Approved by UCB 10-Jun-2008

Clinical Study Summary (CSS) Template

CT Registry ID#: *NCT00238524*
Study No.: SP743

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	Painful distal diabetic neuropathy

Name of Sponsor/Company: UCB

Title of Study:
A multi-center, randomized, double-blind, placebo controlled, parallel-group trial to assess the efficacy and safety of 400mg/day and 600mg/day SPM 927 in subjects with painful distal diabetic neuropathy.

Investigator(s) (number only): 59

Study Center(s) (number only): 52

Length of Study:
Date first patient enrolled: 17 Dec 2003
Date last patient completed: 06 Jan 2005

Phase of Development: 3

Abstract:

This was a multi-center, randomized, double-blind, placebo-controlled trial to assess the efficacy and safety of 400mg/day and 600mg/day of lacosamide (LCM) in subjects with painful distal diabetic neuropathy. Eligible subjects were randomized to receive a maximum of 400 or 600mg/day lacosamide (subjects had their dose titrated to randomized dose during a 6-week Titration Phase) or placebo. Two titration schemes for the 400mg/day lacosamide dose were evaluated to determine if additional tolerability was achieved at a slower titration rate. The target dose was maintained for 12 weeks (down-titration was not permitted) after which the subjects either entered a 2-week Transition Phase (for subjects who elected to continue treatment in an open-label trial) or a 1-week Taper Phase. The Taper Phase was followed by a 2-week Safety Follow-Up Phase.

Of the 411 enrolled subjects, 357 were randomized and received treatment. In all, 246 (68.9%) of the treated randomized subjects completed the trial.

Although the results from the primary efficacy analysis were not statistically significantly different from placebo, data from this trial consistently suggested that lacosamide treatment at doses of both 400mg/day and 600mg/day may be an effective treatment in reducing pain due to diabetic neuropathy, with a sustained effect over a 12-week Maintenance Phase.

Of the 111 (31.1%) subjects who discontinued early from the trial, the most common reason was adverse events (AEs) (52 subjects [14.6%]). Treatment-emergent AEs were most common among all treatment groups in the nervous system disorders SOC with 12.2% (9/74), 22.0% (33/150), and 35.3% (47/133) of subjects in the placebo, 400mg/day LCM, and 600mg/day LCM groups, respectively, reporting at least 1 AE in this SOC.

Number of Patients:

Planned to randomize, N:	**330**
Enrolled, N:	**411**
Randomized, N	**357**
Completed, n(%):	**246 (68.9)**
Number of Patients Withdrawn, n(%):	**111 (31.1)**

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Withdrawn due to Adverse Events, n(%):	**52 (14.6)**
Withdrawn for Other Reasons, n(%):	**10 (2.8)**
Demography:	(If applicable)
Gender (Females/Males):	**173/184**
Age (years), mean(SD):	**57.9 (10.56)**
Race, n(%):	
White	**356 (99.7)**
Other	**1 (0.3)**

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

Treatment Emergent AEs (TEAE)
Patients with at least one TEAE, n(%):

Patients with TEAEs (by Primary System Organ Class)	**Placebo N=74**	**LCM 400mg/day N=150**	**LCM 600mg/day N=133**
	n(%) [n considered drug-related by the Investigator]		
Blood and lymphatic system disorders	*1 (1.4) [0]*	*2 (1.3) [1]*	*1 (0.8) [0]*
Cardiac disorders	*3 (4.1) [0]*	*7 (4.7) [4]*	*6 (4.5) [5]*
Ear and labyrinth disorders	*2 (2.7) [2]*	*11 (7.3) [11]*	*12 (9.0) [7]*
Endocrine disorders	*0*	*1 (0.7) [0]*	*0*
Eye disorders	*4 (5.4) [1]*	*5 (3.3) [4]*	*8 (6.0) [7]*
Gastrointestinal disorders	*8 (10.8) [7]*	*22 (14.7) [18]*	*30 (22.6) [16]*
General disorders and administration site conditions	*11 (14.9) [7]*	*26 (17.3) [20]*	*21 (15.8) [15]*
Hepatobiliary disorders	*1 (1.4) [0]*	*2 (1.3) [0]*	*1 (0.8) [1]*
Immune system disorders	*0*	*1 (0.7) [0]*	*0*
Infections and infestations	*10 (13.5) [1]*	*24 (16.0) [1]*	*13 (9.8) [1]*
Injury, poisoning and procedural complications	*4 (5.4) [0]*	*8 (5.3) [1]*	*9 (6.8) [4]*
Investigations	*6 (8.1) [2]*	*15 (10.0) [7]*	*15 (11.3) [3]*
Metabolism and nutrition disorders	*1 (1.4) [0]*	*3 (2.0) [1]*	*7 (5.3) [2]*
Musculoskeletal and connective tissue disorders	*4 (5.4) [0]*	*11 (7.3) [1]*	*12 (9.0) [4]*
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	*1 (1.4) [0]*	*0*	*0*
Nervous system disorders	*9 (12.2) [5]*	*33 (22.0) [23]*	*47 (35.3) [39]*
Psychiatric disorders	*4 (5.4) [2]*	*4 (2.7) [2]*	*8 (6.0) [5]*
Renal and urinary disorders	*0*	*8 (5.3) [0]*	*3 (2.3) [0]*
Reproductive system and breast disorders	*1 (1.4) [0]*	*2 (1.3) [0]*	*1 (0.8) [0]*
Respiratory, thoracic and mediastinal disorders	*2 (2.7) [0]*	*11 (7.3) [4]*	*1 (0.8) [1]*
Skin and subcutaneous tissue disorders	*3 (4.1) [3]*	*11 (7.3) [6]*	*9 (6.8) [4]*
Social circumstances	*0*	*0*	*1 (0.8) [1]*
Surgical and medical procedures	*2 (2.7) [0]*	*4 (2.7) [0]*	*0*
Vascular disorders	*5 (6.8) [2]*	*7 (4.7) [1]*	*8 (6.0) [1]*

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Death, SAEs, and Other SAEs:
Death, n (%):
Patients with SAEs, n(%):

Patients with SAEs (by Primary System Organ Class)	**Placebo N=74**	**LCM (400mg/day) N=150**	**LCM 600mg/day N=133**
		n(%)	
Cardiac disorders	*0*	*2 (1.3)*	*1 (0.8)*
Gastrointestinal disorders	*0*	*0*	*2 (1.5)*
General disorders and administration site conditions	*0*	*1 (0.7)*	*1 (0.8)*
Injury, poisoning and procedural complications	*0*	*1 (0.7)*	*1 (0.8)*
Investigations	*0*	*0*	*1 (0.8)*
Metabolism and nutrition disorders	*0*	*0*	*1 (0.8)*
Musculoskeletal and connective tissue disorders	*0*	*2 (1.3)*	*0*
Neoplasms benign, malignant and unspecified (uncl cysts and polyps)	*1 (1.4)*	*0*	*0*
Nervous system disorders	*0*	*1 (0.7)*	*3 (2.3)*
Psychiatric disorders	*0*	*0*	*1 (0.8)*
Reproductive system and breast disorders	*0*	*1 (0.7)*	*0*
Surgical and medical procedures	*1 (1.4)*	*2 (1.3)*	*0*
Vascular disorders	*1 (1.4)*	*3 (2.0)*	*1 (0.8)*

Primary & Secondary Outcomes:

The primary efficacy variable was within-subject change in average daily pain score (11-point Likert scale) from the baseline week to the last 4 weeks of the Maintenance Phase. Secondary objectives were to investigate the effect of lacosamide on subjects' perception of pain, sleep, activity, and quality of life, as well as to investigate the pharmacokinetics and safety of lacosamide. The differences in the change from Baseline in average daily pain scores were not statistically significant for the comparison of either of the active treatment groups vs placebo to the last 4 weeks of Maintenance Phase (reduction in LSMean pain score from Baseline of 0.40- and 0.36-point with 400mg/day and 600mg/day lacosamide, respectively), but were statistically significantly different between either lacosamide treatment group and placebo at Visits 5 through 8, in the overall Maintenance Phase and the entire Treatment Phase (descriptive p-values <0.05 not adjusted for multiplicity).

Changes in other secondary efficacy endpoints also indicated that treatment with lacosamide was effective in treating painful distal diabetic neuropathy. The percentage of subjects with $\geq$30% or $\geq$2-point reduction in Likert pain score (a clinically meaningful change, Farrar et al, 2001) from Baseline to the last 4 weeks of the Maintenance Phase was higher in the lacosamide treatment groups than in the placebo group (35.1%, 43.0%, and 50.0% in the placebo, 400mg/day LCM, and 600mg/day LCM groups, respectively). Only the difference between the 600mg/day group and the placebo group was statistically significant (p-value = 0.0409).

Publication Reference(s) based on the study:
None

Date of report: 10-Jun-2008