Clinical trial results:
An open-label extension study to assess the safety and seizure frequency associated with long-term oral lacosamide for uncontrolled primary generalized
tonic-clonic seizures in subjects with idiopathic generalized epilepsy

Summary

EudraCT number	2014-004375-23
Trial protocol	Outside EU/EEA
Global end of trial date	25 October 2012

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	04 July 2015

Trial information

Trial identification

Sponsor protocol code	SP0962

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01118962
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 2173 48 15 15, clinicaltrials@ucb.com
Scientific contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, +49 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	11 December 2012
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	25 October 2012
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The objectives of this study were:
- To obtain data on the safety and seizure frequency associated with long-term oral Lacosamide (LCM) for uncontrolled primary generalized tonic-clonic (PGTC) seizures in subjects with idiopathic generalized epilepsy (IGE)
- To allow subjects who completed SP0961 to continue to receive LCM

Protection of trial subjects:

There were no specific protocol measures in place to protect subjects.

Background therapy:

Not applicable

Evidence for comparator:

Not applicable

Actual start date of recruitment	18 August 2010
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	14 Months
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	United States: 39
Worldwide total number of subjects	39
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)	3

Adults (18-64 years)	36
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

This study began enrollment in August 2010. The study completed in October 2012. The participant flow consists of the Safety Set (SS).

The Safety Set consists of all subjects that were dosed at least once with Lacosamide (LCM).

Pre-assignment

Screening details:

The participant flow refers to the Safety Set, which consists of all subjects that were dosed at least once with Lacosamide (LCM).

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 was supplied as 50 mg and 100 mg tablets. The starting Lacosamide dose was the same dose reached by a subject at the end of SP0961 (NCT01118949). Lacosamide was administered twice daily (approx. 12 hours apart, once in the morning and once in the evening) in 2 equally divided doses.

Arm type	Experimental
Investigational medicinal product name	Lacosamide
Investigational medicinal product code	Lacosamide LCM
Other name	Vimpat
Pharmaceutical forms	Film-coated tablet
Routes of administration	Oral use

Dosage and administration details:

Lacosamide was supplied as 50 mg and 100 mg tablets. The starting Lacosamide dose was the same dose reached by a subject at the end of SP0961 (NCT01118949).
Lacosamide was administered twice daily (approx. 12 hours apart, once in the morning and once in the evening) in 2 equally divided doses.

Number of subjects in period 1	Lacosamide
Started	39
Completed	29
Not completed	10
Non-Fatal, Non-Serious AE	1
Consent withdrawn by subject	4
Non-Fatal, Serious AE	1
Pregnancy	1
Non-compliance with Medicinal Product	1
Lack of efficacy	1

Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Lacosamide

Reporting group description:

Lacosamide was supplied as 50 mg and 100 mg tablets. The starting Lacosamide dose was the same dose reached by a subject at the end of SP0961 (NCT01118949). Lacosamide was administered twice daily (approx. 12 hours apart, once in the morning and once in the evening) in 2 equally divided doses.

Reporting group values	Lacosamide	Total	
Number of subjects	39	39	
Age Categorical Units: Subjects			
<=18 years	3	3	
Between 18 and 65 years	36	36	
>=65 years	0	0	
Age Continuous Units: years			
arithmetic mean	30.3		
standard deviation	± 10.7	-	
Gender Categorical Units: Subjects			
Female	28	28	
Male	11	11	
Region of Enrollment Units: Subjects			
United States	39	39	
Weight Units: Kilograms			
arithmetic mean	77.66		
standard deviation	± 17.58	-	
Height Units: Centimeters			
arithmetic mean	167.88		
standard deviation	± 8.25	-	

End points

End points reporting groups

Reporting group title	Lacosamide

Reporting group description:

Lacosamide was supplied as 50 mg and 100 mg tablets. The starting Lacosamide dose was the same dose reached by a subject at the end of SP0961 (NCT01118949). Lacosamide was administered twice daily (approx. 12 hours apart, once in the morning and once in the evening) in 2 equally divided doses.

Primary: Number of participants with Treatment-emergent Adverse Events (TEAEs) From Visit 1 to the End of Study (approximately 61 weeks)

End point title	Number of participants with Treatment-emergent Adverse Events (TEAEs) From Visit 1 to the End of Study (approximately 61 weeks)[1]

End point description:

End point type	Primary

End point timeframe:

From Visit 1 to the end of study (Approximately 61 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: No formal statistical hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	Lacosamide			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: participants				
TEAEs	37			

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants withdrawn from the study due to Treatment-emergent Adverse Events (TEAEs) From Visit 1 to the End of Study (approximately 61 weeks)

End point title	Number of participants withdrawn from the study due to Treatment-emergent Adverse Events (TEAEs) From Visit 1 to the End of Study (approximately 61 weeks)[2]

End point description:

End point type	Primary

End point timeframe:

From Visit 1 to the end of study (Approximately 61 weeks)

Notes:

[2] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.
Justification: No formal statistical hypothesis testing was planned for this study. Results were summarized in tables as descriptive statistics only.

End point values	Lacosamide			
Subject group type	Reporting group			
Number of subjects analysed	39			
Units: participants				
Participant withdrawn from study due to TEAE	2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected from August 2010 through October 2012.

Adverse Event reporting consists of the Safety Set (SS). The Safety Set consists of all subjects that were dosed at least once with Lacosamide (LCM).

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups

Reporting group title	Lacosamide

Reporting group description:

Lacosamide was supplied as 50 mg and 100 mg tablets. The starting Lacosamide dose was the same dose reached by a subject at the end of SP0961 (NCT01118949).

Lacosamide was administered twice daily (approx. 12 hours apart, once in the morning and once in the evening) in 2 equally divided doses.

Serious adverse events	Lacosamide		
Total subjects affected by serious adverse events			
subjects affected / exposed	3 / 39 (7.69%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Nervous system disorders			
CONVULSION			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
MIGRAINE			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
ABNORMAL BEHAVIOUR			
subjects affected / exposed	1 / 39 (2.56%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			

PNEUMONIA			
subjects affected / exposed	1 / 39 (2.56%)		
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	35 / 39 (89.74%)		
General disorders and administration site conditions			
FATIGUE			
subjects affected / exposed	3 / 39 (7.69%)		
occurrences (all)	4		
GAIT DISTURBANCE			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Immune system disorders			
SEASONAL ALLERGY			
subjects affected / exposed	3 / 39 (7.69%)		
occurrences (all)	3		
Respiratory, thoracic and mediastinal disorders			
DYSPNOEA			
subjects affected / exposed	4 / 39 (10.26%)		
occurrences (all)	4		
RESPIRATORY DISORDER			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Psychiatric disorders			
ANXIETY			
subjects affected / exposed	4 / 39 (10.26%)		
occurrences (all)	5		
CONFUSIONAL STATE			
subjects affected / exposed	4 / 39 (10.26%)		
occurrences (all)	4		
DEPRESSION			

subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Investigations			
ALANINE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
WEIGHT INCREASED			
subjects affected / exposed	4 / 39 (10.26%)		
occurrences (all)	4		
ARTERIAL BRUIT			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
ASPARTATE AMINOTRANSFERASE INCREASED			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
GAMMA-GLUTAMYLTRANSFERASE INCREASED			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Injury, poisoning and procedural complications			
FALL			
subjects affected / exposed	4 / 39 (10.26%)		
occurrences (all)	4		
CONTUSION			
subjects affected / exposed	3 / 39 (7.69%)		
occurrences (all)	3		
JOINT SPRAIN			
subjects affected / exposed	4 / 39 (10.26%)		
occurrences (all)	5		
EXCORIATION			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
MUSCLE STRAIN			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		

SKIN LACERATION subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2		
Cardiac disorders PALPITATIONS subjects affected / exposed occurrences (all)	2 / 39 (5.13%) 2		
Nervous system disorders DIZZINESS subjects affected / exposed occurrences (all) HEADACHE subjects affected / exposed occurrences (all) TREMOR subjects affected / exposed occurrences (all) POSTICTAL STATE subjects affected / exposed occurrences (all)	 10 / 39 (25.64%) 12 7 / 39 (17.95%) 12 6 / 39 (15.38%) 6 2 / 39 (5.13%) 9		
Eye disorders DIPLOPIA subjects affected / exposed occurrences (all)	 3 / 39 (7.69%) 4		
Gastrointestinal disorders NAUSEA subjects affected / exposed occurrences (all) DIARRHOEA subjects affected / exposed occurrences (all)	 5 / 39 (12.82%) 5 2 / 39 (5.13%) 2		
Skin and subcutaneous tissue disorders ALOPECIA subjects affected / exposed occurrences (all)	 2 / 39 (5.13%) 2		
Musculoskeletal and connective tissue disorders			

ARTHRALGIA			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	4		
MUSCULOSKELETAL PAIN			
subjects affected / exposed	3 / 39 (7.69%)		
occurrences (all)	3		
Infections and infestations			
UPPER RESPIRATORY TRACT INFECTION			
subjects affected / exposed	10 / 39 (25.64%)		
occurrences (all)	13		
GASTROENTERITIS VIRAL			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	3		
SINUSITIS			
subjects affected / exposed	3 / 39 (7.69%)		
occurrences (all)	3		
INFLUENZA			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
TOOTH ABSCESS			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		
Metabolism and nutrition disorders			
INCREASED APPETITE			
subjects affected / exposed	2 / 39 (5.13%)		
occurrences (all)	2		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
02 November 2010	Protocol Amendment 1, dated 02 Nov 2010, provided for the following changes: - To remove the variable of percent change in PGTC seizure frequency per 28 days from Baseline - To revise withdrawal criteria and follow-up recommendations for abnormal liver function tests (LFTs) - To increase the number of study sites from 10 to 25 - To remove the 150mg and 200mg LCM doses of study medication - Minor administrative changes Based on the date of the amendment, 1 subject was enrolled in the study prior to this amendment (Table 1.3.1).
24 August 2011	Protocol Amendment 2, dated 24 Aug 2011, provided for the following changes: - To add the Columbia-Suicide Severity Rating Scale (C-SSRS) and accompanying necessary revisions - To add the list of anticipated serious adverse events (SAEs) - To change the Sponsor's name to UCB BIOSCIENCES Inc - Minor administrative changes Based on the date of the amendment, an additional 37 subjects were enrolled in the study prior to this amendment (Table 1.3.1).

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported