Clinical Trial Results Summary
Study EN3220-008

Study Number: EN3220-008	
Title of Study: A Prospective, Open-Label, Multicenter Study of the Effectiveness and Safety of Lidoderm® as Add-on Treatment in Patients with Postherpetic Neuralgia, Diabetic Neuropathy, or Low Back Pain	
Investigators: 9 investigators	
Study Centers: 9 study centers located in the United States	
Publication (reference): None	
Study Period (years): Date of First Enrollment: June 12, 2002 Date of Study Visit: November 8, 2002	**Phase of Development:** Phase IV
Objectives: To assess the effectiveness of Lidoderm® administered once daily (q24h) after 14 days in the treatment of postherpetic neuralgia (PHN), diabetic neuropathy (DN), and low back pain (LBP) in patients who had a partial response (defined as pain >4 on a scale of 0 to 10) to a regimen containing gabapentin; to assess the safety and tolerability of Lidoderm patches applied q24h; to assess the effect of Lidoderm on quality of life (QOL) in patients with PHN, DN, and LBP who had a partial response to a regimen containing gabapentin; and to assess the impact of Lidoderm on various characteristics of pain in patients who are partially responsive to gabapentin.	
Methodology: This multicenter study was conducted using an open-label, non-randomized design in patients with PHN, DN, and LBP who had a partial response to a regimen containing gabapentin. At the screening evaluation (Day –5 to Day –3), patients were enrolled in the study after providing informed consent and completing all screening evaluations. To meet the study objectives, a sufficient number of patients were to be enrolled in the study to ensure that 100 patients completed at least 14 days of treatment including approximately 50 patients with PHN, approximately 25 patients with DN, and approximately 25 patients with LBP. During the 14-day treatment period, patients used up to four Lidoderm patches applied q24h. Patients returned to the study site on Day 7 for study assessments and on Day 14 for the end of study (EOS) assessments.	
Number of Subjects Planned and Analyzed: Planned: A sufficient number of patients were to be enrolled to ensure that 100 patients completed at least 14 days of treatment, including approximately 50 patients with PHN, 25 patients with DN, and 25 patients with LBP. Enrolled: 107 patients (11 with PHN, 49 with DN, and 47 with LBP) Intent-to-Treat population analyzed for effectiveness: 103 patients (11 with PHN, 47 with DN, and 45 with LBP) Treated population analyzed for safety: 107 patients (11 with PHN, 49 with DN, and 47 with LBP)	
Diagnosis and Main Criteria for Inclusion: Patients were males and females with a diagnosis of PHN, DN, or LBP who were currently receiving an analgesic regimen that contained gabapentin.	
Test Product, Dose and Mode of Administration, Batch Number(s): Commercially available Lidoderm (lidocaine patch 5%), up to four patches applied topically once daily (q24h) to the area of maximal peripheral pain. Lot number 1026.	
Duration of Treatment: 2 weeks	

Criteria for Evaluation:

Effectiveness: Average daily pain intensity (Brief Pain Inventory [BPI] Questions 3, 4, 5, and 6), pain quality using the Neuropathic Pain Scale (NPS), Investigator and Patient Global Impression of Change, extent of numbness at the site of pain using the Numbness Questionnaire, and Patient Global Assessment of Pain Relief.

Safety: Adverse events (AEs), discontinuations due to AEs, physical and neurological examination results, vital signs, clinical laboratory data, sensory testing, numbness testing, and dermal assessments.

Quality of Life: Pain interference (BPI Question 9) and Patient Global Assessments of Patch Satisfaction.

Statistical Methods:

Effectiveness: Mean change from baseline in daily pain intensity (BPI Questions 3-6) and NPS were analyzed using paired t-test. All analyses were performed for each of the patient groups separately and combined. Descriptive statistics were performed for Investigator and Patient Global Impression of Change, Numbness Questionnaire and, Patient Global Assessment of Pain Relief.

Safety: The frequency of AEs, treatment-emergent AEs (TEAEs), and treatment-related TEAEs was tabulated by MedDRA® term and body system. The incidence of AEs was summarized using appropriate descriptive statistics. Serious adverse events (SAEs) and discontinuations due to AEs were summarized. All clinical laboratory measurements were summarized by mean values, changes from baseline, and shift changes. Vital signs, physical and neurological examinations, and dermal/sensory assessments were summarized.

QOL: BPI Question 9 was analyzed similarly to the BPI Questions 3, 4, 5, and 6. The Global Assessment of Patch Satisfaction was summarized descriptively by presenting the number and percentage of patients' responses in each patient group.

SUMMARY:

Effectiveness Results: Statistically significant improvement (decrease) was seen for all groups in the mean change in daily pain intensity at Day 14/EOS from baseline (Day 0) as measured by BPI Questions 3, 4, 5, and 6. For each BPI question, the PHN Group demonstrated consistently greater improvement than the other two groups, and the DN Group consistently showed greater improvement than the LBP Group. Mean change from baseline to Day 14/EOS ranged from -2.0 to -2.9, -1.2 to -1.8, and -0.8 to -1.0 over all BPI questions for the PHN, DN, and LBP Groups, respectively.

Statistically significant improvements (decreases) in mean change from baseline to Day 14/EOS were observed in both the DN and LBP Groups for the majority of individual NPS pain item scores. Symptoms where improvements did not reach statistical significance were "cold," "itchy," and "surface pain" for the LBP Group and all symptoms for the PHN Group. Mean changes from baseline to Day 14/EOS for the DN Group were approximately -2.0 across all NPS items.

All NPS composite scores showed statistically significant decreases in the mean change from baseline between baseline and Day 14/EOS for the DN and LBP Groups. No statistically significant results were observed for the PHN Group.

An equal percentage of patients and investigators in the PHN Group (approximately 82%) recorded minimal/moderately, or much improved change in pain. A slightly greater percentage of investigators than patients in the DN (53% versus 49%, respectively) and LBP (38% versus 36%, respectively) Groups reported moderately or much improved change in pain.

Mean baseline scores for numbness were notably higher for the DN Group (5.7) than for either of the PHN (2.5) or LBP (1.2) Groups. Mean change from baseline to Day 14/EOS revealed a statistically significant decrease (improvement) in numbness scores for the DN Group (-1.6, p-value < 0.001). Patients in the DN Group most frequently reported "no change" (45% of patients) or "improved" (40% of patients) numbness. In the LBP Group, most patients (49%) reported "no change" in numbness.

In the PHN Group, equal percentages of patients (36%) reported "no change" and "improved" numbness.

No patients reported complete pain relief, but most reported "a lot" or "moderate" relief.

Quality of Life Results: Statistically significant decreases from baseline to Day 14/EOS were seen in all BPI Question 9 sub-items for all groups except for "walking ability" and the "relations with other people" in the PHN Group. For most sub-items, mean decreases from baseline were notably larger in the PHN Group than either of the DN or LBP Groups.

Most patients reported being satisfied or very satisfied with the patch with the largest percentage of patients reporting these two highest levels of patch satisfaction in the PHN Group (73%) compared to the DN (68%) and LBP Groups (53%).

Safety Results: Overall, 29.0% of patients reported at least one TEAE. Similar percentages of patients reported at least one TEAE across the groups. The most frequently reported TEAEs overall were those associated with the skin and subcutaneous tissue disorders, investigations, and nervous system disorders system organ classes. The most frequent TEAE was dermatitis NOS (in 1 DN patient, 2.0% and 2 LBP patients, 4.3%).

Six patients (5.6%) discontinued prematurely due to TEAEs with similar percentages of patients discontinuing due to TEAEs across the groups (1 patient, 9.1% PHN; 2 patients, 4.1% DN; and 3 patients, 6.4% LBP). Two patients (both in the DN Group) reported SAEs (confusion and mesenteric ischemia).

No clinically notable changes were seen in laboratory tests, vital signs, physical examinations, neurological, dermal, or sensory assessments during the study.