Clinical Trial Results Summary
Study EN3220-011

Study Number: EN3220-011	
Title of Study: A Prospective, Double-Blind, Randomized, Placebo-Controlled, Pilot Study of the Efficacy and Safety of Lidoderm Patch in the Treatment of Low Back Pain	
Investigators: 5 Investigators	
Study Centers: 12 centers in the United States	
Publication (reference): none	
Study Period (years): First patient visit: April 7, 2003 Last patient visit: August 19, 2003	**Phase of Development:** Phase IV

Objectives: The primary objective was to evaluate the analgesic efficacy of the lidocaine patch 5% compared to placebo in patients with moderate to severe chronic low back pain (LBP).

The secondary objectives were to assess:

- The safety and tolerability of continuous 24-hour application of the lidocaine patch 5%
- The impact of treatment with lidocaine patch 5% compared to placebo on quality of life (QOL) in patients with moderate to severe LBP
- The impact of treatment with lidocaine patch 5% compared to placebo on pain qualities reported by patients with moderate to severe LBP
- Patient and investigator global impressions of change after treatment with lidocaine patch 5% compared to placebo

Methodology: This was a multicenter, prospective, pilot study conducted using a double-blind, randomized, placebo-controlled design to assess the efficacy and safety of the lidocaine patch 5% in LBP for 6 weeks.

At the screening evaluation (Day -7), patients with moderate to severe chronic LBP despite current analgesic treatment were enrolled in the study after providing informed consent and completing all screening evaluations. Thereafter, patients were to record average daily pain intensity in a diary for 1 week prior to the baseline visit (Day 0). To be eligible to participate in the study, patients had to have a mean daily pain intensity score during the baseline week of ≥6 on a 0 to 10 scale, with 0 being no pain and 10 being pain as bad as the patients have ever imagined (Question 5 of the Brief Pain Inventory [BPI]).

At the baseline visit, eligible patients were randomized equally to one of two groups: lidocaine patch 5% or matching placebo patch. During the 6-week treatment period, patients used up to three patches daily applied q24h and completed daily diaries to record the number of patches used, average daily pain score, and any concomitant medications used. On Days 7, 14, 28, and 42, patients returned to the study site for study assessments. On Days 21 and 35, site personnel contacted patients by telephone to assess concomitant medication use, adverse events (AEs), and average daily pain intensity. On Days 7 and 42, blood samples were collected just prior to patch application for determination of plasma lidocaine concentrations.

Number of Subjects Planned and Analyzed:

Planned: Approximately 100 patients

Enrolled: 102 (51 Lidocaine and 51 Placebo)

Intent-to-Treat Population Analyzed for Efficacy: 99 (49 Lidocaine and 50 Placebo)

Treated Population Analyzed for Safety: 102 (51 Lidocaine and 51 Placebo)

Diagnosis and Main Criteria for Inclusion: Males or females, 18 years of age or older, with LBP who were currently experiencing moderate/severe pain despite current analgesic treatment.

Test Product, Dose and Mode of Administration, Batch Number(s):
Lidoderm (lidocaine patch 5%), up to three patches applied topically once daily (q24h) to the area of maximal peripheral pain; Lot number: 51292

Reference Therapy, Dose and Mode of Administration, Batch Number(s):
Matching placebo patch up to three patches applied topically once daily (q24h) to the area of maximal peripheral pain; Lot number: 51291

Duration of Treatment: 6 weeks

Criteria for Evaluation:

Efficacy: Mean change in average daily pain intensity (BPI Question 5) from baseline week to the final week of treatment (primary endpoint); mean change from baseline to Week 2 and Week 6/end of study (EOS) in average daily pain intensity (BPI Question 5) and pain relief (BPI Question 8); mean change from baseline to Week 2 and Week 6 in Pain Quality Assessment Scale (PQAS); Patient and Investigator Global Impression of Pain Relief at Week 6.

Safety: AEs, discontinuations as a result of AEs, clinical laboratory tests, vital signs, physical examinations, plasma lidocaine levels, dermal assessments, and skin sensory testing.

Quality of Life: Change from baseline to Week 6 in pain interference with QOL (BPI Question 9) and Profile of Mood States (POMS); Patient and Investigator Global Assessments of Patch Satisfaction.

Statistical Methods:

Efficacy: For the primary endpoint (BPI Question 5 from diary data), BPI Questions 3, 4, 5, 6 and 8 (from visit data), and PQAS composite scores, the mean change from baseline was assessed by analysis of covariance (ANCOVA) or analysis of variance (ANOVA). Least Squares mean (LSmean) differences from ANCOVA and ANOVA models were calculated as LSmeans for lidocaine minus the LSmeans for placebo. Mean change in pain relief (BPI Question 8) from baseline to Week 2 and Week 6/EOS was analyzed using an ANOVA model. Treatment and center were included as effects in the model. Patient and Investigator's Global Assessment of Pain Relief at Week 6 was analyzed using stratified rank-sum test procedure, stratified by center.

Safety: The frequency of AEs, treatment-emergent AEs (TEAEs), and treatment-related TEAEs were 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 examinations, dermal assessments, and skin sensory assessments were summarized.

Quality of Life: BPI Question 9, POMS, and Patient Global Assessment of Patch Satisfaction results were summarized. BPI Question 9 was analyzed similarly to BPI Question 8. The POMS was summarized and change from baseline to Week 2 and Week 6 was summarized and analyzed via paired-t-test. The Global Assessment of Patch Satisfaction was analyzed using stratified rank sum test procedure, stratified by center.

SUMMARY:

Efficacy Results: The Placebo Group demonstrated a greater improvement in average daily pain intensity (BPI Question 5 from daily diary data) from the baseline week to the final week (-2.54) than the Lidocaine Group (-1.91). There were no statistically significant differences between the treatment groups in the changes from baseline to Week 2 and Week 6/EOS for any of the BPI questions.

Mean percent pain relief increased from baseline to each post-baseline assessment in both treatment groups.

Mean PQAS-20, PQAS-18, and PQAS-4 composite scores decreased from baseline to Week 2 and Week 6/EOS for both treatment groups. No statistically significant differences were seen between the treatment groups.

In the patient and investigator assessment of global impression of pain relief, similar percentages of patients reported "moderate improvement", "a lot of improvement", or "complete improvement" in the Lidocaine (54%) and Placebo (58%) Groups. Similar percentages were also seen for the investigator assessment.

Pharmacokinetic Results: Mean plasma Lidocaine concentrations levels for Week 1 were 34.3 ng/mL (SD =22.89) and 0.0 ng/mL (SD = 0.0) for the Lidocaine and Placebo Groups, respectively. Mean plasma lidocaine concentrations levels for Week 6/EOS were 40.5 ng/mL (SD =49.80) and 0.9 ng/mL (SD =4.45) for the Lidocaine and Placebo Groups, respectively.

Safety Results: Overall, 19/51 patients (37.3%) in the Lidocaine Group and 17/51 patients (33.3%) in the Placebo Group reported at least one TEAE. The most frequently reported TEAEs in the Lidocaine Group were hypoaesthesia, application site pruritus, and application site hyperaesthesia (two patients each, 3.9%), and the most frequent events in the Placebo Group were headache (three patients, 5.9%) and application site pruritus, gastroenteritis viral NOS, and cough (two patients each, 3.9%).

No deaths or treatment-emergent SAEs occurred during this study. One patient in the Placebo Group experienced an SAE within 30 days of completing the study. Three patients in the Lidocaine Group and one patient in the Placebo Group discontinued due to AEs. No clinically important changes or trends in laboratory tests, vital signs, physical examinations, dermal assessments, or skin sensory assessments occurred during the study.

Quality of Life Results: BPI Question 9 pain interference scores decreased from baseline at each assessment for both treatment groups; however, no statistically significant differences were seen between the treatment groups in the mean changes from baseline to Week 2 or Week 6/EOS.

All raw POMS composite score mean values showed statistically significant decreases from baseline to Week 2 and Week 6/EOS except Vigor-Activity (which showed slightly positive mean changes in both groups) and Confusion-Bewilderment (for which the decreases from baseline were not statistically significant at Week 6/EOS for either group).

Global assessment of patch satisfaction results were similar between the two treatment groups. Most patients and investigators reported being either "satisfied" or "very satisfied" with the patch.