CT Registry ID#: NCT00135109 *(ClinicalTrials.gov Identifier number)*
Study No.: SP768

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 diabetic neuropathy

Name of Sponsor/Company: Schwarz Pharma

Title of Study:
A multi-center, randomized, double-blind, placebo-controlled, parallel-group trial to assess the efficacy and safety of SPM 927 (200, 400, and 600mg/day) in subjects with painful distal diabetic neuropathy

Investigator(s) (number only): 83

Study Center(s) (number only): 84

Length of Study:
Date first patient enrolled: 02 Nov 2004
Date last patient completed: 28 Dec 2005

Phase of Development: Phase 3

Abstract:

This 18-week randomized, double-blind, placebo-controlled trial evaluated efficacy and safety of 200, 400, and 600mg/day oral lacosamide in 468 patients (18 years or older) with painful peripheral diabetic neuropathy with pain intensity ≥4 on the 11-point Likert scale for the previous ≥7 days. The trial assessed mean within-patient change from Baseline in Likert pain score to the last 4 weeks of the 12-week maintenance period (primary endpoint). Secondary outcomes assessed median reduction in pain scores from Baseline to the last 4 weeks of the trial, reductions in pain score from Baseline to end of each treatment phase. Safety evaluation considered adverse events, physical and laboratory examinations, and ECG. After a 2-week run-in period, eligible patients were randomized to placebo or 200, 400, or 600mg/day of lacosamide to begin a 6-week forced titration period when the dose was escalated from starting dose of 100mg/day to the randomized dose level at weekly intervals in 100mg/day increments. Patients then entered the 12-week maintenance phase, when dose adjustment was not permitted. Thereafter, patients opting to enter the open-label trial underwent a blinded 2-week transition phase on 200mg/day lacosamide or matching placebo. All other patients, including those withdrawing prematurely, entered a 1-week taper-phase followed by a 2-week safety follow-up period. Lacosamide 400 and 600mg/day consistently showed a trend towards efficacy in the primary variable supported by statistically significant non-parametric and post-hoc analysis of the primary variable and significant secondary variables. Overall, in the combined lacosamide treatment groups, dizziness (18.4%), nausea (11.9%), headache (10.4%), tremor (9.4%), somnolence (7.2%), balance disorder (5.7%), and pruritus (5.5%) were the most frequently reported treatment-emergent adverse events. Adverse events of weight change, edema, cognition, and behavior were low.

Publication Reference(s) based on the study:
Manuscript submitted to Journal of Pain.

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Number of Subjects: (If applicable)	**Placebo**	**Lacosamide (mg/day)**			**Total**
		200	**400**	**600**	
Planned, N:	-	-	-	-	652
Enrolled, N:	-	-	-	-	654
Randomized	66	141	125	137	469
Completed, n (%):	45 (68.2)	95 (67.4)	71 (56.8)	46 (33.6)	257 (54.7)
Number of Subjects Withdrawn, n (%):	21 (31.8)	46 (32.6)	54 (43.2)	91 (66.4)	212 (45.2)
Withdrawn due to Adverse Events, n (%):	9 (13.6)	17 (12.1)	30 (24.0)	58 (42.3)	114 (24.3)
Withdrawn for Other Reasons, n (%):	12 (18.2)	29 (20.6)	24 (19.2)	33 (24.1)	98 (20.9)
Demography: (If applicable)					
Gender (Females/Males):	27/39	57/84	53/72	67/70	204/265
Age (years), mean(SD):	59.5 (8.31)	60.2 (11.07)	60.3 (9.88)	59.1 (9.84)	59.8 (10.03)
Race, n (%):					
White	49 (74.2)	111 (78.7)	104 (83.2)	113 (82.5)	377 (80.4)
Black	9 (13.6)	19 (13.5)	12 (9.6)	16 (11.7)	56 (11.9)
Asian	0	1 (0.7)	1 (0.8)	0	2 (0.4)
Other	8 (12.1)	10 (7.1)	8 (6.4)	8 (5.8)	34 (7.2)

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

Treatment Emergent AEs: if applicable	**Placebo**	**Lacosamide**			**Total**
		200 mg/day	**400 mg/day**	**600 mg/day**	
Subjects with at least one TEAE, n (%):	55 (84.6)	113 (80.1)	99 (79.2)	119 (86.9)	386 (82.3)
Subjects with TEAEs (by Primary System Organ Class)	*n (%) [n considered drug-related by the Investigator]*				
Ear and labyrinth disorders	1 (1.5)	2 (1.4)	2 (1.6)	14 (10.2)	19 (4.1)
Eye disorders	2 (3.1)	7 (5.0)	5 (4.0)	12 (8.8)	26 (5.5)
Gastrointestinal disorders	15 (23.1)	35 (24.8)	27 (21.6)	50 (36.5)	127 (27.1)
General disorders and administrative site conditions	9 (13.8)	20 (14.2)	20 (16.0)	30 (21.9)	79 (16.8)
Infections and infestations	17 (26.2)	34 (24.1)	30 (24.0)	26 (19.0)	107 (22.8)
Musculoskeletal and connective tissue disorders	16 (24.6)	26 (18.4)	26 (20.8)	20 (14.6)	88 (18.8)
Nervous system disorders	11 (16.9)	42 (29.8)	60 (48.0)	86 (62.8)	219 (46.7)
Skin and subcutaneous tissue disorders	3 (4.6)	21 (14.9)	20 (16.0)	17 (12.4)	61 (13.0)

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Death, SAEs, and Other SAEs: if applicable	*n (%) [n considered drug-related by the Investigator]*				
Death, n (%):	0	2 (1.4) [0]	0	1 (0.7) [0]	3 (0.6) [0]
Subjects with SAEs, n (%):	4 (6.1)	7 (5.0)	6 (4.8)	9 (6.6)	26 (5.5)
Subjects with SAEs (by Primary System Organ Class)	*n (%) [n considered drug-related by the Investigator]*				
Cardiac disorders	1 (1.5) [0]	1 (0.7) [0]	1 (0.8) [0]	4 (2.9) [1]	7 (1.5) [1]
Gastrointestinal disorders	1 (1.5) [0]	0	0	1 (0.7) [0]	2 (0.4) [0]
Hepatobiliary disorders	1 (1.5) [0]	0	0	0	1 (0.2) [0]
Infections and infestations	0	0	2 (1.6) [0]	0	2 (0.4) [0]
Injury, poisoning and procedural complications	0	0	0	1 (0.7) [0]	1 (0.2) [0]
Investigations	0	0	0	1 (0.7) [1]	1 (0.2) [1]
Metabolism and nutrition disorders	1 (1.5) [0]	1 (0.7) [1]	0	0	2 (0.4) [1]
Musculoskeletal and connective tissue disorders	0	1 (0.7) [0]	1 (0.8) [0]	0	2 (0.4) [0]
Neoplasms benign, malignant, and unspecified (including cysts and polyps)	0	2 (1.4) [0]	0	0	2 (0.4) [0]
Nervous system disorders	1 (1.5) [0]	1 (0.7) [0]	1 (0.8) [0]	2 (1.5) [2]	5 (1.1) [2]
Psychiatric disorders	0	1 (0.7) [1]	1 (0.8) [0]	0	2 (0.4) [1]
Renal and urinary disorders	0	0	1 (0.8) [0]	0	1 (0.2) [0]

Primary outcome analysis showed pain score reductions of 2.01 on lacosamide 200 mg/day (p=0.28), 2.29 on 400 mg/day (p=0.0507), and 2.23 on 600 mg/day (p=0.07) compared with 1.67 on placebo. Median reductions in pain from Baseline to the last 4 weeks of the trial were 1.33 on placebo, 1.94 on lacosamide 200 mg/day (p=0.11), 2.37 on 400 mg/day (p=0.03), and 1.96 on 600 mg/day (p=0.04). Pain score reductions from Baseline over the titration phase were 0.78 on placebo compared with 1.38 on lacosamide 200 mg/day (p=0.014), 1.37 on 400 mg/day (p=0.018), and 1.45 on 600 mg/day (p=0.006). Reductions in pain score from Baseline over the maintenance phase were 1.88 on placebo compared with 2.21 on 200 mg/day (p=0.31), 2.77 on 400 mg/day (p=0.007), and 2.81 on 600 mg/day (p=0.007). Changes in other secondary efficacy endpoints supported the primary efficacy outcome.

Publication(s): Being submitted to Journal of Pain

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