Clinical trial results:
An Open-label, Multicenter Extension Study to Evaluate the Long-term Safety and Efficacy of Lacosamide as Adjunctive Therapy for Uncontrolled Primary Generalized Tonic-Clonic Seizures in Subjects With Idiopathic Generalized Epilepsy

Summary

EudraCT number	2012-001770-29
Trial protocol	SK HU DE ES CZ PT BE PL BG FR RO Outside EU/EEA
Global end of trial date	30 March 2023

Results information

Result version number	v1
This version publication date	14 October 2023
First version publication date	14 October 2023

Trial information

Trial identification

Sponsor protocol code	EP0012

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02408549
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)	Yes
EMA paediatric investigation plan number(s)	EMEA-000402-PIP03-17
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	03 May 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	30 March 2023
Global end of trial reached?	Yes
Global end of trial date	30 March 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

Assess the safety and tolerability of lacosamide (LCM) as an adjunctive therapy for uncontrolled primary generalized tonic-clonic seizures (PGTCS) in subjects with idiopathic generalized epilepsy (IGE) during long-term exposure.

Protection of trial subjects:

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

Background therapy:

Concomitant therapy as permitted in the protocol.

Evidence for comparator:

Not applicable

Actual start date of recruitment	03 August 2015
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	Australia: 15
Country: Number of subjects enrolled	Brazil: 16
Country: Number of subjects enrolled	Bulgaria: 11
Country: Number of subjects enrolled	China: 3
Country: Number of subjects enrolled	Czechia: 16
Country: Number of subjects enrolled	France: 5
Country: Number of subjects enrolled	Germany: 3
Country: Number of subjects enrolled	Hungary: 12
Country: Number of subjects enrolled	Israel: 7
Country: Number of subjects enrolled	Italy: 1
Country: Number of subjects enrolled	Japan: 37
Country: Number of subjects enrolled	Mexico: 1
Country: Number of subjects enrolled	Poland: 16
Country: Number of subjects enrolled	Portugal: 1
Country: Number of subjects enrolled	Romania: 8
Country: Number of subjects enrolled	Russian Federation: 31
Country: Number of subjects enrolled	Slovakia: 11
Country: Number of subjects enrolled	Korea, Republic of: 6
Country: Number of subjects enrolled	Spain: 13

Country: Number of subjects enrolled	Taiwan: 2
Country: Number of subjects enrolled	United States: 24
Worldwide total number of subjects	239
EEA total number of subjects	97

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)	16
Adolescents (12-17 years)	28
Adults (18-64 years)	194
From 65 to 84 years	1
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in August 2015 and concluded in March 2023. Study participants from SP0982 [NCT02408523], who met EP0012 eligibility criteria were enrolled.

Pre-assignment

Screening details:

The Participant Flow refers to the Safety Set. The Safety Set included all study participants who received at least 1 dose of Investigational medicinal product (IMP) during this study.

Period 1

Period 1 title	Overall Study (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Arms

Arm title	All participants (lacosamide)

Arm description:

Participants included in this treatment group received at least one dose of LCM as EP0012 protocol entry criteria. The dose range for pediatric participants weighing <50 kg is from 4 mg/kg/day (oral solution) to 12 mg/kg/day (oral solution), for pediatric participants weighing ≥50 kg, the dose range is from 200 mg/day (tablets) to 600 mg/day (tablets) and for adult participants, the dose range is from 200 mg/day to 800mg/day (tablets) during the Treatment Period. The LCM dose may be increased or decreased at the investigator's discretion after the study participant received the first dose of LCM in the study. Pediatric participants who initially started on oral solution might have transferred to tablets at Investigator's discretion after achieving >=50 kgs. LCM was administered orally, twice daily (bid), up to approximately 5 years. Treatment was continued for at least 2 years for adult participants and up to approximately 5 years for pediatric participants.

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 orally, bid, at pre-defined timepoints during the Treatment Period.

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 orally, bid, at pre-defined timepoints during the Treatment Period.

Number of subjects in period 1	All participants (lacosamide)
Started	239
Completed	157
Not completed	82
Adverse event, serious fatal	4
Adverse event, non-fatal	15
Study terminated at site	1
Withdrawal of consent due to business trip	1
Pregnancy	1
Subject moved to another place, far from site	1
Neurology research program closing at site	1
Lost to follow-up	6
Consent withdrawn	30
Site closure	1
Lack of efficacy	17
Protocol deviation	4

Baseline characteristics

Reporting groups	
Reporting group title	All participants (lacosamide)

Reporting group description:

Participants included in this treatment group received at least one dose of LCM as EP0012 protocol entry criteria. The dose range for pediatric participants weighing <50 kg is from 4 mg/kg/day (oral solution) to 12 mg/kg/day (oral solution), for pediatric participants weighing ≥50 kg, the dose range is from 200 mg/day (tablets) to 600 mg/day (tablets) and for adult participants, the dose range is from 200 mg/day to 800mg/day (tablets) during the Treatment Period. The LCM dose may be increased or decreased at the investigator's discretion after the study participant received the first dose of LCM in the study. Pediatric participants who initially started on oral solution might have transferred to tablets at Investigator's discretion after achieving >=50 kgs. LCM was administered orally, twice daily (bid), up to approximately 5 years. Treatment was continued for at least 2 years for adult participants and up to approximately 5 years for pediatric participants.

Reporting group values	All participants (lacosamide)	Total	
Number of subjects	239	239	
Age Categorical Units: Participants			
≥4-<12 years	16	16	
12-<18 years	28	28	
18-<65 years	194	194	
≥65 years	1	1	
Age Continuous Units: Years			
arithmetic mean	27.9		
standard deviation	± 12.6	-	
Sex: Female, Male Units: Participants			
Female	134	134	
Male	105	105	

End points

End points reporting groups

Reporting group title	All participants (lacosamide)

Reporting group description:

Participants included in this treatment group received at least one dose of LCM as EP0012 protocol entry criteria. The dose range for pediatric participants weighing <50 kg is from 4 mg/kg/day (oral solution) to 12 mg/kg/day (oral solution), for pediatric participants weighing ≥50 kg, the dose range is from 200 mg/day (tablets) to 600 mg/day (tablets) and for adult participants, the dose range is from 200 mg/day to 800mg/day (tablets) during the Treatment Period. The LCM dose may be increased or decreased at the investigator's discretion after the study participant received the first dose of LCM in the study. Pediatric participants who initially started on oral solution might have transferred to tablets at Investigator's discretion after achieving >=50 kgs. LCM was administered orally, twice daily (bid), up to approximately 5 years. Treatment was continued for at least 2 years for adult participants and up to approximately 5 years for pediatric participants.

Primary: Number of study participants with new appearance of absence and/or myoclonic seizures during the Treatment Period

End point title	Number of study participants with new appearance of absence and/or myoclonic seizures during the Treatment Period[1]

End point description:

The number of study participants with appearance of new absence and/or myoclonic seizure types experienced during the Treatment Period but who did not experience in Combined Baseline Period or in seizure classification history, before taking LCM were reported. To determine appearance of new seizure type, the Combined Baseline Period was used. Thus, the participants who directly enrolled into EP0012, the Baseline absence, and/or myoclonic seizure data from SP0982's 4-week Prospective Baseline Period were combined with any reported Baseline absence, and myoclonic seizure information in the daily seizure diary from EP0012 (reported before first dose in EP0012) to recalculate the study participant's Baseline variables such as days with absence, and/or myoclonic seizures per 28 days. The Safety Set included all study participants who received at least 1 dose of IMP during this study.

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to End of Treatment Period (up to approximately 5 years)

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 as descriptive statistics only.

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	239			
Units: participants				
Absence seizures	3			
Myoclonic seizures	5			

Statistical analyses

No statistical analyses for this end point

Primary: Number of study participants withdrawn due to TEAEs

End point title	Number of study participants withdrawn due to TEAEs[2]

End point description:

AEs were considered treatment-emergent if event had onset on or after date of first study medication dose in EP0012 and within 30 days following last study medication dose or events whose intensity worsened on or after date of first study medication dose and within 30 days following date of last study medication administration. Adverse Events were reported spontaneously by the participant and/or caregiver or observed by the investigator. The Safety Set included all study participants who received at least 1 dose of IMP during this study.

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to End of Treatment Period (up to approximately 5 years)

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 as descriptive statistics only.

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	239			
Units: participants	19			

Statistical analyses

No statistical analyses for this end point

Primary: Number of study participants with treatment-emergent adverse events (TEAEs) over the duration of the Treatment Period

End point title	Number of study participants with treatment-emergent adverse events (TEAEs) over the duration of the Treatment Period[3]

End point description:

AEs were considered treatment-emergent if event had onset on or after date of first study medication dose in EP0012 and within 30 days following last study medication dose or events whose intensity worsened on or after date of first study medication dose and within 30 days following date of last study medication administration. Adverse Events were reported spontaneously by the participant and/or caregiver or observed by the investigator. The Safety Set included all study participants who received at least 1 dose of IMP during this study.

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to End of Treatment Period (up to approximately 5 years)

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 as descriptive statistics only.

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	239			
Units: participants	222			

Statistical analyses

No statistical analyses for this end point

Primary: Number of study participants with an increase of greater than (>)25% to 50% in days with absence seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)

End point title	Number of study participants with an increase of greater than (>)25% to 50% in days with absence seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)[4]

End point description:

The number of participants experiencing an increase of >25% to 50% in the number of days with absence seizures per 28 days during the Treatment Period compared to the Prospective Baseline Period (for those participants with absence seizure data reported in the 4-week Prospective Baseline Period in SP0982) were reported. This period started on the day of Visit 1 of SP0982 and ended the day before Visit 2 of SP0982. For the direct enrollers into EP0012, Prospective Baseline ended the day before Visit 1 (or prior to first dose) of EP0012. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Here, Number of participants analyzed included those participants who were evaluable for the assessment (absence seizures).

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to End of Treatment Period (up to approximately 5 years), compared to the Prospective SP0982 Baseline Period

Notes:

[4] - 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 as descriptive statistics only.

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of study participants with an increase of >75% in days with absence seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)

End point title	Number of study participants with an increase of >75% in days with absence seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)[5]

End point description:

The number of participants experiencing an increase of >75% in the number of days with absence

seizures per 28 days during the Treatment Period compared to the Prospective Baseline Period (for those participants with absence seizure data reported in the 4-week Prospective Baseline Period in SP0982) were reported. This period started on the day of Visit 1 of SP0982 and ended the day before Visit 2 of SP0982. For the direct enrollers into EP0012, Prospective Baseline ended the day before Visit 1 (or prior to first dose) of EP0012. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Here, Number of participants analyzed included those participants who were evaluable for the assessment (absence seizures).

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to End of Treatment Period (up to approximately 5 years), compared to the Prospective SP0982 Baseline Period

Notes:

[5] - 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 as descriptive statistics only.

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of study participants with an increase of >50% to 75% in days with absence seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)

End point title	Number of study participants with an increase of >50% to 75% in days with absence seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)[6]

End point description:

The number of participants experiencing an increase of >50% to 75% in the number of days with absence seizures per 28 days during the Treatment Period compared to the Prospective Baseline Period (for those participants with absence seizure data reported in the 4-week Prospective Baseline Period in SP0982) were reported. This period started on the day of Visit 1 of SP0982 and ended the day before Visit 2 of SP0982. For the direct enrollers into EP0012, Prospective Baseline ended the day before Visit 1 (or prior to first dose) of EP0012. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Here, Number of participants analyzed included those participants who were evaluable for the assessment (absence seizures).

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to End of Treatment Period (up to approximately 5 years), compared to the Prospective SP0982 Baseline Period

Notes:

[6] - 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 as descriptive statistics only.

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: participants	0			

Statistical analyses

No statistical analyses for this end point

Primary: Number of study participants with an increase of up to 25% in days with absence seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)

End point title	Number of study participants with an increase of up to 25% in days with absence seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)[7]

End point description:

The number of participants experiencing an increase of up to 25% in the number of days with absence seizures per 28 days during the Treatment Period compared to the Prospective Baseline Period (for those participants with absence seizure data reported in the 4-week Prospective Baseline Period in SP0982) were reported. This period started on the day of Visit 1 of SP0982 and ended the day before Visit 2 of SP0982. For the direct enrollers into EP0012, Prospective Baseline ended the day before Visit 1 (or prior to first dose) of EP0012. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Here, Number of participants analyzed (N) included those participants who were evaluable for the assessment (absence seizures).

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to End of Treatment Period (up to approximately 5 years), compared to the Prospective SP0982 Baseline Period

Notes:

[7] - 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 as descriptive statistics only.

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	93			
Units: participants	5			

Statistical analyses

No statistical analyses for this end point

Primary: Number of study participants with an increase of >50% to 75% in days with myoclonic seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)

End point title	Number of study participants with an increase of >50% to 75% in days with myoclonic seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)[8]

End point description:

The number of participants experiencing an increase of >50% to 75% in the number of days with myoclonic seizures per 28 days during the Treatment Period compared to the Prospective Baseline Period (for those participants with myoclonic seizure data reported in the 4-week Prospective Baseline Period in SP0982) were reported. This period started on the day of Visit 1 of SP0982 and ended the day before Visit 2 of SP0982. For the direct enrollers into EP0012, Prospective Baseline ended the day before Visit 1 (or prior to first dose) of EP0012. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Here, Number of participants analyzed included those participants who were evaluable for the assessment (myoclonic seizures).

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to End of Treatment Period (up to approximately 5 years), compared to the Prospective SP0982 Baseline Period

Notes:

[8] - 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 as descriptive statistics only.

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	96			
Units: participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Number of study participants with an increase of >75% in days with myoclonic seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)

End point title	Number of study participants with an increase of >75% in days with myoclonic seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)[9]

End point description:

The number of participants experiencing an increase of >75% in the number of days with myoclonic seizures per 28 days during the Treatment Period compared to the Prospective Baseline Period (for those participants with myoclonic seizure data reported in the 4-week Prospective Baseline Period in SP0982) were reported. This period started on the day of Visit 1 of SP0982 and ended the day before Visit 2 of SP0982. For the direct enrollers into EP0012, Prospective Baseline ended the day before Visit 1 (or prior to first dose) of EP0012. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Here, Number of participants analyzed included those participants who were evaluable for the assessment (myoclonic seizures).

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to End of Treatment Period (up to approximately 5 years), compared to the Prospective SP0982 Baseline Period

Notes:

[9] - 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 as descriptive statistics only.

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	96			
Units: participants	2			

Statistical analyses

No statistical analyses for this end point

Primary: Number of study participants with an increase of up to 25% in days with myoclonic seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)

End point title	Number of study participants with an increase of up to 25% in days with myoclonic seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)[10]

End point description:

The number of participants experiencing an increase of up to 25% in the number of days with myoclonic seizures per 28 days during the Treatment Period compared to the Prospective Baseline Period (for those participants with myoclonic seizure data reported in the 4-week Prospective Baseline Period in SP0982) were reported. This period started on the day of Visit 1 of SP0982 and ended the day before Visit 2 of SP0982. For the direct enrollers into EP0012, Prospective Baseline ended the day before Visit 1 (or prior to first dose) of EP0012. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Here, Number of participants analyzed included those participants who were evaluable for the assessment (myoclonic seizures).

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to End of Treatment Period (up to approximately 5 years), compared to the Prospective SP0982 Baseline Period

Notes:

[10] - 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 as descriptive statistics only.

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	96			
Units: participants	4			

Statistical analyses

No statistical analyses for this end point

Primary: Number of study participants with an increase of >25% to 50% in days with myoclonic seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)

End point title	Number of study participants with an increase of >25% to 50% in days with myoclonic seizures per 28 days during the Treatment Period as compared to the Prospective Baseline (of study SP0982)[11]

End point description:

The number of participants experiencing an increase of >25% to 50% in the number of days with myoclonic seizures per 28 days during the Treatment Period compared to the Prospective Baseline Period (for those participants with myoclonic seizure data reported in the 4-week Prospective Baseline Period in SP0982) were reported. This period started on the day of Visit 1 of SP0982 and ended the day before Visit 2 of SP0982. For the direct enrollers into EP0012, Prospective Baseline ended the day before Visit 1 (or prior to first dose) of EP0012. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Here, Number of participants analyzed included those participants who were evaluable for the assessment (myoclonic seizures).

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to End of Treatment Period (up to approximately 5 years), compared to the Prospective SP0982 Baseline Period

Notes:

[11] - 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 as descriptive statistics only.

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	96			
Units: participants	1			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of study participants with at least 50% worsening in days with absence seizures

End point title	Percentage of study participants with at least 50% worsening in days with absence seizures[12]

End point description:

Seizure worsening was defined as a participant experiencing >=50% increase in the number of days with absence seizures per 28 days from Prospective Baseline. Percentages for seizure worsening were based on those participants who have reported a history of or an occurrence of absence seizures in Prospective Baseline or the Treatment Period. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Here, Number of participants analyzed included those participants who were evaluable for the assessment (absence seizures).

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to End of Treatment Period (up to approximately 5 years)

Notes:

[12] - 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 as descriptive statistics only.

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	92			
Units: percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Primary: Percentage of study participants with at least 50% worsening in days with myoclonic seizures

End point title	Percentage of study participants with at least 50% worsening in days with myoclonic seizures[13]

End point description:

Seizure worsening was defined as a participant experiencing >=50% increase in the number of days with myoclonic seizures per 28 days from Prospective Baseline. Percentages for seizure worsening were based on those participants who have reported a history of or an occurrence of myoclonic seizures in Prospective Baseline or the Treatment Period. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Here, Number of participants analyzed included those participants who were evaluable for the assessment (myoclonic seizures).

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) to End of Treatment Period (up to approximately 5 years)

Notes:

[13] - 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 as descriptive statistics only.

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	95			
Units: percentage of participants				
number (not applicable)	3.2			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Hemoglobin)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Hemoglobin)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Hematology parameter, Hemoglobin were those that were observed post-Baseline (BL) during the Treatment Period but not present at BL. For the age range, '2 years (y) to <17 years', the abnormality criteria were '<=95' grams/deciliter (g/dL) (Low) and '>160' g/dL (High). For age range, '>=17 years', the abnormality Criteria were '<=85% of lower limit of normal (LLN)' value (Low) and '>=115% of upper limit of normal (ULN)' value (High) of Hemoglobin in blood. Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants

analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of Hematology parameter (Hemoglobin) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	195			
Units: percentage of participants				
number (not applicable)				
Low: Week (Wk) 78 (2-<17 y) (n=7)	14.3			
Low: Wk 0 (>=17 y) (n=27)	3.7			
Low: Wk 2 (>=17 y) (n=195)	0.5			
Low: Wk 118 (>=17 y) (n=123)	0.8			
Low: Wk 166 (>=17 y) (n=81)	1.2			
Low: Wk 214 (>=17 y) (n=40)	2.5			
Low: TV (>=17 y) (n=123)	1.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Hematocrit)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Hematocrit)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Hematocrit were those that were observed post-BL during the Treatment Period but not present at BL. For the age range, '2 years to <17 years', the abnormality criteria were '<=29%' (Low) and '>47%' (High) hematocrit values. For age range, '>=17 years', the abnormality criteria were '<=85% of LLN' (Low) and '>=115% of ULN' (High) of Hematocrit values in blood. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of Hematology parameter (Hematocrit) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	170			
Units: percentage of participants				
number (not applicable)				
High: Wk 22 (2-<17 y) (n=29)	6.9			
High: Wk 46 (2-<17 y) (n=27)	3.7			
Low: Wk 46 (>=17 y) (n=170)	1.2			
Low: Wk 118 (>=17 y) (n=123)	1.6			
Low: Wk 166 (>=17 y) (n=81)	1.2			
Low: TV (>=17 y) (n=123)	0.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Eosinophils Absolute)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Eosinophils Absolute)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Eosinophils Absolute were those that were observed post-BL during the Treatment Period but not present at BL. For the age range, '>1 month', the abnormality criteria were '>=1.0' 10^9/L of Eosinophils in the blood. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of Hematology parameter (Eosinophils Absolute) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	228			
Units: percentage of participants				
number (not applicable)				
>=1.0: Wk 2 (>1 month) (n=228)	0.9			
>=1.0: Wk 22 (>1 month) (n=215)	0.5			
>=1.0: TV (>1 month) (n=134)	1.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Erythrocytes)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Erythrocytes)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Erythrocytes parameter were those that were observed post-BL during the Treatment Period but not present at BL. For the age range, '>=2years', the abnormality criteria were '<3.5' 10^12/L of Erythrocytes value in blood. Early Termination Visit (TV) was last visit in the study (up to approximately 5 years). The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. Data for visit (Early TV) wherein at least 1 TEMA value of Hematology parameter (Erythrocytes) observed during the study was reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	59			
Units: percentage of participants				
number (not applicable)	1.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Platelets)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Platelets)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Platelet count were those that were observed post-BL during the Treatment Period but not present at BL. For the age range of '>1 month', the abnormality criteria were '<=100' 10^9/L and '>=600' 10^9/L of Platelets count value. The Safety Set included all study participants who received at least 1 dose of IMP during this study. No participant had TEMA value (platelets) with markedly abnormal criteria specified at any visit.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	239			
Units: percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Leukocytes)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Leukocytes)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Leukocytes were those that were observed post-BL during the Treatment Period but not present at BL. For all age ranges, the abnormality criteria were ‘<=3.0' 10^9/L (Low) and ‘>= 16.0' 10^9/L (High) of Leukocytes values in blood. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. Data for visit (Week 62-Low) wherein at least 1 TEMA value of Hematology parameter (Leukocytes) observed during the study was reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	191			
Units: percentage of participants				
number (not applicable)	0.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Basophils Absolute)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Basophils Absolute)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Basophils Absolute were those that were observed post-BL during the Treatment Period but not present at BL. For the age range, ‘>1 month’, the abnormality criteria were '>=0.4'

10^9/L of Basophils in blood. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. Data for visit (Week 2) wherein at least 1 TEMA value of Hematology parameter (Basophils Absolute) observed during the study was reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	228			
Units: percentage of participants				
number (not applicable)	0.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Neutrophils Absolute)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Neutrophils Absolute)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Neutrophils Absolute were those that were observed post-BL during the Treatment Period but not present at BL. For the age range, '>1 month', the abnormality criteria was '<1.5' 10^9/L of Neutrophils in blood. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of Hematology parameter (Neutrophils Absolute) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	228			
Units: percentage of participants				
number (not applicable)				
<1.5: Wk 2 (>1 m) (n=228)	0.9			
<1.5: Wk 22 (>1 m) (n=215)	0.5			
<1.5: Wk 46 (>1 m) (n=196)	0.5			
<1.5: Wk 62 (>1 m) (n=191)	0.5			
<1.5: Wk 94 (>1 m) (n=162)	0.6			

<1.5: Wk 214 (>1 m) (n=42)	2.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Monocytes Absolute)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Monocytes Absolute)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Monocytes Absolute were those that are observed post-BL during the Treatment Period but not present at BL. For the age range, '>1 month', the abnormality criteria was '>=2.0' 10^9/L of Monocytes in blood. The Safety Set included all study participants who received at least 1 dose of IMP during this study. No participant had TEMA value (Monocytes Absolute) with markedly abnormal criteria specified at any visit.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	239			
Units: percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Lymphocytes Absolute)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in hematology parameters (Lymphocytes Absolute)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Lymphocytes Absolute were those that were observed post-Baseline (BL) during the Treatment Period but not present at Baseline. For the age range, '2 years - <6 years', the abnormality criteria were '<0.7' 10^9/L (Low) and '>6.9' 10^9/L (High). For age range, '>=6 years', the abnormality criteria were '<0.6' 10^9/L (Low) and '>5.0' 10^9/L (High) for Lymphocytes Absolute in the blood. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein

at least 1 TEMA value of Hematology parameter (Lymphocytes Absolute) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	226			
Units: percentage of participants				
number (not applicable)				
High: Wk 2 (>=6 y) (n=226)	0.4			
High: Wk 78 (>=6 y) (n=63)	3.2			
High: Wk 118 (>=6 y) (n=141)	0.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Sodium)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Sodium)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Sodium were those that were observed post- BL during the Treatment Period but not present at Baseline. For the age range, '>1 month', the abnormality criteria were '<127' mmol/L (Low) and '>151' mmol/L (High) of serum Sodium. The Safety Set included all study participants who received at least 1 dose of IMP during this study. No participant had TEMA value (Sodium) with markedly abnormal criteria specified at any visit.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	239			
Units: percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Calcium)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Calcium)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Calcium were those that were observed post- BL during the Treatment Period but not present at Baseline. For the age range, '1 year -<17 years', the abnormality criteria were '<=1.85' millimoles per litre (mmol/L) and '>=2.95' mmol/L. For age range, '>=17 years', the abnormality criteria was '<=1.9 mmol/L' and '>=2.75 mmol/L' of serum Calcium. The Safety Set included all study participants who received at least 1 dose of IMP during this study. No participant had TEMA value (Calcium) with markedly abnormal criteria specified at any visit.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	239			
Units: percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Potassium)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Potassium)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Potassium were those that were observed post- BL during the Treatment Period but not present at Baseline. For the age range, '>=1 year', the abnormality criteria were '<= 3.0' mmol/L (Low) and '>= 6.0' mmol/L (High) of serum Potassium. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. Data for visit (Week 2-High) wherein at least 1 TEMA value of Serum chemistry parameter (Potassium) observed during the study was reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	230			
Units: percentage of participants				
number (not applicable)	0.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Chloride)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Chloride)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Chloride were those that were observed post- BL during the Treatment Period but not present at Baseline. For the age range, '>1 month', the abnormality criteria were '<=90' mmol/L (Low) and '>=112' mmol/L (High) of serum Chloride. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of serum chemistry parameter (Chloride) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	234			
Units: percentage of participants				
number (not applicable)				
High: Wk 2 (>1 month) (n=234)	1.3			
High: Wk 22 (>1 month) (n=218)	2.3			
High: Wk 46 (>1 month) (n=198)	2.5			
High: Wk 62 (>1 month) (n=194)	1.5			
High: Wk 78 (>1 m) (n=65)	3.1			
High: Wk 94 (>1 m) (n=165)	1.2			
High: Wk 118 (>1 m) (n=145)	3.4			
High: Wk 214 (>1 m) (n=43)	2.3			
High: TV (>1 m) (n=145)	1.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Bicarbonate)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Bicarbonate)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Bicarbonate were those that were observed post- BL during the Treatment Period but not present at Baseline. For the age range, '>1 month-<17 years', the abnormality criteria were '<15' mmol/L (Low) and '>38' mmol/L (High). For age range, '>=17 years', the abnormality criteria were '<18' mmol/L (Low) and '>38' mmol/L (High) of serum Bicarbonate. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of serum chemistry parameter (Bicarbonate) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	180			
Units: percentage of participants				
number (not applicable)				
Low: Wk 2 (>=17 y) (n=180)	1.1			
Low: Wk 46 (>=17 y) (n=161)	1.2			
Low: Wk 62 (>=17 y) (n=158)	1.3			
Low: Wk 94 (>=17 y) (n=136)	0.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Aspartate Aminotransferase)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Aspartate Aminotransferase)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Aspartate Aminotransferase (AST) were those that were observed post- BL during the Treatment Period but not present at Baseline. For all ages, the abnormality criteria were specified as '≥3.0 units per litre (U/L) x ULN' (High A), '≥5.0 U/L x ULN' (High B), and '≥10.0 U/L x ULN' (High C) of serum AST. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of serum chemistry parameter (AST) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	144			
Units: percentage of participants				
number (not applicable)				
High A: All ages (Early TV) (n=58)	1.7			
High A: All ages (TV) (n=144)	0.7			
High B: All ages (TV) (n=144)	0.7			
High C: All ages (TV) (n=144)	0.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Creatinine)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Creatinine)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Creatinine were those that were observed post- BL during the Treatment Period but not present at Baseline. For the age range, '1-<10 years', the abnormality criteria were '>106.8' micromole per litre (umol/L), for '10-<16 years', the abnormality criteria were '>159.12' umol/L and for '>=16 years', the abnormality criteria was '>=176.8' umol/L for serum Creatinine. The Safety Set included all study participants who received at least 1 dose of IMP during this study. No participant had TEMA value (Creatinine) with markedly abnormal criteria specified at any visit.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	239			
Units: percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Alanine Aminotransferase)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Alanine Aminotransferase)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Alanine Aminotransferase (ALT) were those that were observed post- BL during the Treatment Period but not present at Baseline. For all ages, the abnormality criteria were specified as '≥3.0 U/L x ULN' (High A), '≥5.0 U/L x ULN' (High B), and '≥10.0 U/L x ULN' (High C) of serum ALT. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of serum chemistry parameter (ALT) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	234			
Units: percentage of participants				
number (not applicable)				
High A: All ages (Wk 2) (n=234)	0.4			
High A: All ages (Wk 46) (n=198)	0.5			
High A: All ages (Wk 62) (n=192)	0.5			
High A: All ages (Wk 118) (n=144)	0.7			
High A: All ages (TV) (n=144)	0.7			
High B: All ages (Wk 2) (n=234)	0.4			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Gamma Glutamyl Transferase)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Gamma Glutamyl Transferase)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Gamma Glutamyl Transferase (GGT) were those that were observed post- BL during the Treatment Period but not present at Baseline. For the age range, '1 year-<13 years', the abnormality criteria was '>=66' U/L (High A), for '13 years-<17 years', the abnormality criteria was '>=126' U/L (High B) and for '>=17 years', the abnormality criteria was '>=3.0 U/L x ULN' (High C) of serum GGT. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein

at least 1 TEMA value of serum chemistry parameter (GGT) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	198			
Units: percentage of participants				
number (not applicable)				
High A: TV (1-<13 y) (n=6)	16.7			
High C: Wk 2 (>=17 y) (n=198)	1.0			
High C: Wk 22 (>=17 y) (n=189)	0.5			
High C: Wk 62 (>=17 y) (n=169)	1.8			
High C: Wk 78 (>=17 y) (n=58)	3.4			
High C: Wk 118 (>=17 y) (n=125)	0.8			
High C: Wk 166 (>=17 y) (n=89)	1.1			
High C:TV (>=17 y) (n=132)	0.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Alkaline Phosphatase)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Alkaline Phosphatase)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Alkaline Phosphatase were those that were observed post- BL during the Treatment Period but not present at Baseline. For the age range, '4 years -<10 years', the abnormality criteria was '>=834 U/L', for '10 years -<17 years', the abnormality criteria was '>=1761 U/L' and for '>=17 years', the abnormality criteria was '>=3.0 U/L x ULN' of serum alkaline phosphatase. The Safety Set included all study participants who received at least 1 dose of IMP during this study. No participant had TEMA value (Alkaline Phosphatase) with markedly abnormal criteria specified at any visit .

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	239			
Units: percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in chemistry parameters (Total Bilirubin)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in chemistry parameters (Total Bilirubin)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Total Bilirubin were those that were observed post- BL during the Treatment Period but not present at Baseline. For the age range, '>1 month', the abnormality criteria was '≥34.208' umol/L of serum Bilirubin. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. Data for visit (Week 22) wherein at least 1 TEMA value of serum chemistry parameter (Total Bilirubin) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	218			
Units: percentage of participants				
number (not applicable)	0.5			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Glucose)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Glucose)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Glucose were those that were observed post- BL during the Treatment Period but not present at BL. For the age range, '>1 month-<17 years', the abnormality criteria were from '<2.

775’ mmol/L (Low) and ‘>=9.99’ mmol/L (High). For age range, ‘>=17 years’, the abnormality criteria were ‘<2.775’ mmol/L (Low) and ‘>=11.1’ mmol/L (High) of serum Glucose. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of serum chemistry parameter (Glucose) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	195			
Units: percentage of participants				
number (not applicable)				
Low: Wk 2 (>=17 y) (n=195)	0.5			
Low: Wk 62 (>=17 y) (n=168)	0.6			
Low: Wk 94 (>=17 y) (n=143)	0.7			
Low: Wk 118 (>=17 y) (n=123)	0.8			
High: Wk 2 (>=17 y) (n=195)	1.0			
High: Wk 22 (>=17 y) (n=186)	1.1			
High: Wk 46 (>=17 y) (n=166)	1.2			
High: Wk 62 (>=17 y) (n=168)	1.8			
High: Wk 78 (>=17 y) (n=58)	3.4			
High: Wk 94 (>=17 y) (n=143)	0.7			
High: Wk 118 (>=17 y) (n=123)	0.8			
High: Early TV (>=17 y) (n=52)	1.9			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Phosphate)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Phosphate)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Phosphate were those that are observed post- BL during the Treatment Period but not present at Baseline. For the age range, ‘1 year-<17 years’, the abnormality criteria were from ‘<0.5814’ mmol/L (Low) and ‘>2.3902’ mmol/L (High). For age range, ‘>=17 years’, the abnormality Criteria were ‘<=0.646’ mmol/L (Low) and ‘>=1.938’ mmol/L (High) of serum phosphate. The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of serum chemistry parameter (Phosphate) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	141			
Units: percentage of participants				
number (not applicable)				
Low: Wk 94 (>=17 y) (n=141)	0.7			
Low: Wk 118 (>=17 y) (n=123)	0.8			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in 12-lead electrocardiogram (ECG) parameter (QT interval)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in 12-lead electrocardiogram (ECG) parameter (QT interval)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA ECG results of QT interval parameter were those that were observed post- BL during the Treatment Period but not present at Baseline. For the age range, '1 month (m)-<12 years', the abnormality criteria were '>=500 milliseconds (ms)' (Abnormal (Abn) A). For age range, '>=12 years', the abnormality criteria were '>=500 ms' (Abn B) or '>=60 ms increase from Baseline' (Abn C). The abnormality in QT interval was observed at Week 0 as the participant was rolled over from SP0982 study and was constantly having abnormal ECG parameters while in SP0982 and EP0012. Safety Set was analyzed. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of ECG parameter (QT interval) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	216			
Units: percentage of participants				
number (not applicable)				
Abn C: Wk 0 (>=12 years) (n=3)	33.3			
Abn C: Wk 2 (>=12 years) (n=216)	0.5			
Abn C: Wk 14 (>=12 years) (n=209)	3.3			
Abn C: Wk 30 (>=12 years) (n=130)	0.8			
Abn B: Wk 46 (>=12 years) (n=188)	0.5			
Abn C: Wk 46 (>=12 years) (n=188)	2.7			
Abn C: Wk 62 (>=12 years) (n=186)	2.2			

Abn C: Wk 78 (>=12 years) (n=61)	1.6			
Abn C: Wk 94 (>=12 years) (n=162)	2.5			
Abn C: Wk 118 (>=12 years) (n=23)	13.0			
Abn C: Wk 142 (>=12 years) (n=58)	6.9			
Abn C: Wk 190 (>=12 years) (n=31)	3.2			
Abn C: Early TV (>=12 years) (n=52)	3.8			
Abn C: TV (>=12 years) (n=43)	2.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Albumin)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Albumin)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Albumin were those that were observed post- BL during the Treatment Period but not present at Baseline. For the age range, '>=1 year to <17 years', the abnormality criteria were '<24' g/L and '>84' g/L and for age range, '>=17 years', the abnormality criteria was '<26' g/L of serum albumin. The Safety Set included all study participants who received at least 1 dose of IMP during this study. No participant had TEMA value (Albumin) with markedly abnormal criteria specified at any visit.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	239			
Units: percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Total Protein)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in serum chemistry parameters (Total Protein)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA laboratory results of Total Protein were those that were observed post- BL during the Treatment Period but not present at Baseline. For the age range, '1 year to <17 years', the abnormality criteria were

'<43' g/L and '>120' g/L. For age range, '>=17 years', the abnormality criteria were '<43' g/L and '>130' g/L of serum protein. The Safety Set included all study participants who received at least 1 dose of IMP during this study. No participant had TEMA value (Total Protein) with markedly abnormal criteria specified at any visit.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	239			
Units: percentage of participants				
number (not applicable)	0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in 12-lead ECG parameter (QTc(F) interval)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in 12-lead ECG parameter (QTc(F) interval)

End point description:

TEMA values indicated significant deviations from expected range of age-appropriate values. TEMA ECG results of QTc(F) interval were those that are observed post- BL during Treatment Period but not present at BL. For age range '3 years -<12 years' and '>=12 years- <17 years', the abnormality criteria were from '>440 ms' (Abn A) and '>15% increase from BL value (Abn B). For age range, '>=17 years', the abnormality Criteria were '>450 ms' (Abn C), '>480 ms' (Abn D), '>500 ms' (Abn E) or '>=60 ms increase from BL value (Abn F). The abnormality in QTc(F) interval was observed at Week 0 as the participant was rolled over from SP0982 study and was constantly having abnormal ECG parameters while in SP0982 and EP0012. Safety Set was analyzed. N = participants who were evaluable for the assessment. 'n' = participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of QTc(F) interval observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	196			
Units: percentage of participants				
number (not applicable)				
Abn C: Wk 0 (>=17 y) (n=3)	33.3			
Abn D: Wk 0 (>=17 y) (n=3)	33.3			
Abn F: Wk 0 (>=17 y) (n=3)	33.3			

Abn C: Wk 2 (>=17 y) (n=196)	1.5			
Abn F: Wk 2 (>=17 y) (n=196)	1.0			
Abn A: Wk 14 (>=12 y-<17 y) (n=18)	5.6			
Abn C: Wk 14 (>=17 y) (n=191)	2.1			
Abn D: Wk 14 (>=17 y) (n=191)	1.0			
Abn E: Wk 14 (>=17 y) (n=191)	0.5			
Abn F: Wk 14 (>=17 y) (n=191)	3.7			
Abn F: Wk 30 (>=17 y) (n=118)	1.7			
Abn C: Wk 46 (>=17 y) (n=172)	5.2			
Abn D: Wk 46 (>=17 y) (n=172)	1.7			
Abn E: Wk 46 (>=17 y) (n=172)	1.2			
Abn F: Wk 46 (>=17 y) (n=172)	2.3			
Abn A: Wk 62 (>=12 y-<17 y) (n=16)	6.3			
Abn B: Wk 62 (>=12 y-<17 y) (n=16)	6.3			
Abn C: Wk 62 (>=17 y) (n=170)	2.4			
Abn D: Wk 62 (>=17 y) (n=170)	0.6			
Abn F: Wk 62 (>=17 y) (n=170)	1.8			
Abn F: Wk 78 (>=17 y) (n=56)	1.8			
Abn C: Wk 94 (>=17 y) (n=148)	2.7			
Abn D: Wk 94 (>=17 y) (n=148)	2.0			
Abn E: Wk 94 (>=17 y) (n=148)	2.0			
Abn F: Wk 94 (>=17 y) (n=148)	3.4			
Abn C: Wk 118 (>=17 y) (n=21)	9.5			
Abn F: Wk 118 (>=17 y) (n=21)	4.8			
Abn C: Wk 142 (>=17 y) (n=47)	2.1			
Abn F: Wk 142 (>=17 y) (n=47)	2.1			
Abn C: Early TV (>=17 y) (n=49)	6.1			
Abn D: Early TV (>=17 y) (n=49)	2.0			
Abn E: Early TV (>=17 y) (n=49)	2.0			
Abn F: Early TV (>=17 y) (n=49)	4.1			
Abn C: TV (>=17 y) (n=36)	2.8			
Abn F: TV (>=17 y) (n=36)	5.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in 12-lead ECG parameter (QTc(B) interval)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in 12-lead ECG parameter (QTc(B) interval)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA ECG results of QTc(B) interval were those that are observed post- BL during the Treatment Period but not present at BL. For the age range '3 years -<12 years' and '>=12 years- <17 years', the abnormality criteria were '>450 ms' (Abn A) and '>15% increase from BL' value (Abn B). For age range, '>=17 years', the abnormality criteria were '>450 ms' (Abn C), '>480 ms' (Abn D), '>500 ms' (Abn E) or '>=60 ms increase from BL' value (Abn F). The abnormality in QTc(B) interval was observed at Week 0 as the participant was rolled over from SP0982 study and was constantly having abnormal ECG parameters while in SP0982 and EP0012. Safety Set was analyzed. N= participants who were evaluable for the assessment. 'n'=participants who were evaluable at specified time points. Data for visits wherein

at least 1 TEMA value of QTc(B) interval observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	196			
Units: percentage of participants				
number (not applicable)				
Abn C: Wk 0 (>=17 y) (n=3)	33.3			
Abn D: Wk 0 (>=17 y) (n=3)	33.3			
Abn E: Wk 0 (>=17 y) (n=3)	33.3			
Abn F: Wk 0 (>=17 y) (n=3)	33.3			
Abn C: Wk 2 (>=17 y) (n=196)	3.6			
Abn F: Wk 2 (>=17 y) (n=196)	2.0			
Abn A: Wk 14 (>=12 y-<17 y) (n=18)	5.6			
Abn C: Wk 14 (>=17 y) (n=191)	5.8			
Abn D: Wk 14 (>=17 y) (n=191)	1.6			
Abn E: Wk 14 (>=17 y) (n=191)	1.0			
Abn F: Wk 14 (>=17 y) (n=191)	3.7			
Abn C: Wk 30 (>=17 y) (n=118)	2.5			
Abn F: Wk 30 (>=17 y) (n=118)	1.7			
Abn C: Wk 46 (>=17 y) (n=172)	7.0			
Abn D: Wk 46 (>=17 y) (n=172)	2.9			
Abn E: Wk 46 (>=17 y) (n=172)	1.2			
Abn F: Wk 46 (>=17 y) (n=172)	3.5			
Abn A: Wk 62 (>=12 y-<17 y) (n=16)	6.3			
Abn B: Wk 62 (>=12 y-<17 y) (n=16)	6.3			
Abn C: Wk 62 (>=17 y) (n=170)	2.4			
Abn D: Wk 62 (>=17 y) (n=170)	0.6			
Abn E: Wk 62 (>=17 y) (n=170)	0.6			
Abn F: Wk 62 (>=17 y) (n=170)	3.5			
Abn C: Wk 78 (>=17 y) (n=56)	5.4			
Abn F: Wk 78 (>=17 y) (n=56)	1.8			
Abn C: Wk 94 (>=17 y) (n=148)	5.4			
Abn D: Wk 94 (>=17 y) (n=148)	2.0			
Abn E: Wk 94 (>=17 y) (n=148)	2.0			
Abn F: Wk 94 (>=17 y) (n=148)	3.4			
Abn A: Wk 118 (>=12 y-<17 y) (n=2)	50.0			
Abn C: Wk 118 (>=17 y) (n=21)	14.3			
Abn D: Wk 118 (>=17 y) (n=21)	4.8			
Abn E: Wk 118 (>=17 y) (n=21)	4.8			
Abn F: Wk 118 (>=17 y) (n=21)	9.5			
Abn A: Wk 142 (>=12 y-<17 y) (n=11)	9.1			
Abn C: Wk 142 (>=17 y) (n=47)	8.5			
Abn F: Wk 142 (>=17 y) (n=47)	4.3			
Abn F: Wk 166 (>=17 y) (n=3)	33.3			

Abn C: Wk 190 (>=17 y) (n=26)	7.7			
Abn F: Wk 190 (>=17 y) (n=26)	3.8			
Abn C: Early TV (>=17 y) (n=49)	6.1			
Abn D: Early TV (>=17 y) (n=49)	2.0			
Abn E: Early TV (>=17 y) (n=49)	2.0			
Abn F: Early TV (>=17 y) (n=49)	6.1			
Abn C: TV (>=17 y) (n=36)	2.8			
Abn D: TV (>=17 y) (n=36)	2.8			
Abn F: TV (>=17 y) (n=36)	5.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in 12-lead ECG parameter (PR interval)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in 12-lead ECG parameter (PR interval)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA ECG results of PR interval were those that were observed post- BL during the Treatment Period but not present at BL. For the age range, '3 years -<12 years', the abnormality criteria were '>180 ms' (Abn A) and '>25% increase from BL value (Abn B). For the age range, '>=12 years - <17 years', the abnormality criteria were '>200 ms' (Abn C) and '>25% increase from BL value (Abn D). For age range, '>=17 years', the abnormality criteria were treatment-emergent values above '>200 ms' (Abn E), '>220 ms' (Abn F), or '>250 ms' (Abn G). Safety Set was analyzed. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of ECG parameter (PR interval) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	196			
Units: percentage of participants				
number (not applicable)				
Abn B: Wk 2 (3 y-<12 y) (n=16)	6.3			
Abn D: Wk 2 (>=12 y-<17 y) (n=20)	5.0			
Abn E: Wk 2 (>=17 y) (n=196)	1.5			
Abn F: Wk 2 (>=17 y) (n=196)	0.5			
Abn E: Wk 14 (>=17 y) (n=191)	1.0			
Abn E: Wk 30 (>=17 y) (n=117)	1.7			
Abn F: Wk 30 (>=17 y) (n=117)	0.9			
Abn C: Wk 46 (>=12 y-<17 y) (n=16)	6.3			
Abn E: Wk 46 (>=17 y) (n=172)	1.2			
Abn B: Wk 62 (3 y-<12 y) (n=10)	20.0			

Abn C: Wk 62 (>=12 y-<17 y) (n=16)	6.3			
Abn E: Wk 62 (>=17 y) (n=170)	2.9			
Abn F: Wk 62 (>=17 y) (n=170)	0.6			
Abn E: Wk 78 (>=17 y) (n=56)	5.4			
Abn F: Wk 78 (>=17 y) (n=56)	1.8			
Abn G: Wk 78 (>=17 y) (n=56)	1.8			
Abn B: Wk 94 (3 y-<12 y) (n=7)	28.6			
Abn C: Wk 94 (>=12 y-<17 y) (n=14)	7.1			
Abn E: Wk 94 (>=17 y) (n=148)	2.7			
Abn F: Wk 94 (>=17 y) (n=148)	0.7			
Abn G: Wk 94 (>=17 y) (n=148)	0.7			
Abn D: Wk 118 (>=12 y-<17 y) (n=2)	50.0			
Abn E: Wk 142 (>=17 y) (n=46)	8.7			
Abn F: Wk 142 (>=17 y) (n=46)	2.2			
Abn E: Early TV (>=17 y) (n=49)	2.0			
Abn F: Early TV (>=17 y) (n=49)	2.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in 12-lead ECG parameter (QRS interval)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in 12-lead ECG parameter (QRS interval)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA ECG results of QRS interval were those that were observed post- BL during the Treatment Period but not present at BL. For the age range, '3 years -<12 years', the abnormality criteria were '>100 ms' (Abn A) and '>25% increase from BL' value (Abn B). For the age range, '>=12 years - <17 years', the abnormality criteria were '>110 ms' (Abn C) and '>25% increase from BL' (Abn D). For age range, '>=17 years', the abnormality criteria were treatment-emergent values above '>100 ms' (Abn E), '>120 ms' (Abn F), or '>140 ms' (Abn G). Safety Set was analyzed. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of ECG parameter (QRS interval) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	196			
Units: percentage of participants				
number (not applicable)				
Abn E: Wk 2 (>=17 y) (n=196)	5.1			
Abn D: Wk 14 (>=12 y-<17 y) (n=18)	5.6			
Abn E: Wk 14 (>=17 y) (n=191)	9.9			

Abn F: Wk 14 (>=17 y) (n=191)	0.5			
Abn E: Wk 30 (>=17 y) (n=118)	7.6			
Abn A: Wk 46 (3 y-<12 y) (n=12)	8.3			
Abn D: Wk 46 (>=12 y-<17 y) (n=16)	6.3			
Abn E: Wk 46 (>=17 y) (n=172)	7.6			
Abn D: Wk 62 (>=12 y-<17 y) (n=16)	6.3			
Abn E: Wk 62 (>=17 y) (n=170)	10.6			
Abn F: Wk 62 (>=17 y) (n=170)	1.8			
Abn E: Wk 78 (>=17 y) (n=56)	8.9			
Abn F: Wk 78 (>=17 y) (n=56)	1.8			
Abn C: Wk 94 (>=12 y-<17 y) (n=14)	7.1			
Abn D: Wk 94 (>=12 y-<17 y) (n=14)	7.1			
Abn E: Wk 94 (>=17 y) (n=148)	6.1			
Abn F: Wk 94 (>=17 y) (n=148)	0.7			
Abn E: Wk 118 (>=17 y) (n=21)	14.3			
Abn E: Wk 142 (>=17 y) (n=47)	10.6			
Abn E: Early TV (>=17 y) (n=49)	10.2			
Abn E: TV (>=17 y) (n=36)	5.6			
Abn F: TV (>=17 y) (n=36)	5.6			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in 12-lead ECG parameter (Heart rate interval)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in 12-lead ECG parameter (Heart rate interval)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA ECG results of Heart rate interval were those that were observed post- BL during the Treatment Period but not present at Baseline. For the age range, '3 years -<12 years', the abnormality criteria were '<60 beats per minute (bpm)' (Abn A) and '>130 bpm' (Abn B). For the age range, '>=12 years', the abnormality criteria were '<50 bpm' (Abn C) and '>120 bpm' (Abn D). The Safety Set included all study participants who received at least 1 dose of IMP during this study. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of ECG parameter (Heart rate interval) observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	216			
Units: percentage of participants				
number (not applicable)				
Abn C: Wk 2 (>=12 y) (n=216)	1.4			

Abn C: Wk 14 (>=12 y) (n=209)	2.4			
Abn C: Wk 30 (>=12 y) (n=130)	1.5			
Abn C: Wk 46 (>=12 y) (n=188)	0.5			
Abn D: Wk 46 (>=12 y) (n=188)	0.5			
Abn C: Wk 62 (>=12 y) (n=186)	3.2			
Abn D: Wk 62 (>=12 y) (n=186)	0.5			
Abn C: Wk 78 (>=12 y) (n=61)	3.3			
Abn C: Wk 94 (>=12 y) (n=162)	1.2			
Abn C: Wk 118 (>=12 y) (n=23)	4.3			
Abn D: Wk 214 (>=12 y) (n=1)	100			
Abn D: TV (>=12 y) (n=43)	2.3			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in vital sign measurements (Pulse Rate)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in vital sign measurements (Pulse Rate)

End point description:

TEMA values of Pulse rate were those that were observed post- BL during Treatment Period but not present at BL. For age range, '3 years -<12 years', abnormality criteria were '<60 bpm' (Low) and '>130 bpm' (High). For age range, '12 years - <17 years', abnormality criteria were '<=50 bpm' (Low) and '>=120 bpm' (High). For age range, '>=17 years', abnormality criteria were '<=50 bpm and a decrease from BL of >=15 bpm' (Low A), '>=120 bpm and an increase from BL of >=15 bpm' (High A), '<60 bpm' (Low B) and '>100 bpm' (High B). Pulse rate was reported as per positions such as 'Supine 3 minute (Sup 3 min)', 'Standing 1 minute' (Std 1 min), and 'Standing 3 minute' (Std 3 min). Safety Set was analyzed. N= participants who were evaluable for assessment. 'n'=participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of Pulse rate observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	199			
Units: percentage of participants				
number (not applicable)				
Low B: Wk 2 (>=17 y)-Sup 3 min (n=199)	4.5			
High B: Wk 2 (>=17 y)- Sup 3 min (n=199)	0.5			
High: Wk 2 (>=12 y-<17 y)-Std 1 min (n=20)	5.0			
Low B: Wk 2 (>=17 y)-Std 1 min (n=197)	2.5			

High B: Wk 2 (>=17 y)-Std 1 min (n=197)	3.0			
Low B: Wk 2 (>=17 y)-Std 3 min (n=196)	1.5			
High B: Wk 2 (>=17 y)-Std 3 min (n=196)	2.6			
Low A: Wk 6 (>=17 y)-Sup 3 min (n=196)	0.5			
Low B: Wk 6 (>=17 y)-Sup 3 min (n=196)	4.6			
High B: Wk 6 (>=17 y)-Sup 3 min (n=196)	2.0			
High: Wk 6 (>=12 y-<17 y)- Std 1 min (n=21)	4.8			
Low B: Wk 6 (>=17 y)- Std 1 min (n=196)	1.5			
High B: Wk 6 (>=17 y)- Std 1 min (n=196)	3.1			
Low A: Wk 6 (>=17 y)- Std 3 min (n=196)	0.5			
Low B: Wk 6 (>=17 y)- Std 3 min (n=196)	1.0			
High B: Wk 6 (>=17 y)- Std 3 min (n=196)	2.6			
Low B: Wk 14 (>=17 y)- Sup 3 min (n=196)	4.1			
High B: Wk 14 (>=17 y)- Sup 3 min (n=196)	1.0			
High: Wk 14 (>=12 y-<17 y)- Std 1 min (n=18)	5.6			
Low B: Wk 14 (>=17 y)- Std 1 min (n=195)	3.1			
High B: Wk 14 (>=17 y)- Std 1 min (n=195)	2.6			
Low B: Wk 14 (>=17 y)- Std 3 min (n=195)	0.5			
High B: Wk 14 (>=17 y)- Std 3 min (n=195)	4.1			
Low B: Wk 22 (>=17 y)- Sup 3 min (n=189)	3.2			
High B: Wk 22 (>=17 y)- Sup 3 min (n=189)	0.5			
High A: Wk 22 (>=17 y)- Std 1 min (n=189)	0.5			
Low B: Wk 22 (>=17 y)- Std 1 min (n=189)	1.6			
High B: Wk 22 (>=17 y)- Std 1 min (n=189)	4.2			
Low B: Wk 22 (>=17 y)- Std 3 min (n=189)	2.1			
High B: Wk 22 (>=17 y)- Std 3 min (n=189)	3.7			
Low B: Wk 30 (>=17 y)- Sup 3 min (n=119)	1.7			
Low B: Wk 30 (>=17 y)- Std 1 min (n=119)	5.0			
High B: Wk 30 (>=17 y)- Std 1 min (n=119)	3.4			
Low B: Wk 30 (>=17 y)- Std 3 min (n=119)	2.5			
High B: Wk 30 (>=17 y)- Std 3 min (n=119)	1.7			

Low B: Wk 38 (>=17 y)- Sup 3 min (n=108)	3.7			
Low B: Wk 38 (>=17 y)- Std 1 min (n=107)	2.8			
High B: Wk 38 (>=17 y)- Std 1 min (n=107)	5.6			
Low B: Wk 38 (>=17 y)- Std 3 min (n=107)	0.9			
High B: Wk 38 (>=17 y)- Std 3 min (n=107)	2.8			
Low B: Wk 46 (>=17 y)- Sup 3 min (n=174)	5.7			
High B: Wk 46 (>=17 y)- Sup 3 min (n=174)	1.7			
Low A: Wk 46 (>=17 y)- Std 1 min (n=174)	0.6			
High A: Wk 46 (>=17 y)- Std 1 min (n=174)	1.1			
Low B: Wk 46 (>=17 y)- Std 1 min (n=174)	4.0			
High B: Wk 46 (>=17 y)- Std 1 min (n=174)	5.2			
Low B: Wk 46 (>=17 y)- Std 3 min (n=174)	2.9			
High B: Wk 46 (>=17 y)- Std 3 min (n=174)	4.6			
Low B: Wk 62 (>=17 y)- Sup 3 min (n=173)	5.2			
High B: Wk 62 (>=17 y)- Sup 3 min (n=173)	2.3			
Low: Wk 62 (>=12 y-<17 y)- Std 1 min (n=16)	6.3			
High A: Wk 62 (>=17 y)- Std 1 min (n=173)	0.6			
Low B: Wk 62 (>=17 y)- Std 1 min (n=173)	4.6			
High B: Wk 62 (>=17 y)- Std 1 min (n=173)	4.0			
High A: Wk 62 (>=17 y)- Std 3 min (n=173)	0.6			
Low B: Wk 62 (>=17 y)- Std 3 min (n=173)	2.3			
High B: Wk 62 (>=17 y)- Std 3 min (n=173)	2.9			
Low B: Wk 78 (>=17 y)- Sup 3 min (n=60)	6.7			
High B: Wk 78 (>=17 y)- Sup 3 min (n=60)	1.7			
Low B: Wk 78 (>=17 y)- Std 1 min (n=60)	6.7			
High B: Wk 78 (>=17 y)- Std 1 min (n=60)	6.7			
Low B: Wk 78 (>=17 y)- Std 3 min (n=60)	6.7			
High B: Wk 78 (>=17 y)- Std 3 min (n=60)	5.0			
Low B: Wk 94 (>=17 y)- Sup 3 min (n=148)	6.1			
High B: Wk 94 (>=17 y)- Sup 3 min (n=148)	0.7			
Low B: Wk 94 (>=17 y)- Std 1 min (n=148)	2.7			

High B: Wk 94 (>=17 y)- Std 1 min (n=148)	4.1			
Low B: Wk 94 (>=17 y)- Std 3 min (n=148)	1.4			
High B: Wk 94 (>=17 y)- Std 3 min (n=148)	2.7			
Low B: Wk 118 (>=17 y)- Sup 3 min (n=92)	2.2			
High B: Wk 118 (>=17 y)- Sup 3 min (n=92)	2.2			
Low B: Wk 118 (>=17 y)- Std 1 min (n=90)	2.2			
High B: Wk 118 (>=17 y)- Std 1 min (n=90)	3.3			
Low B: Wk 118 (>=17 y)- Std 3 min (n=90)	2.2			
High B: Wk 118 (>=17 y)- Std 3 min (n=90)	4.4			
High A: Wk 142 (>=17 y)- Sup 3 min (n=63)	1.6			
Low B: Wk 142 (>=17 y)- Sup 3 min (n=63)	6.3			
High B: Wk 142 (>=17 y)- Sup 3 min (n=63)	4.8			
High A: Wk 142 (>=17 y)- Std 1 min (n=63)	3.2			
High B: Wk 142 (>=17 y)- Std 1 min (n=63)	7.9			
High A: Wk 142 (>=17 y)- Std 3 min (n=63)	1.6			
Low B: Wk 142 (>=17 y)- Std 3 min (n=63)	3.2			
High B: Wk 142 (>=17 y)- Std 3 min (n=63)	7.9			
Low B: Wk 166 (>=17 y)- Sup 3 min (n=52)	3.8			
High B: Wk 166 (>=17 y)- Sup 3 min (n=52)	1.9			
Low B: Wk 166 (>=17 y)- Std 1 min (n=51)	2.0			
High B: Wk 166 (>=17 y)- Std 1 min (n=51)	5.9			
High B: Wk 166 (>=17 y)- Std 3 min (n=51)	5.9			
Low B: Wk 190 (>=17 y)- Sup 3 min (n=34)	2.9			
High B: Wk 190 (>=17 y)- Sup 3 min (n=34)	8.8			
High B: Wk 190 (>=17 y)- Std 1 min (n=34)	11.8			
High B: Wk 190 (>=17 y)- Std 3 min (n=34)	17.6			
High B: Wk 214 (>=17 y)- Sup 3 min (n=17)	5.9			
High B: Wk 214 (>=17 y)- Std 1 min (n=17)	5.9			
High B: Wk 214 (>=17 y)- Std 3 min (n=17)	5.9			
Low B: Early TV (>=17 y)- Sup 3 min (n=55)	3.6			
High B: Early TV (>=17 y)- Sup 3 min (n=55)	1.8			

High: Early TV (>=12 y-<17 y)- Std 1 min (n=3)	33.3			
Low B: Early TV (>=17 y)- Std 1 min (n=55)	3.6			
High B: Early TV (>=17 y)- Std 1 min (n=55)	5.5			
Low A: TV (>=17 years)- Sup 3 min (n=50)	2.0			
Low B: TV (>=17 years)- Sup 3 min (n=50)	4.0			
High B: TV (>=17 years)- Sup 3 min (n=50)	2.0			
Low B: TV (>=17 years)- Std 1 min (n=50)	2.0			
High B: TV (>=17 years)- Std 1 min (n=50)	4.0			
Low B: TV (>=17 years)- Std 3 min (n=50)	2.0			
High B: TV (>=17 years)- Std 3 min (n=50)	2.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in vital sign measurements (Systolic Blood Pressure)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in vital sign measurements (Systolic Blood Pressure)

End point description:

TEMA values of Systolic Blood Pressure (BP) results were those that were observed post- BL during the Treatment Period but not present at BL. For age range, '3 years -<12 years', abnormality criteria were '<80 millimeters of mercury (mmHg)' (Low) and '>140 mmHg' (High). For age range, '>=12 years - <17 years', abnormality criteria were '<90 mmHg' (Low) and '>160 mmHg' (High). For age range, '>=17 years', abnormality criteria were '<=90 mmHg and decrease from BL of >=20 mmHg' (Low A), '>=180 mmHg and increase from BL of >=20' mmHg (High A), '<90 mmHg' (Low B), '>140 mmHg (High B), and '>160 mmHg' (High C). Systolic BP were reported as per positions such as 'Sup 3 min', 'Std 1 min, and 'Std 3 min'. Safety Set was analyzed. N= participants who were evaluable for assessment. 'n'= signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of Systolic BP observed during study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	199			
Units: percentage of participants				
number (not applicable)				
High B: Wk 2 (>=17 y)- Sup 3 min (n=199)	3.5			

Low B: Wk 2 (>=17 y)- Std 1 min (n=197)	1.0			
High B: Wk 2 (>=17 y)- Std 1 min (n=197)	2.5			
High B: Wk 2 (>=17 y)- Std 3 min (n=196)	3.6			
High B: Wk 6 (>=17 y)- Sup 3 min (n=196)	3.1			
High B: Wk 6 (>=17 y)- Std 1 min (n=196)	2.0			
Low B: Wk 6 (>=17 y)- Std 3 min (n=196)	0.5			
High B: Wk 6 (>=17 y)- Std 3 min (n=196)	3.6			
Low B: Wk 14 (>=17 y)- Sup 3 min (n=196)	0.5			
High B: Wk 14 (>=17 y)- Sup 3 min (n=196)	3.1			
High B: Wk 14 (>=17 y)- Std 1 min (n=195)	3.6			
High B: Wk 14 (>=17 y)- Std 3 min (n=195)	3.6			
High B: Wk 22 (>=17 y)- Sup 3 min (n=189)	4.2			
High B: Wk 22 (>=17 y)- Std 1 min (n=189)	4.2			
High B: Wk 22 (>=17 y)- Std 3 min (n=189)	3.7			
Low B: Wk 30 (>=17 y)- Sup 3 min (n=119)	0.8			
High B: Wk 30 (>=17 y)- Sup 3 min (n=119)	5.9			
High B: Wk 30 (>=17 y)- Std 1 min (n=119)	2.5			
High B: Wk 30 (>=17 y)- Std 3 min (n=119)	5.0			
Low B: Wk 38 (>=17 y)- Sup 3 min (n=108)	0.9			
High B: Wk 38 (>=17 y)- Sup 3 min (n=108)	2.8			
Low B: Wk 38 (>=17 y)- Std 1 min (n=107)	0.9			
High B: Wk 38 (>=17 y)- Std 1 min (n=107)	2.8			
High B: Wk 38 (>=17 y)- Std 3 min (n=107)	3.7			
Low: Wk 46 (>=12 y-<17 y)- Sup 3 min (n=16)	6.3			
High B: Wk 46 (>=17 y)- Sup 3 min (n=174)	2.9			
Low: Wk 46 (>=12 y-<17 y)- Std 1 min (n=16)	6.3			
High B: Wk 46 (>=17 y)- Std 1 min (n=174)	2.3			
Low: Wk 46 (>=12 y-<17 y)- Std 3 min (n=16)	6.3			
High B: Wk 46 (>=17 y)- Std 3 min (n=174)	3.4			
High C: Wk 46 (>=17 y)- Std 3 min (n=174)	0.6			
Low B: Wk 62 (>=17 y)- Sup 3 min (n=173)	0.6			

High B: Wk 62 (>=17 y)- Sup 3 min (n=173)	3.5			
Low: Wk 62 (>=12 y-<17 y)- Std 1 min (n=16)	6.3			
Low A: Wk 62 (>=17 y)- Std 1 min (n=173)	0.6			
Low B: Wk 62 (>=17 y)- Std 1 min (n=173)	0.6			
High B: Wk 62 (>=17 y)- Std 1 min (n=173)	2.3			
Low A: Wk 62 (>=17 y)- Std 3 min (n=173)	0.6			
Low B: Wk 62 (>=17 y)- Std 3 min (n=173)	1.7			
High B: Wk 62 (>=17 y)- Std 3 min (n=173)	1.2			
Low A: Wk 78 (>=17 y)- Sup 3 min (n=60)	1.7			
High B: Wk 78 (>=17 y)- Sup 3 min (n=60)	1.7			
High B: Wk 78 (>=17 y)- Std 1 min (n=60)	1.7			
High B: Wk 78 (>=17 y)- Std 3 min (n=60)	1.7			
High B: Wk 94 (>=17 y)- Sup 3 min (n=148)	4.1			
High B: Wk 94 (>=17 y)- Std 1 min (n=148)	4.1			
High B: Wk 94 (>=17 y)- Std 3 min (n=148)	4.1			
High B: Wk 118 (>=17 y)- Sup 3 min (n=92)	5.4			
High C: Wk 118 (>=17 y)- Sup 3 min (n=92)	1.1			
High B: Wk 118 (>=17 y)- Std 1 min (n=91)	5.5			
High C: Wk 118 (>=17 y)- Std 1 min (n=91)	1.1			
High B: Wk 118 (>=17 y)- Std 3 min (n=91)	6.6			
High C: Wk 118 (>=17 y)- Std 3 min (n=91)	1.1			
High B: Wk 142 (>=17 y)- Sup 3 min (n=63)	6.3			
High B: Wk 142 (>=17 y)- Std 1 min (n=63)	6.3			
High B: Wk 142 (>=17 y)- Std 3 min (n=63)	6.3			
High B: Wk 166 (>=17 y)- Sup 3 min (n=52)	3.8			
High B: Wk 166 (>=17 y)- Std 1 min (n=51)	7.8			
High B: Wk 166 (>=17 y)- Std 3 min (n=51)	7.8			
High B: Wk 190 (>=17 y)- Sup 3 min (n=34)	2.9			
High B: Wk 214 (>=17 y)- Std 1 min (n=17)	5.9			
High C: Wk 214 (>=17 y)- Std 1 min (n=17)	5.9			
High B: Wk 214 (>=17 y)- Std 3 min (n=17)	5.9			

High B: Wk 262 (>=17 y)- Std 3 min (n=1)	100			
High B: Early TV (>=17 y)- Sup 3 min (n=55)	1.8			
High B: Early TV (>=17 y)- Std 1 min (n=55)	1.8			
High B: TV (>=17 y)- Std 1 min (n=50)	4.0			
High B: TV (>=17 y)- Std 3 min (n=50)	2.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in vital sign measurements (Diastolic Blood Pressure)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in vital sign measurements (Diastolic Blood Pressure)

End point description:

TEMA values of Diastolic BP results were those that are observed post- BL during the Treatment Period but not present at BL. For the age range, '3 years -<12 years', the abnormality criteria were '<50 mmHg' (Low) and '>80 mmHg' (High), '>=12 years - <17 years', the abnormality criteria were '<=50 mmHg' (Low) and '>=105 mmHg' (High), and '>=17 years', the abnormality criteria were '<=50 mmHg and decrease from BL of >=15 mmHg' (Low A), '>=105 mmHg and increase from BL of >=15' mmHg (High A), '<50 mmHg' (Low B), '>90 mmHg' (High B), and '>100 mmHg' (High C). Diastolic BP were reported as per positions such as 'Sup 3 min', 'Std 1 min, and 'Std 3 min'. Safety Set was analyzed. Number of participants analyzed included those participants who were evaluable for the assessment. 'n' signifies participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA value of Diastolic BP observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	199			
Units: percentage of participants				
number (not applicable)				
Low: Wk 2 (3 y-<12 y)- Sup 3 min (n=16)	6.3			
Low B: Wk 2 (>=17 y)- Sup 3 min (n=199)	0.5			
High B: Wk 2 (>=17 y)- Sup 3 min (n=199)	2.5			
Low: Wk 2 (3 y-<12 y)- Std 1 min (n=16)	6.3			
High: Wk 2 (3 y-<12 y)- Std 1 min (n=16)	6.3			
High B: Wk 2 (>=17 y)- Std 1 min (n=197)	5.1			
High C: Wk 2 (>=17 y)- Std 1 min (n=197)	0.5			

Low: Wk 2 (3 y-<12 y)- Std 3 min (n=16)	6.3			
High: Wk 2 (3 y-<12 y)- Std 3 min (n=16)	12.5			
High B: Wk 2 (>=17 y)- Std 3 min (n=196)	6.1			
High C: Wk 2 (>=17 y)- Std 3 min (n=196)	0.5			
Low A: Wk 6 (>=17 y)- Sup 3 min (n=196)	0.5			
High B: Wk 6 (>=17 y)- Sup 3 min (n=196)	4.6			
High C: Wk 6 (>=17 y)- Sup 3 min (n=196)	0.5			
Low A: Wk 6 (>=17 y)- Std 1 min (n=196)	0.5			
High A: Wk 6 (>=17 y)- Std 1 min (n=196)	0.5			
High B: Wk 6 (>=17 y)- Std 1 min (n=196)	4.1			
High C: Wk 6 (>=17 y)- Std 1 min (n=196)	0.5			
High: Wk 6 (3 y-<12 y)- Std 3 min (n=14)	7.1			
Low A: Wk 6 (>=17 y)- Std 3 min (n=196)	0.5			
Low B: Wk 6 (>=17 y)- Std 3 min (n=196)	0.5			
High B: Wk 6 (>=17 y)- Std 3 min (n=196)	6.6			
High C: Wk 6 (>=17 y)- Std 3 min (n=196)	0.5			
High: Wk 14 (3 y-<12 y)- Sup 3 min (n=13)	7.7			
High B: Wk 14 (>=17 y)- Sup 3 min (n=196)	2.0			
High C: Wk 14 (>=17 y)- Sup 3 min (n=196)	0.5			
High A: Wk 14 (>=17 y)- Std 1 min (n=195)	0.5			
High B: Wk 14 (>=17 y)- Std 1 min (n=195)	3.1			
High C: Wk 14 (>=17 y)- Std 1 min (n=195)	1.0			
High: Wk 14 (3 y-<12 y)- Std 3 min (n=12)	8.3			
High B: Wk 14 (>=17 y)- Std 3 min (n=195)	4.6			
High C: Wk 14 (>=17 y)- Std 3 min (n=195)	0.5			
High: Wk 22 (3 y-<12 y)- Sup 3 min (n=13)	15.4			
Low: Wk 22 (>=12 y-<17 y)- Sup 3 min (n=16)	6.3			
High B: Wk 22 (>=17 y)- Sup 3 min (n=189)	1.6			
High C: Wk 22 (>=17 y)- Sup 3 min (n=189)	0.5			
High: Wk 22 (3 y-<12 y)- Std 1 min (n=13)	15.4			
Low A: Wk 22 (>=17 y)- Std 1 min (n=189)	1.1			

Low B: Wk 22 (>=17 y)- Std 1 min (n=189)	0.5			
High B: Wk 22 (>=17 y)- Std 1 min (n=189)	7.9			
High C: Wk 22 (>=17 y)- Std 1 min (n=189)	0.5			
High: Wk 22 (3 y-<12 y)- Std 3 min (n=13)	7.7			
Low A: Wk 22 (>=17 y)- Std 3 min (n=189)	0.5			
High B: Wk 22 (>=17 y)- Std 3 min (n=189)	6.3			
High C: Wk 22 (>=17 y)- Std 3 min (n=189)	1.1			
High B: Wk 30 (>=17 y)- Sup 3 min (n=119)	3.4			
High C: Wk 30 (>=17 y)- Sup 3 min (n=119)	0.8			
High: Wk 30 (3 y-<12 y)- Std 1 min (n=7)	14.3			
High A: Wk 30 (>=17 y)- Std 1 min (n=119)	0.8			
High B: Wk 30 (>=17 y)- Std 1 min (n=119)	5.9			
High C: Wk 30 (>=17 y)- Std 1 min (n=119)	0.8			
High B: Wk 30 (>=17 y)- Std 3 min (n=119)	4.2			
High B: Wk 38 (>=17 y)- Sup 3 min (n=108)	2.8			
High: Wk 38 (3 y-<12 y)- Std 1 min (n=5)	20.0			
High B: Wk 38 (>=17 y)- Std 1 min (n=107)	5.6			
High C: Wk 38 (>=17 y)- Std 1 min (n=107)	0.9			
High B: Wk 38 (>=17 y)- Std 3 min (n=107)	9.3			
Low A: Wk 46 (>=17 y)- Sup 3 min (n=174)	0.6			
High B: Wk 46 (>=17 y)- Sup 3 min (n=174)	4.0			
Low: Wk 46 (>=12 y-<17 y)- Std 1 min (n=16)	6.3			
High B: Wk 46 (>=17 y)- Std 1 min (n=174)	8.0			
High C: Wk 46 (>=17 y)- Std 1 min (n=174)	0.6			
High B: Wk 46 (>=17 y)- Std 3 min (n=174)	9.8			
High C: Wk 46 (>=17 y)- Std 3 min (n=174)	1.1			
High A: Wk 62 (>=17 y)- Sup 3 min (n=173)	0.6			
High B: Wk 62 (>=17 y)- Sup 3 min (n=173)	5.2			
High C: Wk 62 (>=17 y)- Sup 3 min (n=173)	1.2			
High: Wk 62 (3 y-<12 y)- Std 1 min (n=10)	20.0			
Low: Wk 62 (>=12 y-<17 y)- Std 1 min (n=16)	6.3			

High A: Wk 62 (>=17 y)- Std 1 min (n=173)	0.6			
High B: Wk 62 (>=17 y)- Std 1 min (n=173)	5.8			
High C: Wk 62 (>=17 y)- Std 1 min (n=173)	1.2			
Low B: Wk 62 (>=17 y)- Std 3 min (n=173)	0.6			
High B: Wk 62 (>=17 y)- Std 3 min (n=173)	5.8			
High C: Wk 62 (>=17 y)- Std 3 min (n=173)	0.6			
Low: Wk 78 (>=12 y-<17 y)- Sup 3 min (n=6)	16.7			
High B: Wk 78 (>=17 y)- Sup 3 min (n=60)	1.7			
High B: Wk 78 (>=17 y)- Std 1 min (n=60)	3.3			
High B: Wk 78 (>=17 y)- Std 3 min (n=60)	3.3			
High C: Wk 78 (>=17 y)- Std 3 min (n=60)	1.7			
High B: Wk 94 (>=17 y)- Sup 3 min (n=148)	1.4			
High B: Wk 94 (>=17 y)- Std 1 min (n=148)	4.1			
High: Wk 94 (3 y-<12 y)- Std 3 min (n=7)	14.3			
High A: Wk 94 (>=17 y)- Std 3 min (n=148)	0.7			
High B: Wk 94 (>=17 y)- Std 3 min (n=148)	4.7			
High C: Wk 94 (>=17 y)- Std 3 min (n=148)	0.7			
Low A: Wk 118 (>=17 y)- Sup 3 min (n=92)	1.1			
High A: Wk 118 (>=17 y)- Sup 3 min (n=92)	1.1			
Low B: Wk 118 (>=17 y)- Sup 3 min (n=92)	1.1			
High B: Wk 118 (>=17 y)- Sup 3 min (n=92)	2.2			
High C: Wk 118 (>=17 y)- Sup 3 min (n=92)	1.1			
Low A: Wk 118 (>=17 y)- Std 1 min (n=91)	1.1			
Low B: Wk 118 (>=17 y)- Std 1 min (n=91)	1.1			
High B: Wk 118 (>=17 y)- Std 1 min (n=91)	4.4			
High B: Wk 118 (>=17 y)- Std 3 min (n=91)	7.7			
High B: Wk 142 (>=17 y)- Sup 3 min (n=63)	6.3			
High B: Wk 142 (>=17 y)- Std 1 min (n=63)	7.9			
High B: Wk 142 (>=17 y)- Std 3 min (n=63)	7.9			
High B: Wk 166 (>=17 y)- Sup 3 min (n=52)	3.8			
High B: Wk 166 (>=17 y)- Std 1 min (n=51)	5.9			

High A: Wk 166 (>=17 y)- Std 3 min (n=51)	2.0			
High B: Wk 166 (>=17 y)- Std 3 min (n=51)	11.8			
High C: Wk 166 (>=17 y)- Std 3 min (n=51)	2.0			
High B: Wk 190 (>=17 y)- Std 3 min (n=34)	2.9			
High B: Wk 214 (>=17 y)- Sup 3 min (n=17)	5.9			
High A: Wk 214 (>=17 y)- Std 1 min (n=17)	5.9			
High B: Wk 214 (>=17 y)- Std 1 min (n=17)	5.9			
High C: Wk 214 (>=17 y)- Std 1 min (n=17)	5.9			
High A: Wk 214 (>=17 y)- Std 3 min (n=17)	5.9			
High B: Wk 214 (>=17 y)- Std 3 min (n=17)	5.9			
High C: Wk 214 (>=17 y)- Std 3 min (n=17)	5.9			
High B: Early TV (>=17 y)- Sup 3 min (n=55)	3.6			
High C: Early TV (>=17 y)- Sup 3 min (n=55)	1.8			
High B: Early TV (>=17 y)- Std 1 min (n=55)	9.1			
High C: Early TV (>=17 y)- Std 1 min (n=55)	1.8			
High A: Early TV (>=17 y)- Std 3 min (n=55)	1.8			
High B: Early TV (>=17 y)- Std 3 min (n=55)	10.9			
High C: Early TV (>=17 y)- Std 3 min (n=55)	3.6			
High: TV (3 y-<12 y)- Sup 3 min (n=6)	16.7			
High B: TV (>=17 y)- Sup 3 min (n=50)	4.0			
High B: TV (>=17 y)- Std 1 min (n=50)	2.0			
High B: TV (>=17 y)- Std 3 min (n=50)	4.0			
High C: TV (>=17 y)- Std 3 min (n=50)	2.0			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in vital sign measurements (Body Weight)

End point title	Percentage of study participants with treatment-emergent marked abnormalities (TEMAs) in vital sign measurements (Body Weight)

End point description:

TEMA values indicated significant deviations from the expected range of age-appropriate values. TEMA vital signs parameter results were those that are observed post- BL during the Treatment Period but not present at Baseline. For the age range, '1 month - <17 years', the abnormality criteria were '<3% of normal body weight' in Kilograms (kg) or '>97% of normal body weight' in kgs. Here, '<3% of normal' is presented as 'Low' and '>97% of normal' is presented as 'High'. For the age range '>=17 years', the

abnormality criteria were 'Increase/decrease of >=10%' body weight in kgs (presented as Inc/Dec A) or 'Increase/decrease of >=7%' body weight in kgs (presented as Inc/Dec B). Safety Set was analyzed. N= participants who were evaluable for the assessment. 'n'= participants who were evaluable at specified time points. Data for visits wherein at least 1 TEMA body weight value observed during the study were reported in this assessment.

End point type	Secondary

End point timeframe:

During the study (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	195			
Units: percentage of participants				
number (not applicable)				
High- Wk 14 (1 m - <17 y) (n=31)	9.7			
Inc/Dec A- Wk 14 (>=17 y) (n=195)	5.6			
Inc/Dec B- Wk 14 (>=17 y) (n=195)	16.4			
High- Wk 30 (1 m - <17 y) (n=19)	10.5			
Inc/Dec A- Wk 30 (>=17 y) (n=119)	5.9			
Inc/Dec B- Wk 30 (>=17 y) (n=119)	19.3			
High- Wk 46 (1 m - <17 y) (n=28)	7.1			
Inc/Dec A- Wk 46 (>=17 y) (n=177)	12.4			
Inc/Dec B- Wk 46 (>=17 y) (n=177)	22.6			
High- Wk 62 (1 m - <17 y) (n=26)	7.7			
Inc/Dec A- Wk 62 (>=17 y) (n=174)	14.9			
Inc/Dec B- Wk 62 (>=17 y) (n=174)	21.8			
Inc/Dec A- Wk 78 (>=17 y) (n=63)	19.0			
Inc/Dec B- Wk 78 (>=17 y) (n=63)	30.2			
High- Wk 94 (1 m - <17 y) (n=23)	13.0			
Inc/Dec A- Wk 94 (>=17 y) (n=152)	16.4			
Inc/Dec B- Wk 94 (>=17 y) (n=152)	30.9			
Low- Wk 118 (1 m - <17 y) (n=19)	5.3			
High- Wk 118 (1 m - <17 y) (n=19)	10.5			
Inc/Dec A- Wk 118 (>=17 y) (n=97)	21.6			
Inc/Dec B- Wk 118 (>=17 y) (n=97)	33.0			
Low- Wk 142 (1 m - <17 y) (n=13)	7.7			
High- Wk 142 (1 m - <17 y) (n=13)	7.7			
Inc/Dec A- Wk 142 (>=17 y) (n=77)	19.5			
Inc/Dec B- Wk 142 (>=17 y) (n=77)	32.5			
High- Wk 166 (1 m - <17 y) (n=10)	10.0			
Inc/Dec A- Wk 166 (>=17 y) (n=60)	25.0			
Inc/Dec B- Wk 166 (>=17 y) (n=60)	45.0			
Low- Wk 190 (1 m - <17 y) (n=6)	16.7			
Inc/Dec A- Wk 190 (>=17 y) (n=46)	26.1			
Inc/Dec B- Wk 190 (>=17 y) (n=46)	50.0			
Low- Wk 214 (1 m - <17 y) (n=2)	50.0			
Inc/Dec A- Wk 214 (>=17 y) (n=22)	31.8			
Inc/Dec B- Wk 214 (>=17 y) (n=22)	54.5			
Inc/Dec A- Wk 238 (>=17 y) (n=6)	16.7			

Inc/Dec B- Wk 238 (>=17 y) (n=6)	50.0			
Inc/Dec A- Wk 262 (>=17 y) (n=3)	33.3			
Inc/Dec B- Wk 262 (>=17 y) (n=3)	33.3			
Inc/Dec A- Early TV (>=17 y) (n=57)	26.3			
Inc/Dec B- Early TV (>=17 y) (n=57)	33.3			
High- TV (1 m - <17 y) (n=14)	21.4			
Inc/Dec A- TV (>=17 y) (n=55)	34.5			
Inc/Dec B- TV (>=17 y) (n=55)	52.7			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in Primary Generalized Tonic-clonic seizure (PGTCS) frequency per 28 days from Combined Baseline

End point title	Percent change in Primary Generalized Tonic-clonic seizure (PGTCS) frequency per 28 days from Combined Baseline

End point description:

The 28-day PGTCS frequency during the relative period was subtracted from the 28-day Combined Baseline PGTCS frequency and the result was divided by 28-day Combined Baseline PGTCS frequency and the result was then multiplied by 100 to get percent change in PGTCS frequency per 28 days from Combined Baseline Period (CB) to the appropriate analysis Period. The CB was defined as the combined 12-week Historical Baseline and 4-week Prospective Baseline periods immediately prior to randomization in the study SP0982 or prior to Visit 1 (first dose) if direct enrollers in EP0012. Full Analysis Set (FAS) was a subset of the Safety Set and included all study participants with seizure diary data for at least 1 day during this study.

End point type	Secondary

End point timeframe:

From Combined Baseline until end of Treatment Period (up to approximately 5 years)

End point values	All participants (lacosamide)			
Subject group type	Reporting group			
Number of subjects analysed	238			
Units: percent change				
median (full range (min-max))	-88.58 (-100.0 to 465.4)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

From Visit 1 (Week 0) to End of Treatment Period (up to approximately 5 years)

Adverse event reporting additional description:

AEs were treatment-emergent if event had onset on or after date of first study medication dose in EP0012 and within 30 days following last study medication dose or events whose intensity worsened on or after date of first study medication dose and within 30 days following date of last study medication administration. TEAEs were assessed on SS.

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	All participants (lacosamide)

Reporting group description:

Participants included in this treatment group received at least one dose of LCM as EP0012 protocol entry criteria. The dose range for pediatric participants weighing <50 kg is from 4 mg/kg/day (oral solution) to 12 mg/kg/day (oral solution), for pediatric participants weighing ≥50 kg, the dose range is from 200 mg/day (tablets) to 600 mg/day (tablets) and for adult participants, the dose range is from 200 mg/day to 800mg/day (tablets) during the Treatment Period. The LCM dose may be increased or decreased at the investigator's discretion after the study participant received the first dose of LCM in the study. Pediatric participants who initially started on oral solution might have transferred to tablets at Investigator's discretion after achieving >=50 kgs. LCM was administered orally, twice daily (bid), up to approximately 5 years. Treatment was continued for at least 2 years for adult participants and up to approximately 5 years for pediatric participants.

Serious adverse events	All participants (lacosamide)		
Total subjects affected by serious adverse events			
subjects affected / exposed	54 / 239 (22.59%)		
number of deaths (all causes)	4		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Bladder cancer			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Uterine leiomyoma			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			

Peripheral ischaemia			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Non-cardiac chest pain			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Death			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Drowning			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Respiratory, thoracic and mediastinal disorders			
Pneumonia aspiration			
subjects affected / exposed	2 / 239 (0.84%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Acute respiratory failure			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory failure			

subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Suicide attempt			
subjects affected / exposed	2 / 239 (0.84%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Mental status changes			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychogenic seizure			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Completed suicide			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Investigations			
Drug level increased			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Weight decreased			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Head injury			
subjects affected / exposed	2 / 239 (0.84%)		
occurrences causally related to treatment / all	0 / 4		
deaths causally related to treatment / all	0 / 0		

Facial bones fracture				
subjects affected / exposed	2 / 239 (0.84%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	2 / 239 (0.84%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Animal bite				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Ankle fracture				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Clavicle fracture				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Epidural haemorrhage				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Face injury				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fall				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fibula fracture				

subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Fracture				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hand fracture				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intentional overdose				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lip injury				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Periorbital contusion				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Spinal column injury				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Stab wound				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				

subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Traumatic intracranial haemorrhage				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Myocardial infarction				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac failure acute				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Cardiac failure				
subjects affected / exposed	1 / 239 (0.42%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Nervous system disorders				
Grand mal convulsion				
subjects affected / exposed	16 / 239 (6.69%)			
occurrences causally related to treatment / all	1 / 20			
deaths causally related to treatment / all	0 / 0			
Status epilepticus				
subjects affected / exposed	4 / 239 (1.67%)			
occurrences causally related to treatment / all	1 / 7			
deaths causally related to treatment / all	0 / 0			
Myoclonic epilepsy				
subjects affected / exposed	2 / 239 (0.84%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Petit mal epilepsy				

subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Benign intracranial hypertension			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain injury			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Convulsion			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cubital tunnel syndrome			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Dizziness			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Migraine			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Multiple sclerosis relapse			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ear and labyrinth disorders			
Vertigo positional			

subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Periorbital oedema			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diplopia			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			
Abdominal pain			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vomiting			
subjects affected / exposed	2 / 239 (0.84%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Small intestinal perforation			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coeliac disease			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain lower			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue			

disorders			
Mixed connective tissue disease			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Osteoarthritis			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Otitis media acute			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Urinary tract infection			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Viral upper respiratory tract infection			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infected dermal cyst			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Escherichia urinary tract infection			
subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			

subjects affected / exposed	1 / 239 (0.42%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Diabetes mellitus			
subjects affected / exposed	1 / 239 (0.42%)		
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	All participants (lacosamide)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	176 / 239 (73.64%)		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	24 / 239 (10.04%)		
occurrences (all)	30		
Laceration			
subjects affected / exposed	12 / 239 (5.02%)		
occurrences (all)	14		
Nervous system disorders			
Migraine			
subjects affected / exposed	13 / 239 (5.44%)		
occurrences (all)	17		
Headache			
subjects affected / exposed	56 / 239 (23.43%)		
occurrences (all)	113		
Dizziness			
subjects affected / exposed	53 / 239 (22.18%)		
occurrences (all)	73		
Somnolence			
subjects affected / exposed	40 / 239 (16.74%)		
occurrences (all)	51		
Grand mal convulsion			

subjects affected / exposed	14 / 239 (5.86%)		
occurrences (all)	16		
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	13 / 239 (5.44%)		
occurrences (all)	15		
Pyrexia			
subjects affected / exposed	13 / 239 (5.44%)		
occurrences (all)	13		
Ear and labyrinth disorders			
Vertigo			
subjects affected / exposed	19 / 239 (7.95%)		
occurrences (all)	30		
Eye disorders			
Diplopia			
subjects affected / exposed	12 / 239 (5.02%)		
occurrences (all)	15		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	16 / 239 (6.69%)		
occurrences (all)	24		
Diarrhoea			
subjects affected / exposed	18 / 239 (7.53%)		
occurrences (all)	23		
Nausea			
subjects affected / exposed	23 / 239 (9.62%)		
occurrences (all)	31		
Musculoskeletal and connective tissue disorders			
Back pain			
subjects affected / exposed	17 / 239 (7.11%)		
occurrences (all)	19		
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	52 / 239 (21.76%)		
occurrences (all)	91		
Influenza			

subjects affected / exposed	18 / 239 (7.53%)		
occurrences (all)	23		
Corona virus infection			
subjects affected / exposed	14 / 239 (5.86%)		
occurrences (all)	16		
Upper respiratory tract infection			
subjects affected / exposed	17 / 239 (7.11%)		
occurrences (all)	18		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
27 January 2015	Global Protocol Amendment 1, dated 27 Jan 2015, provided the following primary and key revisions. No study participants entered the study prior to the date of amendment. The primary purpose of this substantial amendment followed the amendment made to the SP0982 protocol, which was to identify significant changes to the study design and the inclusion of pediatric study participants (≥4 to 12 years of age). The duration of EP0012 was clarified as at least 2 years, and LCM plasma concentration analysis was removed. Clarification on study participants being able to participate in a substudy at some sites, without being withdrawn from EP0012, was added. The use of concomitant medications and treatments was clarified and permitted and prohibited concomitant treatments were clarified to be consistent with SP0982. For pediatric study participants <50 kg, a Dispensation Visit was added 12 weeks after each 24-weekly visit from Year 3 onwards, in order to dispense LCM solution. Behavior Rating Inventory of Executive Function® - Preschool Version (BRIEF®-P) was added and socio-professional data assessment was removed in this study.
09 June 2016	Global Protocol Amendment 2, dated 09 Jun 2016, provided the following primary and key revisions. Thirty study participants entered the study prior to the date of amendment. The protocol was amended following a request from the Taiwanese Ministry of Health and Welfare: for dose escalation, study participants who were eligible Baseline failures from SP0982 had to remain on the dose for ≥7 days before a subsequent dose escalation. Additionally, the purpose of the amendment was to remove superfluous description of a substudy, to clarify the requirement for ECG at subsequent visits, requirement for endocrinology and timing of endocrinology assessments, pregnancy testing, definition of contraceptive methods, and seizure count, and to add a definition of the Enrolled Set (ES). Several assessments were removed from Years 3 to 5, including brief physical examination (complete physical examination instead), complete neurological examination (brief neurological examination instead), and health outcome measures. The protocol was also updated according to the new UCB protocol template, for example, with the addition of text regarding potential drug-induced liver injury (PDILI).

29 November 2017	Global Protocol Amendment 3, dated 29 Nov 2017, provided the following primary and key revisions. One hundred forty-four study participants entered the study prior to the date of amendment. The primary purpose of this amendment was to simplify the assessments and procedures for all study participants during the first 94 weeks of study and to simplify the assessments and procedures for adults after Week 94. Pediatric assessments were kept as they were after Week 94 for regulatory purposes. In addition, the following changes were made: • To allow the Safety Follow-up for study participants tapered in SP0982 after the 125th event occurred in SP0982; the 4-week Safety Follow-up was to be started at Visit 1 of EP0012. • In the schedule of study assessments for treatment Years 1 to 2, a footnote was added to explain that Visit 6, Visit 7, and Visit 10 were not performed according to Protocol Amendment 3. Footnote 'b' had 'vital signs' removed and for footnote 'd,' Week 30, Week 38, and Week 78 were added to the footnote for consistency. • A schedule of study assessments for Years 3 through 5 for EP0012 (Treatment Period, Early Termination (ET) Visit, Termination Visit, and Unscheduled Visit for study participants ≥18 years) was added. • In the schedule of study assessments for Years 3 through 5, footnotes were amended to specify that the Taper Period and Safety Follow-up Visit included some of the study participants who tapered into SP0982 after the 125th event and who consented to enter EP0012 for the Safety Follow-up Visit only. • To restructure the safety variables. • To align the planned number of study participants with the pivotal study SP0982. • To update the introduction section with regulatory information on the marketing authorization of Vimpat and to provide an update on the LCM clinical program. • To clarify the PDILI criteria requiring immediate and permanent discontinuation of the study medication.
13 December 2019	Global Protocol Amendment 4, dated 13 Dec 2019, provided the following primary and key revisions. All study participants entered the study prior to the date of amendment. The primary purpose of this substantial amendment was to extend the treatment of the study participants and have LCM available for the study participants till the main approvals for an extended PGTCS indication was obtained. UCB sought to obtain the approvals in first instance in US, EU, and Japan. In addition, primary generalized tonic-clonic seizures was globally changed to PGTCS.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported