Long-Term Use of Oral Lacosamide in Young Children With Epilepsy Who Received Lacosamide in Previous Trials: Data From a Multicenter, Open-Label, Follow-Up Trial

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Background

- Lacosamide (LCM) has been approved as monotherapy and adjunctive treatment in patients with focal seizures (minimum age varying between 1 month and 18 years, depending on individual country) and as adjunctive treatment for primary generalized tonic-clonic seizures in adult and pediatric patients with idiopathic generalized epilepsy (minimum age of 4 years, depending on individual country).

Objective

- To assess the long-term use of LCM oral solution in pediatric patients with epilepsy.

Methods

TRIAL DESIGN

- EP0151 (ClinicalTrials.gov: NCT04627285) was a Phase III, multicenter, long-term, open-label, follow-up trial for pediatric patients <6 years of age with epilepsy who had received LCM in a previous trial (EP0034 or SP848[1]).
- This trial allowed patients to continue LCM treatment until they reached 6 years of age or until LCM oral solution was approved for patients <4 years of age in the participating country (whichever was earliest).
  - Situations where patients >6 years of age required longer treatment with LCM oral solution (eg, developmental delay, need for precise dosing) were assessed on a case-by-case basis following discussions between the investigator and the sponsor.
- In EP0151, investigators were allowed to increase or decrease the dose of LCM to optimize tolerability and seizure reduction for each patient (minimum dose of 2 mg/kg/day; maximum dose of 12 mg/kg/day or 600 mg/day, whichever was lower).
- The maximum planned trial duration was ~213 weeks, including an ~205-week treatment period and up to 8-week end-of-study period (4-week taper and 30-day safety follow-up).

STATISTICS

- The Safety Set (SS) included all patients who received ≥1 LCM dose during the trial.

OUTCOMES

- Primary safety outcomes were treatment-emergent adverse events (TEAEs), discontinuations due to TEAEs, discontinuations due to serious adverse events (SAEs), modal daily dose, and maximum daily dose.

Results

BASELINE DEMOGRAPHICS

- Of the 48 patients in the SS, 19 (39.6%) were ≥2 to <4 years of age and 29 (60.4%) were ≥4 to <6 years of age at trial entry.
- Patients were enrolled in 6 countries: 22 (45.8%) in Ukraine, 12 (25.0%) in Hungary, 6 (12.5%) in Romania, 5 (10.4%) in Georgia, 2 (4.2%) in Taiwan, and 1 (2.1%) in Moldova.

Baseline demographics (SS)

	≥2 TO <4 YEARS (n=19)	≥4 TO <6 YEARS (n=29)	ALL PATIENTS (N=48)
Age,[a] median (range), years	2.8 (2.2-3.8)	5.4 (4.0-6.0[b])	4.4 (2.2-6.0[b])
Male, n (%)	13 (68.4)	20 (69.0)	33 (68.8)
Weight,[c] median (range), kg	12.3 (9.5-18.9)	16.1 (8.0-24.3)	14.5 (8.0-24.3)

[a]At entry into EP0151; [b]Rounded to 6.0 (patient was <6 years of age at trial entry); [c]At visit 1 of EP0151.

Overview

QUESTION

What is the long-term use of lacosamide (LCM) oral solution in pediatric patients with epilepsy?

INVESTIGATION

EP0151 (NCT04627285) was a Phase III, multicenter, long-term, open-label, follow-up trial for pediatric patients <6 years of age with epilepsy who had received LCM in a previous trial (EP0034 or SP848).

RESULTS

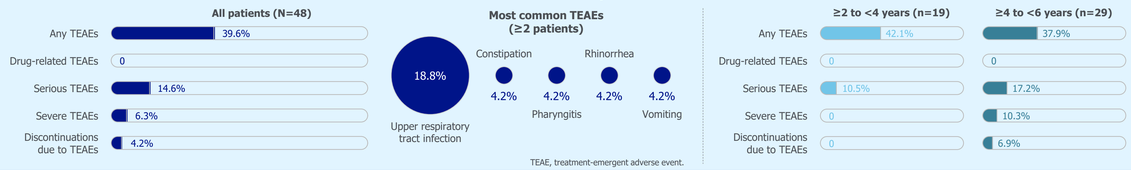
Exposure and dosing in this trial

Mean/median exposure duration
977.6/1093.0 days

Total exposure
128.474 patient-years

Mean modal LCM dose
9.8 mg/kg/day

Tolerability



TEAE, treatment-emergent adverse event.

CONCLUSIONS

Long-term LCM treatment of children with epilepsy (<6 years of age at trial entry) was well tolerated and no new safety signals were identified.

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Antiseizure medications (SS)

	≥2 TO <4 YEARS (n=19)	≥4 TO <6 YEARS (n=29)	ALL PATIENTS (N=48)
Number of concomitant ASMs taken at the time of first dose of LCM in EP0151, n (%)			
0	2 (10.5)	0	2 (4.2)
1	8 (42.1)	12 (41.4)	20 (41.7)
2	5 (26.3)	8 (27.6)	13 (27.1)
3	3 (15.8)	5 (17.2)	8 (16.7)
>3	1 (5.3)	4 (13.8)	5 (10.4)
Most common concomitant ASMs taken at the time of first dose of LCM in EP0151 (taken by ≥10% of patients in either age group),[a] n (%)			
Valproate[b]	13 (68.4)	16 (55.2)	29 (60.4)
Levetiracetam	7 (36.8)	9 (31.0)	16 (33.3)
Topiramate	1 (5.3)	6 (20.7)	7 (14.6)
Carbamazepine	2 (10.5)	3 (10.3)	5 (10.4)
Vigabatrin	2 (10.5)	2 (6.9)	4 (8.3)
Most common concomitant ASMs taken during the treatment period (taken by ≥10% of patients in either age group),[a] n (%)			
Valproate[b]	14 (73.7)	16 (55.2)	30 (62.5)
Levetiracetam	7 (36.8)	9 (31.0)	16 (33.3)
Topiramate	1 (5.3)	6 (20.7)	7 (14.6)
Carbamazepine	2 (10.5)	3 (10.3)	5 (10.4)
Clobazam	2 (10.5)	2 (6.9)	4 (8.3)
Vigabatrin	2 (10.5)	2 (6.9)	4 (8.3)

[a]Patients may have taken >1 concomitant ASM; [b]Included valproic acid, valproate semisodium, valproate sodium, ergenyl chrono, and valpromide. ASM, antiseizure medication.

- Most patients (68.8%) were taking 1-2 concomitant antiseizure medications at the time of first dose of LCM in this trial.

PATIENT DISPOSITION

Patient disposition and discontinuation reasons (SS)

PATIENTS, n (%)	≥2 TO <4 YEARS (n=19)	≥4 TO <6 YEARS (n=29)	ALL PATIENTS (N=48)
Started trial	19 (100)	29 (100)	48 (100)
Treated <12 months	0	5 (17.2)	5 (10.4)
Treated ≥12 months and <24 months	1 (5.3)	4 (13.8)	5 (10.4)
Treated ≥24 months and <36 months	4 (21.1)	4 (13.8)	8 (16.7)
Treated ≥36 months and <48 months	10 (52.6)	12 (41.4)	22 (45.8)
Treated ≥48 months	4 (21.1)	4 (13.8)	8 (16.7)
Completed trial	12 (63.2)	25 (86.2)	37 (77.1)
Discontinued	7 (36.8)	4 (13.8)	11 (22.9)
Primary reason for discontinuation			
Adverse event	0	2 (6.9)	2 (4.2)
Lack of efficacy	0	0	0
Protocol deviation	0	0	0
Lost to follow-up	1 (5.3)	0	1 (2.1)
Withdrawal by patient	1 (5.3)	1 (3.4)	2 (4.2)
Other	5 (26.3)	1 (3.4)	6 (12.5)

Reference

1. Farkas MK, et al. *Epilepsy Behav* 2024;159:109989.

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EXPOSURE AND DOSING

Duration of exposure, maximum daily dose, and modal daily LCM dose (SS)

PATIENTS, n (%)	≥2 TO <4 YEARS (n=19)	≥4 TO <6 YEARS (n=29)	ALL PATIENTS (N=48)
Duration of exposure, days			
Mean (SD)	1142.4 (255.1)	869.7 (473.2)	977.6 (420.1)
Median (range)	1275.0 (573-1406)	1055.0 (1-1501)	1093.0 (1-1501)
Maximum dose, mg/kg/day			
Mean (SD)	9.5 (2.4)	10.1 (2.6)	9.9 (2.5)
Median (range)	10.0 (4-12)	10.0 (3-12)	10.0 (3-12)
Modal dose, mg/kg/day			
Mean (SD)	9.5 (2.4)	10.0 (2.6)	9.8 (2.5)
Median (range)	10.0 (4-12)	10.0 (3-12)	10.0 (3-12)

- In this trial, patients were exposed to LCM for a total of 128.474 patient-years.

SAFETY AND TOLERABILITY

Treatment-emergent adverse events (SS)

PATIENTS, n (%)	≥2 TO <4 YEARS (n=19)	≥4 TO <6 YEARS (n=29)	ALL PATIENTS (N=48)
Any TEAE	8 (42.1)	11 (37.9)	19 (39.6)
Drug-related TEAEs	0	0	0
Serious TEAEs	2 (10.5)	5 (17.2)	7 (14.6)
Severe TEAEs	0	3 (10.3)	3 (6.3)
Discontinuations due to TEAEs	0	2 (6.9)	2 (4.2)
Discontinuations due to SAEs[a]	0	2 (6.9)	2 (4.2)
Deaths (TEAEs leading to death)	0	2 (6.9)	2 (4.2)
TEAEs[b] reported by ≥2 patients			
Upper respiratory tract infection	5 (26.3)	4 (13.8)	9 (18.8)
Constipation	2 (10.5)	0	2 (4.2)
Pharyngitis	2 (10.5)	0	2 (4.2)
Rhinorrhea	1 (5.3)	1 (3.4)	2 (4.2)
Vomiting	1 (5.3)	1 (3.4)	2 (4.2)

[a]Regardless of treatment-emergent; [b]Medical Dictionary for Regulatory Activities Version 16.1 Preferred Term. SAE, serious adverse event; TEAE, treatment-emergent adverse event.

- Seven (14.6%) patients had serious TEAEs; no individual serious TEAE occurred in >1 patient.
- Two (4.2%) patients discontinued due to TEAEs/SAEs.
  - These 2 patients died during the trial (due to acute cardiac failure and sudden death, respectively); neither death was considered related to LCM.

Conclusions

- Long-term LCM treatment of children with epilepsy (<6 years of age at trial entry) was well tolerated and no new safety signals were identified.

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