Clinical trial results:
Quality of life in patients with non-adipocyte soft tissue sarcoma under palliative chemotherapy or pazopanib – a randomized, controlled trial

Summary

EudraCT number	2017-003382-10
Trial protocol	DE
Global end of trial date	06 October 2020

Results information

Result version number	v1 (current)
This version publication date	27 October 2022
First version publication date	27 October 2022

Trial information

Trial identification

Sponsor protocol code	PazoQol

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT03735758
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GWT-TUD GmbH
Sponsor organisation address	Freiberger Strasse 33, Dresden, Germany, 01067
Public contact	Medical Consulting, GWT-TUD GmbH, +49 03515933100, medical.consulting@g-wt.de
Scientific contact	Medical Consulting, GWT-TUD GmbH, +49 03515933100, medical.consulting@g-wt.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	01 October 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 October 2020
Global end of trial reached?	Yes
Global end of trial date	06 October 2020
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

Compare the overall QoL under treatment with pazopanib or physician-preferred chemotherapy after 9 weeks

Protection of trial subjects:

The conduct of this study was in compliance with the Good Clinical Praactice Guidelines and under the guiding principles detailed in the Declaration of Helsinki. The study was also carried out in keeping with applicable local law(s) and regulation(s). All treatments applied in this study were recommended per guidelines and represent equivalent treatment options.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	02 November 2018
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: 9
Country: Number of subjects enrolled	Switzerland: 1
Worldwide total number of subjects	10
EEA total number of subjects	9

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)	5
From 65 to 84 years	5
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Clinical conduct of the study was between 02 Nov 2018 (date of first informed consent) and 06 Oct 2020 (LPLV) at three study sites in Germany and one study site in Switzerland.

Pre-assignment

Screening details:

Subjects were randomized in a 1:1 fashion and allocated to either pazopanib or to guideline-conform chemotherapy (excluding pazopanib).

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	Arm A

Arm description:

Eight patients were randomized into Arm A and received treatment with pazopanib. Six of them were treated with the planned dose of 800 mg per day. For two subjects a dose modification was documented. Overall, the treatment duration was between 40 and 67 days and patients received a cumulative dose between 29200 and 53600 mg pazopanib.

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:

2 x 400 mg once daily, oral, 9 weeks

Arm title	Arm B

Arm description:

Two patients were randomized into Arm B and received guideline-conform, physician-preferred chemotherapy. One of these patients received treatment with trabectedin and the other one received treatment with gemcitabine with or without docetaxel.

Arm type	Active comparator
Investigational medicinal product name	Trabectedin
Investigational medicinal product code	
Other name	Yondelis
Pharmaceutical forms	Powder for concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

for the treatment of soft tissue sarcoma, the recommended dose 1.5 mg/m^2 body surface area, administered as an intravenous infusion over 24 hours with a three-week interval between cycles, in total of 9 weeks

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

Dosage and administration details: 1000 mg/m^2, given by 30-minute intravenous infusion, repeated once weekly for 3 weeks, in total of 9 weeks	
Investigational medicinal product name	Docetaxel
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use
Dosage and administration details: 75 mg/m^2 administered 1-hour, every 3 weeks, in total of 9 weeks	

Number of subjects in period 1	Arm A	Arm B
Started	8	2
Completed	8	1
Not completed	0	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups	
Reporting group title	overall trial

Reporting group description: -

Reporting group values	overall trial	Total	
Number of subjects	10	10	
Age categorical Units: Subjects			
In utero	0	0	
Preterm newborn infants (gestational age < 37 wks)	0	0	
Newborns (0-27 days)	0	0	
Infants and toddlers (28 days-23 months)	0	0	
Children (2-11 years)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	5	5	
From 65-84 years	5	5	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	8	8	
Male	2	2	

End points

End points reporting groups

Reporting group title	Arm A

Reporting group description:

Eight patients were randomized into Arm A and received treatment with pazopanib. Six of them were treated with the planned dose of 800 mg per day. For two subjects a dose modification was documented. Overall, the treatment duration was between 40 and 67 days and patients received a cumulative dose between 29200 and 53600 mg pazopanib.

Reporting group title	Arm B

Reporting group description:

Two patients were randomized into Arm B and received guideline-conform, physician-preferred chemotherapy. One of these patients received treatment with trabectedin and the other one received treatment with gemcitabine with or without docetaxel.

Primary: Quality of Life

End point title	Quality of Life[1][2]

End point description:

The primary endpoint of this study was the overall QoL measured by EORTC QLQ-C30 sum score after 9 weeks of treatment which was defined as end of treatment (EoT) in this study.

End point type	Primary

End point timeframe:

after 9 weeks

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: Because of the low number of patients finally included in this study statistical analysis of group comparisons was not possible. Thus, only descriptive analysis was performed.
[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Because of the low number of patients finally included in this study statistical analyses of group comparisons were not possible. Thus, parameters were only listed and summarized by descriptive statistics for the whole data set (n=10) and for patients treated with pazopanib (n=8).

End point values	Arm A			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: QLQ-C30 sum score				
arithmetic mean (standard deviation)	66.79 (± 22.22)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

9 weeks

Adverse event reporting additional description:

AEs observed, mentioned upon open questioning by a member of the investigator’s team or spontaneously reported by the subject were documented.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	23.1

Reporting groups

Reporting group title	Overall

Reporting group description: -

Serious adverse events	Overall		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 10 (30.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences causally related to treatment / all	2 / 2		
deaths causally related to treatment / all	0 / 0		
Aspartate aminotransferase increased			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Ejection fraction decreased			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Coronary artery stenosis			

subjects affected / exposed	3 / 10 (30.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cytotoxic cardiomyopathy			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Infection			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
subjects affected / exposed	3 / 10 (30.00%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Overall		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	10 / 10 (100.00%)		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Tumour pain			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	1		
Vascular disorders			
Cyanosis			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	1		
Hypertension			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	4		
Subclavian vein thrombosis			

subjects affected / exposed occurrences (all)	10 / 10 (100.00%) 1		
Surgical and medical procedures Coronary arterial stent insertion subjects affected / exposed occurrences (all)	 10 / 10 (100.00%) 1		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all) Chest discomfort subjects affected / exposed occurrences (all) Chest pain subjects affected / exposed occurrences (all) Fatigue subjects affected / exposed occurrences (all) Oedema peripheral subjects affected / exposed occurrences (all) Swelling subjects affected / exposed occurrences (all)	 10 / 10 (100.00%) 1 10 / 10 (100.00%) 1 10 / 10 (100.00%) 1 10 / 10 (100.00%) 3 10 / 10 (100.00%) 1 10 / 10 (100.00%) 1		
Respiratory, thoracic and mediastinal disorders Dyspnoea subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all)	 10 / 10 (100.00%) 2 10 / 10 (100.00%) 1		
Psychiatric disorders Agitation subjects affected / exposed occurrences (all)	 10 / 10 (100.00%) 1		

Anxiety			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	1		
Investigations			
Alanine aminotransferase abnormal			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	3		
Alanine aminotransferase increased			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	2		
Aspartate aminotransferase abnormal			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	1		
Aspartate aminotransferase decreased			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	1		
Aspartate aminotransferase increased			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	3		
C-reactive protein increased			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	2		
Ejection fraction decreased			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	1		
Heart rate decreased			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	1		
Neutrophil count decreased			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	4		
Platelet Count decreased			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	1		
Transaminases			

subjects affected / exposed occurrences (all) White blood cell count decreased subjects affected / exposed occurrences (all) White blood cell count increased subjects affected / exposed occurrences (all) Hypokalaemia subjects affected / exposed occurrences (all)	10 / 10 (100.00%) 1 10 / 10 (100.00%) 5 10 / 10 (100.00%) 1 10 / 10 (100.00%) 1		
Injury, poisoning and procedural complications Procedural pain subjects affected / exposed occurrences (all)	 10 / 10 (100.00%) 2		
Cardiac disorders Cardiac failure chronic subjects affected / exposed occurrences (all) Coronary artery disease subjects affected / exposed occurrences (all) Sinus bradycardia subjects affected / exposed occurrences (all) Toxic cardiomyopathy subjects affected / exposed occurrences (all)	 10 / 10 (100.00%) 1 10 / 10 (100.00%) 1 10 / 10 (100.00%) 1 10 / 10 (100.00%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all) Peripheral sensory neuropathy subjects affected / exposed occurrences (all)	 10 / 10 (100.00%) 2 10 / 10 (100.00%) 1		
Ear and labyrinth disorders			

Vertigo			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Abdominal distension			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	2		
Abdominal pain			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	1		
Diarrhoea			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	7		
Dysphagia			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	1		
Flatulence			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	2		
Nausea			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	5		
Tongue coated			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	3		
Hepatobiliary disorders			
Autoimmune hepatitis			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	1		
Cholecystitis chronic			
subjects affected / exposed	10 / 10 (100.00%)		
occurrences (all)	1		
Hyperbilirubinemia			

subjects affected / exposed occurrences (all)	10 / 10 (100.00%) 1		
Skin and subcutaneous tissue disorders Hyperhidrosis subjects affected / exposed occurrences (all)	 10 / 10 (100.00%) 2		
Renal and urinary disorders Proteinuria subjects affected / exposed occurrences (all)	 10 / 10 (100.00%) 3		
Endocrine disorders Hypothyroidism subjects affected / exposed occurrences (all)	 10 / 10 (100.00%) 3		
Musculoskeletal and connective tissue disorders Arthralgia subjects affected / exposed occurrences (all) Back pain subjects affected / exposed occurrences (all) Joint swelling subjects affected / exposed occurrences (all) Muscle spasms subjects affected / exposed occurrences (all) Muscular weakness subjects affected / exposed occurrences (all)	 10 / 10 (100.00%) 1 10 / 10 (100.00%) 2 10 / 10 (100.00%) 1 10 / 10 (100.00%) 1 10 / 10 (100.00%) 1		
Infections and infestations Infection subjects affected / exposed occurrences (all) Nasopharyngitis	 10 / 10 (100.00%) 1 		

subjects affected / exposed occurrences (all)	10 / 10 (100.00%) 1		
Metabolism and nutrition disorders Decreased appetite subjects affected / exposed occurrences (all)	 10 / 10 (100.00%) 5		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
17 May 2019	Protocol Version 4.0 dated 08 Aug 2018: Changes to improve the understanding of the protocol and to better adapt the vistite procedures to the clinical routine. The changes to the visit plan regarding ECG measurements increase patient safety.

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.

Recruitment into the study was prematurely terminated. The reason for early termination was a substantial delay in recruitment which did not suggest completion of the study in a reasonable time frame.

Notes: