Clinical trial results:
A Multi-center, Open-label, Uncontrolled, Long-term, Extension Study to Evaluate the Safety and Efficacy of Lacosamide as Adjunctive Therapy in Japanese and Chinese Adults With Partial-onset Seizures With or Without Secondary Generalization

Summary

EudraCT number	2019-004756-11
Trial protocol	Outside EU/EEA
Global end of trial date	29 July 2019

Results information

Result version number	v1
This version publication date	12 February 2020
First version publication date	12 February 2020

Trial information

Trial identification

Sponsor protocol code	EP0009

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT01832038
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	UCB Pharma SA
Sponsor organisation address	Allée de la Recherche 60, Brussels, Belgium, B-1070
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Sponsor organisation name	UCB Japan Co. Ltd.
Sponsor organisation address	8-17-1 Nishi-Shinjuku, Tokyo, Japan, 160-0023
Public contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com
Scientific contact	Clin Trial Reg & Results Disclosure, UCB BIOSCIENCES GmbH, clinicaltrials@ucb.com

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	Yes

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	29 August 2019
Is this the analysis of the primary completion data?	Yes
Primary completion date	29 July 2019
Global end of trial reached?	Yes
Global end of trial date	29 July 2019
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of long-term administration of lacosamide at doses up to 400 mg/day in Japanese and Chinese adults with epilepsy who have completed the Treatment and Transition Period of EP0008 [NCT01710657]

Protection of trial subjects:

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

Background therapy:

Background therapy as permitted in the protocol.

Evidence for comparator:

Not Applicable

Actual start date of recruitment	26 March 2013
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	China: 350
Country: Number of subjects enrolled	Japan: 123
Worldwide total number of subjects	473
EEA total number of subjects	0

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	27

Adults (18-64 years)	444
From 65 to 84 years	2
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The study started to enroll participants in March 2013 and concluded in July 2019.

Pre-assignment

Screening details:

Participant Flow refers to the Safety Set.

Period 1

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

Arms

Arm title	Lacosamide

Arm description:

At the completion of EP0008 [NCT01710657], all participants who enrolled in EP0009 were administered a dose of 200 mg/day lacosamide (LCM). The LCM dose may have been decreased to 100 mg/day or increased, no faster than 100 mg/day per week, up to 400 mg/day, at the investigator's discretion.

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

Dosage and administration details:

Lacosamide (LCM) was supplied as immediate-release, film-coated, tablets in strengths of 50 mg (pinkish) and 100 mg (dark yellow). LCM was orally administered bid (once in the morning and once in the evening) in 2 equally divided doses. The LCM dose may have been decreased to 100 mg/day or increased, no faster than 100 mg/day per week, up to 400 mg/day. Increasing the dose of LCM should have been done at a visit (scheduled or unscheduled). The LCM dose must have remained stable during changes to concomitant antiepileptic drugs [AED(s)].

Number of subjects in period 1	Lacosamide
Started	473
Completed	238
Not completed	235
Adverse event, serious fatal	5
Participant was asked to quit	5
Changes of implementation system	3
Subject considered the efficacy was poor	1
Visit non-compliance	2
Prohibited concomitant medication	1
Consent withdrawn by subject	49

Not possible to visit the hospital	1
Low compliance	3
Adverse event, non-fatal	50
Pregnancy	1
Bad mood and has suicidal thought	1
Subject refused to return visit	2
Back home	1
Prohibit procedure	2
Lost to follow-up	10
Pregnancy and abortion in EP0008 study	1
Plan to pregnancy	7
Not convenient to come back to site	2
Lack of efficacy	81
Protocol deviation	7

Baseline characteristics

Reporting groups	
Reporting group title	Lacosamide
Reporting group description:	
At the completion of EP0008 [NCT01710657], all participants who enrolled in EP0009 were administered a dose of 200 mg/day lacosamide (LCM). The LCM dose may have been decreased to 100 mg/day or increased, no faster than 100 mg/day per week, up to 400 mg/day, at the investigator's discretion.	

Reporting group values	Lacosamide	Total	
Number of subjects	473	473	
Age categorical Units: Subjects			
<=18	39	39	
Between 18 and 65 years	432	432	
>=65	2	2	
Age continuous Units: years			
arithmetic mean	32.7		
standard deviation	± 12.0	-	
Gender categorical Units: Subjects			
Male	259	259	
Female	214	214	

End points

End points reporting groups

Reporting group title	Lacosamide

Reporting group description:

At the completion of EP0008 [NCT01710657], all participants who enrolled in EP0009 were administered a dose of 200 mg/day lacosamide (LCM). The LCM dose may have been decreased to 100 mg/day or increased, no faster than 100 mg/day per week, up to 400 mg/day, at the investigator's discretion.

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

Subject analysis set description:

At the completion of EP0008 [NCT01710657], all participants who enrolled in EP0009 were administered a dose of 200 mg/day LCM. The LCM dose may have been decreased to 100 mg/day or increased, no faster than 100 mg/day per week, up to 400 mg/day, at the investigator's discretion. Participants formed the Safety Set (SS).

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

Subject analysis set description:

At the completion of EP0008 [NCT01710657], all participants who enrolled in EP0009 were administered a dose of 200 mg/day LCM. The LCM dose may have been decreased to 100 mg/day or increased, no faster than 100 mg/day per week, up to 400 mg/day, at the investigator's discretion. Participants formed the Full Analysis Set (FAS).

Primary: Number of participants with at least one adverse event reported spontaneously by the subject or observed by the investigator from Baseline until the End of Study Visit

End point title	Number of participants with at least one adverse event reported spontaneously by the subject or observed by the investigator from Baseline until the End of Study Visit[1]

End point description:

An Adverse Event (AE) is any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment. An AE could therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) up to approximately Week 323

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	Lacosamide (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	473			
Units: participants	410			

Statistical analyses

No statistical analyses for this end point

Primary: Number of participants that withdrew due to adverse events from Baseline until the End of Study Visit

End point title	Number of participants that withdrew due to adverse events from Baseline until the End of Study Visit[2]

End point description:

An Adverse Event (AE) is any untoward medical occurrence in a patient or clinical investigation participant administered a pharmaceutical product, which does not necessarily have a causal relationship with this treatment and led to the withdrawal of the participants from the study. An AE could therefore be any unfavorable and unintended sign, symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

End point type	Primary

End point timeframe:

From Visit 1 (Week 0) up to approximately Week 323

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	Lacosamide (SS)			
Subject group type	Subject analysis set			
Number of subjects analysed	473			
Units: participants	49			

Statistical analyses

No statistical analyses for this end point

Secondary: Percent change in partial-onset seizure frequency per 28 days from Baseline of study EP0008 [NCT01710657] until the End of Study Visit in study EP0009

End point title	Percent change in partial-onset seizure frequency per 28 days from Baseline of study EP0008 [NCT01710657] until the End of Study Visit in study EP0009

End point description:

The percent change from Baseline to the Treatment Period was calculated as {[(Seizure frequency per 28 days during the Treatment Period) minus (Seizure frequency per 28 days during Baseline Period)] divided by (Seizure frequency per 28 days during Baseline Period)} multiplied by 100. Baseline was defined as the Baseline Period of study EP0008 [NCT01710657].

End point type	Secondary

End point timeframe:

From Visit 1 in study EP0008 [NCT01710657] up to approximately Week 323 in study EP0009

End point values	Lacosamide (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	471			
Units: Percent change				
arithmetic mean (standard deviation)				
Standard Deviation	-44.47 (± 55.82)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of participants with 50 % response rate in partial-onset seizure frequency per 28 days from Baseline of study EP0008 [NCT01710657] until the End of Study Visit in study EP0009

End point title	Percentage of participants with 50 % response rate in partial-onset seizure frequency per 28 days from Baseline of study EP0008 [NCT01710657] until the End of Study Visit in study EP0009

End point description:

A responder is a subject experiencing a greater than or equal to (≥) 50 % reduction in partial-onset seizure frequency per 28 days from baseline. Baseline was defined as the Baseline Period of study EP0008 [NCT01710657].

End point type	Secondary

End point timeframe:

From Visit 1 in study EP0008 [NCT01710657] up to approximately Week 323 in study EP0009

End point values	Lacosamide (FAS)			
Subject group type	Subject analysis set			
Number of subjects analysed	471			
Units: percentage of participants				
number (not applicable)	57.1			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse Events were collected from Visit 1 (Week 0) up to approximately Week 323

Assessment type	Non-systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	16.1

Reporting groups

Reporting group title	Lacosamide (SS)

Reporting group description:

At the completion of EP0008 [NCT01710657], all participants who enrolled in EP0009 were administered a dose of 200 mg/day LCM. The LCM dose may have been decreased to 100 mg/day or increased, no faster than 100 mg/day per week, up to 400 mg/day, at the investigator's discretion. Participants formed the Safety Set (SS).

Serious adverse events	Lacosamide (SS)		
Total subjects affected by serious adverse events			
subjects affected / exposed	78 / 473 (16.49%)		
number of deaths (all causes)	5		
number of deaths resulting from adverse events	2		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Colon cancer			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemangioma			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meigs' syndrome			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metastatic glioma			

subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ovarian fibroma			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Ovarian germ cell teratoma			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Varicose vein			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Venous occlusion			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Wisdom teeth removal			
subjects affected / exposed	2 / 473 (0.42%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Pregnancy, puerperium and perinatal conditions			
Abortion spontaneous			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Pregnancy on contraceptive			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

General disorders and administration site conditions			
Sudden death			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 1		
Reproductive system and breast disorders			
Prostatitis			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			
Asthma			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemoptysis			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nasal septum deviation			
subjects affected / exposed	2 / 473 (0.42%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Rhinitis allergic			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vocal cord leukoplakia			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Psychiatric disorders			
Epileptic psychosis			

subjects affected / exposed	2 / 473 (0.42%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Hallucination			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Mental disorder			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Suicidal ideation			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Suicide attempt			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Injury, poisoning and procedural complications			
Ankle fracture			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Brain contusion			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Burns third degree			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Clavicle fracture			

subjects affected / exposed	2 / 473 (0.42%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Craniocerebral injury				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Face injury				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Facial bones fracture				
subjects affected / exposed	2 / 473 (0.42%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Fibula fracture				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Foreign body				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 3			
deaths causally related to treatment / all	0 / 0			
Head injury				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Heat stroke				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Humerus fracture				

subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury				
subjects affected / exposed	2 / 473 (0.42%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Jaw fracture				
subjects affected / exposed	2 / 473 (0.42%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Spinal compression fracture				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subdural haemorrhage				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Thermal burn				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Tibia fracture				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Toxicity to various agents				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Congenital, familial and genetic disorders				
Hamartoma				

subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cardiac disorders			
Sinus bradycardia			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nervous system disorders			
Cerebral haemorrhage			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Cerebral infarction			
subjects affected / exposed	2 / 473 (0.42%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	1 / 1		
Complex partial seizures			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Convulsion			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Epilepsy			
subjects affected / exposed	10 / 473 (2.11%)		
occurrences causally related to treatment / all	3 / 10		
deaths causally related to treatment / all	0 / 0		
Grand mal convulsion			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhage intracranial			

subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Headache				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Hypoxic-ischaemic encephalopathy				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Intracranial haematoma				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Partial seizures with secondary generalisation				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Seizure cluster				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Status epilepticus				
subjects affected / exposed	10 / 473 (2.11%)			
occurrences causally related to treatment / all	3 / 12			
deaths causally related to treatment / all	1 / 2			
Subarachnoid haemorrhage				
subjects affected / exposed	2 / 473 (0.42%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Temporal lobe epilepsy				

subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Transient ischaemic attack				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Visual field defect				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Eye disorders				
Blindness unilateral				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastrointestinal disorders				
Duodenitis				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Dyspepsia				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastric ulcer				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Gastritis				
subjects affected / exposed	2 / 473 (0.42%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Gastritis atrophic				

subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal necrosis			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal pain			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Haemorrhoids			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hypertrophic anal papilla			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Inguinal hernia, obstructive			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Large intestine polyp			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal polyp			

subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal prolapse			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reflux gastritis			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal impairment			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Rhabdomyolysis			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Bacterial prostatitis			

subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Chronic sinusitis				
subjects affected / exposed	2 / 473 (0.42%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Erysipelas				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Gastroenteritis				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Lung infection				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Orchitis				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonitis				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Peritonsillar abscess				
subjects affected / exposed	1 / 473 (0.21%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Pneumonia				

subjects affected / exposed	6 / 473 (1.27%)		
occurrences causally related to treatment / all	1 / 6		
deaths causally related to treatment / all	0 / 0		
Retroperitoneal infection			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Tuberculosis of genitourinary system			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Upper respiratory tract infection			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Decreased appetite			
subjects affected / exposed	1 / 473 (0.21%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Lacosamide (SS)		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	350 / 473 (74.00%)		
Investigations			
Protein urine present			
subjects affected / exposed	18 / 473 (3.81%)		
occurrences (all)	24		
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	26 / 473 (5.50%)		
occurrences (all)	36		
Nervous system disorders			

Dizziness			
subjects affected / exposed	125 / 473 (26.43%)		
occurrences (all)	318		
Headache			
subjects affected / exposed	76 / 473 (16.07%)		
occurrences (all)	175		
Somnolence			
subjects affected / exposed	41 / 473 (8.67%)		
occurrences (all)	80		
Tremor			
subjects affected / exposed	20 / 473 (4.23%)		
occurrences (all)	22		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	41 / 473 (8.67%)		
occurrences (all)	53		
Eye disorders			
Vision blurred			
subjects affected / exposed	22 / 473 (4.65%)		
occurrences (all)	29		
Gastrointestinal disorders			
Abdominal pain upper			
subjects affected / exposed	28 / 473 (5.92%)		
occurrences (all)	57		
Diarrhoea			
subjects affected / exposed	41 / 473 (8.67%)		
occurrences (all)	64		
Constipation			
subjects affected / exposed	21 / 473 (4.44%)		
occurrences (all)	35		
Nausea			
subjects affected / exposed	30 / 473 (6.34%)		
occurrences (all)	46		
Toothache			
subjects affected / exposed	38 / 473 (8.03%)		
occurrences (all)	47		

Vomiting			
subjects affected / exposed	36 / 473 (7.61%)		
occurrences (all)	65		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	27 / 473 (5.71%)		
occurrences (all)	43		
Oropharyngeal pain			
subjects affected / exposed	27 / 473 (5.71%)		
occurrences (all)	48		
Psychiatric disorders			
Insomnia			
subjects affected / exposed	26 / 473 (5.50%)		
occurrences (all)	31		
Infections and infestations			
Gastroenteritis			
subjects affected / exposed	27 / 473 (5.71%)		
occurrences (all)	36		
Nasopharyngitis			
subjects affected / exposed	155 / 473 (32.77%)		
occurrences (all)	508		
Pharyngitis			
subjects affected / exposed	22 / 473 (4.65%)		
occurrences (all)	38		
Upper respiratory tract infection			
subjects affected / exposed	99 / 473 (20.93%)		
occurrences (all)	206		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported