Clinical trial results:
An open-label multi-center single agent panobinostat roll-over protocol for patients who have completed a previous Novartis-sponsored panobinostat study and are judged by the investigator to benefit from continued single agent panobinostat treatment

Summary

EudraCT number	2012-005252-41
Trial protocol	ES NL
Global end of trial date	19 November 2018

Results information

Result version number	v1
This version publication date	18 December 2019
First version publication date	18 December 2019

Trial information

Trial identification

Sponsor protocol code	CLBH589B2402B

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01802879
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Study Director, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com
Scientific contact	Study Director, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com

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	19 November 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	19 November 2018
Global end of trial reached?	Yes
Global end of trial date	19 November 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate long term safety data (serious adverse events and adverse events)

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	24 June 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	Israel: 1
Country: Number of subjects enrolled	Netherlands: 1
Country: Number of subjects enrolled	Spain: 2
Country: Number of subjects enrolled	United States: 4
Worldwide total number of subjects	8
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)	5
From 65 to 84 years	3

85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

There was no screening period. Patients enrolled into trial directly from the parent protocol.

Period 1

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

Arms

Arm title	Panobinostat - 10 to 40 mg/day TIW QoW

Arm description:

10 to 40mg/day TIW QoW (3 times/week every other week) as per parent protocol design

Arm type	Experimental
Investigational medicinal product name	Panobinostat
Investigational medicinal product code	LBH589
Other name	
Pharmaceutical forms	Capsule, hard
Routes of administration	Oral use

Dosage and administration details:

10 - 40 mg/day TIW QoW (three times a week every other week)

Number of subjects in period 1	Panobinostat - 10 to 40 mg/day TIW QoW
Started	8
Completed	0
Not completed	8
Disease progression	6
Administrative problems	2

Baseline characteristics

Reporting groups	
Reporting group title	Panobinostat - 10 to 40 mg/day TIW QoW
Reporting group description:	
10 to 40mg/day TIW QoW (3 times/week every other week) as per parent protocol design	

Reporting group values	Panobinostat - 10 to 40 mg/day TIW QoW	Total	
Number of subjects	8	8	
Age categorical Units: Subjects			
Adults (18-64 years)	5	5	
From 65-84 years	3	3	
Age Continuous Units: years			
arithmetic mean	54		
standard deviation	± 14.5	-	
Sex: Female, Male Units: Subjects			
Female	4	4	
Male	4	4	
Parent protocol participants Units: Subjects			
CLBH589B2201	2	2	
CLBH589B2207	3	3	
CLBH589E2214	1	1	
CLBH589X2105	2	2	

End points

End points reporting groups

Reporting group title	Panobinostat - 10 to 40 mg/day TIW QoW

Reporting group description:

10 to 40mg/day TIW QoW (3 times/week every other week) as per parent protocol design

Primary: Overview of adverse events (Safety Set)

End point title	Overview of adverse events (Safety Set)[1]

End point description:

Adverse events were collected from baseline up to 30 days post treatment at scheduled visits. Severity of adverse events was assessed according to the current version of Common Terminology Criteria for Adverse Events (CTCAE). If CTCAE grading did not exist for an adverse event, the severity of mild, moderate, severe, and life-threatening, corresponding to Grades 1 - 4, was used

End point type	Primary

End point timeframe:

Baseline up to approximately 60 months

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: No statistical analysis was done

End point values	Panobinostat - 10 to 40 mg/day TIW QoW			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: participants				
Any adverse event (AE)	6			
Any treatment related AE	2			
Any serious adverse event (SAE)	2			
Grade 3 or 4 AE	3			
Grade 3 or 4 AE - suspected to be related	1			
AEs leading discontinuation	0			
AEs leading to dose adjust/ temp dose interruption	2			
On-treatment death	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of patients with clinical benefit as assessed by the investigator.

End point title	Percentage of patients with clinical benefit as assessed by the investigator.

End point description:

Patients were assessed by investigators at scheduled visits to determine if patient continued to benefit from panobinostat therapy.

End point type	Secondary

End point timeframe:

baseline up to approximately 5 years

End point values	Panobinostat - 10 to 40 mg/day TIW QoW			
Subject group type	Reporting group			
Number of subjects analysed	8			
Units: participants				
Participants with clinical benefit	7			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from first dose of study treatment until end of study treatment plus 30 days post treatment, up to maximum duration of 60 months

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.0

Reporting groups

Reporting group title	Panobinostat - 10 to 40 mg/day TIW QoW

Reporting group description:

10 to 40mg/day TIW QoW (3 times/week every other week) as per parent protocol design

Serious adverse events	Panobinostat - 10 to 40 mg/day TIW QoW		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 8 (25.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			
Nervous system disorders			
Cerebrovascular accident			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 8 (12.50%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Panobinostat - 10 to 40 mg/day TIW QoW		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 8 (50.00%)		

Investigations Blood creatinine increased subjects affected / exposed occurrences (all) Platelet count decreased subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Neoplasms benign, malignant and unspecified (incl cysts and polyps) Benign muscle neoplasm subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Nervous system disorders Neuropathy peripheral subjects affected / exposed occurrences (all)	 2 / 8 (25.00%) 1		
Blood and lymphatic system disorders Neutropenia subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
General disorders and administration site conditions Asthenia subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Gastrointestinal disorders Diarrhoea subjects affected / exposed occurrences (all) Gastric disorder subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Skin and subcutaneous tissue disorders Pruritus subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		
Psychiatric disorders Insomnia			

subjects affected / exposed occurrences (all)	1 / 8 (12.50%) 1		
Musculoskeletal and connective tissue disorders Bone pain subjects affected / exposed occurrences (all) Osteoarthritis subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1 1 / 8 (12.50%) 1		
Infections and infestations Nasopharyngitis subjects affected / exposed occurrences (all)	 1 / 8 (12.50%) 1		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
11 March 2016	The main purpose of the amendment is to change the primary endpoint to safety to better characterize the long-term safety of the compound. In addition, the protocol has been amended to include the collection of all AEs (including nonserious AEs) and an investigator descriptive attestation of continued clinical benefit (Yes/No).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported