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