Clinical trial results:
A Multicenter, Open-label, Follow-up Study to Assess the Long-term Use of Lacosamide (Flexible Dose From 200 to 600 mg/Day) Used as Monotherapy in Subjects Who Completed SP0994 and Received Lacosamide Monotherapy Treatment

Summary

EudraCT number	2015-001549-96
Trial protocol	FI SE DE LV BG PL FR RO
Global end of trial date	06 January 2020

Results information

Result version number	v1 (current)
This version publication date	26 December 2020
First version publication date	26 December 2020

Trial information

Trial identification

Sponsor protocol code	SP1042

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02582866
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB BioPharma SPRL
Sponsor organisation address	Allée de la Recherche 60, Brussels, Belgium, B-1070
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, 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	04 February 2020
Is this the analysis of the primary completion data?	Yes
Primary completion date	06 January 2020
Global end of trial reached?	Yes
Global end of trial date	06 January 2020
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the long-term safety and tolerability of lacosamide dosed at 200 mg/day to 600 mg/day when used as monotherapy in subjects, with partial-onset seizures or generalized tonic-clonic seizures (without clear focal origin), who completed SP0994

Protection of trial subjects:

During the conduct of the study all participants were closely monitored.

Background therapy:

Not Applicable

Evidence for comparator:

Not Applicable

Actual start date of recruitment	18 January 2016
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	Bulgaria: 4
Country: Number of subjects enrolled	Finland: 6
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Germany: 14
Country: Number of subjects enrolled	Japan: 6
Country: Number of subjects enrolled	Latvia: 1
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	Philippines: 8
Country: Number of subjects enrolled	Poland: 4
Country: Number of subjects enrolled	Romania: 19
Country: Number of subjects enrolled	Russian Federation: 11
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Sweden: 13
Country: Number of subjects enrolled	Switzerland: 4
Country: Number of subjects enrolled	Ukraine: 7
Worldwide total number of subjects	106
EEA total number of subjects	64

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)	92
From 65 to 84 years	13
85 years and over	1

Subject disposition

Recruitment

Recruitment details:

The study started to enroll study participants in January 2016 and concluded in January 2020.

Pre-assignment

Screening details:

Participant Flow refers to the Safety Set.

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 (LCM) was administered orally, twice daily from 200 mg/day to 600 mg/day, in 2 divided doses at approximately 12 hour intervals in the morning and in the evening. The investigator may have maintained the subject's LCM dose, decreased
the dose in decrements of 100 mg/day per week to a minimum dose of LCM 200 mg/day, or increased the dose in increments of 100 mg/day per week up to a maximum dose of LCM 600 mg/day.
Participants stopping LCM should have been tapered off LCM at recommended decreasing steps of 200 mg/day/week. A slower taper (eg, 100 mg/day/week) or faster taper was permitted but the duration of tapering should not have exceeded 6 weeks.

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

Dosage and administration details:

Lacosamide (LCM) was administered orally twice daily from 200 mg/day to 600 mg/day (at approximately 12 hour intervals in the morning and in the evening) in 2 divided doses.

Number of subjects in period 1	Lacosamide
Started	106
Completed	84
Not completed	22
Adverse event, serious fatal	1
Consent withdrawn by subject	7
Pregnancy	2
Withdrawal due to personal reasons	1
Investigator decision	5
Participant wants to get pregnant	1
Lost to follow-up	2

Sponsor decision	1
Lack of efficacy	2

Baseline characteristics

Reporting groups	
Reporting group title	Lacosamide

Reporting group description:

Lacosamide (LCM) was administered orally, twice daily from 200 mg/day to 600 mg/day, in 2 divided doses at approximately 12 hour intervals in the morning and in the evening. The investigator may have maintained the subject's LCM dose, decreased
the dose in decrements of 100 mg/day per week to a minimum dose of LCM 200 mg/day, or increased the dose in increments of 100 mg/day per week up to a maximum dose of LCM 600 mg/day.
Participants stopping LCM should have been tapered off LCM at recommended decreasing steps of 200 mg/day/week. A slower taper (eg, 100 mg/day/week) or faster taper was permitted but the duration of tapering should not have exceeded 6 weeks.

Reporting group values	Lacosamide	Total	
Number of subjects	106	106	
Age categorical Units: Subjects			
<=18 years	2	2	
Between 18 and 65 years	90	90	
>=65 years	14	14	
Age continuous Units: years			
arithmetic mean	43.5		
standard deviation	± 17.1	-	
Gender categorical Units: Subjects			
Female	48	48	
Male	58	58	

End points

End points reporting groups

Reporting group title	Lacosamide

Reporting group description:

Lacosamide (LCM) was administered orally, twice daily from 200 mg/day to 600 mg/day, in 2 divided doses at approximately 12 hour intervals in the morning and in the evening. The investigator may have maintained the subject's LCM dose, decreased
the dose in decrements of 100 mg/day per week to a minimum dose of LCM 200 mg/day, or increased the dose in increments of 100 mg/day per week up to a maximum dose of LCM 600 mg/day.
Participants stopping LCM should have been tapered off LCM at recommended decreasing steps of 200 mg/day/week. A slower taper (eg, 100 mg/day/week) or faster taper was permitted but the duration of tapering should not have exceeded 6 weeks.

Subject analysis set title	Lacosamide (SS)
Subject analysis set type	Safety analysis

Subject analysis set description:

Lacosamide (LCM) was administered orally, twice daily from 200 mg/day to 600 mg/day, in 2 divided doses at approximately 12 hour intervals in the morning and in the evening. The investigator may have maintained the subject's LCM dose, decreased
the dose in decrements of 100 mg/day per week to a minimum dose of LCM 200 mg/day, or increased the dose in increments of 100 mg/day per week up to a maximum dose of LCM 600 mg/day.
Participants stopping LCM should have been tapered off LCM at recommended decreasing steps of 200 mg/day/week. A slower taper (eg, 100 mg/day/week) or faster taper was permitted but the duration of tapering should not have exceeded 6 weeks.
Participants formed the Safety Set (SS).

Primary: Percentage of participants experiencing any Adverse Events (AEs) reported spontaneously by the subject and/or caregiver or observed by Investigator

End point title	Percentage of participants experiencing any Adverse Events (AEs) reported spontaneously by the subject and/or caregiver or observed by Investigator[1]

End point description:

An Adverse Event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study medication, whether or not considered related to the study medication. An AE could, therefore, be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study medication.
The SS consisted of all study participants in the ES who received at least 1 dose of study medication in SP1042.

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to Final Visit (up to Week 158)

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 (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	106			
Units: percentage of participants				
number (not applicable)	59.4			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants experiencing any Serious Adverse Events (SAEs) reported spontaneously by the subject and/or caregiver or observed by Investigator

End point title	Percentage of participants experiencing any Serious Adverse Events (SAEs) reported spontaneously by the subject and/or caregiver or observed by Investigator[2]

End point description:

A Serious Adverse Event (SAE) is any untoward medical occurrence that at any dose:
- Results in death
- Is life-threatening
- Requires in patient hospitalization or prolongation of existing hospitalization
- Is a congenital anomaly or birth defect
- Is an infection that requires treatment parenteral antibiotics
- Other important medical events which based on medical or scientific judgement may jeopardize the study participants, or may require medical or surgical intervention to prevent any of the above.
The SS consisted of all study participants in the ES who received at least 1 dose of study medication in SP1042.

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to Final Visit (up to Week 158)

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 (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	106			
Units: percentage of participants				
number (not applicable)	14.2			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants that withdrew due to Adverse Events (AEs)

End point title	Percentage of participants that withdrew due to Adverse Events (AEs)[3]

End point description:

An Adverse Event (AE) is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study medication, whether or not considered related to the study medication. An AE could, therefore, be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study medication.
The SS consisted of all study participants in the ES who received at least 1 dose of study medication in SP1042.

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to Final Visit (up to Week 158)

Notes:

[3] - 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 (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	106			
Units: percentage of participants				
number (not applicable)	0.9			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from Visit 1 (Week 0) to Final Visit (up to Week 158)

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Lacosamide (SS)

Reporting group description:

Lacosamide (LCM) was administered orally, twice daily from 200 mg/day to 600 mg/day, in 2 divided doses at approximately 12 hour intervals in the morning and in the evening. The investigator may have maintained the subject's LCM dose, decreased
the dose in decrements of 100 mg/day per week to a minimum dose of LCM 200 mg/day, or increased the dose in increments of 100 mg/day per week up to a maximum dose of LCM 600 mg/day.
Participants stopping LCM should have been tapered off LCM at recommended decreasing steps of 200 mg/day/week. A slower taper (eg, 100 mg/day/week) or faster taper was permitted but the duration of tapering should not have exceeded 6 weeks.
Participants formed the Safety Set (SS).

Serious adverse events	Lacosamide (SS)		
Total subjects affected by serious adverse events			
subjects affected / exposed	15 / 106 (14.15%)		
number of deaths (all causes)	1		
number of deaths resulting from adverse events	0		
Investigations			
Arteriogram Coronary			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Breast Cancer			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Forearm Fracture			

subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post Gastric Surgery Syndrome			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tibia Fracture			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac Failure			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Atrial Flutter			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myocardial Infarction			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ventricular Tachycardia			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Knee Arthroplasty			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			

Epilepsy				
subjects affected / exposed	2 / 106 (1.89%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Ischaemic Stroke				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peripheral Sensorimotor Neuropathy				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
General disorders and administration site conditions				
Device Dislocation				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sudden Unexplained Death In Epilepsy				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Gastrointestinal disorders				
Diarrhoea				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrooesophageal Reflux Disease				
subjects affected / exposed	1 / 106 (0.94%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Umbilical Hernia				

subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Acute Respiratory Distress Syndrome			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dyspnoea			
subjects affected / exposed	1 / 106 (0.94%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	2 / 106 (1.89%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Hypoglycaemia			
subjects affected / exposed	1 / 106 (0.94%)		
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 (SS)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	19 / 106 (17.92%)		
Nervous system disorders			
Headache			
subjects affected / exposed	11 / 106 (10.38%)		
occurrences (all)	11		
Infections and infestations			

Nasopharyngitis subjects affected / exposed occurrences (all)	8 / 106 (7.55%) 17		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported