Study Number: EN3260-001	
Title of Study: A Randomized, Double-Blind, Pilot Study Comparing the Efficacy and Safety of Lidocaine 5% Patch With Placebo in Patients With Pain From Osteoarthritis of the Knee	
Investigators: 25 investigators	
Study Centers: 25 study centers in the United States	
Publication (reference): None.	
Study Period (years): August 9, 2004 to September 1, 2005	**Phase of Development:** II
Objectives: The primary objective of the study was to assess the efficacy of lidocaine 5% patch compared with placebo in the treatment of pain from osteoarthritis (OA) of the knee. The secondary objectives were to assess: the impact of treatment with lidocaine 5% patch compared with placebo on various qualities of pain, the safety of lidocaine 5% patch compared with placebo, the patient and investigator global impression of change in OA pain after treatment with lidocaine 5% patch compared with placebo, and the impact of treatment with lidocaine 5% patch compared with placebo on quality of life (QOL).	
Methodology: This randomized, double-blind, placebo-controlled pilot study was conducted at multiple investigational sites in patients with moderate-to-severe pain from OA of one or both knees. At the screening visit (Day –14), patients provided written informed consent and completed all screening evaluations, including the identification of the index joint, i.e., the knee to be used for all OA pain assessments throughout the study. (For patients with OA of both knees, the index joint was the knee with more severe pain.) Patients who met eligibility criteria entered an open-label, placebo run-in period for up to 14 days and discontinued use of all analgesic medications, chondroitin, and glucosamine. (Patients were permitted to use a stable dose of aspirin daily for cardiac prophylaxis.) All patients applied 1⅓ placebo patches on each affected knee once every 24 hours (q24h) at approximately the same time of day. Patients recorded average daily pain intensity in the index joint in a diary (at bedtime). Site personnel contacted patients at least every other day (via telephone) to monitor average daily pain intensity scores, adverse events (AEs), and to ensure that analgesic medications were not used. When patients' average daily pain intensity score was 6 or greater (on a scale of 0 to 10 using Question 5 of the Brief Pain Inventory [BPI]) for 3 days out of the 5 consecutive days immediately prior to the baseline visit, and they had an OA severity score of 7 or greater (on a composite scale of 0 to 24 using the Index of Severity for Osteoarthrosis of the Knee), baseline procedures were conducted. After all baseline assessments were completed, eligible patients were randomly allocated to receive one of two treatments for 12 weeks: lidocaine 5% patch or matching placebo patch. Patients returned to the study site at Weeks 2, 4, 6, and 8 for study assessments and again at Week 12 for end-of-study (EOS) assessments.	
Number of Patients Planned and Analyzed: Planned: approximately 200 patients (100 per treatment arm) Entered Placebo Run-In: 443 Randomized: 224 (112 active, 112 placebo) Analyzed for efficacy based on MITT: 213 (108 active, 105 placebo) Analyzed for safety based on treated population: 224 (112 active, 112 placebo)	
Diagnosis and Main Criteria for Inclusion: Patients 18 years of age or older who were in generally good health with unilateral or bilateral OA of the knee diagnosed according to the American College of Rheumatology (ACR) criteria based on clinical and radiographic evidence (presence of osteophytes on	

x-ray and written evaluation) of OA and who had a functional capacity class rating of I, II, or III according to ACR classification criteria.

Test Product, Dose and Mode of Administration, Batch Number(s): Lidocaine 5% patch (Lidoderm®, Endo Pharmaceuticals Inc.), 1⅓ patches applied on each affected knee once every 24 hours; lot number Y3112

Reference Therapy, Dose and Mode of Administration, Batch Number(s): Matching placebo patch, 1⅓ patches applied on each affected knee once every 24 hours; lot number Y3111

Duration of Treatment: 12 weeks

Criteria for Evaluation:

Efficacy

- Western Ontario and McMaster Universities (WOMAC) OA Index
- Pain intensity and pain relief (BPI Questions 3, 4, 5, 6, and 8)
- Pain Quality Assessment Scale (PQAS)
- Patient-rated and Investigator-rated Global Impression of Change in OA pain (categorical scale)
- Patient-rated and Investigator-rated Global Assessment of Treatment Satisfaction (categorical scale)

Safety

- AEs
- Dermal assessments
- Clinical laboratory tests, including urinalysis
- Vital sign measurements
- Physical examination results
- Plasma lidocaine concentrations

QOL

- Pain interference on activities of daily living using Question 9 of the BPI
- Beck Depression Inventory (BDI)
- Quality of Sleep (QOS)

Statistical Methods: Statistical analyses were performed and summary tables and data listings were prepared using SAS® software (Version 8.2). A result was determined to be statistically significant when the accompanying statistical test (two-tailed) yielded a probability of less than 0.05. P-values are shown to three decimal places to assess statistical significance against the criterion ($p<0.050$).

Descriptive statistics were used to summarize treatment group characteristics. Number and percent of patients were presented for categorical variables. Percentages were based on non-missing data. Mean, standard deviation, median, and range are presented for continuous data. For height and weight, non-missing baseline values were used; however, if the baseline value was missing, the screening value was used.

SUMMARY:

Efficacy Results: The primary efficacy endpoint, mean change in WOMAC pain subscale score from baseline to Week 12, was not statistically significant (p-value = 0.096). Although the mean WOMAC pain subscale scores for lidocaine patients improved from baseline to Week 12 (11.3 to 7.9), placebo patients' pain scores also improved from baseline to Week 12 (12.1 to 7.2), and at a similar rate to lidocaine patients' pain scores.

Safety Results: The lidocaine 5% patch was well tolerated compared to placebo. The incidence of treatment related AEs was similar in both groups, and low overall. Eight patients (4 lidocaine, 4 placebo) out of 224 total randomized patients discontinued due to AEs. Two serious AEs (SAEs) were reported during the study by 2 patients. Both SAEs were assessed to be unlikely related to the study drug.