



Clinical trial results:

A Multicenter, Open-label Extension Trial to Assess the Long-term Safety and Tolerability of Lacosamide as Adjunctive Therapy in Subjects With Partial-onset Seizures

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2014-004384-21 |
| Trial protocol | Outside EU/EEA |
| Global end of trial date | 15 June 2010 |

Results information

| | |
|--------------------------------|--------------|
| Result version number | v1 (current) |
| This version publication date | 30 June 2016 |
| First version publication date | 17 May 2015 |

Trial information

Trial identification

| | |
|-----------------------|--------|
| Sponsor protocol code | SP0926 |
|-----------------------|--------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT00655486 |
| 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, 0049 2173 48 15 15, clinicaltrials@ucb.com |
| Scientific contact | Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 0049 2173 48 15 15, 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? | Yes |

Notes:

Results analysis stage

| | |
|--|----------------|
| Analysis stage | Final |
| Date of interim/final analysis | 10 August 2010 |
| Is this the analysis of the primary completion data? | No |
| Global end of trial reached? | Yes |
| Global end of trial date | 15 June 2010 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

The objectives of this study were to:

- Allow subjects who completed the SP925 study or terminated from the study (Cohorts 2, 3, and 4 only) due to an intolerable adverse event(s) (AE[s]) to continue Lacosamide (LCM)
- Obtain additional long-term safety information for LCM

Protection of trial subjects:

Subject's informed consent was obtained and documented in accordance with local regulations, ICH-GCP requirements, and the ethical principles that have their origin in the principles of the Declaration of Helsinki.

Prior to obtaining informed consent, information was given in a language and at a level of complexity understandable to the subject in both oral and written form by the investigator or designee. Each subject had the opportunity to discuss the trial and its alternatives with the investigator.

Background therapy:

N/A

Evidence for comparator:

N/A

| | |
|---|---------------|
| Actual start date of recruitment | 22 April 2008 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-------------------|
| Country: Number of subjects enrolled | United States: 97 |
| Worldwide total number of subjects | 97 |
| EEA total number of subjects | 0 |

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) | 1 |
| Adults (18-64 years) | 96 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

Subject disposition

Recruitment

Recruitment details:

The study started in April 2008 with enrollment occurring in the United States only. The study completed June 2010

Pre-assignment

Screening details:

N/A

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 100 to 800 mg/day, flexible dosing, administered twice daily throughout the duration of the study (up to 2 years)

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Lacosamide |
| Investigational medicinal product code | SPM 927 |
| Other name | Vimpat |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Subjects' dose of Lacosamide may be increased or decreased as needed to maintain a subject's effective and tolerable dose during the study. Tablets are 50 mg or 100 mg each; Dose is 100 mg/day up to 800 mg/day administered twice daily throughout the study (up to 2 years).

| Number of subjects in period 1 | Lacosamide |
|---|------------|
| Started | 97 |
| Completed | 69 |
| Not completed | 28 |
| Consent withdrawn by subject | 4 |
| Non-Fatal, Non-Serious AE | 9 |
| Non-Fatal, Serious AE | 1 |
| Unsatisfactory compliance | 2 |
| Other: Pregnancy | 1 |
| Other: Could not tolerate BID dosing | 1 |
| Lack of efficacy | 8 |
| Protocol deviation | 1 |
| Other: Abnormal electrocardiogram (ECG) | 1 |

Baseline characteristics

Reporting groups

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

Reporting group description:

Lacosamide 100 to 800 mg/day, flexible dosing, administered twice daily throughout the duration of the study (up to 2 years)

| Reporting group values | Lacosamide | Total | |
|-------------------------|------------|-------|--|
| Number of subjects | 97 | 97 | |
| Age Categorical | | | |
| Units: Subjects | | | |
| <=18 years | 2 | 2 | |
| Between 18 and 65 years | 95 | 95 | |
| Age Continuous | | | |
| Units: years | | | |
| arithmetic mean | 38.8 | | |
| standard deviation | ± 11.7 | - | |
| Gender categorical | | | |
| Units: Subjects | | | |
| Female | 47 | 47 | |
| Male | 50 | 50 | |

End points

End points reporting groups

| | |
|--|------------|
| Reporting group title | Lacosamide |
| Reporting group description: | |
| Lacosamide 100 to 800 mg/day, flexible dosing, administered twice daily throughout the duration of the study (up to 2 years) | |

Primary: Number of subjects with at least one adverse event during this open-label extension study (maximum study duration 2 years)

| | |
|-----------------|---|
| End point title | Number of subjects with at least one adverse event during this open-label extension study (maximum study duration 2 years) ^[1] |
|-----------------|---|

End point description:

An Adverse Event (AE) is any untoward medical occurrence (eg, noxious or pathological changes) in a subject or clinical investigation subject compared with pre-existing conditions, that occurs during any period of a clinical trial including Pre-treatment, Run-In, Wash-Out, or Follow-Up Periods. An AE is defined as being independent of assumption of any causality (eg, to study or concomitant medication, primary or concomitant disease, or study design).

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

End point timeframe:

2 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: The primary variables for this study were all aimed at evaluating the long-term safety of LCM using descriptive data summaries. No statistical comparisons were planned based on the nature of the study design (no treatment comparator, open label flexible dosing, etc).

| End point values | Lacosamide | | | |
|-----------------------------|-----------------|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 97 | | | |
| Units: subjects | | | | |
| number | 93 | | | |

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects who withdrew from the study due to an adverse event (maximum study duration 2 years)

| | |
|-----------------|--|
| End point title | Number of subjects who withdrew from the study due to an adverse event (maximum study duration 2 years) ^[2] |
|-----------------|--|

End point description:

An Adverse Event (AE) is any untoward medical occurrence (eg, noxious or pathological changes) in a subject or clinical investigation subject compared with pre-existing conditions, that occurs during any period of a clinical trial including Pre-treatment, Run-In, Wash-Out, or Follow-Up Periods. An AE is defined as being independent of assumption of any causality (eg, to study or concomitant medication, primary or concomitant disease, or study design).

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

End point timeframe:

2 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: The primary variables for this study were all aimed at evaluating the long-term safety of LCM using descriptive data summaries. No statistical comparisons were planned based on the nature of the study design (no treatment comparator, open label flexible dosing, etc).

| | | | | |
|-----------------------------|-----------------|--|--|--|
| End point values | Lacosamide | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 97 | | | |
| Units: subjects | | | | |
| number | 10 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

2 years

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

Dictionary used

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

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

Reporting groups

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

Reporting group description:

Lacosamide 100 to 800 mg/day, flexible dosing, administered twice daily throughout the duration of the study (up to 2 years)

| Serious adverse events | Lacosamide | | |
|---|------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 10 / 97 (10.31%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | 0 | | |
| Injury, poisoning and procedural complications | | | |
| Post procedural bile leak | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Arrhythmia supraventricular | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Atrial fibrillation | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Nervous system disorders | | | |
| Convulsion | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 2 / 97 (2.06%) | | |
| occurrences causally related to treatment / all | 1 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Lethargy | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Chest pain | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Drug interaction | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Hallucination | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Homicidal ideation | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Paranoia | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Depression suicidal | | | |
| subjects affected / exposed | 1 / 97 (1.03%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |

| | | | |
|---|----------------------------------|--|--|
| Infections and infestations Giardiasis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 97 (1.03%) 0 / 1 0 / 0 | | |
| Pneumonia subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 97 (1.03%) 0 / 1 0 / 0 | | |
| Sepsis subjects affected / exposed occurrences causally related to treatment / all deaths causally related to treatment / all | 1 / 97 (1.03%) 0 / 1 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 | 88 / 97 (90.72%) | | |
| Investigations | | | |
| Weight increased | | | |
| subjects affected / exposed | 6 / 97 (6.19%) | | |
| occurrences (all) | 6 | | |
| Injury, poisoning and procedural complications | | | |
| Contusion | | | |
| subjects affected / exposed | 5 / 97 (5.15%) | | |
| occurrences (all) | 5 | | |
| Nervous system disorders | | | |
| Dizziness | | | |
| subjects affected / exposed | 43 / 97 (44.33%) | | |
| occurrences (all) | 50 | | |
| Somnolence | | | |
| subjects affected / exposed | 12 / 97 (12.37%) | | |
| occurrences (all) | 13 | | |
| Coordination abnormal | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 11 / 97 (11.34%) | | |
| occurrences (all) | 13 | | |
| Headache | | | |
| subjects affected / exposed | 11 / 97 (11.34%) | | |
| occurrences (all) | 11 | | |
| Balance disorder | | | |
| subjects affected / exposed | 11 / 97 (11.34%) | | |
| occurrences (all) | 13 | | |
| Tremor | | | |
| subjects affected / exposed | 8 / 97 (8.25%) | | |
| occurrences (all) | 10 | | |
| Memory impairment | | | |
| subjects affected / exposed | 5 / 97 (5.15%) | | |
| occurrences (all) | 5 | | |
| Hypoaesthesia | | | |
| subjects affected / exposed | 5 / 97 (5.15%) | | |
| occurrences (all) | 7 | | |
| General disorders and administration site conditions | | | |
| Fatigue | | | |
| subjects affected / exposed | 12 / 97 (12.37%) | | |
| occurrences (all) | 12 | | |
| Chest pain | | | |
| subjects affected / exposed | 8 / 97 (8.25%) | | |
| occurrences (all) | 9 | | |
| Irritability | | | |
| subjects affected / exposed | 5 / 97 (5.15%) | | |
| occurrences (all) | 6 | | |
| Ear and labyrinth disorders | | | |
| Tinnitus | | | |
| subjects affected / exposed | 5 / 97 (5.15%) | | |
| occurrences (all) | 5 | | |
| Eye disorders | | | |
| Diplopia | | | |
| subjects affected / exposed | 17 / 97 (17.53%) | | |
| occurrences (all) | 18 | | |
| Vision blurred | | | |

| | | | |
|--|------------------------|--|--|
| subjects affected / exposed occurrences (all) | 10 / 97 (10.31%) 10 | | |
| Gastrointestinal disorders | | | |
| Vomiting | | | |
| subjects affected / exposed | 16 / 97 (16.49%) | | |
| occurrences (all) | 18 | | |
| Nausea | | | |
| subjects affected / exposed | 13 / 97 (13.40%) | | |
| occurrences (all) | 14 | | |
| Diarrhoea | | | |
| subjects affected / exposed | 12 / 97 (12.37%) | | |
| occurrences (all) | 13 | | |
| Constipation | | | |
| subjects affected / exposed | 5 / 97 (5.15%) | | |
| occurrences (all) | 6 | | |
| Skin and subcutaneous tissue disorders | | | |
| Rash | | | |
| subjects affected / exposed | 5 / 97 (5.15%) | | |
| occurrences (all) | 5 | | |
| Psychiatric disorders | | | |
| Insomnia | | | |
| subjects affected / exposed | 9 / 97 (9.28%) | | |
| occurrences (all) | 9 | | |
| Confusional state | | | |
| subjects affected / exposed | 8 / 97 (8.25%) | | |
| occurrences (all) | 8 | | |
| Depression | | | |
| subjects affected / exposed | 7 / 97 (7.22%) | | |
| occurrences (all) | 7 | | |
| Infections and infestations | | | |
| Upper respiratory tract infection | | | |
| subjects affected / exposed | 14 / 97 (14.43%) | | |
| occurrences (all) | 17 | | |
| Sinusitis | | | |
| subjects affected / exposed | 8 / 97 (8.25%) | | |
| occurrences (all) | 11 | | |
| Urinary tract infection | | | |

| | | | |
|-----------------------------|----------------|--|--|
| subjects affected / exposed | 7 / 97 (7.22%) | | |
| occurrences (all) | 8 | | |
| Nasopharyngitis | | | |
| subjects affected / exposed | 6 / 97 (6.19%) | | |
| occurrences (all) | 7 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date | Amendment |
|-----------------|---|
| 01 October 2008 | <p>SP0926 protocol amendment 1 included the following key changes:</p> <ul style="list-style-type: none">• Administrative changes including contact and title information for the Associate Clinical Program Director, the Sr. Clinical Project Manager, the Clinical Trial Biostatistician, and the Associate Medical Director (Medical Therapeutics) were incorporated in the protocol• Current information on the Central Laboratory Services and Central Electrocardiogram Services were included in the protocol• Information in the protocol text was corrected to state that in SP925, subjects in Cohort 2 received Lacosamide (LCM) 300 mg/day (not 200 mg/day) and subjects in Cohort 3 received LCM 400mg/day (not 300 mg/day)• For consistency with the Phase 3 LCM epilepsy adjunctive therapy program, text was added to permit subjects who withdrew from Cohort 2 or 3 in SP0925 due to lack of tolerability to begin SP0926 at a dose as low as LCM 100mg/day increasing the dose no faster than 100 mg/day per week up to a maximum dose of LCM 800 mg/day, based on tolerability• To clarify that IVRS was to be contacted during Unscheduled Visits irrespective of drug dispensation, the wording 'if applicable' was removed from Section 5.1.6.• To allow consistency in the observations of the neurological exam between this oral LCM epilepsy study and the oral LCM epilepsy Phase 2/3 program, conduct of the neurological examination was modified to be performed by clinicians with documented training in neurological exams• For clarification, '8 weeks' was added to the Frequency of Visits under 'Term' in the Schedule of Procedures (Section 15.1)• For consistency with the LCM epilepsy adjunctive therapy program, as well as appropriate safety oversight, additional phone calls were included where there was a significant time period between visits/frequency of visits had decreased• Information on the window periods was added to the individual visits in Section 5.1 for clarity |
| 06 October 2009 | <p>SP926 protocol amendment 2 included the following key changes:</p> <ul style="list-style-type: none">• Detail was added to the protocol to allow subjects who, in consultation with the investigator, chose to initiate treatment with commercially available Lacosamide (LCM) at the end of the study, to do so without taper. In addition, details were added for subjects who chose not to initiate treatment with commercial LCM at the end of the study• The liver function test (LFT) withdrawal criteria were revised to reflect the Sponsor's current understanding of the safety profile of LCM based on a comprehensive review of the data from clinical studies• The Adverse Events (AE)s of special interest were revised to reflect the Sponsor's current understanding of the potential risks of LCM based on a comprehensive review of the data from clinical studies and commitments to regulatory agencies• Lacosamide was classified as a controlled substance in the US; thus, it was necessary to add this information to the protocol |

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported