Clinical trial results:
Phase II Clinical Trial of Pazopanib to evaluate the activity and tolerability in patients with advanced and/or metastatic liposarcoma who have relapsed following standard therapies or for whom no standard therapy exists

Summary

EudraCT number	2012-002745-38
Trial protocol	ES DE
Global end of trial date	02 March 2018

Results information

Result version number	v1 (current)
This version publication date	27 November 2019
First version publication date	27 November 2019
Summary attachment (see zip file)	Clinical Study Report Summary (GEIS-30 - CLINICAL STUDY REPORTS - SYNOPSIS_03Dic2018.pdf)

Trial information

Trial identification

Sponsor protocol code	GEIS-30

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01692496
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	GRUPO ESPAÑOL DE INVESTIGACIÓN EN SARCOMAS - GEIS
Sponsor organisation address	C/ Velázquez nº7, 3ª planta, Madrid, Spain, 28001
Public contact	Secretaría GEIS, GRUPO ESPAÑOL DE INVESTIGACIÓN EN SARCOMAS - GEIS, 34 934344412, investigacion@mfar.net
Scientific contact	Secretaría GEIS, GRUPO ESPAÑOL DE INVESTIGACIÓN EN SARCOMAS - GEIS, 34 934344412, investigacion@mfar.net

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	23 July 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 December 2017
Global end of trial reached?	Yes
Global end of trial date	02 March 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the activity of Pazopanib in patients with advanced and/or metastatic liposarcoma by means of progression-free survival (PFS) assessed 12 weeks after start of treatment. (According the RECIST criteria 1.1 and central radiology review).

Protection of trial subjects:

Subjects will receive investigational product until any of the following occur:
• Subject experiences disease progression according to RECIST V 1.1
• Subject experiences unacceptable toxicities or an adverse experience that would, in the judgement of the investigator, make continued administration of the study regimen an unacceptable risk.
• Subject is considered

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 January 2013
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	Spain: 39
Country: Number of subjects enrolled	Germany: 13
Worldwide total number of subjects	52
EEA total number of subjects	52

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)	52

From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 17 eligible and treated patients will be included in each stratum. Total duration of recruitment period: 30 months.

Pre-assignment

Screening details:

Once a patient has signed the biological samples consent form, at least one representative formaline fixed paraffin embedded tumour block and haematoxylin/eosin slides from all the different areas of the tumor will be collected for central pathological review in order to confirm histological type of sarcoma.

Period 1

Period 1 title	Baseline
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Investigational arm

Arm description:

Single arm (two cohorts) of Pazopanib 800 mg (2x400mg or 4x200 mg) given as a single agent administered once daily.

Arm type	Experimental
Investigational medicinal product name	Pazopanib mono-hydrochloride salt
Investigational medicinal product code	GW786034B)
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Pazopanib 800 mg (2x400mg or 4 x 200 mg) per day, once a day, should be taken orally without food at least one hour before or two hours after a meal until disease progression, the development of unacceptable toxicity, non-compliance, withdrawal of consent by the patient, or investigator decision.

Number of subjects in period 1	Investigational arm
Started	52
Completed	52

Period 2

Period 2 title	End of trial
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Pazopanib

Arm description:

Single arm (two cohorts) of Pazopanib 800 mg (2x400mg or 4x200 mg) given as a single agent administered once daily.

Arm type	Experimental
Investigational medicinal product name	Pazopanib mono-hydrochloride salt
Investigational medicinal product code	GW786034B)
Other name	
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Pazopanib 800 mg (2x400mg or 4 x 200 mg) per day, once a day, should be taken orally without food at least one hour before or two hours after a meal until disease progression, the development of unacceptable toxicity, non-compliance, withdrawal of consent by the patient, or investigator decision.

Number of subjects in period 2	Pazopanib
Started	52
Completed	52

Baseline characteristics

Reporting groups	
Reporting group title	Baseline

Reporting group description: -

Reporting group values	Baseline	Total	
Number of subjects	52	52	
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	58.3		
standard deviation	± 13.5	-	
Gender categorical Units: Subjects			
Female	24	24	
Male	28	28	
Tumour location Units: Subjects			
Pelvis	1	1	
Upper extremities	4	4	
Lower extremities	10	10	
Retroperitoneum	26	26	
Others	11	11	
Histological type Units: Subjects			
Well-differentiated Liposarcoma	6	6	
Well-differentiated Liposarcoma/undifferentiated	8	8	
Undifferentiated Liposarcoma	23	23	
Mixoid Liposarcoma	15	15	
First treatment Units: Subjects			
Yes	42	42	
No	10	10	
Previous chemotherapy Units: Subjects			
Yes	15	15	

No	37	37	

End points

End points reporting groups	
Reporting group title	Investigational arm
Reporting group description:	
Single arm (two cohorts) of Pazopanib 800 mg (2x400mg or 4x200 mg) given as a single agent administered once daily.	
Reporting group title	Pazopanib
Reporting group description:	
Single arm (two cohorts) of Pazopanib 800 mg (2x400mg or 4x200 mg) given as a single agent administered once daily.	
Subject analysis set title	Cohort A
Subject analysis set type	Per protocol
Subject analysis set description:	
Patients with well-differentiated/undiferentiated lyposarcoma (ALT-WD)	
Subject analysis set title	Cohort B
Subject analysis set type	Per protocol
Subject analysis set description:	
Mixoid lyposarcoma/round cells lyposarcoma	

Primary: Progression-free survival (PFS) at 12 weeks	
End point title	Progression-free survival (PFS) at 12 weeks
End point description:	
End point type	Primary
End point timeframe:	
12 weeks after start of treatment	

End point values	Pazopanib	Cohort A	Cohort B	
Subject group type	Reporting group	Subject analysis set	Subject analysis set	
Number of subjects analysed	52	37	15	
Units: Percentage	54	54	40	

Statistical analyses

Statistical analysis title	Comparison on PFS among cohorts
Comparison groups	Cohort A v Cohort B
Number of subjects included in analysis	52
Analysis specification	Pre-specified
Analysis type	other
P-value	< 0.05
Method	Logrank
Parameter estimate	Log risk ratio

Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Secondary: Progression-free survival (PFS)

End point title	Progression-free survival (PFS)
End point description: Weeks	
End point type	Secondary
End point timeframe: 24 months	

End point values	Investigational arm	Pazopanib	Cohort A	Cohort B
Subject group type	Reporting group	Reporting group	Subject analysis set	Subject analysis set
Number of subjects analysed	52	52	37	52
Units: weeks				
median (full range (min-max))	11.86 (2.3 to 195.7)	11.86 (2.3 to 195.7)	15 (5.3 to 217.3)	11.86 (2.3 to 195.7)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival
End point description:	
End point type	Secondary
End point timeframe: 24 months	

End point values	Investigational arm			
Subject group type	Reporting group			
Number of subjects analysed	35			
Units: weeks				
median (full range (min-max))	70.43 (2.3 to 217.3)			

Statistical analyses

No statistical analyses for this end point

Secondary: Growth modulation index

End point title	Growth modulation index

End point description:

End point type	Secondary

End point timeframe:

24 months

End point values	Investigational arm			
Subject group type	Reporting group			
Number of subjects analysed	52			
Units: units				
median (full range (min-max))	0.4 (0.1 to 18.6)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Throughout the study period

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Cohort A
Reporting group description: -	
Reporting group title	Cohort B

Reporting group description: -

Serious adverse events	Cohort A	Cohort B	
Total subjects affected by serious adverse events			
subjects affected / exposed	9 / 37 (24.32%)	5 / 15 (33.33%)	
number of deaths (all causes)	26	7	
number of deaths resulting from adverse events	2	0	
Investigations			
Alanine aminotransferase increased			
subjects affected / exposed	1 / 37 (2.70%)	1 / 15 (6.67%)	
occurrences causally related to treatment / all	1 / 1	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Cardiac disorder	Additional description: Cardiac dysrhytmia and chest pain		
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
General disorders and administration site conditions			
General disorders and administration site conditions - Other, specify	Additional description: General status deterioration		
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Fatigue			

subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Pain			
subjects affected / exposed	1 / 37 (2.70%)	1 / 15 (6.67%)	
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			
Febrile neutropenia			
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Gastric hemorrhage			
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 1	0 / 0	
Ascites			
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (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			
Tumour budding	Additional description: Tumour abscess		
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences causally related to treatment / all	0 / 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	Cohort A	Cohort B	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	28 / 37 (75.68%)	15 / 15 (100.00%)	
Investigations			
Alanine aminotransferase increased	Additional description: Grade 3		

subjects affected / exposed	2 / 37 (5.41%)	1 / 15 (6.67%)	
occurrences (all)	2	2	
Aspartate aminotransferase increased	Additional description: Grade 3		
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Blood bilirubin increased	Additional description: Grade 3		
subjects affected / exposed	1 / 37 (2.70%)	1 / 15 (6.67%)	
occurrences (all)	1	1	
Gamma-glutamyltransferase increased	Additional description: Grade 3		
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Neutrophil count decreased	Additional description: Grade 3		
subjects affected / exposed	2 / 37 (5.41%)	1 / 15 (6.67%)	
occurrences (all)	2	1	
Injury, poisoning and procedural complications			
Fracture	Additional description: Femur, Grade 3		
subjects affected / exposed	0 / 37 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Vascular disorders			
Hypertension	Additional description: Grade 3		
subjects affected / exposed	5 / 37 (13.51%)	2 / 15 (13.33%)	
occurrences (all)	5	2	
Cardiac disorders			
Chest pain	Additional description: Grade 3		
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Myocardial infarction	Additional description: Grade 3		
subjects affected / exposed	0 / 37 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Blood and lymphatic system disorders			
Anemia	Additional description: Grade 3		
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
General disorders and administration site conditions			

Ascites	Additional description: Grade 3		
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Fatigue	Additional description: Also reported as Asthenia		
subjects affected / exposed	3 / 37 (8.11%)	0 / 15 (0.00%)	
occurrences (all)	3	0	
Malaise	Additional description: Reported as "General Status Deterioration", grade 5		
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Diarrhoea	Additional description: Grade 3		
subjects affected / exposed	3 / 37 (8.11%)	1 / 15 (6.67%)	
occurrences (all)	3	1	
Lower gastrointestinal haemorrhage	Additional description: Grade 5		
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Nausea	Additional description: Grade 3		
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Toothache	Additional description: Grade 3		
subjects affected / exposed	0 / 37 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Vomiting	Additional description: Grade 3		
subjects affected / exposed	0 / 37 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Back pain	Additional description: Grade 3		
subjects affected / exposed	0 / 37 (0.00%)	1 / 15 (6.67%)	
occurrences (all)	0	1	
Generalized muscle weakness	Additional description: Grade 3		
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Soft tissue infection	Additional description: Abscess of tumor mass		
subjects affected / exposed	1 / 37 (2.70%)	0 / 15 (0.00%)	
occurrences (all)	1	0	

Metabolism and nutrition disorders Anorexia nervosa subjects affected / exposed occurrences (all)	 1 / 37 (2.70%) 1	 0 / 15 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
08 April 2013	Modification of visits calendar to improve hepathic monitoring
20 May 2014	Update of safety information
28 December 2016	Update of safety information

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.

Further analysis in larger populations (ex. in countries were pazopanib is approved in this setting) should be considered.

Notes: