Approved by UCB 13-Nov-2008

Clinical Study Summary (CSS) Template

CT Registry ID#: *NCT00151879*
Study No.: SP757

These results are supplied for informational purposes only. Prescribing decisions should be made based on the approved package insert.

Proprietary Drug Name	**INN**	**Therapeutic area and indication(s)**
Vimpat®	Lacosamide (SPM 927)	Epilepsy; Partial-onset seizures with or without secondary generalization

Name of Sponsor/Company: UCB

Title of Study:
A multicenter, open-label trial to investigate the safety and tolerability of intravenous SPM 927 as replacement for oral SPM 927 in subjects with partial seizures with or without secondary generalization

Investigator(s) (number only): Multicenter trial (26)

Study Center(s) (number only): 26

Length of Study:
Date first patient enrolled: 03-Feb-2005
Date last patient completed: 10-May-2006

Phase of Development: 3

Abstract:

This was a multicenter, open-label, inpatient trial to investigate the safety and tolerability of intravenous (iv) lacosamide (LCM) as replacement for oral LCM in subjects with partial-onset seizures with or without secondary generalization.

The objectives of this trial were to evaluate the safety and tolerability of LCM when given as iv infusions in subjects who were receiving oral LCM in addition to up to 3 concomitant antiepileptic drugs (AEDs) for partial-onset seizures with or without secondary generalization. LCM doses from 200mg/day up to 800mg/day were evaluated.

The trial was designed to administer LCM at progressively faster infusion durations under the direction of a Data Monitoring Committee. Subjects were enrolled into serial cohorts of progressively shorter infusion durations with the goal of identifying the appropriate infusion duration for LCM.

Subjects entered into a 1-day Screening Phase followed by a 2 to 5 day Treatment Phase, during which subjects received iv LCM infused over 10, 15, or 30 minutes twice daily (depending on cohort). The dose of iv LCM was the same as the subject's current daily dose in the open-label extension trial of oral LCM. Subjects receiving 700mg/day or 800mg/day were allowed to enter the trial only after review of the safety data from the first 3 cohorts. End of Trial Phase assessments were performed the day after the Treatment Phase was completed, after which subjects continued in the open-label extension trial (SP615, SP756, or SP774) where they resumed dosing with oral LCM as stipulated in that protocol.

Of the 160 subjects enrolled, all subjects were treated and 157 (98%) subjects completed the trial. Of the 160 treated subjects, 3 subjects discontinued the trial prematurely, 2 subjects discontinued due to adverse events (AEs), and 1 subject discontinued due to a change in concomitant AED. In the 30-, 15-, and 10-minute infusion duration groups, 43%, 24%, and 35% of subjects, respectively, reported at least 1 treatment-emergent AE (TEAE) during the Treatment Phase. The frequency of AEs did not increase with more days of exposure, nor with shorter infusion durations. Headache and dizziness were the most common AEs reported during the Treatment Phase. All AEs were assessed by the investigator as mild or moderate in intensity. There was

CT Registry ID#: *NCT00151879*
Study No.: SP757

1 serious adverse event (SAE) reported during the trial (bradycardia [transient]).

Number of Patients:

Planned, N:	**160**
Enrolled, N:	**160**
Treated, N (%):	**160 (100)**
Completed, n (%):	**157 (98)**
Number of Patients Withdrawn, n (%):	**3 (2)**
Withdrawn due to Adverse Events, n (%):	**2 (1)**
Withdrawn for Other Reasons, n (%):	**1 (1)**

Demography:

Gender (Females/Males):		**78/82**
Age (years), mean (SD):		**39.4 (11.24)**
Race, n (%):		
	White	**152 (95)**
	Black	**5 (3)**
	Other	**3 (2)**

Safety Outcomes:
- Summary of treatment emergent adverse events, deaths, other serious adverse events and certain other significant adverse events:

Treatment Emergent AEs (TEAE):

Number of Patients with TEAEs During the Treatment Phase (by Primary System Organ Class)	**LCM infusion duration (all days)**		
	30 minute N=40	**15 minute N=100**	**10 minute N=20**
	N (%) [n considered drug-related by the Investigator]		
Any System Organ Class (patients who experienced at least one TEAE)	17 (43) [15]	24 (24) [15]	7 (35) [2]
Cardiac disorders	2 (5) [2]	2 (2) [2]	0
Eye disorders	2 (5) [1]	7 (7) [7]	0
Gastrointestinal disorders	4 (10) [4]	6 (6) [3]	3 (15) [0]
General disorders and administration site conditions	2 (5)[2]	6 (6) [3]	3 (15) [0]
Infections and infestations	1 (3) [1]	1 (1) [0]	0
Investigations	2 (5) [0]	1 (1) [1]	0
Musculoskeletal and connective tissue disorders	1 (3) [1]	3 (3) [1]	1 (5) [1]
Nervous system disorders	13 (33) [11]	12 (12) [5]	3 (15) [1]
Respiratory, thoracic and mediastinal disorders	1 (3) [0]	0	0
Skin and subcutaneous tissue disorders	1 (3) [1]	1 (1) [0]	0
Vascular disorders	0	2 (2) [1]	0

Death, SAEs, and Other SAEs :

Death, n (%):	**0**
Patients with SAEs, n (%):	**1 (0.6)**

Approved by UCB 13-Nov-2008

CT Registry ID#: *NCT00151879*
Study No.: SP757

Nimber of Patients with SAEs During the Treatment Phase (by Primary System Organ Class)	**LCM infusion duration**		
	30 minute N=40	**15 minute N=100**	**10 minute N=20**
	N (%)		
Cardiac disorders	0	1 (1)	0

Primary & Secondary Outcomes:

Overall, this comprehensive evaluation supports the safety of iv LCM at doses of 200mg/day to 600mg/day (100mg to 300mg bid, respectively) at infusion durations of 30 minutes, 15 minutes, and 10 minutes as a short-term (2 to 5 days) replacement for oral LCM in patients with partial-onset seizures. Similar findings were observed at doses of LCM 700mg/day to 800mg/day at an infusion duration of 15 minutes for up to 4 days; however, there was a limited number of exposures at these doses.

Publication Reference(s) based on the study:
None

Date of report: 13-Nov-2008