Clinical trial results:
Phase II Studie zur Wirksamkeit und Verträglichkeit von Vorinostat bei Patienten mit fortgeschrittenen, metastasierten Weichteilsarkomen.
English title:
A Phase II Study to Investigate the Efficacy and Tolerability of Vorinostat in Patients Suffering from Advanced, Metastatic Soft Tissue Sarcoma.

Summary

EudraCT number	2008-008513-19
Trial protocol	DE
Global end of trial date	20 November 2013

Results information

Result version number	v1 (current)
This version publication date	24 June 2022
First version publication date	24 June 2022

Trial information

Trial identification

Sponsor protocol code	SAHA-I

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00918489
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Universitätsklinikum Heidelberg
Sponsor organisation address	Im Neuenheimer Feld 672, Heidelberg, Germany, 69120
Public contact	Prof. Dr. G. Egerer, Universitätsklinikum Heidelberg Medizinische Klinik und Poliklinik V, +496221 56 8002, Gerlinde.Egerer@med.uni-heidelberg.de
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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	05 August 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 November 2013
Global end of trial reached?	Yes
Global end of trial date	20 November 2013
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Investigation of progression-free survival on the basis of RECIST criteria 1 year after treatment start

Protection of trial subjects:

Adverse events were monitored.
A Data and Safety Monitoring Committee was establshed.

Background therapy: -

Evidence for comparator:

not applicable

Actual start date of recruitment	02 June 2010
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Germany: 40
Worldwide total number of subjects	40
EEA total number of subjects	40

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)	30
From 65 to 84 years	9
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

Patients with metastatic soft tissue sarcoma failing 1 °-line anthracycline-based chemotherapy

Pre-assignment

Screening details:

Criteria for inclusion:

- Histologically proven advanced or metastatic soft tissue sarcoma
- Age: 18 years
- Previous anthracycline-based, 1°-line chemotherapy
- Life expectancy >/= 12 weeks
- Adequate bone marrow, liver- and renal function
- Negative pregnancy test

Period 1

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

Blinding implementation details:

not applicable

Arms

Arm title	Therapy

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Vorinostat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

400 mg per o, followed by a therapy-free period 7 dayss for 28 days

Number of subjects in period 1	Therapy
Started	40
Completed	23
Not completed	17
death (no SAE)	17

Baseline characteristics

Reporting groups	
Reporting group title	Therapy

Reporting group description: -

Reporting group values	Therapy	Total	
Number of subjects	40	40	
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)	30	30	
From 65-84 years	9	9	
85 years and over	1	1	
Gender categorical Units: Subjects			
Female	19	19	
Male	21	21	

End points

End points reporting groups

Reporting group title	Therapy

Reporting group description: -

Primary: Progression-free survival

End point title	Progression-free survival[1]

End point description:

Disease status was assessed by CT and/or MRI scans applying RECIST criteria every three months. Progression-free survival was defined as time from treatment start to disease progression or patient's death.

End point type	Primary

End point timeframe:

1 year after start of study

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: Single arm study, no comparative statistics applicable (feasibility study)

End point values	Therapy			
Subject group type	Reporting group			
Number of subjects analysed	40[2]			
Units: percent				
arithmetic mean (confidence interval 95%)	0.480 (0.302 to 0.631)			

Notes:

[2] - The numer displayed as arithmetic mean is actually the proportion (48% progression free survival)

Statistical analyses

No statistical analyses for this end point

Secondary: Overall survival

End point title	Overall survival

End point description:

Overall survival was defined as time from treatment start patient's death or last follow-up.

End point type	Secondary

End point timeframe:

1 year

End point values	Therapy			
Subject group type	Reporting group			
Number of subjects analysed	40[3]			
Units: percent				
number (confidence interval 95%)	0.580 (0.381 to 0.724)			

Notes:

[3] - number displayed as result is proportion of patients with overall survival as defined in description

Statistical analyses

No statistical analyses for this end point

Secondary: Pharmacokinetic analyses

End point title	Pharmacokinetic analyses

End point description:

Data on pharmacokinetics were available for 8 subjects (male=4. female=4. median age=62 years) . In plasma samples, mean Gmax (maximum concentration) , tmax (time to reach max. concentration), AUG (area under the plasma- concentration time curve), t112 (elimination half-life) and GI/F (apparent total clearance) were 350 ng/ml , 101 min, 71.1 min*µg/ml , 103 min and 5903 ml/ min. The corresponding parameters in PBMGs were 558 ng/ml , 97.5 min, 208.4 min*µg/ml , 286 min and 2475 ml /min, respectively. The AUG plasma/PBMG ratio was 2.93, indicating accumulation of vorinostat in PBMGs. Differences in AUG (p=.008) and t112 (p= . 01) reached statistical significance.
It was not possible to enter these data as measurable due to technical reasons (no dispersion values available).

End point type	Secondary

End point timeframe:

Subset of 8 patients, examined within study period

End point values	Therapy			
Subject group type	Reporting group			
Number of subjects analysed	40[4]			
Units: patients in this substudy	8			

Notes:

[4] - The count displayed here is the number of patients included in pharmacokinetics substudy.

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

During treatment and follow-up

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.0

Reporting groups

Reporting group title	Therapy

Reporting group description: -

Serious adverse events	Therapy		
Total subjects affected by serious adverse events			
subjects affected / exposed	20 / 40 (50.00%)		
number of deaths (all causes)	17		
number of deaths resulting from adverse events	1		
Vascular disorders			
Haemorrhage			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Shock	Additional description: unknown etiology		
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Aphasia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Blood and lymphatic system disorders			
Leukopenia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Pancytopenia				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thrombopenia				
subjects affected / exposed	3 / 40 (7.50%)			
occurrences causally related to treatment / all	3 / 4			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Death				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Gastrointestinal disorders				
Diarrhoea				
subjects affected / exposed	2 / 40 (5.00%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Intussusception				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subileus				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 0			
deaths causally related to treatment / all	0 / 0			
Vomiting				
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Pain	Additional description: pain in extremities			
subjects affected / exposed	1 / 40 (2.50%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			

Respiratory, thoracic and mediastinal disorders			
Dyspnoea exertional			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumothorax			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Candidiasis	Additional description: Candidiasis of oral mucosa		
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Febrile infection			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	2 / 40 (5.00%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 1		
Metabolism and nutrition disorders			
Abnormal loss of weight			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Decreased appetite			

subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Dehydration			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 3		
deaths causally related to treatment / all	0 / 0		
Hyperglycaemia			
subjects affected / exposed	1 / 40 (2.50%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Therapy		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	40 / 40 (100.00%)		
Surgical and medical procedures			
Surgical and medical procedures	Additional description: All AEs in this SOC		
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
General disorders and administration site conditions			
General disorders and administration site conditions	Additional description: All AEs in this SOC		
subjects affected / exposed	30 / 40 (75.00%)		
occurrences (all)	59		
Respiratory, thoracic and mediastinal disorders			
Respiratory, thoracic and mediastinal disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	13 / 40 (32.50%)		
occurrences (all)	25		
Psychiatric disorders			
Psychiatric disoders	Additional description: All AEs in this SOC		
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	3		
Investigations			

Investigations	Additional description: All AEs in this SOC		
subjects affected / exposed	17 / 40 (42.50%)		
occurrences (all)	29		
Injury, poisoning and procedural complications			
Injury, poisoning and procedural complications	Additional description: All AEs in this SOC		
subjects affected / exposed	5 / 40 (12.50%)		
occurrences (all)	5		
Cardiac disorders			
Cardiac Disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	2 / 40 (5.00%)		
occurrences (all)	2		
Nervous system disorders			
Nervous system disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	14 / 40 (35.00%)		
occurrences (all)	27		
Blood and lymphatic system disorders			
Blood and lymphatic system disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	11 / 40 (27.50%)		
occurrences (all)	14		
Ear and labyrinth disorders			
Ear and labyrinth disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	4 / 40 (10.00%)		
occurrences (all)	4		
Eye disorders			
Eye disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	3 / 40 (7.50%)		
occurrences (all)	5		
Gastrointestinal disorders			
Gastrointestinal disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	27 / 40 (67.50%)		
occurrences (all)	65		
Skin and subcutaneous tissue disorders			
Skin and subcutaneous tissue disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	13 / 40 (32.50%)		
occurrences (all)	17		
Renal and urinary disorders			

Renal and urinary disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	6 / 40 (15.00%)		
occurrences (all)	6		
Musculoskeletal and connective tissue disorders			
Musculoskeletal and connective tissue disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	15 / 40 (37.50%)		
occurrences (all)	24		
Infections and infestations			
Infections and infestations	Additional description: All AEs in this SOC		
subjects affected / exposed	10 / 40 (25.00%)		
occurrences (all)	15		
Metabolism and nutrition disorders			
Metabolism and nutrition disorders	Additional description: All AEs in this SOC		
subjects affected / exposed	16 / 40 (40.00%)		
occurrences (all)	24		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
01 March 2010	Study Protocol: More detailed description of the statistical evaluation of study data ICF: More detailed description of possible risks related to the study medication, deletion of the currative approach of the trial, information of sufficient anticontraception in male volunteers, report obligation of investigator in case of positive serology for hepatitis and HIV.
20 April 2010	Samples for pharmacokinetic examination

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/27367154