Clinical trial results:
An Open-label Extension Trial to Determine Safety and Efficacy of Long-term Oral SPM 927 in Patients With Partial Seizures

Summary

EudraCT number	2014-004398-18
Trial protocol	Outside EU/EEA
Global end of trial date	28 October 2009

Results information

Result version number	v1 (current)
This version publication date	30 June 2016
First version publication date	16 May 2015

Trial information

Trial identification

Sponsor protocol code	SP0756

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT00522275
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	SCHWARZ BIOSCIENCES INC.
Sponsor organisation address	8010 Arco Corporate Drive, Raleigh, United States, 27617
Public contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 0049 2173 48 15 15, clinicaltrials@ucb.com
Scientific contact	Clinical Trial Registries and Results Disclosure, UCB BIOSCIENCES GmbH, 0049 2173 48 15 15,

Notes:

Paediatric regulatory details

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

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	14 January 2010
Is this the analysis of the primary completion data?	No

Global end of trial reached?	Yes
Global end of trial date	28 October 2009
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

- To obtain information about the safety of Lacosamide (LCM) during long-term exposure
- To obtain data on seizure reduction and the maintenance of efficacy by LCM during long-term exposure
- To allow subjects who had completed an LCM epilepsy study to receive LCM

Protection of trial subjects:

Subject's informed consent was obtained and documented in accordance with local regulations, ICH-GCP requirements, and to the ethical principles that have their origin in the principles of the Declaration of Helsinki.

Prior to obtaining informed consent, information was given in a language and at a level of complexity understandable to the subject in both oral and written form by the investigator or designee. Each subject had the opportunity to discuss the trial and its alternatives with the investigator.

Background therapy:

N/A

Evidence for comparator:

N/A

Actual start date of recruitment	04 October 2004
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	United States: 308
Worldwide total number of subjects	308
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)	4
Adults (18-64 years)	297
From 65 to 84 years	7
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

The SP0756 study began recruitment in October 2004 and concluded in October 2009. Recruitment occurred in the United States.

Pre-assignment

Screening details:

N/A

Period 1

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

Arms

Arm title	Lacosamide

Arm description:

Up to 800 mg/day lacosamide (flexible dosing)

Arm type	Experimental
Investigational medicinal product name	Lacosamide
Investigational medicinal product code	SPM 927
Other name	Vimpat
Pharmaceutical forms	Tablet
Routes of administration	Oral use

Dosage and administration details:

Up to 800 mg/day Lacosamide (flexible dosing).

Number of subjects in period 1	Lacosamide
Started	308
Completed	138
Not completed	170
Other: Site / clinic closed	4
Other: Sponsor request	2
Non-Fatal, Non-Serious AE	25
Other: Subject is pregnant	2
Non-Fatal, Serious AE	8
Other: Subject had surgery for epilepsy	2
Unsatisfactory compliance	11
Other: Subject relocated	2
Subject withdrew consent	16
Other: Subject arrested	1

Fatal, Serious AE	2
Lost to follow-up	8
Other: Subject wants to become pregnant	2
Other: Travel to / from site difficulty	3
Other: Subject ran out of medication	1
Lack of efficacy	80
Protocol deviation	1

Baseline characteristics

Reporting groups	
Reporting group title	Lacosamide
Reporting group description:	
Up to 800 mg/day lacosamide (flexible dosing)	

Reporting group values	Lacosamide	Total	
Number of subjects	308	308	
Age Categorical Units: Subjects			
<=18 years	10	10	
Between 18 and 65 years	291	291	
>=65 years	7	7	
Age Continuous Units: years			
arithmetic mean	37.7		
standard deviation	± 12.5	-	
Gender categorical Units: Subjects			
Female	146	146	
Male	162	162	
Region of Enrollment Units: Subjects			
Asian	5	5	
Black	29	29	
White	251	251	
Other/ mixed	23	23	

End points

End points reporting groups

Reporting group title	Lacosamide
Reporting group description:	
Up to 800 mg/day lacosamide (flexible dosing)	

Primary: Number of subjects reporting at least 1 Treatment-Emergent Adverse Event (TEAE) during the treatment period (Maximum 6 years)

End point title	Number of subjects reporting at least 1 Treatment-Emergent Adverse Event (TEAE) during the treatment period (Maximum 6 years)[1]
End point description:	
Adverse events are any untoward medical occurrences in a subject administered study treatment, whether or not these events are related to treatment.	
End point type	Primary
End point timeframe:	
During the Treatment Period (Maximum 6 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: The primary variables for this study were all aimed at evaluating the long term safety of LCM using descriptive data summaries. Analysis of seizure reduction was considered secondary/ exploratory and was descriptive only. No statistical comparisons were planned based on the nature of the study design (no treatment comparator, open label flexible dosing, etc).

End point values	Lacosamide			
Subject group type	Reporting group			
Number of subjects analysed	308			
Units: subjects				
number	288			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects prematurely discontinuing due to a Treatment-Emergent Adverse Event (TEAE) during the treatment period (maximum 6 years)

End point title	Number of subjects prematurely discontinuing due to a Treatment-Emergent Adverse Event (TEAE) during the treatment period (maximum 6 years)[2]
End point description:	
Adverse events are any untoward medical occurrences in a subject administered study treatment, whether or not these events are related to treatment.	
End point type	Primary
End point timeframe:	
During the Treatment Period (Maximum 6 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: The primary variables for this study were all aimed at evaluating the long term safety of LCM using descriptive data summaries. Analysis of seizure reduction was considered secondary/ exploratory and was descriptive only. No statistical comparisons were planned based on the nature of the study design (no treatment comparator, open label flexible dosing, etc).

End point values	Lacosamide			
Subject group type	Reporting group			
Number of subjects analysed	308			
Units: subjects				
number	33			

Statistical analyses

No statistical analyses for this end point

Primary: Number of subjects reporting at least 1 Serious Adverse Event (SAE) during the treatment period (maximum 6 years)

End point title	Number of subjects reporting at least 1 Serious Adverse Event (SAE) during the treatment period (maximum 6 years)[3]

End point description:

Serious adverse events are any untoward serious medical occurrences in a subject administered study treatment, whether or not these events are related
to treatment.

End point type	Primary

End point timeframe:

During the Treatment Period (Maximum 6 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: The primary variables for this study were all aimed at evaluating the long term safety of LCM using descriptive data summaries. Analysis of seizure reduction was considered secondary/ exploratory and was descriptive only. No statistical comparisons were planned based on the nature of the study design (no treatment comparator, open label flexible dosing, etc).

End point values	Lacosamide			
Subject group type	Reporting group			
Number of subjects analysed	308			
Units: subjects				
number	71			

Statistical analyses

No statistical analyses for this end point

Secondary: Median percentage change from baseline in 28-day seizure frequency during the treatment period (Maximum 6 years)

End point title	Median percentage change from baseline in 28-day seizure

	frequency during the treatment period (Maximum 6 years)

End point description:

Negative changes from Baseline indicate an improvement (i.e., a reduction) in 28-day seizure frequency.

End point type	Secondary

End point timeframe:

Baseline (8-week Baseline Period from the parent study SP0754), Treatment Period (Maximum 6 years)

End point values	Lacosamide			
Subject group type	Reporting group			
Number of subjects analysed	307			
Units: percentage change				
median (full range (min-max))				
median (full range)	-48.5 (-100 to 567.7)			

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of at least 50 % Responders during the treatment period (maximum 6 years)

End point title	Percentage of at least 50 % Responders during the treatment period (maximum 6 years)

End point description:

At least 50 percent response is based on the percentage reduction in 28-day seizure frequency during the Treatment Period of the open-label extension relative to the Baseline Phase of the prior study.

End point type	Secondary

End point timeframe:

Treatment Period (Maximum 6 years)

End point values	Lacosamide			
Subject group type	Reporting group			
Number of subjects analysed	307			
Units: percentage of subjects				
number (not applicable)				
percentage	48.2			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Maximum of 6 years	
Assessment type	Non-systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	9.1

Reporting groups	
Reporting group title	Lacosamide
Reporting group description: Up to 800 mg/day lacosamide (flexible dosing)	

Serious adverse events	Lacosamide		
Total subjects affected by serious adverse events			
subjects affected / exposed	71 / 308 (23.05%)		
number of deaths (all causes)	2		
number of deaths resulting from adverse events	0		
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Testis cancer			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Basal cell carcinoma			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Breast cancer			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Vascular disorders			
Thrombosis			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Surgical and medical procedures			
Vagal nerve stimulator implantation			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
General disorders and administration site conditions			
Chest pain			
subjects affected / exposed	5 / 308 (1.62%)		
occurrences causally related to treatment / all	0 / 6		
deaths causally related to treatment / all	0 / 0		
Asthenia			
subjects affected / exposed	2 / 308 (0.65%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Pyrexia			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Immune system disorders			
Hypersensitivity			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Reproductive system and breast disorders			
Ovarian cyst			
subjects affected / exposed	2 / 308 (0.65%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Priapism			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Respiratory, thoracic and mediastinal disorders			

Pneumothorax				
subjects affected / exposed	2 / 308 (0.65%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Pulmonary oedema				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Haemoptysis				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 2			
deaths causally related to treatment / all	0 / 0			
Psychiatric disorders				
Mental status changes				
subjects affected / exposed	3 / 308 (0.97%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Suicidal ideation				
subjects affected / exposed	3 / 308 (0.97%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Depression				
subjects affected / exposed	2 / 308 (0.65%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Aggression				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Suicide attempt				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Psychotic disorder				

subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Sleep attacks				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Abnormal behaviour				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Paranoia				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Anxiety				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Investigations				
Hepatic enzyme increased				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Electrocardiogram QT corrected interval prolonged				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Blood pressure increased				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Injury, poisoning and procedural complications				

Fall				
subjects affected / exposed	2 / 308 (0.65%)			
occurrences causally related to treatment / all	1 / 2			
deaths causally related to treatment / all	0 / 0			
Drug toxicity				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Facial bones fracture				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skin laceration				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Traumatic haematoma				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Excoriation				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Limb injury				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Skull fracture				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Multiple fractures				

subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Accidental overdose				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Operative haemorrhage				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Subdural haematoma				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Burns third degree				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Hip fracture				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Jaw fracture				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Cardiac disorders				
Atrial fibrillation				
subjects affected / exposed	2 / 308 (0.65%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Ventricular extrasystoles				

subjects affected / exposed	2 / 308 (0.65%)			
occurrences causally related to treatment / all	2 / 2			
deaths causally related to treatment / all	0 / 0			
Angina pectoris				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Coronary artery stenosis				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 0			
Supraventricular tachycardia				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	1 / 1			
deaths causally related to treatment / all	0 / 0			
Cardio-respiratory arrest				
subjects affected / exposed	1 / 308 (0.32%)			
occurrences causally related to treatment / all	0 / 1			
deaths causally related to treatment / all	0 / 1			
Nervous system disorders				
Convulsion				
subjects affected / exposed	11 / 308 (3.57%)			
occurrences causally related to treatment / all	4 / 13			
deaths causally related to treatment / all	0 / 1			
Status epilepticus				
subjects affected / exposed	3 / 308 (0.97%)			
occurrences causally related to treatment / all	1 / 3			
deaths causally related to treatment / all	0 / 0			
Dizziness				
subjects affected / exposed	4 / 308 (1.30%)			
occurrences causally related to treatment / all	4 / 4			
deaths causally related to treatment / all	0 / 0			
Complex partial seizures				

subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Coordination abnormal			
subjects affected / exposed	2 / 308 (0.65%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Headache			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Transient ischaemic attack			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Myoclonus			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Grand mal convulsion			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Subarachnoid haemorrhage			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Eye disorders			
Diplopia			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal disorders			

Vomiting			
subjects affected / exposed	4 / 308 (1.30%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Nausea			
subjects affected / exposed	2 / 308 (0.65%)		
occurrences causally related to treatment / all	1 / 2		
deaths causally related to treatment / all	0 / 0		
Gastrointestinal haemorrhage			
subjects affected / exposed	2 / 308 (0.65%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Dyspepsia			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Small intestinal obstruction			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Abdominal pain			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		
Haematemesis			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Mesenteric vein thrombosis			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Peptic ulcer			

subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Rectal haemorrhage			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Gastrooesophagitis			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Hepatobiliary disorders			
Cholecystitis			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Chronic hepatitis			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Angioneurotic oedema			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal and urinary disorders			
Renal failure acute			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Nephrolithiasis			
subjects affected / exposed	2 / 308 (0.65%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Haematuria			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Renal failure			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Musculoskeletal and connective tissue disorders			
Intervertebral disc protrusion			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Pneumonia			
subjects affected / exposed	5 / 308 (1.62%)		
occurrences causally related to treatment / all	0 / 5		
deaths causally related to treatment / all	0 / 0		
Enterobacter pneumonia			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Cystitis			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Meningitis viral			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Wound infection			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		

Influenza			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Salpingitis			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Metabolism and nutrition disorders			
Dehydration			
subjects affected / exposed	3 / 308 (0.97%)		
occurrences causally related to treatment / all	1 / 4		
deaths causally related to treatment / all	0 / 0		
Anorexia			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		
Hyponatraemia			
subjects affected / exposed	1 / 308 (0.32%)		
occurrences causally related to treatment / all	1 / 1		
deaths causally related to treatment / all	0 / 0		

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

Non-serious adverse events	Lacosamide		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	265 / 308 (86.04%)		
Investigations			
Weight increased			
subjects affected / exposed	17 / 308 (5.52%)		
occurrences (all)	17		
Gamma-glutamyltransferase increased			
subjects affected / exposed	17 / 308 (5.52%)		
occurrences (all)	17		
Injury, poisoning and procedural			

complications			
Fall			
subjects affected / exposed	47 / 308 (15.26%)		
occurrences (all)	93		
Contusion			
subjects affected / exposed	57 / 308 (18.51%)		
occurrences (all)	90		
Joint sprain			
subjects affected / exposed	19 / 308 (6.17%)		
occurrences (all)	20		
Excoriation			
subjects affected / exposed	18 / 308 (5.84%)		
occurrences (all)	38		
Skin laceration			
subjects affected / exposed	38 / 308 (12.34%)		
occurrences (all)	69		
Head injury			
subjects affected / exposed	17 / 308 (5.52%)		
occurrences (all)	21		
Nervous system disorders			
Dizziness			
subjects affected / exposed	154 / 308 (50.00%)		
occurrences (all)	260		
Headache			
subjects affected / exposed	67 / 308 (21.75%)		
occurrences (all)	91		
Convulsion			
subjects affected / exposed	44 / 308 (14.29%)		
occurrences (all)	62		
Tremor			
subjects affected / exposed	41 / 308 (13.31%)		
occurrences (all)	57		
Balance disorder			
subjects affected / exposed	41 / 308 (13.31%)		
occurrences (all)	51		
Nystagmus			

subjects affected / exposed	34 / 308 (11.04%)		
occurrences (all)	37		
Coordination abnormal			
subjects affected / exposed	26 / 308 (8.44%)		
occurrences (all)	30		
Memory impairment			
subjects affected / exposed	20 / 308 (6.49%)		
occurrences (all)	21		
Somnolence			
subjects affected / exposed	25 / 308 (8.12%)		
occurrences (all)	28		
General disorders and administration site conditions			
Irritability			
subjects affected / exposed	19 / 308 (6.17%)		
occurrences (all)	21		
Fatigue			
subjects affected / exposed	36 / 308 (11.69%)		
occurrences (all)	45		
Gait disturbance			
subjects affected / exposed	18 / 308 (5.84%)		
occurrences (all)	22		
Eye disorders			
Vision blurred			
subjects affected / exposed	28 / 308 (9.09%)		
occurrences (all)	39		
Diplopia			
subjects affected / exposed	46 / 308 (14.94%)		
occurrences (all)	72		
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	56 / 308 (18.18%)		
occurrences (all)	78		
Vomiting			
subjects affected / exposed	47 / 308 (15.26%)		
occurrences (all)	66		
Diarrhoea			

subjects affected / exposed	25 / 308 (8.12%)		
occurrences (all)	32		
Constipation			
subjects affected / exposed	22 / 308 (7.14%)		
occurrences (all)	22		
Respiratory, thoracic and mediastinal disorders			
Cough			
subjects affected / exposed	20 / 308 (6.49%)		
occurrences (all)	23		
Pharyngolaryngeal pain			
subjects affected / exposed	27 / 308 (8.77%)		
occurrences (all)	29		
Skin and subcutaneous tissue disorders			
Rash			
subjects affected / exposed	20 / 308 (6.49%)		
occurrences (all)	21		
Psychiatric disorders			
Anxiety			
subjects affected / exposed	17 / 308 (5.52%)		
occurrences (all)	20		
Depression			
subjects affected / exposed	35 / 308 (11.36%)		
occurrences (all)	45		
Insomnia			
subjects affected / exposed	28 / 308 (9.09%)		
occurrences (all)	38		
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	18 / 308 (5.84%)		
occurrences (all)	26		
Back pain			
subjects affected / exposed	34 / 308 (11.04%)		
occurrences (all)	46		
Pain in extremity			
subjects affected / exposed	16 / 308 (5.19%)		
occurrences (all)	24		

Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	53 / 308 (17.21%)		
occurrences (all)	83		
Upper respiratory tract infection			
subjects affected / exposed	40 / 308 (12.99%)		
occurrences (all)	54		
Sinusitis			
subjects affected / exposed	32 / 308 (10.39%)		
occurrences (all)	46		
Influenza			
subjects affected / exposed	26 / 308 (8.44%)		
occurrences (all)	28		
Urinary tract infection			
subjects affected / exposed	25 / 308 (8.12%)		
occurrences (all)	37		
Bronchitis			
subjects affected / exposed	17 / 308 (5.52%)		
occurrences (all)	23		

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
05 April 2005	This amendment provided information regarding an additional study (SP0757) with an iv formulation of LCM in which subjects at selected sites of the SP0756 study were eligible to participate. In addition, the number of subjects allowed to enroll in the prerequisite double-blind study (SP754) was increased, leading to a longer enrollment period for the SP756 study. Therefore, the estimated number of subjects and the duration of this study were increased.
19 May 2006	This amendment provided further specifications concerning the withdrawal criteria regarding cardiac function. Administrative changes were also made.
20 March 2008	This amendment provided information regarding an extension of the study duration by 2 years to ensure that all subjects had access to LCM until it was otherwise (eg, commercially) available.
12 January 2009	This amendment provided additional detail for the procedures to be followed for subjects who discontinued from the study prematurely and for subjects who completed the study.

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported

Online references

http://www.ncbi.nlm.nih.gov/pubmed/22372628