Clinical trial results:
The Safety and Efficacy of The Histone Deacetylase Inhibitor Panobinostat for Purging HIV-1 from The Latent Reservoir (CLEAR) Study

Summary

EudraCT number	2012-000240-94
Trial protocol	DK
Global end of trial date	16 January 2014

Results information

Result version number	v1 (current)
This version publication date	27 November 2021
First version publication date	27 November 2021

Trial information

Trial identification

Sponsor protocol code	CLEAR0001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Aarhus University Hospital
Sponsor organisation address	Palle Juul-Jensens Boulevard 99, Aarhus, Denmark, 8200
Public contact	Department of Infectious Diseases, Aarhus University Hospital, 0045 78452841, thomrasm@rm.dk
Scientific contact	Department of Infectious Diseases, Aarhus University Hospital, 0045 78452841, thomrasm@rm.dk

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	15 August 2014
Is this the analysis of the primary completion data?	Yes
Primary completion date	16 January 2014
Global end of trial reached?	Yes
Global end of trial date	16 January 2014
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To re-activate HIV transcription in latently infected CD4+ T-cells as measured by an increase >0.5 log10 from baseline in copies of unspliced HIV-RNA/µg total RNA in the CD4+ T-cells of HIV-infected patients on suppressive HAART

Protection of trial subjects:

Frequent clinical and lab test monitoring; strategy for dose-reduction; exclusion of participants with conditions believed to enhance risks of participation.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 May 2012
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	Denmark: 15
Worldwide total number of subjects	15
EEA total number of subjects	15

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)	15
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Written information and advertisements approved by The Research Ethics Committee and Investigator databases may be used for recruitment purposes. Eligible study subjects will receive written invitation to participate in the study unless the subject has asked not be contacted in such matters.

Pre-assignment

Screening details:

5.1 Inclusion Criteria
- Documented HIV-1 infection
- Age >18 years
- HIV-1 plasma RNA <50 copies/ml for at least 2 years with at least 2 viral load measures per year. Episodes of a single HIV plasma RNA 50-199 copies/ml will not exclude participation if the subsequent HIV plasma RNA was <50 copies/ml
- Receiving HAART, defined as at least 2 nu

Pre-assignment period milestones

Number of subjects started	15
Number of subjects completed	15

Period 1

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

Arms

Arm title	Intervention arm (single-arm study)
Arm description: -	
Arm type	Experimental
Investigational medicinal product name	Panobinostat
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

20 mg 3 times per week every other week

Number of subjects in period 1	Intervention arm (single-arm study)
Started	15
Completed	15

Baseline characteristics

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Reporting group values	Overall trial	Total	
Number of subjects	15	15	
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)	15	15	
From 65-84 years	0	0	
85 years and over	0	0	
Age continuous Units: years			
median	47		
full range (min-max)	28 to 53	-	
Gender categorical Units: Subjects			
Male	15	15	
Female	0	0	

Subject analysis sets

Subject analysis set title	Pre-therapy
Subject analysis set type	Full analysis

Subject analysis set description:
Before starting Panobinostat

Reporting group values	Pre-therapy		
Number of subjects	15		
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)	15		

From 65-84 years	0		
85 years and over	0		

Age continuous			
Units: years			
median	47		
full range (min-max)	28 to 53		
Gender categorical			
Units: Subjects			
Male	15		
Female	0		

End points

End points reporting groups

Reporting group title	Intervention arm (single-arm study)
Reporting group description: -	
Subject analysis set title	Pre-therapy
Subject analysis set type	Full analysis
Subject analysis set description: Before starting Panobinostat	

Primary: Cell-associated HIV RNA

End point title	Cell-associated HIV RNA
End point description:	
End point type	Primary
End point timeframe: During 8 weeks of study therapy	

End point values	Intervention arm (single-arm study)	Pre-therapy		
Subject group type	Reporting group	Subject analysis set		
Number of subjects analysed	15	15		
Units: Maximum fold-change from baseline				
geometric mean (full range (min-max))	3.5 (2.1 to 14.4)	1 (1 to 1)		

Statistical analyses

Statistical analysis title	repeated measures anova
Comparison groups	Intervention arm (single-arm study) v Pre-therapy
Number of subjects included in analysis	30
Analysis specification	Pre-specified
Analysis type	superiority
P-value	< 0.001
Method	ANOVA
Parameter estimate	Fold-change from baseline
Confidence interval	
level	95 %
sides	2-sided
Variability estimate	Standard deviation

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Oct 2012 - Jan 2014

Assessment type	Systematic

Dictionary used

Dictionary name	CTCAE
Dictionary version	4

Reporting groups

Reporting group title	Overall trial

Reporting group description: -

Serious adverse events	Overall trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	1 / 15 (6.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
Headache			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

Non-serious adverse events	Overall trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	14 / 15 (93.33%)		
Cardiac disorders			
Palpitations	Additional description: Cardiac assessment normal		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Nervous system disorders			
Post lumbar puncture headache			
subjects affected / exposed	4 / 15 (26.67%)		
occurrences (all)	7		
Headache			

subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
General disorders and administration site conditions			
Malaise			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	7 / 15 (46.67%)		
occurrences (all)	8		
Insomnia			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Immune system disorders			
Fever			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Gastrointestinal disorders			
Polyp found during sigmoidoscopy			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Nausea			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
stomach ache			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Vomiting			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Respiratory, thoracic and mediastinal disorders			
sinusitis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Skin and subcutaneous tissue disorders			
Skin lesion			

subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Rash			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		
Fungal skin infection			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Psychiatric disorders			
Emotional stress			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Endocrine disorders			
Increased TSH			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Hypoglycaemia	Additional description: Postprandial		
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Musculoskeletal and connective tissue disorders			
Lower back ache after lumbar puncture			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Fracture			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Infections and infestations			
Influenza like illness			
subjects affected / exposed	3 / 15 (20.00%)		
occurrences (all)	3		
Pharyngitis			
subjects affected / exposed	1 / 15 (6.67%)		
occurrences (all)	1		
Upper respiratory tract infection			
subjects affected / exposed	2 / 15 (13.33%)		
occurrences (all)	2		

Diarrhoea subjects affected / exposed occurrences (all)	3 / 15 (20.00%) 3		
Syphilis subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1		

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