Clinical trial results:
A Multicenter, Double-blind, Randomized, Placebo-controlled, Parallel-group Study to Investigate the Efficacy and Safety of Lacosamide as Adjunctive Therapy in Subjects with Epilepsy >=4 Years to <17 Years of Age with Partial-Onset Seizures

Summary

EudraCT number	2012-004996-38
Trial protocol	HU SK BE IT LV EE CZ ES PL GB LT BG RO Outside EU/EEA SI HR FR
Global end of trial date	24 January 2017

Results information

Result version number	v2 (current)
This version publication date	01 April 2018
First version publication date	09 August 2017
Version creation reason	• Correction of full data set For consistency between registries

Trial information

Trial identification

Sponsor protocol code	SP0969

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01921205
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	13 February 2017
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	24 January 2017
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the efficacy of Lacosamide (LCM) administered concomitantly with 1 to <=3 antiepileptic drugs (AEDs) in subjects with epilepsy >=4 years to <17 years of age who currently have uncontrolled partial-onset seizures.

Protection of trial subjects:

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

Background therapy:

Background therapy was permitted as defined in the study protocol. Patients were treated with 1-3 concomitant antiepileptic drugs (AEDs).

Evidence for comparator:

Not applicable.

Actual start date of recruitment	29 August 2013
Long term follow-up planned	Yes
Long term follow-up rationale	Safety
Long term follow-up duration	2 Years
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Argentina: 9
Country: Number of subjects enrolled	Australia: 8
Country: Number of subjects enrolled	Belgium: 5
Country: Number of subjects enrolled	Bulgaria: 3
Country: Number of subjects enrolled	Colombia: 3
Country: Number of subjects enrolled	Croatia: 16
Country: Number of subjects enrolled	Czech Republic: 8
Country: Number of subjects enrolled	Estonia: 3
Country: Number of subjects enrolled	Georgia: 29
Country: Number of subjects enrolled	Hungary: 29
Country: Number of subjects enrolled	Israel: 6
Country: Number of subjects enrolled	Italy: 8
Country: Number of subjects enrolled	Latvia: 13
Country: Number of subjects enrolled	Lithuania: 4
Country: Number of subjects enrolled	Mexico: 8
Country: Number of subjects enrolled	Montenegro: 2

Country: Number of subjects enrolled	Poland: 36
Country: Number of subjects enrolled	Romania: 15
Country: Number of subjects enrolled	Russian Federation: 16
Country: Number of subjects enrolled	Serbia: 12
Country: Number of subjects enrolled	Slovakia: 16
Country: Number of subjects enrolled	Slovenia: 3
Country: Number of subjects enrolled	Korea, Republic of: 12
Country: Number of subjects enrolled	Taiwan: 15
Country: Number of subjects enrolled	Thailand: 33
Country: Number of subjects enrolled	Ukraine: 17
Country: Number of subjects enrolled	United Kingdom: 2
Country: Number of subjects enrolled	United States: 12
Worldwide total number of subjects	343
EEA total number of subjects	161

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)	182
Adolescents (12-17 years)	161
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 patients in August 2013 and concluded in January 2017.

Pre-assignment

Screening details:

The Participant Flow refers to the Safety Set which included all randomized subjects who took at least 1 dose of study medication.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Placebo

Arm description:

This arm includes subjects with epilepsy, who received a flexible dose of Placebo oral solution or tablets, administered twice a day. Appearance of Placebo oral solution and tablets matched the Lacosamide oral solution and tablets.

Arm type	Placebo
Investigational medicinal product name	Placebo - solution
Investigational medicinal product code	PBO - solution
Other name	
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

Placebo solution matching LCM solution.

Investigational medicinal product name	Placebo - tablet
Investigational medicinal product code	PBO - tablet
Other name	
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Placebo tablets matching LCM tablets.

Arm title	Lacosamide

Arm description:

This arm includes subjects with epilepsy, who received a flexible dose of Lacosamide (LCM) oral solution or tablets, administered twice a day. Subjects weighing <30kg received 8mg/kg/day to 12mg/kg/day Lacosamide (LCM) oral solution; subjects weighing >=30kg to <50kg received 6mg/kg/day to 8mg/kg/day LCM oral solution; and subjects weighing >=50kg received 300mg/day to 400mg/day LCM tablets, or if unable or unwilling to swallow tablets may have received LCM oral solution, however, they were not permitted to exceed the maximum dose of LCM 400mg/day. The subject's body weight at Baseline (Visit 2) was used to determine the dose throughout the study.

Arm type	Experimental

Investigational medicinal product name	Lacosamide - solution
Investigational medicinal product code	LCM - solution
Other name	Vimpat
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

6mg/kg/day to 12 mg/kg/day determined by subject´s body weight at Baseline.

Investigational medicinal product name	Lacosamide - tablet
Investigational medicinal product code	LCM - tablet
Other name	Vimpat
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

300mg/day to 400mg/day determined by subject´s body weight at Baseline.

Number of subjects in period 1	Placebo	Lacosamide
Started	172	171
Completed	151	151
Not completed	21	20
Use Of Prohibited Medication	-	1
Consent withdrawn by subject	6	5
The Excessive Use Of Rescue Medication	-	1
Non Compliance Of Child	-	1
Adverse event, non-fatal	12	7
Lost to follow-up	1	1
Non Compliance Of The Parent	-	1
Lack of efficacy	1	-
Protocol deviation	1	3

Baseline characteristics

Reporting groups	
Reporting group title	Placebo

Reporting group description:

This arm includes subjects with epilepsy, who received a flexible dose of Placebo oral solution or tablets, administered twice a day. Appearance of Placebo oral solution and tablets matched the Lacosamide oral solution and tablets.

Reporting group title	Lacosamide

Reporting group description:

This arm includes subjects with epilepsy, who received a flexible dose of Lacosamide (LCM) oral solution or tablets, administered twice a day. Subjects weighing <30kg received 8mg/kg/day to 12mg/kg/day Lacosamide (LCM) oral solution; subjects weighing >=30kg to <50kg received 6mg/kg/day to 8mg/kg/day LCM oral solution; and subjects weighing >=50kg received 300mg/day to 400mg/day LCM tablets, or if unable or unwilling to swallow tablets may have received LCM oral solution, however, they were not permitted to exceed the maximum dose of LCM 400mg/day. The subject's body weight at Baseline (Visit 2) was used to determine the dose throughout the study.

Reporting group values	Placebo	Lacosamide	Total
Number of subjects	172	171	343
Age Categorical Units: Subjects			
<=18 years	172	171	343
Between 18 and 65 years	0	0	0
>=65 years	0	0	0
Age Continuous Units: years			
arithmetic mean	10.9	10.5	
standard deviation	± 3.5	± 3.6	-
Gender Categorical Units: Subjects			
Male	99	91	190
Female	73	80	153

End points

End points reporting groups

Reporting group title	Placebo

Reporting group description:

This arm includes subjects with epilepsy, who received a flexible dose of Placebo oral solution or tablets, administered twice a day. Appearance of Placebo oral solution and tablets matched the Lacosamide oral solution and tablets.

Reporting group title	Lacosamide

Reporting group description:

This arm includes subjects with epilepsy, who received a flexible dose of Lacosamide (LCM) oral solution or tablets, administered twice a day. Subjects weighing <30kg received 8mg/kg/day to 12mg/kg/day Lacosamide (LCM) oral solution; subjects weighing >=30kg to <50kg received 6mg/kg/day to 8mg/kg/day LCM oral solution; and subjects weighing >=50kg received 300mg/day to 400mg/day LCM tablets, or if unable or unwilling to swallow tablets may have received LCM oral solution, however, they were not permitted to exceed the maximum dose of LCM 400mg/day. The subject's body weight at Baseline (Visit 2) was used to determine the dose throughout the study.

Subject analysis set title	Placebo (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm includes subjects with epilepsy, who received a flexible dose of Placebo oral solution or tablets, administered twice a day. Appearance of Placebo oral solution and tablets matched the Lacosamide oral solution and tablets.

Subject analysis set title	Lacosamide (FAS)
Subject analysis set type	Full analysis

Subject analysis set description:

This arm includes subjects with epilepsy, who received a flexible dose of Lacosamide (LCM) oral solution or tablets, administered twice a day. Subjects weighing <30kg received 8mg/kg/day to 12mg/kg/day Lacosamide (LCM) oral solution; subjects weighing >=30kg to <50kg received 6mg/kg/day to 8mg/kg/day LCM oral solution; and subjects weighing >=50kg received 300mg/day to 400mg/day LCM tablets, or if unable or unwilling to swallow tablets may have received LCM oral solution, however, they were not permitted to exceed the maximum dose of LCM 400mg/day. The subject's body weight at Baseline (Visit 2) was used to determine the dose throughout the study.

Primary: Change in partial onset seizure (POS) frequency per 28 days from Baseline to the Maintenance Period

End point title	Change in partial onset seizure (POS) frequency per 28 days from Baseline to the Maintenance Period

End point description:

The POS frequency is standardized to a 28-day duration. Negative values indicate improvement from Baseline.

End point type	Primary

End point timeframe:

Baseline to Week 16 (or last value on treatment)

End point values	Placebo (FAS)	Lacosamide (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	170		
Units: Seizures per 28 days				
median (full range (min-max))				
Median (full range)	-1.55 (-318.7 to 690)	-3.05 (-302.9 to 210.4)		

Statistical analyses

Statistical analysis title	Statistical Analysis 1
Comparison groups	Placebo (FAS) v Lacosamide (FAS)
Number of subjects included in analysis	338
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.0003
Method	ANCOVA
Parameter estimate	Percent reduction over Placebo
Point estimate	31.72
Confidence interval	
level	95 %
sides	2-sided
lower limit	16.342
upper limit	44.277

Secondary: Proportion of responders where a responder is defined as a participant with >= 50% reduction in partial onset seizure frequency per 28 days from Baseline to the Maintenance Period

End point title	Proportion of responders where a responder is defined as a participant with >= 50% reduction in partial onset seizure frequency per 28 days from Baseline to the Maintenance Period

End point description:

Proportion of responders is presented as percentage of participants. A responder is a subject experiencing a 50 % or greater reduction in partial onset seizure frequency per 28 days from Baseline to the Maintenance Period.

End point type	Secondary

End point timeframe:

Baseline to Week 16 (or last value on treatment)

End point values	Placebo (FAS)	Lacosamide (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	168	170		
Units: percentage of participants				
number (not applicable)				
Percentage of participants	33.3	52.9		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects experiencing a >=25 % to <50 %, 50 % to 75 %, or >75 % reduction in partial onset seizure frequency per 28 days from Baseline to the end of Maintenance Period

End point title	Proportion of subjects experiencing a >=25 % to <50 %, 50 % to 75 %, or >75 % reduction in partial onset seizure frequency per 28 days from Baseline to the end of Maintenance Period

End point description:

Proportion of subjects is presented as percentage of participants.
A >=25%-<50% response in the Maintenance Period is defined as >=25% to <50% reduction in POS frequency per 28 days from Baseline to end of Maintenance Period. A >=50%-<=75% response in the Maintenance Period is defined as >=50% to <=75% reduction in POS frequency per 28 days from Baseline to end of Maintenance Period. A 75% response in the Maintenance Period is defined as >75% reduction in POS frequency per 28 days from Baseline to end of Maintenance Period.

End point type	Secondary

End point timeframe:

Baseline to Week 16 (or last value on treatment)

End point values	Placebo (FAS)	Lacosamide (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	170	170		
Units: percentage of participants				
number (not applicable)				
>=25% - <50%	14.7	11.8		
>=50% - <=75%	17.1	21.8		
>75%	15.9	31.2		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in partial onset seizure frequency per 28 days from Baseline to the entire treatment (ie, Titration+Maintenance Periods)

End point title	Change in partial onset seizure frequency per 28 days from Baseline to the entire treatment (ie, Titration+Maintenance Periods)

End point description:

The POS frequency is standardized to a 28-day duration. Negative values indicate improvement from Baseline.

End point type	Secondary

End point timeframe:

Baseline to Week 16 (or last value on treatment)

End point values	Placebo (FAS)	Lacosamide (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	169	170		
Units: Seizures per 28 days				
median (full range (min-max))				
Median (full range)	-1.22 (-250.6 to 477)	-2.46 (-219.2 to 210.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects experiencing a >=25 % to <50 %, 50 % to 75 %, or >75 % reduction in partial onset seizure frequency per 28 days from Baseline to the entire treatment (ie, Titration+Maintenance Periods)

End point title	Proportion of subjects experiencing a >=25 % to <50 %, 50 % to 75 %, or >75 % reduction in partial onset seizure frequency per 28 days from Baseline to the entire treatment (ie, Titration+Maintenance Periods)

End point description:

Proportion of subjects is presented as percentage of participants.
A >=25%-<50% response in the Treatment Period is defined as >=25% to <50% reduction in POS frequency per 28 days from Baseline to end of Treatment Period. A >=50%-<=75% response in the Treatment Period is defined as >=50% to <=75% reduction in POS frequency per 28 days from Baseline to end of Treatment Period. A 75% response in the Treatment Period is defined as >75% reduction in POS frequency per 28 days from Baseline to end of Treatment Period.

End point type	Secondary

End point timeframe:

Baseline to Week 16 (or last value on treatment)

End point values	Placebo (FAS)	Lacosamide (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	170	170		
Units: percentage of participants				
number (not applicable)				
>=25% - <50%	15.3	16.5		
>=50% - <=75%	20.6	20.6		
>75%	8.8	23.5		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects experiencing no change in partial onset seizure frequency (between <25 % reduction and <25 % increase) per 28 days from Baseline to the entire treatment (ie, Titration+Maintenance Periods)

End point title	Proportion of subjects experiencing no change in partial onset seizure frequency (between <25 % reduction and <25 % increase) per 28 days from Baseline to the entire treatment (ie, Titration+Maintenance Periods)

End point description:

Proportion of subjects is presented as percentage of participants.
No change is defined as between <25% reduction and <25% increase in POS frequency per 28 days from Baseline to the entire Treatment Period, otherwise not between <25% reduction and <25% increase is defined as a change.

End point type	Secondary

End point timeframe:

Baseline to Week 16 (or last value on treatment)

End point values	Placebo (FAS)	Lacosamide (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	169	170		
Units: percentage of participants				
number (not applicable)				
Percentage of participants	32	20.6		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects experiencing an increase in partial onset seizure frequency per 28 days of >=25 % from Baseline to the entire treatment (ie, Titration+Maintenance Periods)

End point title	Proportion of subjects experiencing an increase in partial onset seizure frequency per 28 days of >=25 % from Baseline to the entire treatment (ie, Titration+Maintenance Periods)

End point description:

Proportion of subjects is presented as percentage of participants.
An increase is defined as a >=25% increase in POS frequency per 28 days from Baseline to the entire Treatment Period, otherwise <25% increase is defined as no increase.

End point type	Secondary

End point timeframe:

Baseline to Week 16 (or last value on treatment)

End point values	Placebo (FAS)	Lacosamide (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	169	170		
Units: percentage of participants				
number (not applicable)				
Percentage of participants	23.1	18.8		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in partial onset seizure frequency per 28 days from Baseline to the entire treatment (ie, Titration+Maintenance Periods) for Simple Partial Seizures

End point title	Change in partial onset seizure frequency per 28 days from Baseline to the entire treatment (ie, Titration+Maintenance Periods) for Simple Partial Seizures

End point description:

The POS frequency is standardized to a 28-day duration. Negative values indicate improvement from Baseline.

End point type	Secondary

End point timeframe:

Baseline to Week 16 (or last value on treatment)

End point values	Placebo (FAS)	Lacosamide (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	68	77		
Units: Seizures per 28 days				
median (full range (min-max))				
Median (full range)	-1.14 (-250.6 to 477)	-1.25 (-217.4 to 100.2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in partial onset seizure frequency per 28 days from Baseline to the entire treatment (ie, Titration+Maintenance Periods) for Complex Partial Seizures

End point title	Change in partial onset seizure frequency per 28 days from Baseline to the entire treatment (ie, Titration+Maintenance Periods) for Complex Partial Seizures

End point description:

The POS frequency is standardized to a 28-day duration. Negative values indicate improvement from Baseline.

End point type	Secondary

End point timeframe:

Baseline to Week 16 (or last value on treatment)

End point values	Placebo (FAS)	Lacosamide (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	99	109		
Units: Seizures per 28 days				
median (full range (min-max))				
Median (full range)	-0.98 (-78 to 239.7)	-2.06 (-131.8 to 210.4)		

Statistical analyses

No statistical analyses for this end point

Secondary: Change in partial onset seizure frequency per 28 days from Baseline to the entire treatment (ie, Titration+Maintenance Periods) for Secondary Generalized Seizures

End point title	Change in partial onset seizure frequency per 28 days from Baseline to the entire treatment (ie, Titration+Maintenance Periods) for Secondary Generalized Seizures

End point description:

The POS frequency is standardized to a 28-day duration. Negative values indicate improvement from Baseline.

End point type	Secondary

End point timeframe:

Baseline to Week 16 (or last value on treatment)

End point values	Placebo (FAS)	Lacosamide (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	69	63		
Units: Seizures per 28 days				
median (full range (min-max))				
Median (full range)	-1 (-204.7 to 39.8)	-2.81 (-99.3 to 72.7)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of seizure free days during the Maintenance Period for subjects who completed the Maintenance Period

End point title	Proportion of seizure free days during the Maintenance Period for subjects who completed the Maintenance Period

End point description:

The proportion of seizure free days is calculated as (days with number of seizures = 0) divided by (days with recorded data in the subject diary), where 'days with recorded data in the subject diary' excludes any days where 'Not Done' is recorded.

End point type	Secondary

End point timeframe:

Week 7 to Week 16

End point values	Placebo (FAS)	Lacosamide (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154	152		
Units: days				
arithmetic mean (standard deviation)				
Mean (standard deviation)	0.65 (± 0.35)	0.71 (± 0.32)		

Statistical analyses

No statistical analyses for this end point

Secondary: Proportion of subjects who achieved "seizure free" status (yes/no) for subjects who completed the Maintenance Period

End point title	Proportion of subjects who achieved "seizure free" status (yes/no) for subjects who completed the Maintenance Period

End point description:

The proportion of seizure free days is calculated as (days with number of seizures = 0) divided by (days with recorded data in the subject diary), where 'days with recorded data in the subject diary' excludes any days where 'Not Done' is recorded.

End point type	Secondary

End point timeframe:

Week 7 to Week 16

End point values	Placebo (FAS)	Lacosamide (FAS)		
Subject group type	Subject analysis set	Subject analysis set		
Number of subjects analysed	154	152		
Units: percentage of participants				
number (not applicable)				
Percentage of participants	9.7	15.1		

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 until Safety Follow-Up Visit up to week 24.	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups	
Reporting group title	Placebo
Reporting group description:	
This arm includes subjects with epilepsy, who received a flexible dose of Placebo oral solution or tablets, administered twice a day. Appearance of Placebo oral solution and tablets matched the Lacosamide oral solution and tablets.	
Reporting group title	Lacosamide
Reporting group description:	
This arm includes subjects with epilepsy, who received a flexible dose of Lacosamide (LCM) oral solution or tablets, administered twice a day. Subjects weighing <30kg received 8mg/kg/day to 12mg/kg/day Lacosamide (LCM) oral solution; subjects weighing >=30kg to <50kg received 6mg/kg/day to 8mg/kg/day LCM oral solution; and subjects weighing >=50kg received 300mg/day to 400mg/day LCM tablets, or if unable or unwilling to swallow tablets may have received LCM oral solution, however, they were not permitted to exceed the maximum dose of LCM 400mg/day. The subject's body weight at Baseline (Visit 2) was used to determine the dose throughout the study.	

Serious adverse events	Placebo	Lacosamide	
Total subjects affected by serious adverse events			
subjects affected / exposed	13 / 172 (7.56%)	11 / 171 (6.43%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	
Injury, poisoning and procedural complications			
Postoperative respiratory distress			
subjects affected / exposed	1 / 172 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Cardiac disorders			
Bradycardia			
subjects affected / exposed	0 / 172 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Nervous system disorders			
Convulsion			

subjects affected / exposed	4 / 172 (2.33%)	2 / 171 (1.17%)	
occurrences causally related to treatment / all	0 / 5	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dystonia			
subjects affected / exposed	1 / 172 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Partial seizures			
subjects affected / exposed	0 / 172 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 4	
deaths causally related to treatment / all	0 / 0	0 / 0	
Syncope			
subjects affected / exposed	0 / 172 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	2 / 172 (1.16%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Vomiting			
subjects affected / exposed	1 / 172 (0.58%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 2	1 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Constipation			
subjects affected / exposed	1 / 172 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastrointestinal inflammation			
subjects affected / exposed	0 / 172 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Hepatobiliary disorders			

Hepatitis			
subjects affected / exposed	1 / 172 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Skin and subcutaneous tissue disorders			
Rash maculo-papular			
subjects affected / exposed	1 / 172 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Psychiatric disorders			
Emotional disorder of childhood			
subjects affected / exposed	1 / 172 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	1 / 172 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Infections and infestations			
Pneumonia			
subjects affected / exposed	2 / 172 (1.16%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 2	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Urinary tract infection			
subjects affected / exposed	1 / 172 (0.58%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchitis			
subjects affected / exposed	0 / 172 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Bronchopneumonia			

subjects affected / exposed	0 / 172 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Dengue fever			
subjects affected / exposed	0 / 172 (0.00%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 0	0 / 1	
deaths causally related to treatment / all	0 / 0	0 / 0	
Gastroenteritis			
subjects affected / exposed	1 / 172 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Respiratory tract infection			
subjects affected / exposed	1 / 172 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Tonsillitis			
subjects affected / exposed	1 / 172 (0.58%)	0 / 171 (0.00%)	
occurrences causally related to treatment / all	0 / 1	0 / 0	
deaths causally related to treatment / all	0 / 0	0 / 0	
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	1 / 172 (0.58%)	1 / 171 (0.58%)	
occurrences causally related to treatment / all	0 / 1	0 / 2	
deaths causally related to treatment / all	0 / 0	0 / 0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Placebo	Lacosamide	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	61 / 172 (35.47%)	85 / 171 (49.71%)	
Nervous system disorders			
Somnolence			
subjects affected / exposed	11 / 172 (6.40%)	28 / 171 (16.37%)	
occurrences (all)	14	42	
Dizziness			

subjects affected / exposed	13 / 172 (7.56%)	18 / 171 (10.53%)	
occurrences (all)	14	26	
Headache			
subjects affected / exposed	15 / 172 (8.72%)	14 / 171 (8.19%)	
occurrences (all)	25	19	
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	10 / 172 (5.81%)	17 / 171 (9.94%)	
occurrences (all)	11	21	
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	11 / 172 (6.40%)	17 / 171 (9.94%)	
occurrences (all)	15	22	
Diarrhoea			
subjects affected / exposed	9 / 172 (5.23%)	8 / 171 (4.68%)	
occurrences (all)	13	15	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	10 / 172 (5.81%)	20 / 171 (11.70%)	
occurrences (all)	10	29	
Upper respiratory tract infection			
subjects affected / exposed	10 / 172 (5.81%)	10 / 171 (5.85%)	
occurrences (all)	14	13	
Pharyngitis			
subjects affected / exposed	5 / 172 (2.91%)	10 / 171 (5.85%)	
occurrences (all)	5	13	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 March 2015	The main purpose of this substantial amendment was to add details to the statistics section regarding sample size re-estimation and statistical evaluation of secondary and other efficacy variables based on the clarifications made by the South Korean Ministry of Health and align the wording with the SP0967 protocol (a double-blind, randomized, placebo-controlled, parallel-group study to investigate the efficacy and safety of LCM as adjunctive therapy in subjects with epilepsy >=1 month to <4 years of age with partial-onset seizures). Based on recommendations made by the US FDA, the creatinine clearance was changed from less than 50mL/min to less than 30mL/min in Exclusion Criterion number 10. In addition, as per request from the Swedish Ministry of Health, Exclusion Criterion number 20 (excluding subjects with epilepsy secondary to a progressing cerebral disease or any other progressively neurodegenerative disease, such as Rasmussen Syndrome) was removed because it was considered to be a duplicate of Exclusion Criterion number 23 (Section 3.3.2). Exclusion Criterion number 22 was reworded to clarify that the excluded sodium channelopathies were cardiac.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported