Clinical trial results:
A pilot study of peroral Vorinostat (Zolinza) in patients with refractory histone deacetylase-positive uterine sarcoma.

Summary

EudraCT number	2016-000782-22
Trial protocol	AT
Global end of trial date	06 July 2018

Results information

Result version number	v1 (current)
This version publication date	27 March 2019
First version publication date	27 March 2019

Trial information

Trial identification

Sponsor protocol code	SAHA-Pilot-2016

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Medical University of Graz
Sponsor organisation address	Auenbruggerplatz 2, Graz, Austria, 8036
Public contact	Trial Center, Medical University of Graz, Department of Obstetrics and Gynecology, 0043 31638581082, edgar.petru@medunigraz.at
Scientific contact	Trial Center, Medical University of Graz, Department of Obstetrics and Gynecology, 0043 31638571780, martina.dieber@medunigraz.at

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	04 February 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 July 2018
Global end of trial reached?	Yes
Global end of trial date	06 July 2018
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The main purpose is to test the efficacy of the hydroxamic acid-based HDAC inhibitor Vorinostat as monotherapy in patients with histone deacetylase-positive, progressive, metastatic uterine sarcomas after prior anti-proliferative therapy.

Protection of trial subjects:

Close monitoring of blood chemistry and cardiac function according to the study protocol

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	27 November 2017
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	Austria: 3
Worldwide total number of subjects	3
EEA total number of subjects	3

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)	3
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Only 3 patients were enrolled. Uterine sarcoma are rated among the very rare diseases. Study was prematuraly closed due to the sluggish patient recruitment and the difficult acquisition of the IMP.

Pre-assignment

Screening details:

There were no screening failures in the course of the study

Period 1

Period 1 title	Start of treatment (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	Treatment
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Zolinza (Vorinostat)
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

400 mg (4 capsules á 100mg of Zolinza) orally once daily with food for the first 14 days of a 21 day cycle
Treatment will be continued for 4 cycles (treatment period 1)
Patients with a response or stable disease after 4 cycles will be continued on vorinostat therapy at the tolerated schedule and dosage until disease progression, unacceptable toxicity or patients' withdrawal of the consent. At the maximum, a total of 12 cycles will be administered over a 9 months period (treatment periods 2 and 3).

Number of subjects in period 1	Treatment
Started	3
Completed	1
Not completed	2
Adverse event, serious fatal	2

Baseline characteristics

Reporting groups

Reporting group title	Start of treatment

Reporting group description: -

Reporting group values	Start of treatment	Total	
Number of subjects	3	3	
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)	3	3	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	3	3	
Male	0	0	

Subject analysis sets

Subject analysis set title	End of period
Subject analysis set type	Per protocol

Subject analysis set description:

Assessment of tumor by CT at the end of a Treatment perid (4 cycles of medication)

Reporting group values	End of period		
Number of subjects	1		
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)	1		
From 65-84 years	0		
85 years and over	0		

Gender categorical Units: Subjects			
Female	1		
Male	0		

End points

End points reporting groups

Reporting group title	Treatment
Reporting group description: -	
Subject analysis set title	End of period
Subject analysis set type	Per protocol
Subject analysis set description:	
Assessment of tumor by CT at the end of a Treatment perid (4 cycles of medication)	

Primary: Progression-free survival (PFS) at 3 months

End point title	Progression-free survival (PFS) at 3 months
End point description:	
End point type	Primary
End point timeframe:	
3 months	

End point values	Treatment	End of period		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	1[1]	1[2]		
Units: mm				
number (not applicable)	3	1		

Notes:

[1] - 2 patients died before reaching the first end point due to their progressive underlying disease

[2] - Only 1 patient reached end Point 1 , but was progressive

Statistical analyses

Statistical analysis title	PFS
Statistical analysis description:	
Statistical evaluation was not possible as only 1 Patient reached end point 1. The study was prematurately closed	
Comparison groups	Treatment v End of period
Number of subjects included in analysis	2
Analysis specification	Pre-specified
Analysis type	other[3]
P-value	< 0.05 [4]
Method	descriptive

Notes:

[3] - Statistical evaluation was not possible as only 1 Patient reached end point 1.

[4] - This was a prematurely ended pilot study. Only 3 patients were enrolled. Only 1 patient reached the first primary end Point.(Tumor size Evaluation according to RECIST Version 1.1)
No statistical Analysis can be performed

Primary: PFS at 6 months

End point title	PFS at 6 months[5]

End point description:

End point type	Primary

End point timeframe:

6 months

Notes:

[5] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No Patient reached this end point

End point values	Treatment	End of period		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	0[6]	0[7]		
Units: mm				
number (not applicable)				

Notes:

[6] - No Patient reached end Point 2

[7] - No Patient reached this end point

Statistical analyses

No statistical analyses for this end point

Primary: PFS at 9 months

End point title	PFS at 9 months[8]

End point description:

End point type	Primary

End point timeframe:

9 months

Notes:

[8] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No Patient reached this end point

End point values	Treatment	End of period		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	0[9]	0[10]		
Units: mm				
number (not applicable)				

Notes:

[9] - No Patient reached end Point 3

[10] - No Patient reached end Point 3

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]

Timeframe for reporting adverse events:

Until study completion

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21

Reporting groups

Reporting group title	All study patients

Reporting group description: -

Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.
Justification: All adverse events lead to hospitalisation , therefore were reported as serious adverse events.

Serious adverse events	All study patients		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events			
Reproductive system and breast disorders			
abscess of the vaginal vault			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Death of uterine sarcoma	Additional description: Death of the underlying disease (refractory uterine sarcoma)		
subjects affected / exposed	2 / 3 (66.67%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 2		
Respiratory, thoracic and mediastinal disorders			
pleural effusion			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	All study patients		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 3 (0.00%)		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported