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 occuring 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	1 / 97 (1.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pneumonia			
subjects affected / exposed	1 / 97 (1.03%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Sepsis			
subjects affected / exposed	1 / 97 (1.03%)		
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	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	10 / 97 (10.31%)		
occurrences (all)	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	SP0926 protocol amendment 1 included the following key changes: • 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	SP926 protocol amendment 2 included the following key changes: • 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