Clinical trial results:
A MULTICENTER, OPEN-LABEL, LONG-TERM EXTENSION STUDY TO INVESTIGATE THE EFFICACY AND SAFETY OF LACOSAMIDE AS ADJUNCTIVE THERAPY IN PEDIATRIC SUBJECTS WITH EPILEPSY WITH PARTIAL-ONSET SEIZURES

Summary

EudraCT number	2012-005012-26
Trial protocol	BE IT CZ SK HU ES EE PL GB LV RO BG LT Outside EU/EEA SE SI HR DE FR GR PT DK FI
Global end of trial date	13 April 2022

Results information

Result version number	v1 (current)
This version publication date	16 October 2022
First version publication date	16 October 2022

Trial information

Trial identification

Sponsor protocol code	EP0034

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01964560
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB BIOSCIENCES Inc.
Sponsor organisation address	8010 Arco Corporate Drive, Raleigh, United States, NC 27617
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?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 May 2022
Is this the analysis of the primary completion data?	Yes
Primary completion date	13 April 2022
Global end of trial reached?	Yes
Global end of trial date	13 April 2022
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 in pediatric subjects

Protection of trial subjects:

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

Background therapy:

1 to 3 concomitant antiepileptic drugs (AEDs) as permitted in the protocol

Evidence for comparator:

Not applicable

Actual start date of recruitment	13 August 2014
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	Argentina: 9
Country: Number of subjects enrolled	Australia: 6
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Brazil: 6
Country: Number of subjects enrolled	Bulgaria: 1
Country: Number of subjects enrolled	China: 14
Country: Number of subjects enrolled	Colombia: 1
Country: Number of subjects enrolled	Croatia: 20
Country: Number of subjects enrolled	Czechia: 9
Country: Number of subjects enrolled	Estonia: 3
Country: Number of subjects enrolled	France: 4
Country: Number of subjects enrolled	Georgia: 47
Country: Number of subjects enrolled	Greece: 2
Country: Number of subjects enrolled	Hungary: 51
Country: Number of subjects enrolled	Israel: 8
Country: Number of subjects enrolled	Italy: 13
Country: Number of subjects enrolled	Latvia: 12
Country: Number of subjects enrolled	Lithuania: 4
Country: Number of subjects enrolled	Mexico: 36
Country: Number of subjects enrolled	Montenegro: 2

Country: Number of subjects enrolled	Poland: 33
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	Korea, Republic of: 17
Country: Number of subjects enrolled	Moldova, Republic of: 2
Country: Number of subjects enrolled	Philippines: 2
Country: Number of subjects enrolled	Romania: 24
Country: Number of subjects enrolled	Russian Federation: 29
Country: Number of subjects enrolled	Serbia: 19
Country: Number of subjects enrolled	Slovakia: 14
Country: Number of subjects enrolled	Slovenia: 3
Country: Number of subjects enrolled	Taiwan: 16
Country: Number of subjects enrolled	Thailand: 34
Country: Number of subjects enrolled	Ukraine: 74
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 17
Worldwide total number of subjects	540
EEA total number of subjects	199

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)	103
Children (2-11 years)	287
Adolescents (12-17 years)	150
Adults (18-64 years)	0
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in August 2014 and concluded in April 2022.

Pre-assignment

Screening details:

The Participant Flow refers to the Safety Set (SS). The SS included all enrolled study participants who took at least 1 dose of lacosamide (LCM) in this long-term extension 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 (All subjects)

Arm description:

Participants who participated in primary study [SP0967 (NCT02477839) or SP0969 (NCT01921205)] consented and met requirements to participate in current study received LCM 10 milligram/kilogram/day (mg/kg/day) as an oral solution for study participants weighing <30 kg, LCM 6 mg/kg/day as an oral solution for study participants weighing >=30 kg to <50 kg, and LCM 300 mg/day as tablets for study participants weighing >=50 kg. LCM was administered twice daily (bid) up to Week 96. After 1 week the investigator might adjust the LCM dose during the Treatment based on clinical judgment within a range of 2 mg/kg/day to 12 mg/kg/day for the oral solution and 100 mg/day to 600 mg/day for the tablets.

Arm type	Experimental
Investigational medicinal product name	Lacosamide
Investigational medicinal product code	LCM
Other name	VIMPAT
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Participants received LCM administered orally at pre-defined timepoints.

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:

Participants received LCM administered orally at pre-defined timepoints.

Number of subjects in period 1	Lacosamide (All subjects)
Started	540
Completed	395
Not completed	145
Consent withdrawn by subject	64
Adverse event, non-fatal	23

Surgery-hemispherotomy	1
Protocol deviation	2
Patient and Investigator choice	1
Participant moved to another country	1
Seizures appeared resolved with epilepsy surgery	1
Patient was prescribed CBD	1
Lost to follow-up	4
Surgery	1
Lack of efficacy	46

Baseline characteristics

Reporting groups	
Reporting group title	Lacosamide (All subjects)

Reporting group description:

Participants who participated in primary study [SP0967 (NCT02477839) or SP0969 (NCT01921205)] consented and met requirements to participate in current study received LCM 10 milligram/kilogram/day (mg/kg/day) as an oral solution for study participants weighing <30 kg, LCM 6 mg/kg/day as an oral solution for study participants weighing >=30 kg to <50 kg, and LCM 300 mg/day as tablets for study participants weighing >=50 kg. LCM was administered twice daily (bid) up to Week 96. After 1 week the investigator might adjust the LCM dose during the Treatment based on clinical judgment within a range of 2 mg/kg/day to 12 mg/kg/day for the oral solution and 100 mg/day to 600 mg/day for the tablets.

Reporting group values	Lacosamide (All subjects)	Total	
Number of subjects	540	540	
Age Categorical Units: participants			
>=28 days - <24 months	103	103	
>=24 months - <12 years	287	287	
>=12 - <18 years	150	150	
Age Continuous Units: years			
arithmetic mean	7.486		
standard deviation	± 5.415	-	
Sex: Female, Male Units: participants			
Female	236	236	
Male	304	304	

End points

End points reporting groups

Reporting group title	Lacosamide (All subjects)

Reporting group description:

Participants who participated in primary study [SP0967 (NCT02477839) or SP0969 (NCT01921205)] consented and met requirements to participate in current study received LCM 10 milligram/kilogram/day (mg/kg/day) as an oral solution for study participants weighing <30 kg, LCM 6 mg/kg/day as an oral solution for study participants weighing >=30 kg to <50 kg, and LCM 300 mg/day as tablets for study participants weighing >=50 kg. LCM was administered twice daily (bid) up to Week 96. After 1 week the investigator might adjust the LCM dose during the Treatment based on clinical judgment within a range of 2 mg/kg/day to 12 mg/kg/day for the oral solution and 100 mg/day to 600 mg/day for the tablets.

Primary: Percentage of participants with treatment-emergent adverse events (TEAEs)

End point title	Percentage of participants with treatment-emergent adverse events (TEAEs)[1]

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product that does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product. Treatment-emergent is defined as starting on or after the date of first dose of LCM in EP0034, and within 30 days of last dose. The Safety Set (SS) included all enrolled study participants who took at least 1 dose of LCM in this long-term extension study.

End point type	Primary

End point timeframe:

From Week 0 to the End of Safety Follow-Up (up to Week 104)

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 (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	540			
Units: percentage of participants				
number (not applicable)	77.2			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with serious TEAEs

End point title	Percentage of participants with serious TEAEs[2]

End point description:

A serious adverse event (SAE) must meet 1 or more of the following criteria: • Death, • Life-threatening (Life-threatening does not include a reaction that might have caused death had it occurred in a more severe form.), • Significant or persistent disability/incapacity, • Congenital anomaly/birth defect

(including that occurring in a fetus), • Important medical event that, based upon appropriate medical judgment, may jeopardize the patient or participant and may require medical or surgical intervention to prevent 1 of the other outcomes listed in the definition of serious., • Initial inpatient hospitalization or prolongation of hospitalization. Treatment-emergent is defined as starting on or after the date of first dose of LCM in EP0034, and within 30 days of last dose. The SS included all enrolled study participants who took at least 1 dose of LCM in this long-term extension study.

End point type	Primary

End point timeframe:

From Week 0 to the End of Safety Follow-Up (up to Week 104)

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 (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	540			
Units: percentage of participants				
number (not applicable)	20.6			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of participants with TEAEs leading to study discontinuation

End point title	Percentage of participants with TEAEs leading to study discontinuation[3]

End point description:

An adverse event (AE) is any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment. AEs leading to study discontinuation. Treatment-emergent is defined as starting on or after the date of first dose of LCM in EP0034, and within 30 days of last dose. The SS included all enrolled study participants who took at least 1 dose of LCM in this long-term extension study. Here, only those participants who discontinued the study due to TEAEs starting on or after the date of first dose of LCM in EP0034, and within 30 days of last dose of LCM are reported.

End point type	Primary

End point timeframe:

From Week 0 to the End of Safety Follow-Up (up to Week 104)

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 (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	540			
Units: percentage of participants				
number (not applicable)	4.1			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of seizure-free days during the study

End point title	Percentage of seizure-free days during the study

End point description:

The number of seizure-free days was the total number of days within an interval for which daily diary data were available and no seizures were reported. The percentage of seizure-free days was computed as 100 times the number of seizure-free days in the interval divided by the number of days in the interval for which daily diary data were available. Percentage of seizure-free days was measured using data obtained from participant diaries from EP0034 and is presented for the overall Treatment only. The Full Analysis Set (FAS) was used for the analysis of seizure data and included all study participants in the SS who had at least 1 completed post-Baseline seizure diary. Study participants whose efficacy data could not be source verified were excluded from the FAS. Here, Number of participants analyzed included those participants who were evaluable for the assessment.

End point type	Secondary

End point timeframe:

From Week 0 to End of Treatment (up to Week 96)

End point values	Lacosamide (All subjects)			
Subject group type	Reporting group			
Number of subjects analysed	537			
Units: percentage of seizure free days				
arithmetic mean (standard deviation)	66.96 (± 36.18)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Week 0 to the End of Safety Follow-Up (up to Week 104)

Adverse event reporting additional description:

TEAEs were events which started on or after date of first EP0034 dose of LCM, or whose intensity worsened on or after date of first EP0034 dose of LCM. AEs occurring within 30 days after last dose of LCM were considered treatment-emergent. SS included all enrolled study participants who took at least 1 dose of LCM in the long-term extension study.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Lacosamide (All subjects)

Reporting group description:

Participants who participated in primary study [SP0967 (NCT02477839) or SP0969 (NCT01921205)] consented and met requirements to participate in current study received LCM 10 milligram/kilogram/day (mg/kg/day) as an oral solution for study participants weighing <30 kg, LCM 6 mg/kg/day as an oral solution for study participants weighing >=30 kg to <50 kg, and LCM 300 mg/day as tablets for study participants weighing >=50 kg. LCM was administered twice daily (bid) up to Week 96. After 1 week the investigator might adjust the LCM dose during the Treatment based on clinical judgment within a range of 2 mg/kg/day to 12 mg/kg/day for the oral solution and 100 mg/day to 600 mg/day for the tablets.

Serious adverse events	Lacosamide (All subjects)		
Total subjects affected by serious adverse events			
subjects affected / exposed	111 / 540 (20.56%)		
number of deaths (all causes)	7		
number of deaths resulting from adverse events	0		
Vascular disorders			
Deep vein thrombosis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypotension			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Brain operation			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Device malfunction			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Cyst			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Device breakage			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Device occlusion			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Respiratory distress			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		

Respiratory failure				
subjects affected / exposed	3 / 540 (0.56%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 2			
Pneumonia aspiration				
subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 1			
Apnoea				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchospasm				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chylothorax				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspnoea				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Epistaxis				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoventilation				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxia				

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Interstitial lung disease			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tonsillar hypertrophy			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Disorientation			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Emotional disorder of childhood			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Investigations			
Blood bicarbonate decreased			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Liver function test abnormal			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Urine output decreased			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Clavicle fracture			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Head injury			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Joint dislocation			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Lip injury			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Post procedural fistula			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tooth fracture			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Toxicity to various agents			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper limb fracture			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Congenital, familial and genetic disorders			
Cerebral palsy			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Talipes			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Cardiac arrest			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Nervous system disorders			
Convulsion			
subjects affected / exposed	24 / 540 (4.44%)		
occurrences causally related to treatment / all	1 / 30		
deaths causally related to treatment / all	0 / 0		
Status epilepticus			
subjects affected / exposed	9 / 540 (1.67%)		
occurrences causally related to treatment / all	0 / 11		
deaths causally related to treatment / all	0 / 2		
Epilepsy			
subjects affected / exposed	7 / 540 (1.30%)		
occurrences causally related to treatment / all	1 / 10		
deaths causally related to treatment / all	0 / 0		

Partial seizures				
subjects affected / exposed	4 / 540 (0.74%)			
occurrences causally related to treatment / all	0 / 4			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	3 / 540 (0.56%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Partial seizures with secondary generalisation				
subjects affected / exposed	3 / 540 (0.56%)			
occurrences causally related to treatment / all	0 / 5			
deaths causally related to treatment / all	0 / 0			
Febrile convulsion				
subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Hemiparesis				
subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Somnolence				
subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Altered state of consciousness				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Cognitive disorder				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Grand mal convulsion				

subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hypotonia				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intracranial haematoma				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Motor dysfunction				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Myoclonic epilepsy				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subdural hygroma				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Tonic convulsion				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Blood and lymphatic system disorders				
Idiopathic thrombocytopenic purpura				

subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lymphadenopathy				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Blepharitis				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diplopia				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Parophthalmia				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Vomiting				
subjects affected / exposed	10 / 540 (1.85%)			
occurrences causally related to treatment / all	1 / 12			
deaths causally related to treatment / all	0 / 0			
Nausea				
subjects affected / exposed	4 / 540 (0.74%)			
occurrences causally related to treatment / all	2 / 4			
deaths causally related to treatment / all	0 / 0			
Abdominal pain				
subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Constipation				

subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Diarrhoea				
subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Dyspepsia				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dysphagia				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterocolitis				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal motility disorder				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gingival bleeding				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intestinal obstruction				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stomatitis				

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper gastrointestinal haemorrhage			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Dermatitis			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Drug reaction with eosinophilia and systemic symptoms			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Pyuria			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure acute			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vesicoureteric reflux			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Muscle haemorrhage			

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	11 / 540 (2.04%)		
occurrences causally related to treatment / all	0 / 14		
deaths causally related to treatment / all	0 / 0		
Bronchitis			
subjects affected / exposed	5 / 540 (0.93%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	4 / 540 (0.74%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Bronchopneumonia			
subjects affected / exposed	3 / 540 (0.56%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		
Dengue fever			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 3		
deaths causally related to treatment / all	0 / 0		
Gastroenteritis viral			
subjects affected / exposed	2 / 540 (0.37%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Influenza			

subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Rhinovirus infection				
subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Abscess neck				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Acute tonsillitis				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Adenovirus infection				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Amoebic dysentery				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Bronchiolitis				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Corona virus infection				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Device related sepsis				

subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Diarrhoea infectious				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ear infection				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Enterovirus infection				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis rotavirus				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal infection				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Helicobacter infection				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nasopharyngitis				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Oral herpes				

subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Otitis media				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Otitis media acute				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Periorbital cellulitis				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pharyngotonsillitis				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia influenzal				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Pneumonia pneumococcal				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia respiratory syncytial viral				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia viral				

subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pyelonephritis acute				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Respiratory syncytial virus infection				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sepsis				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Urinary tract infection				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Viral infection				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Metabolism and nutrition disorders				
Dehydration				
subjects affected / exposed	2 / 540 (0.37%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Acetonaemia				
subjects affected / exposed	1 / 540 (0.19%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Decreased appetite				

subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Enteral feeding intolerance			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypoglycaemia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypophagia			
subjects affected / exposed	1 / 540 (0.19%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolic acidosis			
subjects affected / exposed	1 / 540 (0.19%)		
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 (All subjects)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	289 / 540 (53.52%)		
Nervous system disorders			
Somnolence			
subjects affected / exposed	30 / 540 (5.56%)		
occurrences (all)	42		
Headache			
subjects affected / exposed	29 / 540 (5.37%)		
occurrences (all)	89		
Convulsion			

subjects affected / exposed	27 / 540 (5.00%)		
occurrences (all)	33		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	86 / 540 (15.93%)		
occurrences (all)	149		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	56 / 540 (10.37%)		
occurrences (all)	113		
Diarrhoea			
subjects affected / exposed	42 / 540 (7.78%)		
occurrences (all)	54		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	38 / 540 (7.04%)		
occurrences (all)	49		
Infections and infestations			
Upper respiratory tract infection			
subjects affected / exposed	83 / 540 (15.37%)		
occurrences (all)	167		
Nasopharyngitis			
subjects affected / exposed	57 / 540 (10.56%)		
occurrences (all)	92		
Pharyngitis			
subjects affected / exposed	39 / 540 (7.22%)		
occurrences (all)	68		
Bronchitis			
subjects affected / exposed	33 / 540 (6.11%)		
occurrences (all)	46		
Influenza			
subjects affected / exposed	28 / 540 (5.19%)		
occurrences (all)	35		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
30 June 2015	Protocol Amendment 1, dated 30 Jun 2015, provided the following key changes. Based on the date of the amendment, 63 study participants were screened (enrolled into EP0034) prior to this amendment (Table 1.5). The primary purpose of this substantial amendment was to add further clarification regarding the addition of extra procedures electrocardiograms (ECGs) in case of LCM dose increases to ≥8 mg/kg/day and ≥400 mg/day or in case of addition of new concomitant antiepileptic drugs (AEDs), in accordance with the Food and Drug Administration (FDA) request and based on program specific guidelines. Furthermore, at the request of the Spanish Independent Ethics Committee (IEC), additional inclusion criteria (Inclusion Criterion #5 and #6) were added to clarify age and diagnosis requirements for enrollment. Additional changes were implemented for consistency with other protocols in the LCM pediatric program and administrative changes including the update of the study team and minor corrections, and update of the Sponsor Declaration for electronic signature, were made.
24 March 2017	Protocol Amendment 2, dated 24 Mar 2017, provided the following key changes. Based on the date of the amendment, 362 study participants were screened (enrolled into EP0034) prior to this amendment (Table 1.5). The primary purpose of this substantial amendment was to allow administration of the Pediatric Quality of Life Inventory (PedsQL) to study participants under 2 years of age and to implement language regarding potential drug-induced liver injury (PDILI) events, based on new standard language which was applied across all protocols at UCB. Addition of this language was to align with FDA guidance regarding monitoring of potential drug-induced liver injury (PDILI) events and did not reflect a change in the liver safety signal for LCM. Permitted and prohibited concomitant medications were also updated and language clarified; neuroleptics (except for clozapine) were allowed during the study and cannabidiols (not approved or indicated for epilepsy by local health authority) were prohibited during the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported