Clinical trial results:
A Randomized, Placebo-Controlled, Double-Blind, Parallel-Group, Phase 2 Study to Evaluate the Safety and Efficacy of R-Verapamil in the Prophylaxis of Episodic Cluster Headache

Summary

EudraCT number	2012-003729-62
Trial protocol	GB
Global end of trial date	04 September 2017

Results information

Result version number	v1 (current)
This version publication date	15 September 2018
First version publication date	15 September 2018

Trial information

Trial identification

Sponsor protocol code	R-Verapamil-001

Additional study identifiers

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

Notes:

Sponsors

Sponsor organisation name	Center Laboratories, Inc.
Sponsor organisation address	7F, No. 3-2, Park Street, Nangang District, 115, Taipei city, Taiwan,
Public contact	Paul Bookbinder, Emas Pharma Limited T/A Bionical, +44 (0) 1462 424406 , clinicaltrials@bionical-emas.com
Scientific contact	Paul Bookbinder, Emas Pharma Limited T/A Bionical, +44 (0) 1462 424406 , clinicaltrials@bionical-emas.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	04 September 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	21 March 2014
Global end of trial reached?	Yes
Global end of trial date	04 September 2017
Was the trial ended prematurely?	Yes

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the safety of R-verapamil. The safety assessments include:
- adverse events
- clinical laboratory measurements (chemistry and hematology)
- vital signs
- physical examinations
- ECGs (will be obtained on Day 8 prior to the single 75 mg dose of R-verapamil and at 1 hour post dose and at the end of study visit)

Protection of trial subjects:

Signed and dated informed consent was obtained from enrolled-subjects prior to study participation. All study-related procedures were conducted only after a signed and dated ICF by the subject has been received and is counter-signed by the study investigator.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	26 February 2014
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	United Kingdom: 1
Worldwide total number of subjects	1
EEA total number of subjects	1

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)	1
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The actual start date of the study was 21 Nov 2013 with first subject first visit occurring on 26 Feb 2014. The subject has been randomized on 07 Mar 2014 and has completed the study. Due to the difficulty in patient recruitment, a substantial amendment to request a temporary halt of trial R-Verapamil-001 was submitted on 12 Feb 2015.

Pre-assignment

Screening details:

Eligible subject was consented and screened against the eligibility criteria and patient randomly assigned to one treatment group.

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, Monitor, Data analyst, Carer, Assessor

Blinding implementation details:

The investigator kept individual blinded envelopes containing the actual drug assignments for each subject. The sponsor also retained a full set of envelopes. These envelopes were kept in a secure place with limited access in order to minimize the risk of inadvertently opening the envelopes. The randomization code was not disclosed to the investigator or any personnel involved in the conduct of the study.

Arms

Arm title	Blinded

Arm description:

Group I: R-verapamil HCl tablet or
Group II: Placebo tablet

Arm type	Blinded
Investigational medicinal product name	RV Tablet
Investigational medicinal product code	R-verapamil HCl
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Dosage: 375 mg/day
Group I: R-verapamil hydrochloride as one 75 mg tablet in the morning and two 75 mg tablets in the afternoon and two 75 mg tablets at bedtime daily during Days 8-21

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

Dosage and administration details:

1 placebo tablet in the morning and 2 placebo tablets in the afternoon and 2 placebo tablets at bedtime daily during Days 8-21.

Number of subjects in period 1	Blinded
Started	1
Screening	1
Completed	1

Baseline characteristics

Reporting groups	
Reporting group title	Overall Trial

Reporting group description:

Group I: R-verapamil hydrochloride as one 75 mg tablet in the morning and two 75 mg tablets in the afternoon and two 75 mg tablets at bedtime daily during Days 8-21
Group II: Placebo as 1 placebo in the morning and 2 placebo tablets in the afternoon and 2 placebo tablets at bedtime daily during Days 8-21

Reporting group values	Overall Trial	Total	
Number of subjects	1	1	
Age categorical			
Age of subject population			
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)	1	1	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical			
Units: Subjects			
Female	0	0	
Male	1	1	

End points

End points reporting groups

Reporting group title	Blinded

Reporting group description:

Group I: R-verapamil HCl tablet or
Group II: Placebo tablet

Primary: Change in the average daily frequency of attacks between the baseline run-in period and the end of the 2 week treatment period

End point title	Change in the average daily frequency of attacks between the baseline run-in period and the end of the 2 week treatment period[1]

End point description:

No values are reported because only 1 patient completed the study.

End point type	Primary

End point timeframe:

The mean change from baseline to visit 4 will be summarized

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: Early termination of the study due to poor recruitment, only 1 patient was enrolled. Data cannot be interpreted.

End point values	Blinded			
Subject group type	Reporting group			
Number of subjects analysed	1			
Units: Frequency of attacks	1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

The adverse event reporting period was between March 14, 2014 and March 20, 2014 (period during which the patient was enrolled in the trial).

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	1

Reporting groups

Reporting group title	Blinded

Reporting group description:

Group I: R-verapamil HCl tablet or
Group II: Placebo tablet

Serious adverse events	Blinded		
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 1 (0.00%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		

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

Non-serious adverse events	Blinded		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	1 / 1 (100.00%)		
Nervous system disorders			
Dysgeusia	Additional description: Unpleasant taste in mouth		
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	1		
Gastrointestinal disorders			
Dry mouth			
subjects affected / exposed	1 / 1 (100.00%)		
occurrences (all)	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? Yes

Date	Interruption	Restart date
12 February 2015	A temporary halt of trial R-Verapamil-001 was submitted on 10-Feb-2015 to the REC and on 12-Feb-2015 to the MHRA, whilst the Sponsor considered possibilities to increase recruitment. The trial was then terminated on 4-Sep-2017 due to poor recruitment.	-

Notes:

Limitations and caveats

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

Early termination of the study due to poor recruitment, only 1 patient was enrolled. Data cannot be interpreted.

Notes: