Approved by UCB 18-Nov-2008

Clinical Study Summary (CSS) Template

CT Registry ID#: NCT00800215
Study No.: SP616

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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, double-blind, double-dummy, randomized trial to investigate the safety, tolerability and pharmacokinetics 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 (7)

Study Center(s) (number only): 7

Length of Study:
Date first patient enrolled: 04-Mar-2004
Date last patient completed: 17-Aug-2004

Phase of Development: 2

Abstract:

This was a multicenter, double-blind, double-dummy, randomized trial to investigate the safety, tolerability, and pharmacokinetics 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, tolerability, and pharmacokinetics of LCM when given as iv infusions compared with oral administration of the same dose strengths in subjects who were receiving oral LCM in addition to 1 or 2 concomitant antiepileptic drugs (AEDs) for partial seizures with or without secondary generalization.

A total of 60 subjects, who were participating in an open-label extension trial of oral LCM, were enrolled. The subjects were randomized in a 2:1 ratio to iv LCM plus placebo tablets twice daily (bid) or iv placebo plus oral LCM bid, respectively. Subjects were enrolled into 1 of 2 cohorts (30 subjects to Cohort A and 30 subjects to Cohort B). Subjects in Cohort A received 60-minute infusions of trial medication; whereas Cohort B received 30-minute infusions of trial medication. The dose of LCM (200 to 600mg/day; 100 to 300mg bid) during SP616 was the same as the subject's current daily dose in the open-label extension trial of oral LCM. Safety data from Cohort A were examined by a Data Monitoring Committee prior to the enrollment of the last 30 subjects in Cohort B. All enrolled subjects were randomized, had Baseline and post-Baseline data, and received at least 1 dose of trial medication.

Of the 60 subjects enrolled, all subjects were treated and 59 subjects completed the trial. Of the 60 subjects, 1 subject was prematurely discontinued due to a lack of venous access. No subjects discontinued due to adverse events (AEs). Few AEs were reported during the trial. A total of 8 subjects (27%) in Cohort A and 8 subjects (27%) in Cohort B experienced at least 1 treatment-emergent AE (TEAE). In general, the incidences of AEs were comparable between the cohorts and between the treatment groups. Events reported by 2 or more subjects within a treatment group/cohort included injection site pain, dizziness, headache, back pain, and somnolence. No AEs were severe in intensity. No serious adverse events (SAEs) were reported.

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Number of Patients:

Planned, N:	**60**
Enrolled, N:	**60**
Treated, N (%):	**60 (100)**
Completed, n (%):	**59 (98)**
Number of Patients Withdrawn, n (%):	**1 (2)**
Withdrawn due to Adverse Events, n (%):	**0**
Withdrawn for Other Reasons, n (%):	**1 (2)**

Demography:

Gender (Females/Males):	**35/25**
Age (years), mean (SD):	**41.7 (9.80)**
Race, n (%):	
White	**53 (88)**
Black	**6 (10)**
Asian	**1 (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 Body System)	**Cohort A (60 min)**		**Cohort B (30 min)**	
	Oral LCM + iv placebo N=10	**iv LCM + oral placebo N=20**	**Oral LCM + iv placebo N=11**	**iv LCM + oral placebo N=19**
	N (%)[n considered drug-related by the Investigator]			
Any System Organ Class (patients who experienced at least one TEAE)	3 (30) [1]	5 (25) [1]	2 (18) [1]	6 (32) [6]
Application site disorders	0	0	0	2 (11) [2]
Autonomic nervous system disorders	1 (10) [1]	0	1 (9) [1]	1 (5)[1]
Body as a whole – general disorders	0	1 (5) [0]	0	0
Cardiovascular disorders, general	1 (10) [0]	0	0	0
Central and peripheral nervous system disorders	0	2 (10) [1]	1 (9) [0]	5 (26) [4]
Gastrointestinal system disorders	2 (20) [1]	2 (10) [0]	1 (9) [1]	0 [0]
Musculo-skeletal system disorders	0	2 (10) [0]	0	0
Psychiatric disorders	0	0	0	2 (11) [1]
Reproductive disorders, female	0	1 (5) [0]	0	0
Respiratory system disorders	1 (10) [0]	0	0	0
Secondary terms	0	1 (5) [0]	0	0
Skin and appendages disorders	0	0	0	1 (5) [0]
Vision disorders	0	0	0	2 (11) [1]

Death, SAEs, and Other SAEs:

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

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Primary & Secondary Outcomes:

Overall, safety evaluations showed no safety issues of clinical concern when iv LCM was delivered during a 60-minute infusion or a 30-minute infusion. Results of this trial support the conclusion that iv LCM at doses of 200 to 600mg/day (100 to 300mg bid) is well tolerated as a replacement therapy for oral LCM at infusion rates of 60 minutes. This is also true for 200-400mg/day at an infusion rate of 30 minutes; however, additional exposures are needed to extend this conclusion to subjects receiving 500-600mg/day at a 30-minute infusion rate.

Publication Reference(s) based on the study:
Biton V, Rosenfeld WE, Whitesides J, Fountain NB, Vaiciene N, Rudd GD. Intravenous lacosamide as replacement for oral lacosamide in patients with partial-onset seizures. Epilepsia. 2008 Mar;49(3):418-24.

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