



## Clinical trial results:

### A Double-Blind, Randomized, Placebo-Controlled Study of the Efficacy, Safety/Tolerability, and Pharmacokinetic Profile of UCB0942 in Adults with Highly Drug-Resistant Focal Epilepsy

#### Summary

|                          |                   |
|--------------------------|-------------------|
| EudraCT number           | 2014-003330-12    |
| Trial protocol           | DE BE NL HU ES IT |
| Global end of trial date | 18 July 2017      |

#### Results information

|                                |                |
|--------------------------------|----------------|
| Result version number          | v1 (current)   |
| This version publication date  | 03 August 2018 |
| First version publication date | 03 August 2018 |

#### Trial information

##### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | EP0069 |
|-----------------------|--------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT02495844 |
| WHO universal trial number (UTN)   | -           |

Notes:

##### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | UCB Biopharma SPRL  |
| Sponsor organisation address | Allée de la Recherche 60, Brussels, Belgium, B-1070                                       |
| Public contact               | Clin Trial Reg & Results Disclosure<br>, UCB BIOSCIENCES GmbH<br>, clinicaltrials@ucb.com |
| Scientific contact           | Clin Trial Reg & Results Disclosure<br>, UCB BIOSCIENCES GmbH<br>, 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:

## Results analysis stage

|  |              |
|--|--------------|
| Analysis stage                                       | Final        |
| Date of interim/final analysis                       | 31 July 2017 |
| Is this the analysis of the primary completion data? | No           |

|                                  |              |
|----------------------------------|--------------|
| Global end of trial reached?     | Yes          |
| Global end of trial date         | 18 July 2017 |
| Was the trial ended prematurely? | No           |

Notes:

## General information about the trial

Main objective of the trial:

The primary objective was to evaluate the efficacy of UCB0942 administered concomitantly with each subject's current, stable antiepileptic drug (AED) regimen in subjects who had 4 or more focal seizures with or without secondary generalization per week and who failed to achieve seizure control with  $\geq 4$  AED regimens of adequate dose and duration.

Protection of trial subjects:

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

Background therapy:

Patients remained on their background antiepileptic medications during the entire study.

Evidence for comparator: -

|   |                |
|---|----------------|
| Actual start date of recruitment                          | 28 August 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 | Belgium: 8     |
| Country: Number of subjects enrolled | Bulgaria: 5    |
| Country: Number of subjects enrolled | Germany: 13    |
| Country: Number of subjects enrolled | Hungary: 4     |
| Country: Number of subjects enrolled | Netherlands: 3 |
| Country: Number of subjects enrolled | Spain: 22      |
| Worldwide total number of subjects   | 55             |
| EEA total number of subjects         | 55             |

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)      | 55 |
| From 65 to 84 years       | 0  |
| 85 years and over         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

Enrollment started in August 2015 and concluded in July 2017.

### Pre-assignment

Screening details:

Participant Flow refers to the Randomized Set.

### Period 1

|                              |  |
|------------------------------|--|
| Period 1 title               | Overall Study (overall period)         |
| Is this the baseline period? | Yes                                    |
| Allocation method            | Randomised - controlled                |
| Blinding used                | Double blind                           |
| Roles blinded                | Subject, Investigator, Carer, Assessor |

### Arms

|                              |                 |
|------------------------------|-----------------|
| Are arms mutually exclusive? | Yes             |
| <b>Arm title</b>             | Placebo/UCB0942 |

Arm description:

After 2-week in the Inpatient Period, Placebo subjects received the experimental medicine (UCB0942).

|  |                    |
|--|--------------------|
| Arm type                               | Placebo            |
| Investigational medicinal product name | UCB0942            |
| Investigational medicinal product code | UCB0942            |
| Other name                             | Padsevonil         |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Tablets in 2 strengths: 100 mg and 200 mg.

100 mg and 200 mg tablets have the same size and appearance.

|                  |                 |
|------------------|-----------------|
| <b>Arm title</b> | UCB0942/UCB0942 |
|------------------|-----------------|

Arm description:

Subjects received UCB0942.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | UCB0942            |
| Investigational medicinal product code | UCB0942            |
| Other name                             | Padsevonil         |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Tablets in 2 strengths: 100 mg and 200 mg.

100 mg and 200 mg tablets have the same size and appearance.

| <b>Number of subjects in period 1</b> | Placebo/UCB0942 | UCB0942/UCB0942 |
|---------------------------------------|-----------------|-----------------|
| Started                               | 27              | 28              |
| Completed                             | 26              | 24              |
| Not completed                         | 1               | 4               |
| AE, non-fatal                         | -               | 1               |
| Hepatitis Positivity                  | -               | 1               |
| Lack of efficacy                      | 1               | 2               |

## Baseline characteristics

### Reporting groups

|  |                 |
|--|-----------------|
| Reporting group title  | Placebo/UCB0942 |
| Reporting group description:   |                 |
| After 2-week in the Inpatient Period, Placebo subjects received the experimental medicine (UCB0942). |                 |
| Reporting group title  | UCB0942/UCB0942 |
| Reporting group description:   |                 |
| Subjects received UCB0942.   |                 |

| Reporting group values                    | Placebo/UCB0942 | UCB0942/UCB0942 | Total |
|---|-----------------|-----------------|-------|
| Number of subjects                        | 27              | 28              | 55    |
| Age categorical                           |                 |                 |       |
| Units: Subjects                           |                 |                 |       |
| <=18 years                                | 0               | 0               | 0     |
| Between 18 and 65 years                   | 27              | 28              | 55    |
| >=65 years                                | 0               | 0               | 0     |
| Age continuous                            |                 |                 |       |
| Units: years                              |                 |                 |       |
| arithmetic mean                           | 35.2            | 36.2            | -     |
| standard deviation                        | ± 8.7           | ± 11.4          | -     |
| Gender categorical                        |                 |                 |       |
| Units: Subjects                           |                 |                 |       |
| Male                                      | 13              | 13              | 26    |
| Female                                    | 14              | 15              | 29    |
| Race (NIH/OMB)                            |                 |                 |       |
| Units: Subjects                           |                 |                 |       |
| American Indian or Alaska Native          | 0               | 0               | 0     |
| Asian                                     | 0               | 0               | 0     |
| Native Hawaiian or Other Pacific Islander | 0               | 0               | 0     |
| Black or African American                 | 0               | 1               | 1     |
| White                                     | 27              | 25              | 52    |
| More than one race                        | 0               | 2               | 2     |
| Unknown or Not Reported                   | 0               | 0               | 0     |
| Race/Ethnicity, Customized                |                 |                 |       |
| Units: Subjects                           |                 |                 |       |
| Hispanic or Latino                        | 1               | 3               | 4     |
| Not Hispanic or Latino                    | 26              | 25              | 51    |
| BMI (kg/m^2)                              |                 |                 |       |
| Units: units on a scale                   |                 |                 |       |
| arithmetic mean                           | 25.66           | 27.20           | -     |
| standard deviation                        | ± 4.82          | ± 4.32          | -     |

## End points

### End points reporting groups

|   |                       |
|---|-----------------------|
| Reporting group title   | Placebo/UCB0942       |
| Reporting group description:<br>After 2-week in the Inpatient Period, Placebo subjects received the experimental medicine (UCB0942).      |                       |
| Reporting group title   | UCB0942/UCB0942       |
| Reporting group description:<br>Subjects received UCB0942.  |                       |
| Subject analysis set title  | Placebo/UCB0942 (FAS) |
| Subject analysis set type   | Full analysis         |
| Subject analysis set description:<br>After 2-week in the Inpatient Period, Placebo subjects received the experimental medicine (UCB0942). |                       |
| Subject analysis set title  | UCB0942/UCB0942 (FAS) |
| Subject analysis set type   | Full analysis         |
| Subject analysis set description:<br>Subjects received UCB0942.   |                       |
| Subject analysis set title  | Placebo/UCB0942 (SS)  |
| Subject analysis set type   | Safety analysis       |
| Subject analysis set description:<br>After 2-week in the Inpatient Period, Placebo subjects received the experimental medicine (UCB0942). |                       |
| Subject analysis set title  | UCB0942/UCB0942 (SS)  |
| Subject analysis set type   | Safety analysis       |
| Subject analysis set description:<br>Subjects received UCB0942.   |                       |

### Primary: 75 % responder rate during the 2-week Inpatient Period

|   |  |
|---|--|
| End point title   | 75 % responder rate during the 2-week Inpatient Period |
| End point description:<br>The 75% responder rate is defined as the percentage of subjects with a 75 % or greater reduction in focal seizure frequency during the 2-week Inpatient Period compared with the Baseline Period. |  |
| End point type  | Primary  |
| End point timeframe:<br>During the 2-week Inpatient Period  |  |

| End point values                  | Placebo/UCB0942 (FAS) | UCB0942/UCB0942 (FAS) |  |  |
|-----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                | Subject analysis set  | Subject analysis set  |  |  |
| Number of subjects analysed       | 27                    | 28                    |  |  |
| Units: percentage of participants |                       |                       |  |  |
| number (not applicable)           |                       |                       |  |  |
| 75% responder rate                | 11.1                  | 30.8                  |  |  |

## Statistical analyses

|   |   |
|---|---|
| <b>Statistical analysis title</b>       | Statistical Analysis 1                        |
| Comparison groups                       | Placebo/UCB0942 (FAS) v UCB0942/UCB0942 (FAS) |
| Number of subjects included in analysis | 55  |
| Analysis specification                  | Pre-specified                                 |
| Analysis type                           | superiority                                   |
| P-value                                 | = 0.0679                                      |
| Method                                  | Regression, Logistic                          |
| Parameter estimate                      | Odds ratio (OR)                               |
| Point estimate                          | 4.14  |
| Confidence interval                     |   |
| level                                   | 95 %  |
| sides                                   | 2-sided                                       |
| lower limit                             | 0.9   |
| upper limit                             | 19.06   |

### Secondary: Median percent change in weekly focal seizure frequency during the 2-week Inpatient Period

|                        |  |
|------------------------|--|
| End point title        | Median percent change in weekly focal seizure frequency during the 2-week Inpatient Period |
| End point description: | A negative value in median percent change reflects a reduction from Baseline.              |
| End point type         | Secondary  |
| End point timeframe:   | During the 2-week Inpatient Period   |

| End point values                      | Placebo/UCB0942 (FAS)   | UCB0942/UCB0942 (FAS)     |  |  |
|---------------------------------------|-------------------------|---------------------------|--|--|
| Subject group type                    | Subject analysis set    | Subject analysis set      |  |  |
| Number of subjects analysed           | 27                      | 26                        |  |  |
| Units: percentage of change           |                         |                           |  |  |
| median (inter-quartile range (Q1-Q3)) |                         |                           |  |  |
| Median (Inter-Quartile Range)         | -12.5 (-57.14 to 41.11) | -53.68 (-84.61 to -22.73) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Median percent change in weekly focal seizure frequency during the Outpatient Maintenance Period

|                        |  |
|------------------------|--|
| End point title        | Median percent change in weekly focal seizure frequency during the Outpatient Maintenance Period |
| End point description: | A negative value in median percent change reflects a reduction from Baseline.                    |
| End point type         | Secondary  |



End point timeframe:

During the Outpatient Maintenance Period (8 weeks)

| End point values                      | Placebo/UCB0942 (FAS)     | UCB0942/UCB0942 (FAS)    |  |  |
|---------------------------------------|---------------------------|--------------------------|--|--|
| Subject group type                    | Subject analysis set      | Subject analysis set     |  |  |
| Number of subjects analysed           | 27                        | 25                       |  |  |
| Units: percentage of change           |                           |                          |  |  |
| median (inter-quartile range (Q1-Q3)) |                           |                          |  |  |
| Median (Inter-Quartile Range)         | -57.94 (-76.23 to -29.09) | -26.32 (-77.38 to -3.07) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Median percent change in weekly focal seizure frequency during the On-UCB0942 Overall Period

|                 |  |
|-----------------|--|
| End point title | Median percent change in weekly focal seizure frequency during the On-UCB0942 Overall Period |
|-----------------|--|

End point description:

A negative value in median percent change reflects a reduction from Baseline.

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

End point timeframe:

During the On-UCB0942 Overall Period (approximately 11 weeks)

| End point values                      | Placebo/UCB0942 (FAS)     | UCB0942/UCB0942 (FAS)     |  |  |
|---------------------------------------|---------------------------|---------------------------|--|--|
| Subject group type                    | Subject analysis set      | Subject analysis set      |  |  |
| Number of subjects analysed           | 27                        | 27                        |  |  |
| Units: percentage of change           |                           |                           |  |  |
| median (inter-quartile range (Q1-Q3)) |                           |                           |  |  |
| Median (Inter-Quartile Range)         | -53.85 (-78.01 to -34.48) | -29.87 (-76.39 to -11.36) |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Seizure-free rate (all seizures) during the 2-week Inpatient Period

|                 |   |
|-----------------|---|
| End point title | Seizure-free rate (all seizures) during the 2-week Inpatient Period |
|-----------------|---|

End point description:

Seizure-free rate is reported as the percentage of seizure-free participants during the 2-week Inpatient Period.

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

End point timeframe:

During the 2-week Inpatient Period

| End point values                  | Placebo/UCB0942 (FAS) | UCB0942/UCB0942 (FAS) |  |  |
|-----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                | Subject analysis set  | Subject analysis set  |  |  |
| Number of subjects analysed       | 27                    | 27                    |  |  |
| Units: percentage of participants |                       |                       |  |  |
| number (not applicable)           |                       |                       |  |  |
| percentage of participants        | 3.7                   | 7.4                   |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Seizure-free rate (all seizures) during the last 4 weeks of the Outpatient Maintenance Period

|                 |   |
|-----------------|---|
| End point title | Seizure-free rate (all seizures) during the last 4 weeks of the Outpatient Maintenance Period |
|-----------------|---|

End point description:

Seizure-free rate is reported as the percentage of seizure-free participants during the last 4 weeks of the Outpatient Maintenance Period.

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

End point timeframe:

During the last 4 weeks of the Outpatient Maintenance Period

| End point values                  | Placebo/UCB0942 (FAS) | UCB0942/UCB0942 (FAS) |  |  |
|-----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                | Subject analysis set  | Subject analysis set  |  |  |
| Number of subjects analysed       | 27                    | 25                    |  |  |
| Units: percentage of participants |                       |                       |  |  |
| number (not applicable)           |                       |                       |  |  |
| percentage of participants        | 0                     | 0                     |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Seizure-free rate (all seizures) during the On-UCB0942 Overall Period

|  |   |
|--|---|
| End point title  | Seizure-free rate (all seizures) during the On-UCB0942 Overall Period |
| End point description:<br>Seizure-free rate is reported as the percentage of seizure-free participants during the On-UCB0942 Overall Period. |   |
| End point type   | Secondary   |
| End point timeframe:<br>During the On-UCB0942 Overall Period (approximately 11 weeks)  |   |

| End point values                  | Placebo/UCB0942 (FAS) | UCB0942/UCB0942 (FAS) |  |  |
|-----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                | Subject analysis set  | Subject analysis set  |  |  |
| Number of subjects analysed       | 27                    | 28                    |  |  |
| Units: percentage of participants |                       |                       |  |  |
| number (not applicable)           |                       |                       |  |  |
| percentage of participants        | 0                     | 0                     |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: 75 % responder rate during the last 4 weeks of the Outpatient Maintenance Period

|  |  |
|--|--|
| End point title  | 75 % responder rate during the last 4 weeks of the Outpatient Maintenance Period |
| End point description:<br>The 75 % responder rate is defined as the percentage of subjects who achieve a 75 % or greater reduction in focal seizure frequency. |  |
| End point type   | Secondary  |
| End point timeframe:<br>During the last 4 weeks of the Outpatient Maintenance Period   |  |

| End point values                  | Placebo/UCB0942 (FAS) | UCB0942/UCB0942 (FAS) |  |  |
|-----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                | Subject analysis set  | Subject analysis set  |  |  |
| Number of subjects analysed       | 27                    | 24                    |  |  |
| Units: percentage of participants |                       |                       |  |  |
| number (not applicable)           |                       |                       |  |  |
| 75% responder rate                | 33.3                  | 29.2                  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: 75 % responder rate during the On-UCB0942 Overall Period

|                 |  |
|-----------------|--|
| End point title | 75 % responder rate during the On-UCB0942 Overall Period |
|-----------------|--|

End point description:

The 75 % responder rate is defined as the percentage of subjects who achieve a 75 % or greater reduction in focal seizure frequency.

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

End point timeframe:

During the On-UCB0942 Overall Period (approximately 11 weeks)

| End point values                  | Placebo/UCB0942 (FAS) | UCB0942/UCB0942 (FAS) |  |  |
|-----------------------------------|-----------------------|-----------------------|--|--|
| Subject group type                | Subject analysis set  | Subject analysis set  |  |  |
| Number of subjects analysed       | 27                    | 27                    |  |  |
| Units: percentage of participants |                       |                       |  |  |
| number (not applicable)           |                       |                       |  |  |
| 75% responder rate                | 25.9                  | 25.9                  |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of seizure free days (all seizures) during the 2-week Inpatient Period

|                 |   |
|-----------------|---|
| End point title | Percentage of seizure free days (all seizures) during the 2-week Inpatient Period |
|-----------------|---|

End point description:

For the active group, the 2-week Inpatient Period refers to the last 2 weeks of the Inpatient Period, while for the Placebo group, it refers to the first 2 weeks of the Inpatient Period.

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

End point timeframe:

During the 2-week Inpatient Period

| End point values                      | Placebo/UCB0942 (FAS) | UCB0942/UCB0942 (FAS)  |  |  |
|---------------------------------------|-----------------------|------------------------|--|--|
| Subject group type                    | Subject analysis set  | Subject analysis set   |  |  |
| Number of subjects analysed           | 27                    | 27                     |  |  |
| Units: percentage of days             |                       |                        |  |  |
| median (inter-quartile range (Q1-Q3)) |                       |                        |  |  |
| Median (Inter-Quartile Range)         | 21.43 (7.14 to 57.14) | 57.14 (28.57 to 78.57) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Percentage of seizure-free days (all seizures) during the Outpatient Maintenance Period

|                 |   |
|-----------------|---|
| End point title | Percentage of seizure-free days (all seizures) during the Outpatient Maintenance Period |
|-----------------|---|

End point description:

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

End point timeframe:

During the Outpatient Maintenance Period (8 weeks)

| End point values                      | Placebo/UCB0942 (FAS)  | UCB0942/UCB0942 (FAS)  |  |  |
|---------------------------------------|------------------------|------------------------|--|--|
| Subject group type                    | Subject analysis set   | Subject analysis set   |  |  |
| Number of subjects analysed           | 27                     | 26                     |  |  |
| Units: percentage of days             |                        |                        |  |  |
| median (inter-quartile range (Q1-Q3)) |                        |                        |  |  |
| Median (Inter-Quartile Range)         | 51.79 (15.79 to 80.70) | 51.35 (29.82 to 69.64) |  |  |

## Statistical analyses

No statistical analyses for this end point

### Secondary: Number of patients reporting at least one Serious Adverse Event (SAE) during the course of the study

|                 |  |
|-----------------|--|
| End point title | Number of patients reporting at least one Serious Adverse Event (SAE) during the course of the study |
|-----------------|--|

End point description:

Number of subjects experiencing at least one serious adverse event (reported by the subject and/or caregiver or observed by the Investigator or inpatient staff).

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

End point timeframe:

All study duration (approximately 19 to 20 weeks)

| End point values            | Placebo/UCB0942 (SS) | UCB0942/UCB0942 (SS) |  |  |
|-----------------------------|----------------------|----------------------|--|--|
| Subject group type          | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed | 27                   | 28                   |  |  |
| Units: Participants         |                      |                      |  |  |
| participants                | 0                    | 2                    |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Number of subject withdrawals due to Adverse Events (AEs) during the course of the study

|                 |  |
|-----------------|--|
| End point title | Number of subject withdrawals due to Adverse Events (AEs) during the course of the study |
|-----------------|--|

End point description:

Number of subjects who withdrew from the study due adverse event (reported by the subject and/or caregiver or observed by the Investigator or inpatient staff).

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

End point timeframe:

All study duration (approximately 19 to 20 weeks)

| End point values            | Placebo/UCB0942 (SS) | UCB0942/UCB0942 (SS) |  |  |
|-----------------------------|----------------------|----------------------|--|--|
| Subject group type          | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed | 27                   | 28                   |  |  |
| Units: Participants         |                      |                      |  |  |
| participants                | 0                    | 1                    |  |  |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected from Baseline until Safety Follow Up Visit (up to Week 28).

Adverse event reporting additional description:

Baseline Characteristics refer to the Safety Set consisting of all subjects in the Randomized Set who received at least 1 dose of Investigational Medicinal Product (IMP). 2 subjects reported multiple Serious Adverse Events (SAEs).

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

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 19.1 |
|--------------------|------|

### Reporting groups

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | UCB0942/UCB0942 |
|-----------------------|-----------------|

Reporting group description:

Subjects received UCB0942.

|                       |                 |
|-----------------------|-----------------|
| Reporting group title | Placebo/UCB0942 |
|-----------------------|-----------------|

Reporting group description:

After 2-week in the Inpatient Period, Placebo subjects received the experimental medicine (UCB0942).

| Serious adverse events                            | UCB0942/UCB0942 | Placebo/UCB0942 |  |
|---|-----------------|-----------------|--|
| Total subjects affected by serious adverse events |                 |                 |  |
| subjects affected / exposed                       | 2 / 28 (7.14%)  | 0 / 27 (0.00%)  |  |
| number of deaths (all causes)                     | 0               | 0               |  |
| number of deaths resulting from adverse events    | 0               | 0               |  |
| Nervous system disorders                          |                 |                 |  |
| Judgement impaired                                |                 |                 |  |
| subjects affected / exposed                       | 1 / 28 (3.57%)  | 0 / 27 (0.00%)  |  |
| occurrences causally related to treatment / all   | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0           |  |
| Status epilepticus                                |                 |                 |  |
| subjects affected / exposed                       | 1 / 28 (3.57%)  | 0 / 27 (0.00%)  |  |
| occurrences causally related to treatment / all   | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0           |  |
| Psychiatric disorders                             |                 |                 |  |
| Delirium  |                 |                 |  |
| subjects affected / exposed                       | 1 / 28 (3.57%)  | 0 / 27 (0.00%)  |  |
| occurrences causally related to treatment / all   | 1 / 1           | 0 / 0           |  |
| deaths causally related to treatment / all        | 0 / 0           | 0 / 0           |  |

|   |                |                |  |
|---|----------------|----------------|--|
| Dysphoria                                       |                |                |  |
| subjects affected / exposed                     | 1 / 28 (3.57%) | 0 / 27 (0.00%) |  |
| occurrences causally related to treatment / all | 1 / 1          | 0 / 0          |  |
| deaths causally related to treatment / all      | 0 / 0          | 0 / 0          |  |

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

| <b>Non-serious adverse events</b>                     | UCB0942/UCB0942  | Placebo/UCB0942  |  |
|---|------------------|------------------|--|
| Total subjects affected by non-serious adverse events |                  |                  |  |
| subjects affected / exposed                           | 27 / 28 (96.43%) | 26 / 27 (96.30%) |  |
| Investigations  |                  |                  |  |
| Weight increased                                      |                  |                  |  |
| subjects affected / exposed                           | 1 / 28 (3.57%)   | 3 / 27 (11.11%)  |  |
| occurrences (all)                                     | 1                | 3                |  |
| Vascular disorders                                    |                  |                  |  |
| Hypotension   |                  |                  |  |
| subjects affected / exposed                           | 2 / 28 (7.14%)   | 1 / 27 (3.70%)   |  |
| occurrences (all)                                     | 3                | 1                |  |
| Nervous system disorders                              |                  |                  |  |
| Somnolence  |                  |                  |  |
| subjects affected / exposed                           | 17 / 28 (60.71%) | 12 / 27 (44.44%) |  |
| occurrences (all)                                     | 24               | 16               |  |
| Dizziness   |                  |                  |  |
| subjects affected / exposed                           | 14 / 28 (50.00%) | 12 / 27 (44.44%) |  |
| occurrences (all)                                     | 19               | 51               |  |
| Headache  |                  |                  |  |
| subjects affected / exposed                           | 10 / 28 (35.71%) | 6 / 27 (22.22%)  |  |
| occurrences (all)                                     | 13               | 9                |  |
| Tremor  |                  |                  |  |
| subjects affected / exposed                           | 2 / 28 (7.14%)   | 3 / 27 (11.11%)  |  |
| occurrences (all)                                     | 2                | 3                |  |
| Disturbance in attention                              |                  |                  |  |
| subjects affected / exposed                           | 3 / 28 (10.71%)  | 1 / 27 (3.70%)   |  |
| occurrences (all)                                     | 3                | 2                |  |
| Dysarthria  |                  |                  |  |



|  |                 |                 |  |
|--|-----------------|-----------------|--|
| subjects affected / exposed                          | 3 / 28 (10.71%) | 2 / 27 (7.41%)  |  |
| occurrences (all)                                    | 5               | 2               |  |
| Memory impairment                                    |                 |                 |  |
| subjects affected / exposed                          | 3 / 28 (10.71%) | 1 / 27 (3.70%)  |  |
| occurrences (all)                                    | 6               | 2               |  |
| Nystagmus  |                 |                 |  |
| subjects affected / exposed                          | 1 / 28 (3.57%)  | 3 / 27 (11.11%) |  |
| occurrences (all)                                    | 1               | 3               |  |
| Amnesia  |                 |                 |  |
| subjects affected / exposed                          | 2 / 28 (7.14%)  | 1 / 27 (3.70%)  |  |
| occurrences (all)                                    | 2               | 1               |  |
| Paraesthesia   |                 |                 |  |
| subjects affected / exposed                          | 2 / 28 (7.14%)  | 1 / 27 (3.70%)  |  |
| occurrences (all)                                    | 2               | 2               |  |
| Simple partial seizures                              |                 |                 |  |
| subjects affected / exposed                          | 2 / 28 (7.14%)  | 1 / 27 (3.70%)  |  |
| occurrences (all)                                    | 5               | 1               |  |
| Seizure  |                 |                 |  |
| subjects affected / exposed                          | 3 / 28 (10.71%) | 0 / 27 (0.00%)  |  |
| occurrences (all)                                    | 3               | 0               |  |
| Ataxia   |                 |                 |  |
| subjects affected / exposed                          | 2 / 28 (7.14%)  | 0 / 27 (0.00%)  |  |
| occurrences (all)                                    | 3               | 0               |  |
| Restless legs syndrome                               |                 |                 |  |
| subjects affected / exposed                          | 2 / 28 (7.14%)  | 0 / 27 (0.00%)  |  |
| occurrences (all)                                    | 2               | 0               |  |
| General disorders and administration site conditions |                 |                 |  |
| Fatigue  |                 |                 |  |
| subjects affected / exposed                          | 4 / 28 (14.29%) | 9 / 27 (33.33%) |  |
| occurrences (all)                                    | 23              | 14              |  |
| Gait disturbance                                     |                 |                 |  |
| subjects affected / exposed                          | 3 / 28 (10.71%) | 2 / 27 (7.41%)  |  |
| occurrences (all)                                    | 17              | 2               |  |
| Asthenia   |                 |                 |  |

|   |                      |                     |  |
|---|----------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)  | 2 / 28 (7.14%)<br>2  | 2 / 27 (7.41%)<br>2 |  |
| Pyrexia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 28 (0.00%)<br>0  | 2 / 27 (7.41%)<br>2 |  |
| Eye disorders<br>Diplopia<br>subjects affected / exposed<br>occurrences (all)                                 | 2 / 28 (7.14%)<br>2  | 1 / 27 (3.70%)<br>1 |  |
| Vision blurred<br>subjects affected / exposed<br>occurrences (all)  | 2 / 28 (7.14%)<br>5  | 1 / 27 (3.70%)<br>1 |  |
| Gastrointestinal disorders<br>Constipation<br>subjects affected / exposed<br>occurrences (all)                | 3 / 28 (10.71%)<br>3 | 1 / 27 (3.70%)<br>2 |  |
| Dry mouth<br>subjects affected / exposed<br>occurrences (all)   | 2 / 28 (7.14%)<br>2  | 1 / 27 (3.70%)<br>1 |  |
| Nausea<br>subjects affected / exposed<br>occurrences (all)  | 2 / 28 (7.14%)<br>2  | 0 / 27 (0.00%)<br>0 |  |
| Abdominal pain upper<br>subjects affected / exposed<br>occurrences (all)                                      | 0 / 28 (0.00%)<br>0  | 2 / 27 (7.41%)<br>4 |  |
| Diarrhoea<br>subjects affected / exposed<br>occurrences (all)   | 0 / 28 (0.00%)<br>0  | 2 / 27 (7.41%)<br>3 |  |
| Dyspepsia<br>subjects affected / exposed<br>occurrences (all)   | 0 / 28 (0.00%)<br>0  | 2 / 27 (7.41%)<br>4 |  |
| Reproductive system and breast disorders<br>Dysmenorrhoea<br>subjects affected / exposed<br>occurrences (all) | 3 / 28 (10.71%)<br>4 | 0 / 27 (0.00%)<br>0 |  |
| Psychiatric disorders   |                      |                     |  |

|   |                 |                 |  |
|---|-----------------|-----------------|--|
| Irritability                                    |                 |                 |  |
| subjects affected / exposed                     | 5 / 28 (17.86%) | 4 / 27 (14.81%) |  |
| occurrences (all)                               | 5               | 5               |  |
| Insomnia  |                 |                 |  |
| subjects affected / exposed                     | 4 / 28 (14.29%) | 0 / 27 (0.00%)  |  |
| occurrences (all)                               | 5               | 0               |  |
| Depressed mood                                  |                 |                 |  |
| subjects affected / exposed                     | 2 / 28 (7.14%)  | 1 / 27 (3.70%)  |  |
| occurrences (all)                               | 2               | 1               |  |
| Nervousness                                     |                 |                 |  |
| subjects affected / exposed                     | 1 / 28 (3.57%)  | 2 / 27 (7.41%)  |  |
| occurrences (all)                               | 1               | 3               |  |
| Disorientation                                  |                 |                 |  |
| subjects affected / exposed                     | 2 / 28 (7.14%)  | 0 / 27 (0.00%)  |  |
| occurrences (all)                               | 3               | 0               |  |
| Mood swings                                     |                 |                 |  |
| subjects affected / exposed                     | 2 / 28 (7.14%)  | 0 / 27 (0.00%)  |  |
| occurrences (all)                               | 2               | 0               |  |
| Parasomnia                                      |                 |                 |  |
| subjects affected / exposed                     | 2 / 28 (7.14%)  | 0 / 27 (0.00%)  |  |
| occurrences (all)                               | 3               | 0               |  |
| Aggression                                      |                 |                 |  |
| subjects affected / exposed                     | 0 / 28 (0.00%)  | 2 / 27 (7.41%)  |  |
| occurrences (all)                               | 0               | 2               |  |
| Musculoskeletal and connective tissue disorders |                 |                 |  |
| Back pain                                       |                 |                 |  |
| subjects affected / exposed                     | 1 / 28 (3.57%)  | 2 / 27 (7.41%)  |  |
| occurrences (all)                               | 2               | 2               |  |
| Musculoskeletal pain                            |                 |                 |  |
| subjects affected / exposed                     | 0 / 28 (0.00%)  | 3 / 27 (11.11%) |  |
| occurrences (all)                               | 0               | 5               |  |
| Infections and infestations                     |                 |                 |  |
| Nasopharyngitis                                 |                 |                 |  |
| subjects affected / exposed                     | 2 / 28 (7.14%)  | 0 / 27 (0.00%)  |  |
| occurrences (all)                               | 2               | 0               |  |
| Metabolism and nutrition disorders              |                 |                 |  |

|                             |                |                 |  |
|-----------------------------|----------------|-----------------|--|
| Decreased appetite          |                |                 |  |
| subjects affected / exposed | 2 / 28 (7.14%) | 3 / 27 (11.11%) |  |
| occurrences (all)           | 2              | 3               |  |
| Hyponatraemia               |                |                 |  |
| subjects affected / exposed | 2 / 28 (7.14%) | 2 / 27 (7.41%)  |  |
| occurrences (all)           | 2              | 2               |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date              | Amendment   |
|-------------------|---|
| 16 September 2015 | <p>Protocol Amendment 1 (dated 16-Sep-2015) was implemented after the date of first patient first visit (FPFV on 28-Aug-2015). Two subjects were randomized at the time of the amendment. The rationale for this amendment was to add an echocardiogram during dosing in response to a request from the Federal Institute for Drugs and Medical Devices (Bundesinstitut für Arzneimittel und Medizinprodukte). This echocardiogram was added at Day OP22.</p> <p>In addition, the following changes were made:</p> <ul style="list-style-type: none"><li>- It was clarified that either urine or serum pregnancy tests could be used for all visits.</li><li>- It was pointed out that the decision to continue in the OLE study (EP0073) occurred at Day OP43.</li><li>- Clarification on the procedure for dose reduction in cases of poor tolerability of UCB0942 400 mg bid (ie, reduction to UCB0942 200 mg bid and in some cases to UCB0942 100 mg bid).</li><li>- The withdrawal criteria for elevated transaminases were reworded as the previous description was not clear.</li></ul>  |
| 19 November 2015  | <p>Protocol Amendment 2 (dated 19-Nov-2015) was implemented after 22 subjects were randomized. The rationale for this amendment was to make the video monitoring language in the protocol more flexible so that sites/Investigators could perform this according to their usual practice. This new language also allowed video- electroencephalogram (EEG) monitoring as some sites did not perform video-only monitoring. A second change was the wording of the drug misuse exclusion criterion. As is customary in most UCB protocols, exclusion for drug misuse is only applicable if the Investigator deems that study participation is either a risk to the subject or that the drug misuse could confound the outcomes measured in the study. The wording of this exclusion criterion was changed to match that of other UCB studies.</p>  |
| 13 May 2016       | <p>Protocol Amendment 3 (dated-13 May-2016) was implemented after 35 subjects were randomized. The rationale for this amendment was to add and describe an optional interim analysis for purposes of planning and designing of future studies. Other reasons for the amendment included the following:</p> <ul style="list-style-type: none"><li>- To add an exploratory objective, variable and associated assessment (Diary Addendum).</li></ul> <p>Note that this was already part of the study, but not clearly described in the protocol.</p> <ul style="list-style-type: none"><li>- To clarify procedures for dosing when there was intolerance to IMP during the Inpatient Period.</li><li>- To allow and specify flexibility in dosing during the Outpatient Maintenance Period.</li><li>- To further specify which subjects required an echocardiogram at 6 months after the last dose of UCB0942.</li><li>- To expand the range of body mass index (BMI) allowed for inclusion in the study.</li><li>- To revise procedures for assessment of suicidality using the Columbia-Suicide Severity Rating Scale (C-SSRS) (specifically, the C-SSRS withdrawal criterion) in line with revision to UCB SOP, which became effective on 01-Apr-2016.</li><li>- To update the protocol information pertaining to potential drug-induced liver injury (PDILI)</li></ul> <p>(exclusion criteria, withdrawal criteria, adverse events (AEs) of special interest, and assessments) based on new standard language which was being applied across all protocols at UCB. Note that these additions do not reflect a change in the known safety of the compound.</p> |

|                 |   |
|-----------------|---|
| 10 October 2016 | <p>Protocol Amendment 4 (dated 10-Oct-2016) was implemented after all subjects were randomized. The rationale for this amendment was to describe a tiered approach to database lock and unblinding.</p> <p>Other changes included:</p> <ul style="list-style-type: none"> <li>- Correction of an inconsistency between the Summary section and the Study Design section pertaining to allowable dose changes</li> <li>- Clarification of the reporting period for AEs</li> <li>- Specification that the Baseline version of the Seizure Severity Questionnaire (SSQ) was to be used in all instances where it was administered</li> <li>- Correction of the number of questions in the SSQ from 11 to 10</li> <li>- Correction of several cross references</li> <li>- Other minor administrative changes</li> </ul> |
|-----------------|---|

Notes:

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## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

None reported