	
These secondary endpoints were analyzed in an exploratory manner.	
End point type	Secondary

End point timeframe:
from randomisation until death

End point values	Pazopanib+GEM	Pazopanib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: Months				
median (confidence interval 95%)	13.1 (7.3 to 17.9)	11.2 (7.2 to 20.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: time to progression (TTP) after randomisation

End point title	time to progression (TTP) after randomisation

End point description:
These secondary endpoints were analyzed in an exploratory manner.

End point type	Secondary

End point timeframe:
from randomisation until progression

End point values	Pazopanib+GEM	Pazopanib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: Months				
median (confidence interval 95%)	5.6 (4.1 to 8.5)	2.0 (1.6 to 3.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: best overall response

End point title	best overall response

End point description:
best overall response was CR or PR

End point type	Secondary

End point timeframe:
from randomisation until progression

End point values	Pazopanib+GEM	Pazopanib		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	43	43		
Units: N				
CR+PR	5	2		
SD+PD+death	38	41		

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

AEs: from the informed consent until 28 days after the last administration of study treatment. Additionally all SAEs related to study medication (SAR) were recorded through the entire follow-up period, 18 months after last administration of treatment.

Adverse event reporting additional description:

AEs were summarized by System Organ Class (SOC) and Preferred Term (PT), grade, and relationship to study treatment. In the summary by grade, only the worst case per PT for each patient will was counted, if a patient experiences more than one AE within a PT. All AEs were included in the summary by relationship to study treatment.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	14.1

Reporting groups

Reporting group title	Safety analysis Pazopanib+GEM
Reporting group description: -	
Reporting group title	Safety Analysis Pazopanib

Reporting group description: -

Serious adverse events	Safety analysis Pazopanib+GEM	Safety Analysis Pazopanib	
Total subjects affected by serious adverse events			
subjects affected / exposed	26 / 43 (60.47%)	21 / 44 (47.73%)	
number of deaths (all causes)	34	37	
number of deaths resulting from adverse events	3	5	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Metastatic pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Neoplasm progression			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Tumour pain			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Vascular disorders			
Hypertension			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombosis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
Multi-organ failure			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Impaired healing			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Chest pain			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Disease progression			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Fatigue			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General physical health deterioration			
subjects affected / exposed	1 / 43 (2.33%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	1 / 1	0 / 1	

Pyrexia			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory, thoracic and mediastinal disorders			
Pneumothorax			
subjects affected / exposed	2 / 43 (4.65%)	3 / 44 (6.82%)	
occurrences causally related to treatment / all	1 / 6	4 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Acute respiratory distress syndrome			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	1 / 1	0 / 0	
Cough			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pleural effusion			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pulmonary embolism			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Investigations			
Hepatic enzyme increased			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Alanine aminotransferase increased			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	

Transaminases increased			
subjects affected / exposed	1 / 43 (2.33%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Postoperative wound complication			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (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			
Paraparesis			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 1	
Somnolence			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Syncope			
subjects affected / exposed	1 / 43 (2.33%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Blood and lymphatic system disorders			
Anaemia			

subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Febrile neutropenia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Thrombocytopenia			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Eye disorders			
Vitreous haemorrhage			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 43 (2.33%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	1 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Diarrhoea			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal pain			
subjects affected / exposed	1 / 43 (2.33%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Anal fistula			

subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatotoxicity			
subjects affected / exposed	1 / 43 (2.33%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Jaundice cholestatic			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal and urinary disorders			
Bladder perforation			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Renal failure			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	2 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	0 / 43 (0.00%)	2 / 44 (4.55%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Fistula			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	

Muscular weakness			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (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			
Diverticulitis			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	1 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Abdominal abscess			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infection			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 3	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pneumonia			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	0 / 43 (0.00%)	1 / 44 (2.27%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Metabolic disorder			
subjects affected / exposed	1 / 43 (2.33%)	0 / 44 (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: 5 %

Non-serious adverse events	Safety analysis Pazopanib+GEM	Safety Analysis Pazopanib	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	43 / 43 (100.00%)	44 / 44 (100.00%)	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	3 / 43 (6.98%)	3 / 44 (6.82%)	
occurrences (all)	3	3	
Vascular disorders			
Haematoma			
subjects affected / exposed	3 / 43 (6.98%)	0 / 44 (0.00%)	
occurrences (all)	4	0	
Hypertension			
subjects affected / exposed	8 / 43 (18.60%)	9 / 44 (20.45%)	
occurrences (all)	12	12	
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	4 / 43 (9.30%)	4 / 44 (9.09%)	
occurrences (all)	5	4	
Chills			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Fatigue			
subjects affected / exposed	14 / 43 (32.56%)	17 / 44 (38.64%)	
occurrences (all)	25	18	
General physical health deterioration			
subjects affected / exposed	4 / 43 (9.30%)	1 / 44 (2.27%)	
occurrences (all)	4	1	
Local Swelling			
subjects affected / exposed	1 / 43 (2.33%)	2 / 44 (4.55%)	
occurrences (all)	1	3	
Localised oedema			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Mucosal inflammation			
subjects affected / exposed	3 / 43 (6.98%)	3 / 44 (6.82%)	
occurrences (all)	4	3	

Oedema			
subjects affected / exposed	2 / 43 (4.65%)	3 / 44 (6.82%)	
occurrences (all)	4	3	
Pain			
subjects affected / exposed	4 / 43 (9.30%)	4 / 44 (9.09%)	
occurrences (all)	4	4	
Pyrexia			
subjects affected / exposed	10 / 43 (23.26%)	2 / 44 (4.55%)	
occurrences (all)	13	3	
Oedema peripheral			
subjects affected / exposed	10 / 43 (23.26%)	0 / 44 (0.00%)	
occurrences (all)	11	0	
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	15 / 43 (34.88%)	8 / 44 (18.18%)	
occurrences (all)	18	13	
Dysphonia			
subjects affected / exposed	1 / 43 (2.33%)	2 / 44 (4.55%)	
occurrences (all)	1	2	
Dyspnoea			
subjects affected / exposed	9 / 43 (20.93%)	6 / 44 (13.64%)	
occurrences (all)	11	6	
Dyspnoea exertional			
subjects affected / exposed	4 / 43 (9.30%)	4 / 44 (9.09%)	
occurrences (all)	4	5	
Epistaxis			
subjects affected / exposed	7 / 43 (16.28%)	0 / 44 (0.00%)	
occurrences (all)	11	0	
Oropharyngeal pain			
subjects affected / exposed	2 / 43 (4.65%)	2 / 44 (4.55%)	
occurrences (all)	2	2	
Pleural effusion			
subjects affected / exposed	4 / 43 (9.30%)	2 / 44 (4.55%)	
occurrences (all)	4	3	
Pneumothorax			

subjects affected / exposed	2 / 43 (4.65%)	3 / 44 (6.82%)	
occurrences (all)	6	5	
Respiratory distress			
subjects affected / exposed	4 / 43 (9.30%)	1 / 44 (2.27%)	
occurrences (all)	4	3	
Psychiatric disorders			
Depression			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Insomnia			
subjects affected / exposed	1 / 43 (2.33%)	2 / 44 (4.55%)	
occurrences (all)	1	2	
Sleep disorder			
subjects affected / exposed	2 / 43 (4.65%)	1 / 44 (2.27%)	
occurrences (all)	3	1	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	10 / 43 (23.26%)	5 / 44 (11.36%)	
occurrences (all)	19	8	
Aspartate aminotransferase increased			
subjects affected / exposed	11 / 43 (25.58%)	4 / 44 (9.09%)	
occurrences (all)	27	6	
Blood alkaline phosphatase increased			
subjects affected / exposed	7 / 43 (16.28%)	2 / 44 (4.55%)	
occurrences (all)	8	2	
Blood bilirubin increased			
subjects affected / exposed	4 / 43 (9.30%)	1 / 44 (2.27%)	
occurrences (all)	7	1	
Blood creatinine increased			
subjects affected / exposed	5 / 43 (11.63%)	0 / 44 (0.00%)	
occurrences (all)	8	0	
Gamma-glutamyltransferase increased			
subjects affected / exposed	10 / 43 (23.26%)	4 / 44 (9.09%)	
occurrences (all)	19	7	
Platelet count decreased			

subjects affected / exposed	3 / 43 (6.98%)	0 / 44 (0.00%)	
occurrences (all)	7	0	
Weight decreased			
subjects affected / exposed	12 / 43 (27.91%)	11 / 44 (25.00%)	
occurrences (all)	15	12	
White blood cell count decreased			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences (all)	5	0	
Injury, poisoning and procedural complications			
Humerus fracture			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Nervous system disorders			
Burning sensation			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Dizziness			
subjects affected / exposed	4 / 43 (9.30%)	1 / 44 (2.27%)	
occurrences (all)	4	1	
Dysgeusia			
subjects affected / exposed	5 / 43 (11.63%)	7 / 44 (15.91%)	
occurrences (all)	5	7	
Headache			
subjects affected / exposed	7 / 43 (16.28%)	3 / 44 (6.82%)	
occurrences (all)	8	3	
Hypoaesthesia			
subjects affected / exposed	3 / 43 (6.98%)	2 / 44 (4.55%)	
occurrences (all)	3	2	
Paraesthesia			
subjects affected / exposed	1 / 43 (2.33%)	3 / 44 (6.82%)	
occurrences (all)	1	3	
Somnolence			
subjects affected / exposed	19 / 43 (44.19%)	11 / 44 (25.00%)	
occurrences (all)	27	13	
Blood and lymphatic system disorders			

Anaemia			
subjects affected / exposed	16 / 43 (37.21%)	4 / 44 (9.09%)	
occurrences (all)	26	7	
Leukopenia			
subjects affected / exposed	20 / 43 (46.51%)	3 / 44 (6.82%)	
occurrences (all)	53	12	
Lymph node pain			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Neutropenia			
subjects affected / exposed	11 / 43 (25.58%)	2 / 44 (4.55%)	
occurrences (all)	36	6	
Thrombocytopenia			
subjects affected / exposed	25 / 43 (58.14%)	6 / 44 (13.64%)	
occurrences (all)	69	12	
Eye disorders			
Visual impairment			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	5 / 43 (11.63%)	3 / 44 (6.82%)	
occurrences (all)	6	3	
Abdominal pain			
subjects affected / exposed	6 / 43 (13.95%)	6 / 44 (13.64%)	
occurrences (all)	7	6	
Abdominal pain lower			
subjects affected / exposed	4 / 43 (9.30%)	1 / 44 (2.27%)	
occurrences (all)	4	1	
Abdominal pain upper			
subjects affected / exposed	5 / 43 (11.63%)	6 / 44 (13.64%)	
occurrences (all)	5	6	
Constipation			
subjects affected / exposed	12 / 43 (27.91%)	3 / 44 (6.82%)	
occurrences (all)	13	3	
Diarrhoea			

subjects affected / exposed	26 / 43 (60.47%)	18 / 44 (40.91%)	
occurrences (all)	42	28	
Dry mouth			
subjects affected / exposed	3 / 43 (6.98%)	1 / 44 (2.27%)	
occurrences (all)	3	1	
Dyspepsia			
subjects affected / exposed	2 / 43 (4.65%)	3 / 44 (6.82%)	
occurrences (all)	2	3	
Nausea			
subjects affected / exposed	22 / 43 (51.16%)	18 / 44 (40.91%)	
occurrences (all)	28	22	
Vomiting			
subjects affected / exposed	11 / 43 (25.58%)	8 / 44 (18.18%)	
occurrences (all)	16	11	
Hepatobiliary disorders			
Hepatotoxicity			
subjects affected / exposed	1 / 43 (2.33%)	2 / 44 (4.55%)	
occurrences (all)	1	2	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	2 / 43 (4.65%)	1 / 44 (2.27%)	
occurrences (all)	2	1	
Erythema			
subjects affected / exposed	3 / 43 (6.98%)	2 / 44 (4.55%)	
occurrences (all)	3	2	
Hair colour changes			
subjects affected / exposed	4 / 43 (9.30%)	3 / 44 (6.82%)	
occurrences (all)	4	3	
Hyperhidrosis			
subjects affected / exposed	1 / 43 (2.33%)	2 / 44 (4.55%)	
occurrences (all)	1	2	
Nail disorder			
subjects affected / exposed	0 / 43 (0.00%)	2 / 44 (4.55%)	
occurrences (all)	0	2	
Night sweats			

subjects affected / exposed	4 / 43 (9.30%)	3 / 44 (6.82%)	
occurrences (all)	5	4	
Palmar-plantar erythrodysaesthesia syndrome			
subjects affected / exposed	2 / 43 (4.65%)	2 / 44 (4.55%)	
occurrences (all)	5	4	
Petechiae			
subjects affected / exposed	2 / 43 (4.65%)	1 / 44 (2.27%)	
occurrences (all)	2	1	
Pruritus			
subjects affected / exposed	2 / 43 (4.65%)	2 / 44 (4.55%)	
occurrences (all)	2	2	
Rash			
subjects affected / exposed	4 / 43 (9.30%)	2 / 44 (4.55%)	
occurrences (all)	4	2	
Renal and urinary disorders			
Dysuria			
subjects affected / exposed	2 / 43 (4.65%)	1 / 44 (2.27%)	
occurrences (all)	2	2	
Nocturia			
subjects affected / exposed	3 / 43 (6.98%)	0 / 44 (0.00%)	
occurrences (all)	3	0	
Renal failure			
subjects affected / exposed	3 / 43 (6.98%)	0 / 44 (0.00%)	
occurrences (all)	4	0	
Endocrine disorders			
Hypothyroidism			
subjects affected / exposed	7 / 43 (16.28%)	5 / 44 (11.36%)	
occurrences (all)	7	6	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	2 / 43 (4.65%)	2 / 44 (4.55%)	
occurrences (all)	3	3	
Back pain			
subjects affected / exposed	5 / 43 (11.63%)	5 / 44 (11.36%)	
occurrences (all)	6	8	
Muscle spasms			

subjects affected / exposed	4 / 43 (9.30%)	4 / 44 (9.09%)	
occurrences (all)	4	4	
Muscular weakness			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal chest pain			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Musculoskeletal pain			
subjects affected / exposed	2 / 43 (4.65%)	4 / 44 (9.09%)	
occurrences (all)	3	4	
Myalgia			
subjects affected / exposed	0 / 43 (0.00%)	3 / 44 (6.82%)	
occurrences (all)	0	4	
Pain in extremity			
subjects affected / exposed	2 / 43 (4.65%)	7 / 44 (15.91%)	
occurrences (all)	2	9	
Infections and infestations			
Bronchitis			
subjects affected / exposed	2 / 43 (4.65%)	2 / 44 (4.55%)	
occurrences (all)	3	2	
Febrile infection			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Infection			
subjects affected / exposed	10 / 43 (23.26%)	5 / 44 (11.36%)	
occurrences (all)	13	8	
Nasopharyngitis			
subjects affected / exposed	11 / 43 (25.58%)	3 / 44 (6.82%)	
occurrences (all)	12	5	
Oral herpes			
subjects affected / exposed	3 / 43 (6.98%)	0 / 44 (0.00%)	
occurrences (all)	3	0	
Pneumonia			
subjects affected / exposed	3 / 43 (6.98%)	0 / 44 (0.00%)	
occurrences (all)	3	0	

Urinary tract infection			
subjects affected / exposed	3 / 43 (6.98%)	5 / 44 (11.36%)	
occurrences (all)	7	9	
Metabolism and nutrition disorders			
Abnormal loss of weight			
subjects affected / exposed	3 / 43 (6.98%)	2 / 44 (4.55%)	
occurrences (all)	3	2	
Cachexia			
subjects affected / exposed	2 / 43 (4.65%)	0 / 44 (0.00%)	
occurrences (all)	2	0	
Decreased appetite			
subjects affected / exposed	12 / 43 (27.91%)	8 / 44 (18.18%)	
occurrences (all)	14	8	
Hyperuricaemia			
subjects affected / exposed	3 / 43 (6.98%)	0 / 44 (0.00%)	
occurrences (all)	3	0	
Hypokalaemia			
subjects affected / exposed	4 / 43 (9.30%)	0 / 44 (0.00%)	
occurrences (all)	4	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 July 2014	Protocol Amendment N01 (17.07.2014) to protocol 2.0 (06-2011), submission of changes regarding the time frame of the analysis of the primary end-point. "The analysis of the primary end-point (progression free survival rate after 12 weeks) will be done after the last subject has obtained the End of Treatment. Secondary end-points (OS, TTP, response rate, toxicity and quality of live) will be analysed if the last subject has finished the follow-up period (last patient, last visit)", approved by the EC on 28.08.2014, implicit approval by CA.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? Yes

Date	Interruption	Restart date
15 August 2013	Temporary halt of the trial due to a fatal hepatic SAE which occurred in a further clinical study investigating the combination of gemcitabine and pazopanib for the treatment of patients with advanced soft tissue sarcoma	19 December 2013

Notes:

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/33355646