Clinical trial results:
Effectiveness of CALMVALERA HEVERT as measured by quantitative EEG in 24 subjects during audio-visual cognitive and emotional challenges. A double-blind, randomized, placebo-controlled, 2-armed, Phase IV study in parallel design

Summary

EudraCT number	2014-004840-36
Trial protocol	DE
Global end of trial date	03 November 2015

Results information

Result version number	v1 (current)
This version publication date	13 August 2022
First version publication date	13 August 2022
Summary attachment (see zip file)	CHDE-1 Synopsis (CHDE-1 - Synopsis.pdf)

Trial information

Trial identification

Sponsor protocol code	CHDE-1

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Hevert-Arzneimittel GmbH & Co. KG
Sponsor organisation address	In der Weiherwiese 1, N, Germany, 55569
Public contact	Klinische Forschung Dr. Tausend, Hevert-Arzneimittel GmbH & Co. KG, 0049 6751910389, stausend@hevert.de
Scientific contact	Klinische Forschung Dr. Tausend, Hevert-Arzneimittel GmbH & Co. KG, 0049 6751910389, stausend@hevert.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	30 November 2015
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	03 November 2015
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Anxiolytic effects of CALMVALERA HEVERT tablets shall be tested in subjects suffering from test anxiety after single intake by aid of a newly developed, validated method consisting of a combination of Eye-Tracking (following glances) with Neurocode-Tracking (quantitative EEG with a time resolution of 364 ms) termed "EnkephaloVision".
Comparison of verum and placebo is performed on electric power in 17 different brain regions using six frequency ranges defined as target parameters in the presence of different stress inducing cognitive tests and emotional video scenes (i.e. quiz, memory test, Stroop test). With respect to cognition and emotion changes in frontal and temporal spectral beta power are evaluated.

Protection of trial subjects:

No specific measures needed to be taken.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 October 2015
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	Germany: 24
Worldwide total number of subjects	24
EEA total number of subjects	24

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)	24
From 65 to 84 years	0

85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Healthy subjects aged 18-40 years, were recruited by NeuroCode AG, Sportparkstr. 9, D - 35578 Wetzlar, Germany

Pre-assignment

Screening details:

Subjects with an axiety test questionnaire “PAF” (for pre-selection of subjects) - values above T > 60 were screened.

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Calmvalera Hevert

Arm description:

Single dose of Calmvalera Hevert

Arm type	Experimental
Investigational medicinal product name	Calmvalera Hevert
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Subject took a single dose of 6 tablets of Calmvalera Hevert

Arm title	Placebo

Arm description:

Single dose of plabebo tablets

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

Dosage and administration details:

Subjects receive a single dose of 6 placebo tablets

Number of subjects in period 1	Calmvalera Hevert	Placebo
Started	12	12
Completed	12	12

Baseline characteristics

Reporting groups

Reporting group title	Treatment period

Reporting group description: -

Reporting group values	Treatment period	Total	
Number of subjects	24	24	
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)		0	
From 65-84 years		0	
85 years and over		0	
Age continuous Units: years			
arithmetic mean	24.9		
standard deviation	± 4.21	-	
Gender categorical Units: Subjects			
Female	14	14	
Male	10	10	

End points

End points reporting groups

Reporting group title	Calmvalera Hevert
Reporting group description: Single dose of Calmvalera Hevert	
Reporting group title	Placebo
Reporting group description: Single dose of plabebo tablets	

Primary: Memory test

End point title	Memory test[1]

End point description:

The primary endpoint was the change in 17-channel EEG recording combined with eye-tracking after intake of Calmvalera in comparison to placebo.
Method: Quantitative-topographical EEG by measurement of current source density during different cognitive and emotional challenges. Combination of Neurocode-Tracking (quantitative-topographic EEG with epoch length of 364 ms) with Eye-Tracking (following eye gazes) termed "EnkephaloVision. The results cannot be presented as numbers and units.
A statistical significant increase of alpha1 and alpha2 activity was observed (see attached chart) after intake of Calmvalera, but not of delta-theta or beta electric activity nor psychometric performance.

End point type	Primary

End point timeframe:

The memory test was a secondary endpoint, primary endpoint was the EEG evaluation, see description below.

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 test was performed for the memory test.

End point values	Calmvalera Hevert	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	12	12		
Units: Score points				
arithmetic mean (standard deviation)	89.58 (± 16.71)	97.92 (± 7.22)		

Attachments (see zip file)	Effect of active and placebo /Effect of Placebo or Verum.pdf

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information[1]	
Timeframe for reporting adverse events:	
From screening to final examination	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	17.1

Reporting groups	
Reporting group title	Calmvalera
Reporting group description: -	
Reporting group title	Placebo
Reporting group description: -	

Serious adverse events	Calmvalera	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 0 %

Non-serious adverse events	Calmvalera	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	0 / 12 (0.00%)	0 / 12 (0.00%)	

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: No AEs were reported.

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