



## Clinical trial results:

**An open-label, multinational, multicenter, follow-up study to evaluate the long-term safety and efficacy of brivaracetam used at a flexible dose up to a maximum of 200 mg/day in subjects aged 16 years or older suffering from epilepsy.**

### Summary

|                          |                            |
|--------------------------|----------------------------|
| EudraCT number           | 2008-001433-98             |
| Trial protocol           | BE CZ SE ES FR HU FI IT DE |
| Global end of trial date | 20 March 2017              |

### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 05 April 2018 |
| First version publication date | 05 April 2018 |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | N01315 |
|-----------------------|--------|

#### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT00761774 |
| WHO universal trial number (UTN)   | -           |

Notes:

### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | UCB Biosciences, Inc  |
| Sponsor organisation address | 8010 Arco Corporate Drive, Raleigh, United States, NC 27617                       |
| Public contact               | Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com |
| Scientific contact           | Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.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                       | 10 July 2017  |
| Is this the analysis of the primary completion data? | No            |
| Global end of trial reached?                         | Yes           |
| Global end of trial date                             | 20 March 2017 |
| Was the trial ended prematurely?                     | No            |

Notes:

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**General information about the trial**

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Main objective of the trial:

To evaluate the long-term safety and tolerability of Brivaracetam (BRV) at individualized doses with a maximum of 200 mg/day in subjects suffering from epilepsy.

Protection of trial subjects:

During the conduct of the study all subjects were closely monitored.

Background therapy:

Not applicable.

Evidence for comparator:

Not applicable.

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 19 November 2008 |
| 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 | Australia: 7       |
| Country: Number of subjects enrolled | Belgium: 4         |
| Country: Number of subjects enrolled | Canada: 6          |
| Country: Number of subjects enrolled | Czech Republic: 10 |
| Country: Number of subjects enrolled | France: 2          |
| Country: Number of subjects enrolled | Germany: 14        |
| Country: Number of subjects enrolled | Hungary: 4         |
| Country: Number of subjects enrolled | Italy: 7           |
| Country: Number of subjects enrolled | Spain: 1           |
| Country: Number of subjects enrolled | Sweden: 10         |
| Country: Number of subjects enrolled | United States: 43  |
| Worldwide total number of subjects   | 108                |
| EEA total number of subjects         | 52                 |

Notes:

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**Subjects enrolled per age group**

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|  |   |
|--|---|
| In utero                               | 0 |
| Preterm newborn - gestational age < 37 | 0 |

|  |     |
|--|-----|
| wk                                       |     |
| 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)                     | 103 |
| From 65 to 84 years                      | 5   |
| 85 years and over                        | 0   |

## Subject disposition

### Recruitment

Recruitment details:

The study started to enroll patients in November 2008 and concluded in March 2017.

### Pre-assignment

Screening details:

Participant Flow refers to the Safety Set, which consisted of all subjects who took at least 1 dose of study drug.

### Period 1

|                              |                                |
|------------------------------|--------------------------------|
| Period 1 title               | Overall Study (overall period) |
| Is this the baseline period? | Yes                            |
| Allocation method            | Not applicable                 |
| Blinding used                | Not blinded                    |

### Arms

|           |              |
|-----------|--------------|
| Arm title | Brivaracetam |
|-----------|--------------|

Arm description:

This arm consisted of subjects who received Brivaracetam (BRV) at flexible dosing up to 200 mg/day.

|  |              |
|--|--------------|
| Arm type                               | Experimental |
| Investigational medicinal product name | Brivaracetam |
| Investigational medicinal product code | BRV          |
| Other name                             |              |
| Pharmaceutical forms                   | Tablet       |
| Routes of administration               | Oral use     |

Dosage and administration details:

Personalized daily doses of the investigational product (IP) Brivaracetam (BRV) were divided into 2 equal intakes (morning and evening). The suggested individual starting dose of each subject was 100 mg/day. Up- and down-titration could be made by increments of a maximum 50 mg/day on a weekly basis and up to a maximum dose of 200 mg/day.

| Number of subjects in period 1  | Brivaracetam |
|---------------------------------|--------------|
| Started                         | 108          |
| Completed                       | 29           |
| Not completed                   | 79           |
| Subject IP non-compliance       | 1            |
| End of study                    | 2            |
| Patient moved out of study area | 1            |
| Sponsor decision                | 1            |
| Investigator clinical judgement | 1            |
| Consent withdrawn by subject    | 9            |
| Adverse event, non-fatal        | 17           |
| Reclassification of seizures    | 1            |
| Non-compliance                  | 4            |

|  |    |
|--|----|
| Lost to follow-up                      | 2  |
| Coordinator leaving site               | 1  |
| Medical decision to read SUSAR reports | 1  |
| IP stopped by hospital physician       | 1  |
| Lack of efficacy                       | 37 |

## Baseline characteristics

### Reporting groups

|                       |              |
|-----------------------|--------------|
| Reporting group title | Brivaracetam |
|-----------------------|--------------|

Reporting group description:

This arm consisted of subjects who received Brivaracetam (BRV) at flexible dosing up to 200 mg/day.

| Reporting group values  | Brivaracetam | Total |  |
|-------------------------|--------------|-------|--|
| Number of subjects      | 108          | 108   |  |
| Age categorical         |              |       |  |
| Units: Subjects         |              |       |  |
| <=18 years              | 0            | 0     |  |
| Between 18 and 65 years | 103          | 103   |  |
| >=65 years              | 5            | 5     |  |
| Age continuous          |              |       |  |
| Units: years            |              |       |  |
| arithmetic mean         | 40.8         |       |  |
| standard deviation      | ± 13         | -     |  |
| Gender categorical      |              |       |  |
| Units: Subjects         |              |       |  |
| Female                  | 56           | 56    |  |
| Male                    | 52           | 52    |  |

## End points

### End points reporting groups

|  |                   |
|--|-------------------|
| Reporting group title  | Brivaracetam      |
| Reporting group description:<br>This arm consisted of subjects who received Brivaracetam (BRV) at flexible dosing up to 200 mg/day.      |                   |
| Subject analysis set title   | Brivaracetam (SS) |
| Subject analysis set type  | Safety analysis   |
| Subject analysis set description:<br>This arm consisted of subjects who received Brivaracetam (BRV) at flexible dosing up to 200 mg/day. |                   |
| Subject analysis set title   | Brivaracetam (ES) |
| Subject analysis set type  | Full analysis     |
| Subject analysis set description:<br>This arm consisted of subjects who received Brivaracetam (BRV) at flexible dosing up to 200 mg/day. |                   |

### Primary: Percentage of subjects with at least one Treatment-emergent Adverse Event (TEAE) during the Evaluation Period from Entry Visit 1 through End of Treatment (up to 9 years)

|   |  |
|---|--|
| End point title   | Percentage of subjects with at least one Treatment-emergent Adverse Event (TEAE) during the Evaluation Period from Entry Visit 1 through End of Treatment (up to 9 years) <sup>[1]</sup> |
| End point description:<br>Treatment-emergent Adverse events (TEAE) are any untoward medical occurrences in a subject during administered study treatment, whether or not these events are related to study treatment. |  |
| End point type  | Primary  |
| End point timeframe:<br>During the Evaluation Period (up to 9 years)  |  |

#### 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 formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

| End point values                  | Brivaracetam (SS)    |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 108                  |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (not applicable)           |                      |  |  |  |
| percentage of participants        | 90.7                 |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects who withdrew due to Adverse Event (AE) during the Evaluation Period from Entry Visit 1 through End of Treatment (up to 9 years)

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects who withdrew due to Adverse Event (AE) during the Evaluation Period from Entry Visit 1 through End of Treatment (up to 9 years) <sup>[2]</sup> |
|-----------------|---|

End point description:

Adverse Events (AE) are any untoward medical occurrences in a subject during administered study treatment, whether or not these events are related to study treatment.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

During the Evaluation Period (up to 9 years)

Notes:

[2] - 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 formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

| End point values                  | Brivaracetam (SS)    |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 108                  |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (not applicable)           |                      |  |  |  |
| percentage of participants        | 15.7                 |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Primary: Percentage of subjects with a Serious Adverse Event (SAE) during the Evaluation Period from Entry Visit 1 through End of Treatment (up to 9 years)

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects with a Serious Adverse Event (SAE) during the Evaluation Period from Entry Visit 1 through End of Treatment (up to 9 years) <sup>[3]</sup> |
|-----------------|---|

End point description:

An SAE was any untoward medical occurrence that, at any dose resulted in death, was life threatening, required in-subject hospitalization or prolongation of existing hospitalization, resulted in persistent or significant disability/incapacity, or was a congenital anomaly/birth defect.

|                |         |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

During the Evaluation Period (up to 9 years)

Notes:

[3] - 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 formal statistical hypothesis testing was planned for this study. Results were summarized as descriptive statistics only.

| End point values                  | Brivaracetam (SS)    |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 108                  |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (not applicable)           |                      |  |  |  |
| percentage of participants        | 24.1                 |  |  |  |



## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects on continuous Brivaracetam monotherapy for at least 3 months of the Evaluation Period (up to 9 years)

|                 |  |
|-----------------|--|
| End point title | Percentage of subjects on continuous Brivaracetam monotherapy for at least 3 months of the Evaluation Period (up to 9 years) |
|-----------------|--|

End point description:

BRV monotherapy is defined as continuous treatment with BRV only (ie, no treatment with another anti-epileptic drug (AED)). Use of rescue AED for a duration of no more than 2 consecutive days will not disqualify a subject from being defined as on continuous monotherapy provided the use of rescue AED does not exceed more than 1 time per week.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the Evaluation Period (up to 9 years)

| End point values                  | Brivaracetam (ES)    |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 108                  |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (not applicable)           |                      |  |  |  |
| percentage of participants        | 38.89                |  |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects on continuous Brivaracetam monotherapy for at least 6 months, of the Evaluation Period (up to 9 years)

|                 |   |
|-----------------|---|
| End point title | Percentage of subjects on continuous Brivaracetam monotherapy for at least 6 months, of the Evaluation Period (up to 9 years) |
|-----------------|---|

End point description:

BRV monotherapy is defined as continuous treatment with BRV only (ie, no treatment with another anti-epileptic drug (AED)). Use of rescue AED for a duration of no more than 2 consecutive days will not disqualify a subject from being defined as on continuous monotherapy provided the use of rescue AED does not exceed more than 1 time per week.

|                |           |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

During the Evaluation Period (up to 9 years)

| End point values                  | Brivaracetam (ES)    |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 108                  |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (not applicable)           |                      |  |  |  |
| percentage of participants        | 32.41                |  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of subjects on continuous Brivaracetam monotherapy for at least 12 months of the Evaluation Period (up to 9 years)

|   |   |
|---|---|
| End point title   | Percentage of subjects on continuous Brivaracetam monotherapy for at least 12 months of the Evaluation Period (up to 9 years) |
| End point description:<br>BRV monotherapy is defined as continuous treatment with BRV only (ie, no treatment with another anti-epileptic drug (AED)). Use of rescue AED for a duration of no more than 2 consecutive days will not disqualify a subject from being defined as on continuous monotherapy provided the use of rescue AED does not exceed more than 1 time per week. |   |
| End point type  | Secondary   |
| End point timeframe:<br>During the Evaluation Period (up to 9 years)  |   |

| End point values                  | Brivaracetam (ES)    |  |  |  |
|-----------------------------------|----------------------|--|--|--|
| Subject group type                | Subject analysis set |  |  |  |
| Number of subjects analysed       | 108                  |  |  |  |
| Units: percentage of participants |                      |  |  |  |
| number (not applicable)           |                      |  |  |  |
| percentage of participants        | 25                   |  |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected throughout the study (up to 9 years).

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 15.0 |
|--------------------|------|

### Reporting groups

|                       |                   |
|-----------------------|-------------------|
| Reporting group title | Brivaracetam (SS) |
|-----------------------|-------------------|

Reporting group description:

This arm consisted of subjects who received Brivaracetam (BRV) at flexible dosing up to 200 mg/day.

| Serious adverse events  | Brivaracetam (SS) |  |  |
|---|-------------------|--|--|
| Total subjects affected by serious adverse events                   |                   |  |  |
| subjects affected / exposed   | 26 / 108 (24.07%) |  |  |
| number of deaths (all causes)                                       | 1                 |  |  |
| number of deaths resulting from adverse events                      | 0                 |  |  |
| Neoplasms benign, malignant and unspecified (incl cysts and polyps) |                   |  |  |
| Basal cell carcinoma  |                   |  |  |
| subjects affected / exposed   | 1 / 108 (0.93%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1             |  |  |
| deaths causally related to treatment / all                          | 0 / 0             |  |  |
| Malignant melanoma  |                   |  |  |
| subjects affected / exposed   | 1 / 108 (0.93%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1             |  |  |
| deaths causally related to treatment / all                          | 0 / 0             |  |  |
| General disorders and administration site conditions                |                   |  |  |
| Sudden unexplained death in epilepsy                                |                   |  |  |
| subjects affected / exposed   | 1 / 108 (0.93%)   |  |  |
| occurrences causally related to treatment / all                     | 0 / 1             |  |  |
| deaths causally related to treatment / all                          | 0 / 1             |  |  |
| Social circumstances  |                   |  |  |
| Pregnancy of partner  |                   |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Respiratory, thoracic and mediastinal disorders |                 |  |  |
| Chronic obstructive pulmonary disease           |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Epistaxis                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Psychiatric disorders                           |                 |  |  |
| Anxiety   |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Factitious disorder                             |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Psychotic disorder                              |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Somnambulism                                    |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Suicide attempt                                 |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Injury, poisoning and procedural complications  |                 |  |  |
| Contusion                                       |                 |  |  |
| subjects affected / exposed                     | 2 / 108 (1.85%) |  |  |
| occurrences causally related to treatment / all | 0 / 3           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Craniocerebral injury                           |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Facial bones fracture                           |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Intentional overdose                            |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Joint injury                                    |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Laceration                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Snake bite                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cardiac disorders                               |                 |  |  |
| Angina pectoris                                 |                 |  |  |
| subjects affected / exposed                     | 3 / 108 (2.78%) |  |  |
| occurrences causally related to treatment / all | 1 / 3           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Atrial fibrillation                             |                 |  |  |
| subjects affected / exposed                     | 2 / 108 (1.85%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cardiac failure congestive                      |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Nervous system disorders                        |                 |  |  |
| Convulsion                                      |                 |  |  |
| subjects affected / exposed                     | 5 / 108 (4.63%) |  |  |
| occurrences causally related to treatment / all | 2 / 7           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Dysarthria                                      |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Epilepsy  |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Grand mal convulsion                            |                 |  |  |
| subjects affected / exposed                     | 2 / 108 (1.85%) |  |  |
| occurrences causally related to treatment / all | 2 / 4           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hemiparesis                                     |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Migraine  |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Monoplegia                                      |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Postictal state                                 |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Gastrointestinal disorders                      |                 |  |  |
| Abdominal pain                                  |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pancreatitis acute                              |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 1 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Vomiting  |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Hepatobiliary disorders                         |                 |  |  |
| Cholecystitis                                   |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cholecystitis acute                             |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Cholelithiasis                                  |                 |  |  |
| subjects affected / exposed                     | 2 / 108 (1.85%) |  |  |
| occurrences causally related to treatment / all | 0 / 2           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Renal and urinary disorders                     |                 |  |  |

|   |                 |  |  |
|---|-----------------|--|--|
| Nephrolithiasis                                 |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Musculoskeletal and connective tissue disorders |                 |  |  |
| Back pain                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Pain in extremity                               |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Infections and infestations                     |                 |  |  |
| Pneumonia                                       |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |
| Urinary tract infection                         |                 |  |  |
| subjects affected / exposed                     | 1 / 108 (0.93%) |  |  |
| occurrences causally related to treatment / all | 0 / 1           |  |  |
| deaths causally related to treatment / all      | 0 / 0           |  |  |

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

|   |                   |  |  |
|---|-------------------|--|--|
| <b>Non-serious adverse events</b>                     | Brivaracetam (SS) |  |  |
| Total subjects affected by non-serious adverse events |                   |  |  |
| subjects affected / exposed                           | 81 / 108 (75.00%) |  |  |
| Investigations  |                   |  |  |
| Weight increased                                      |                   |  |  |
| subjects affected / exposed                           | 6 / 108 (5.56%)   |  |  |
| occurrences (all)                                     | 6                 |  |  |
| Injury, poisoning and procedural complications        |                   |  |  |



|  |                         |  |  |
|--|-------------------------|--|--|
| Fall<br>subjects affected / exposed<br>occurrences (all)   | 15 / 108 (13.89%)<br>19 |  |  |
| Contusion<br>subjects affected / exposed<br>occurrences (all)  | 9 / 108 (8.33%)<br>11   |  |  |
| Vascular disorders<br>Hypertension<br>subjects affected / exposed<br>occurrences (all)                                 | 6 / 108 (5.56%)<br>8    |  |  |
| Nervous system disorders<br>Convulsion<br>subjects affected / exposed<br>occurrences (all)                             | 17 / 108 (15.74%)<br>28 |  |  |
| Headache<br>subjects affected / exposed<br>occurrences (all)   | 15 / 108 (13.89%)<br>20 |  |  |
| Dizziness<br>subjects affected / exposed<br>occurrences (all)  | 14 / 108 (12.96%)<br>18 |  |  |
| Migraine<br>subjects affected / exposed<br>occurrences (all)   | 7 / 108 (6.48%)<br>11   |  |  |
| Paraesthesia<br>subjects affected / exposed<br>occurrences (all)   | 6 / 108 (5.56%)<br>6    |  |  |
| Tremor<br>subjects affected / exposed<br>occurrences (all)   | 6 / 108 (5.56%)<br>7    |  |  |
| General disorders and administration<br>site conditions<br>Fatigue<br>subjects affected / exposed<br>occurrences (all) | 17 / 108 (15.74%)<br>19 |  |  |
| Chest pain<br>subjects affected / exposed<br>occurrences (all)   | 9 / 108 (8.33%)<br>10   |  |  |

|   |                         |  |  |
|---|-------------------------|--|--|
| Oedema peripheral<br>subjects affected / exposed<br>occurrences (all) | 6 / 108 (5.56%)<br>7    |  |  |
| Gastrointestinal disorders  |                         |  |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)         | 12 / 108 (11.11%)<br>16 |  |  |
| Abdominal pain<br>subjects affected / exposed<br>occurrences (all)    | 9 / 108 (8.33%)<br>12   |  |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)            | 9 / 108 (8.33%)<br>11   |  |  |
| Toothache<br>subjects affected / exposed<br>occurrences (all)         | 7 / 108 (6.48%)<br>10   |  |  |
| Vomiting<br>subjects affected / exposed<br>occurrences (all)          | 6 / 108 (5.56%)<br>9    |  |  |
| Skin and subcutaneous tissue disorders                                |                         |  |  |
| Rash<br>subjects affected / exposed<br>occurrences (all)              | 13 / 108 (12.04%)<br>16 |  |  |
| Psychiatric disorders   |                         |  |  |
| Depression<br>subjects affected / exposed<br>occurrences (all)        | 18 / 108 (16.67%)<br>21 |  |  |
| Anxiety<br>subjects affected / exposed<br>occurrences (all)           | 15 / 108 (13.89%)<br>24 |  |  |
| Insomnia<br>subjects affected / exposed<br>occurrences (all)          | 15 / 108 (13.89%)<br>16 |  |  |
| Suicidal ideation<br>subjects affected / exposed<br>occurrences (all) | 6 / 108 (5.56%)<br>7    |  |  |
| Musculoskeletal and connective tissue                                 |                         |  |  |

|                                   |                   |  |  |
|-----------------------------------|-------------------|--|--|
| disorders                         |                   |  |  |
| Back pain                         |                   |  |  |
| subjects affected / exposed       | 12 / 108 (11.11%) |  |  |
| occurrences (all)                 | 12                |  |  |
| Arthralgia                        |                   |  |  |
| subjects affected / exposed       | 10 / 108 (9.26%)  |  |  |
| occurrences (all)                 | 16                |  |  |
| Infections and infestations       |                   |  |  |
| Nasopharyngitis                   |                   |  |  |
| subjects affected / exposed       | 19 / 108 (17.59%) |  |  |
| occurrences (all)                 | 42                |  |  |
| Bronchitis                        |                   |  |  |
| subjects affected / exposed       | 8 / 108 (7.41%)   |  |  |
| occurrences (all)                 | 13                |  |  |
| Upper respiratory tract infection |                   |  |  |
| subjects affected / exposed       | 8 / 108 (7.41%)   |  |  |
| occurrences (all)                 | 11                |  |  |
| Viral infection                   |                   |  |  |
| subjects affected / exposed       | 6 / 108 (5.56%)   |  |  |
| occurrences (all)                 | 8                 |  |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date           | Amendment   |
|----------------|---|
| 18 June 2010   | Updated the protocol with regard to 5 areas: <ul style="list-style-type: none"><li>- Study personnel and contact details</li><li>- Duration of the study and duration of participation were amended due to termination of the N01276 and N01306 studies</li><li>- Typographical and spelling errors were corrected</li><li>- Details concerning the Phase 3 partial onset seizures (POS) and Unverricht-Lundborg Disease (ULD) studies as those studies had completed since the start of this study</li><li>- Further instruction was given with regard to visit windows</li></ul>  |
| 02 August 2011 | <ul style="list-style-type: none"><li>- Increased maximum dose of BRV to 200 mg/day (instead of 150 mg/day)</li><li>- Reduced the number of assessments for the subjects</li><li>- Updated procedures for reporting serious adverse events (SAEs) to implement the Food and Drug Administration (FDA) Final Rule requirements</li><li>- Added Columbia-Suicide Severity Rating Scale (C-SSRS) to address the requirement of the FDA that prospective assessments for suicidality should be included in clinical studies involving all drugs for neurological indications</li><li>- Updated information on laboratory assessments, statistical analyses, and contact information</li><li>- Further (minor) changes were made throughout the protocol for consistency between BRV studies</li></ul> |
| 25 March 2015  | <ul style="list-style-type: none"><li>- Study personnel and contact details were updated</li><li>- The ability of the Sponsor to sign electronically was added</li><li>- Outdated safety information was removed</li><li>- Protocol language was updated to include the possibility of a named patient or compassionate use program (or similar) as a reason for ending the study duration</li><li>- Language was revised regarding Investigator deviation from the protocol in the event of a medical emergency to align with the current UCB language</li></ul>   |

Notes:

### Interruptions (globally)

Were there any global interruptions to the trial? No

### Limitations and caveats

None reported