Clinical trial results:
Proof of concept study for evaluation of the effect of ketamine intranasal spray in treatment of chronic Cluster Headache (CCH)

Summary

EudraCT number	2019-001260-29
Trial protocol	DK
Global end of trial date	01 July 2020

Results information

Result version number	v1 (current)
This version publication date	28 July 2021
First version publication date	28 July 2021

Trial information

Trial identification

Sponsor protocol code	CCH01

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Lionheart Pharmaceuticals ApS
Sponsor organisation address	Groendals Parkvej 54, Vanloese, Denmark, 2720
Public contact	Chief Scientific Officer, CCH Pharmaceuticals, 45 27772988,
Scientific contact	Chief Scientific Officer, CCH Pharmaceuticals, 45 27772988,
Sponsor organisation name	Lionheart Pharmaceuticals ApS
Sponsor organisation address	Groendals Parkvej 54, Vanloese, Denmark, 2720
Public contact	CEO, Lionheart Pharmaceuticals ApS, 45 27772988, ph@lionheart-pharmaceuticals.com
Scientific contact	CEO, Lionheart Pharmaceuticals ApS, 45 27772988, ph@lionheart-pharmaceuticals.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	01 June 2021
Is this the analysis of the primary completion data?	Yes
Primary completion date	01 July 2020
Global end of trial reached?	Yes
Global end of trial date	01 July 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objective of this open pilot study is to evaluate whether ketamine administered as an intranasal spray in sub-anesthetic doses is effective in treatment of chronic CH

Protection of trial subjects:

Rescue medication ready and patients allowed to withdrawn from the study if desired or if severe adverse effects are observed

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	01 December 2019
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: 23
Worldwide total number of subjects	23
EEA total number of subjects	23

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)	23
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

According to inclusion/exclusion criteria

Pre-assignment period milestones

Number of subjects started	23
Number of subjects completed	23

Period 1

Period 1 title	Overall trial (intervention) (overall period)
Is this the baseline period?	Yes
Allocation method	Non-randomised - controlled
Blinding used	Not blinded

Arms

Arm title	Intervention

Arm description:

The treatment is initiated under a cluster headache attack when the headache pain NRS ≥ 6 on an NRS pain scale. The first intranasal dose of 15 mg is given at time 0 and at time intervals of 6 minutes with a maximum of 5 times (maximum total dose of 75 mg).

Arm type	Experimental
Investigational medicinal product name	Ketamine
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Nasal spray, solution
Routes of administration	Intranasal use

Dosage and administration details:

15 mg R,S ketamine base per intranasal spray (100 microliter). Dosed in one nose nostril at intervals of 6 minutes (15 mg per dose), maximal 5 times (total of 75 mg).

Number of subjects in period 1	Intervention
Started	23
IMP administration	20
Completed	20
Not completed	3
No attack during admission	3

Baseline characteristics

Reporting groups	
Reporting group title	Overall trial (intervention)

Reporting group description: -

Reporting group values	Overall trial (intervention)	Total	
Number of subjects	23	23	
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)	23	23	
From 65-84 years	0	0	
85 years and over	0	0	
Adults	0	0	
Gender categorical Units: Subjects			
Female	7	7	
Male	16	16	

End points

End points reporting groups

Reporting group title	Intervention

Reporting group description:

The treatment is initiated under a cluster headache attack when the headache pain NRS ≥ 6 on an NRS pain scale. The first intranasal dose of 15 mg is given at time 0 and at time intervals of 6 minutes with a maximum of 5 times (maximum total dose of 75 mg).

Primary: Reduction in pain from time point 0 minutes to time point 15 minutes

End point title	Reduction in pain from time point 0 minutes to time point 15 minutes[1]

End point description:

End point type	Primary

End point timeframe:

15 minutes

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: The endpoint looked at the mean percent difference from baseline (timepoint 0 min) to Timepoint 15. No statistical analysis was performed on this percent change. Analyzing the the difference in actual numbers from t0 to t15 with a paired t test resulted in a p value of 0.188.
Primary endpoint was not met in the study.

End point values	Intervention			
Subject group type	Reporting group			
Number of subjects analysed	20			
Units: percent				
arithmetic mean (standard deviation)	11.8 (± 46.2)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From first drug administration and for the 3 following hours. Further there was a follow up conversation with the patient via telephone a week after treatment.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	24.0

Reporting groups

Reporting group title	Reporting group

Reporting group description: -

Serious adverse events	Reporting group		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 20 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events			

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

Non-serious adverse events	Reporting group		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	20 / 20 (100.00%)		
Injury, poisoning and procedural complications			
Intoxication			
subjects affected / exposed	20 / 20 (100.00%)		
occurrences (all)	7		
Cardiac disorders			
Palpitations			
subjects affected / exposed	20 / 20 (100.00%)		
occurrences (all)	1		
Nervous system disorders			
Dizziness			
subjects affected / exposed	20 / 20 (100.00%)		
occurrences (all)	12		
Parasthesia			

subjects affected / exposed	20 / 20 (100.00%)		
occurrences (all)	4		
Lethargy			
subjects affected / exposed	20 / 20 (100.00%)		
occurrences (all)	1		
Aphasia			
subjects affected / exposed	20 / 20 (100.00%)		
occurrences (all)	1		
tension headache			
subjects affected / exposed	20 / 20 (100.00%)		
occurrences (all)	1		
headache			
subjects affected / exposed	20 / 20 (100.00%)		
occurrences (all)	1		
General disorders and administration site conditions			
Hangover			
subjects affected / exposed	20 / 20 (100.00%)		
occurrences (all)	1		
Asthenia			
subjects affected / exposed	20 / 20 (100.00%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	20 / 20 (100.00%)		
occurrences (all)	1		
Feeling of relaxation			
subjects affected / exposed	20 / 20 (100.00%)		
occurrences (all)	1		
Eye disorders			
Ocular discomfort			
subjects affected / exposed	20 / 20 (100.00%)		
occurrences (all)	1		
Visual impairment			
subjects affected / exposed	20 / 20 (100.00%)		
occurrences (all)	1		
Gastrointestinal disorders			

Nausea subjects affected / exposed occurrences (all) Vomiting subjects affected / exposed occurrences (all) Abdominal pain subjects affected / exposed occurrences (all) Dry mouth subjects affected / exposed occurrences (all)	20 / 20 (100.00%) 4 20 / 20 (100.00%) 2 20 / 20 (100.00%) 2 20 / 20 (100.00%) 1		
Respiratory, thoracic and mediastinal disorders Nasopharyngitis subjects affected / exposed occurrences (all) Epistaxis subjects affected / exposed occurrences (all) Rhinalgia subjects affected / exposed occurrences (all) Respiration abnormal subjects affected / exposed occurrences (all)	 20 / 20 (100.00%) 2 20 / 20 (100.00%) 1 20 / 20 (100.00%) 1 20 / 20 (100.00%) 1		
Psychiatric disorders Euphoric mood subjects affected / exposed occurrences (all) Confusional state subjects affected / exposed occurrences (all)	 20 / 20 (100.00%) 3 20 / 20 (100.00%) 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