



## 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:

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**Results analysis stage**

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|  |                   |
|--|-------------------|
| 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:

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**General information about the trial**

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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:

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**Population of trial subjects**

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**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:

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**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.

| <b>Number of subjects in period 1</b> | 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 <sup>[1]</sup> |
| 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.

|                             |                 |  |  |  |
|-----------------------------|-----------------|--|--|--|
| <b>End point values</b>     | 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

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### 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: