



Clinical trial results:

A PROSPECTIVE, MULTINATIONAL, OPEN-LABEL, SINGLE-ARM, EXPLORATIVE STUDY TO EVALUATE THE TOLERABILITY AND EFFICACY OF LACOSAMIDE WHEN ADDED TO LEVETIRACETAM WITH WITHDRAWAL OF THE CONCOMITANT SODIUM CHANNEL BLOCKING ANTIEPILEPTIC DRUG IN SUBJECTS WITH UNCONTROLLED PARTIAL-ONSET SEIZURES

Summary

| | |
|--------------------------|-------------------------|
| EudraCT number | 2011-002461-37 |
| Trial protocol | DE SE AT ES NL DK BG HU |
| Global end of trial date | 10 January 2014 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 30 June 2016 |
| First version publication date | 09 July 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | SP0980 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01484977 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|---|
| Sponsor organisation name | UCB BIOSCIENCES Inc |
| Sponsor organisation address | 8010 Arco Corporate Drive, Raleigh, United States, 27617 |
| Public contact | Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, +49 217348 1515, clinicaltrials@ucb.com |
| Scientific contact | Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, +49 217348 1515, 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 | 10 March 2014 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 10 January 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to assess the overall effectiveness of Lacosamide (optimized within the range of 200 mg/day to 600 mg/day) when added to a stable dose of Levetiracetam (in the label range of 1000 mg/day to 3000 mg/day) with withdrawal of the concomitant Sodium Channel Blocking Antiepileptic Drug (SCB-AED) in subjects with partial-onset seizures not adequately controlled on their dual LEV and SCB-AED regimen.

Protection of trial subjects:

Data privacy measures in place

Background therapy:

Concomitant AED therapy at baseline with LEV and SCB (CBZ, OXC, PHT, LTG or ESL)

Evidence for comparator:

Not applicable

| | |
|---|------------------|
| Actual start date of recruitment | 01 December 2011 |
| 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 | Spain: 12 |
| Country: Number of subjects enrolled | Sweden: 3 |
| Country: Number of subjects enrolled | Bulgaria: 20 |
| Country: Number of subjects enrolled | Denmark: 4 |
| Country: Number of subjects enrolled | France: 8 |
| Country: Number of subjects enrolled | Germany: 3 |
| Country: Number of subjects enrolled | United States: 53 |
| Country: Number of subjects enrolled | Romania: 12 |
| Country: Number of subjects enrolled | Australia: 5 |
| Worldwide total number of subjects | 120 |
| EEA total number of subjects | 62 |

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) | 115 |
| From 65 to 84 years | 5 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The recruitment for the SP0980 study began in December 2011. It concluded in December 2013. This was a multicenter study with subjects enrolled by 30 sites across North America, 12 in Western Europe, 10 in Eastern Europe, and 2 in Oceania.

Pre-assignment

Screening details:

The SP0980 study enrolled 147 patients. Out of the 147 enrolled patients, there were 27 screen failures. This resulted in 120 eligible patients for this study.

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 | Lacosamide |
|-----------|------------|

Arm description:

Lacosamide will be added to levetiracetam while withdrawing the sodium channel blocking antiepileptic drug (AED).

| | |
|--|------------------------------|
| Arm type | Experimental |
| Investigational medicinal product name | Lacosamide |
| Investigational medicinal product code | SPM927 |
| Other name | VIMPAT®, SPM927, Harkoseride |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

50 mg and 100 mg lacosamide tablets will be combined and taken in two equal doses per day to provide the required total daily dosage of 100 - 600 mg/day.

Maximum duration of study drug administration is approximately 23 weeks.

| Number of subjects in period 1 | Lacosamide |
|--------------------------------|------------|
| Started | 120 |
| Completed | 93 |
| Not completed | 27 |
| Moving Overseas | 1 |
| Consent withdrawn by subject | 4 |
| Lack of Compliance | 1 |
| Low White Blood Cell Count | 1 |
| Subject Protocol Non-compliant | 1 |
| Lost to follow-up | 1 |
| Non-Fatal, Non-Serious AE(s) | 8 |

| | |
|--------------------|---|
| Lack of efficacy | 4 |
| Protocol deviation | 6 |

Baseline characteristics

Reporting groups

| | |
|---|------------|
| Reporting group title | Lacosamide |
| Reporting group description: | |
| Lacosamide will be added to levetiracetam while withdrawing the sodium channel blocking antiepileptic drug (AED). | |

| Reporting group values | Lacosamide | Total | |
|---|------------|-------|--|
| Number of subjects | 120 | 120 | |
| Age categorical | | | |
| The Baseline characteristics consist of subjects in the Safety Set (SS). The SS is all subjects who received at least 1 dose of lacosamide. | | | |
| Units: Subjects | | | |
| <=18 | 1 | 1 | |
| >18-<65 | 114 | 114 | |
| >=65 | 5 | 5 | |
| Age continuous | | | |
| The Baseline characteristics consist of subjects in the Safety Set (SS). The SS is all subjects who received at least 1 dose of lacosamide. | | | |
| Units: years | | | |
| arithmetic mean | 39.7 | | |
| standard deviation | ± 12.6 | - | |
| Gender categorical | | | |
| The Baseline characteristics consist of subjects in the Safety Set (SS). The SS is all subjects who received at least 1 dose of lacosamide. | | | |
| Units: Subjects | | | |
| Female | 74 | 74 | |
| Male | 46 | 46 | |
| Racial Group | | | |
| The Baseline characteristics consist of subjects in the Safety Set (SS). The SS is all subjects who received at least 1 dose of lacosamide. | | | |
| Units: Subjects | | | |
| American Indian/ Alaskan Native | 1 | 1 | |
| Asian | 3 | 3 | |
| Black | 8 | 8 | |
| Native Hawaiian or other Pacific Islander | 0 | 0 | |
| White | 96 | 96 | |
| Other/Mixed | 12 | 12 | |
| Ethnicity | | | |
| The Baseline characteristics consist of subjects in the Safety Set (SS). The SS is all subjects who received at least 1 dose of lacosamide. | | | |
| Units: Subjects | | | |
| Hispanic or Latino | 17 | 17 | |
| Not Hispanic or Latino | 103 | 103 | |
| Weight | | | |
| The Baseline characteristics consist of subjects in the Safety Set (SS). The SS is all subjects who received at least 1 dose of lacosamide. | | | |
| Units: kilogram(s) | | | |
| arithmetic mean | 76.39 | | |

| | | | |
|---|-------------|---|--|
| standard deviation | ± 19.98 | - | |
| Height | | | |
| The Baseline characteristics consist of subjects in the Safety Set (SS). The SS is all subjects who received at least 1 dose of lacosamide. | | | |
| Units: Centimeters | | | |
| arithmetic mean | 168.02 | | |
| standard deviation | ± 10.55 | - | |
| BMI | | | |
| The Baseline characteristics consist of subjects in the Safety Set (SS). The SS is all subjects who received at least 1 dose of lacosamide. | | | |
| Units: kilogram(s)/square meter | | | |
| arithmetic mean | 27 | | |
| standard deviation | ± 6.45 | - | |

End points

End points reporting groups

| | |
|---|------------|
| Reporting group title | Lacosamide |
| Reporting group description: Lacosamide will be added to levetiracetam while withdrawing the sodium channel blocking antiepileptic drug (AED). | |

Primary: Retention at the end of the 21-week Treatment Period

| | |
|---|---|
| End point title | Retention at the end of the 21-week Treatment Period ^[1] |
| End point description: Retention is a summary measure that integrates both the patient's and clinician's assessment of efficacy and tolerability in epilepsy clinical studies to provide a measure of effectiveness. | |
| End point type | Primary |
| End point timeframe: Duration of the Treatment Period (21 Weeks) | |

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: Due to system limitations, a single arm study statistical analysis was not entered.

Percentage (retention rate (RR) and its 95 % CI), of subjects remaining in the study through the 21-Week Treatment Period will be calculated. Subjects retained through Week 21 will be counted in the numerator. All subjects in the relevant population will be used as the denominator.

n=120

RR (95 % CI): 73.3 (65.42, 81.25).

| | | | | |
|-----------------------------------|-----------------|--|--|--|
| End point values | Lacosamide | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 120 | | | |
| Units: Percentage of Participants | | | | |
| number (not applicable) | 73.3 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Treatment-emergent Adverse Events (TEAEs) were recorded during the course of the SP0980 study, which began in December 2011 and concluded in December 2013.

Adverse event reporting additional description:

TEAE reporting refers to the Safety Set (SS). The SS is all subjects who received at least 1 dose of lacosamide.

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

Dictionary used

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

| | |
|--------------------|-----|
| Dictionary version | 9.1 |
|--------------------|-----|

Reporting groups

| | |
|-----------------------|------------|
| Reporting group title | Lacosamide |
|-----------------------|------------|

Reporting group description:

Lacosamide will be added to levetiracetam while withdrawing the sodium channel blocking antiepileptic drug (AED).

| Serious adverse events | Lacosamide | | |
|---|-----------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 8 / 120 (6.67%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Cardiac disorders | | | |
| Acute myocardial infarction | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Angina pectoris | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Leukocytosis | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 1 / 120 (0.83%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Gastrointestinal disorders | | | |
| Toothache | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Asthma | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Migraine | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anxiety | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Mental status changes | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Suicidal ideation | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Pneumonia | | | |

| | | | |
|---|-----------------|--|--|
| subjects affected / exposed | 2 / 120 (1.67%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infection | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Urinary tract infection | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vulvovaginitis trichomonal | | | |
| subjects affected / exposed | 1 / 120 (0.83%) | | |
| 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 %

| Non-serious adverse events | Lacosamide | | |
|---|-------------------|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 48 / 120 (40.00%) | | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 28 / 120 (23.33%) | | |
| occurrences (all) | 40 | | |
| Headache | | | |
| subjects affected / exposed | 18 / 120 (15.00%) | | |
| occurrences (all) | 21 | | |
| Convulsion | | | |

| | | | |
|--|------------------------|--|--|
| subjects affected / exposed occurrences (all) | 7 / 120 (5.83%) 8 | | |
| General disorders and administration site conditions Fatigue subjects affected / exposed occurrences (all) | 10 / 120 (8.33%) 13 | | |
| Gastrointestinal disorders Nausea subjects affected / exposed occurrences (all) | 7 / 120 (5.83%) 7 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|--|
| 18 October 2010 | Protocol Amendment 1, 18 Oct 2011 The protocol was amended in order to revise the age inclusion criterion, which limited enrollment to the adult population (≥ 18 years). In addition, a withdrawal criterion was added. The withdrawal criterion clarified that subjects must have been withdrawn from the study if their VNS settings were no longer constant or subject required a change to the VNS Settings. |
| 07 June 2013 | Protocol Amendment 2, 07 Jun 2013 The protocol was amended in order to revise the planned termination of the study. Due to difficulty with enrollment, the initially planned enrollment period was extended approximately 6 months. Despite this extension, it was projected that only approximately 100 total subjects would be enrolled instead of the initially intended subject number of approximately 300. Because of the change in the anticipated number of subjects, the study would not have sufficient power to detect a 50 % reduction in the all-cause discontinuation rate and all analyses would have been exploratory in nature. In addition, administrative changes were made to update study personnel and 24-hour safety contact information. Revisions were also made to reflect UCB BIOSCIENCES department name change from Global Clinical Safety and Pharmacovigilance (GCSP) to Drug Safety, to clarify wording in Exclusion Criterion #11, and to clarify the temperature log recording requirements. Minor typographical revisions were also made. |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported