Clinical trial results:
Oral cannabidivarin (CBDV) solution for treatment of HIV-associated neuropathic pain – a randomized, double-blind, placebo-controlled phase II study.

Summary

EudraCT number	2014-005344-17
Trial protocol	DE
Global end of trial date	31 January 2020

Results information

Result version number	v1 (current)
This version publication date	29 August 2020
First version publication date	29 August 2020
Summary attachment (see zip file)	Eibach + supplement accepted (Eibach + supplement accepted.pdf)

Trial information

Trial identification

Sponsor protocol code	CBDV_2014

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Charité Universitätsmedizin Berlin
Sponsor organisation address	Hindenburgdamm 30, Berlin, Germany, D-12200
Public contact	Prof. Dr. Christoph Stein, Anaesthesiology, Charité Campus Benjamin Franklin, christoph.stein@charite.de
Scientific contact	Prof. Dr. Christoph Stein, Anaesthesiology, Charité Campus Benjamin Franklin, christoph.stein@charite.de

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 January 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	31 January 2019
Global end of trial reached?	Yes
Global end of trial date	31 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Modulation of neuropathic pain by cannabidivarin (CBDV) as compared to placebo

Protection of trial subjects:

all patients provided written informed consent after extensive information about possible adverse events, as described in detail in the manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)

Background therapy:

treatment of HIV by antiviral agents

Evidence for comparator: -

Actual start date of recruitment	01 April 2015
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: 32
Worldwide total number of subjects	32
EEA total number of subjects	32

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)	32
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

as described in the manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)

Pre-assignment

Screening details:

as described in the manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)

Pre-assignment period milestones

Number of subjects started	32
Number of subjects completed	32

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Data analyst, Carer, Assessor

Blinding implementation details:

as described in the manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)

Arms

Are arms mutually exclusive?	No
Arm title	CBDV

Arm description:

as described in the manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)

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

Dosage and administration details:

as described in the manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)

Arm title	Placebo

Arm description:

as described in manuscript posted on medRxiv:
https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Oral liquid
Routes of administration	Oral use

Dosage and administration details:

see posted on medRxiv: https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1

Number of subjects in period 1	CBDV	Placebo
Started	32	32
Completed	32	32

Baseline characteristics

Reporting groups	
Reporting group title	CBDV
Reporting group description:	
as described in the manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)	
Reporting group title	Placebo
Reporting group description:	
as described in manuscript posted on medRxiv: https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1	

Reporting group values	CBDV	Placebo	Total
Number of subjects	32	32	32
Age categorical			
as described in the manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)			
Units: Subjects			
Adults (18-64 years)	32	32	32
From 65-84 years	0	0	0
Gender categorical			
described in manuscript: https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1			
Units: Subjects			
Female	1	1	1
Male	31	31	31
pain			
described in manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)			
Units: described in manuscript			
arithmetic mean			
standard deviation	±	±	-

Subject analysis sets	
Subject analysis set title	all subjects
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
as described in the manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)	
Subject analysis set title	Pain intensity
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
see https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1	
Subject analysis set title	Pain characteristics
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
see https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1	
Subject analysis set title	supplemental medication
Subject analysis set type	Intention-to-treat
Subject analysis set description:	
see https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1	
Subject analysis set title	SF 36
Subject analysis set type	Intention-to-treat

Subject analysis set description:
see https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1

Reporting group values	all subjects	Pain intensity	Pain characteristics
Number of subjects	32	32	32
Age categorical			
as described in the manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)			
Units: Subjects			
Adults (18-64 years)	32	32	32
From 65-84 years	0	0	0
Gender categorical			
described in manuscript: https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1			
Units: Subjects			
Female	1	1	1
Male	31	31	31
pain			
described in manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)			
Units: described in manuscript			
arithmetic mean	2.74	2.74	
standard deviation	± 1.47	± 1.47	±

Reporting group values	supplemental medication	SF 36	
Number of subjects	32	32	
Age categorical			
as described in the manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)			
Units: Subjects			
Adults (18-64 years)	32	32	
From 65-84 years	0	0	
Gender categorical			
described in manuscript: https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1			
Units: Subjects			
Female	1	1	
Male	31	31	
pain			
described in manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)			
Units: described in manuscript			
arithmetic mean			
standard deviation	±	±	

End points

End points reporting groups

Reporting group title	CBDV
Reporting group description: as described in the manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)	
Reporting group title	Placebo
Reporting group description: as described in manuscript posted on medRxiv: https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1	
Subject analysis set title	all subjects
Subject analysis set type	Intention-to-treat
Subject analysis set description: as described in the manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)	
Subject analysis set title	Pain intensity
Subject analysis set type	Intention-to-treat
Subject analysis set description: see https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1	
Subject analysis set title	Pain characteristics
Subject analysis set type	Intention-to-treat
Subject analysis set description: see https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1	
Subject analysis set title	supplemental medication
Subject analysis set type	Intention-to-treat
Subject analysis set description: see https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1	
Subject analysis set title	SF 36
Subject analysis set type	Intention-to-treat
Subject analysis set description: see https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1	

Primary: pain

End point title	pain
End point description: see: https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1	
End point type	Primary
End point timeframe: described in manuscript (https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1)	

End point values	CBDV	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	32	32		
Units: https://medrxiv.org/cgi/content/short/2				
number (not applicable)				
https://medrxiv.org/cgi/content/short/2019.12.20.1	32	32		

Statistical analyses

Statistical analysis title	Pain intensity

Statistical analysis description:

Sample size was calculated by nQuery Advisor® 7.0 based on the primary endpoint (NRS scale) and the cross-over study-design. According to previous literature, a pain reduction by 20% upon verum compared to placebo and a common standard deviation (SD) for the period differences of 2.5 seemed to be achievable and would have been clinical meaningful

Comparison groups	CBDV v Placebo
Number of subjects included in analysis	64
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	< 0.05 [2]
Method	t-test, 2-sided
Parameter estimate	Mean difference (final values)
Point estimate	0.2
Confidence interval	
level	95 %
sides	2-sided
lower limit	-0.27
upper limit	1.51
Variability estimate	Standard deviation
Dispersion value	2.62

Notes:

[1] - Sample size was calculated by nQuery Advisor® 7.0 based on the primary endpoint (NRS scale) and the cross-over study-design. According to previous literature, a pain reduction by 20% upon verum compared to placebo and a common standard deviation (SD) for the period differences of 2.5 seemed to be achievable and would have been clinical meaningful

[2] - We calculated that 21 patients per sequence group were sufficient to show this effect (e.g. a reduction of 20% from 6 points to 4.8 points) with a power of 85% and a two-sided type-I-error of 0.05 using a paired t-test for 2x2 crossover designs

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events: see: https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	2

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

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: justified in: https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1

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

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

see: https://medrxiv.org/cgi/content/short/2019.12.20.19015495v1

Notes: