

Clinical Trial Results Summary  
 Study EN3220-013

<b>Study Number:</b> EN3220-013	
<b>Title of Study:</b> A Randomized, Open-Label Study Comparing the Efficacy and Safety of Lidocaine Patch 5% With Celecoxib 200 mg in Patients With Chronic Axial Low Back Pain	
<b>Investigators:</b> 18 investigators	
<b>Study Centers:</b> 18 study centers in the United States	
<b>Publication (reference):</b> Nicholson B, Gammaitoni A, Oleka N, <i>et al.</i> A randomized, open-label, pilot study comparing the efficacy and safety of lidocaine patch 5% with celecoxib 200 mg/day in patients with chronic axial low back pain. <i>Medscape General Medicine</i> (in press).	
<b>Study Period (years):</b> July 26, 2004 to November 15, 2004	<b>Phase of Development:</b> IV
<p><b>Objectives:</b> The primary objective of the study was to assess the efficacy of the lidocaine patch 5% compared to celecoxib 200 mg in treating chronic axial low back pain (LBP) with and without radiation. A secondary objective was to assess the safety and tolerability of the lidocaine patch 5% compared to celecoxib 200 mg. Additional secondary objectives included comparative assessment of the impact of either treatment on the quality of life and functionality. Only the safety and tolerability objectives are presented in this report.</p>	
<p><b>Methodology:</b> This multicenter study was conducted using a randomized, open-label, active-controlled, parallel-group design consisting of a maximum 14-day washout period followed by a 12-week active treatment period.</p> <p>After the screening visit, patients who provided written informed consent and met eligibility criteria entered a washout period for up to 14 days. During this period, patients discontinued use of all analgesic medications (except use of a stable daily dose of aspirin for cardiac prophylaxis, if indicated), glucosamine, and chondroitin. Also during this period, patients recorded average daily pain intensity associated with LBP in a diary at bedtime. When patients' pain intensity reached a score of 5 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, they were randomly allocated to one of two treatments and received either lidocaine 5% patch or celecoxib 200 mg daily for 12 weeks. Patients were contacted by telephone at specified time points during the washout and treatment periods to monitor adverse events (AEs) and ensure compliance with the study protocol.</p> <p>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.</p> <p>While this study was underway, rofecoxib, a cyclooxygenase-2 (COX-2) inhibitor, was withdrawn from the market due to safety concerns. As a result of unresolved concerns about COX-2 inhibitors as a class, the sponsor decided to halt the study in November 2004 prior to the completion of enrollment. Therefore, an abbreviated clinical study report (CSR) was prepared, which includes only the safety evaluation.</p>	
<p><b>Number of Subjects Planned and Analyzed:</b></p> <p>Planned: Approximately 200 patients (100 in each treatment arm)</p> <p>Entered Washout: 122 patients</p> <p>Randomized to Treatment: 98 (50 lidocaine, 48 celecoxib)</p> <p>Analyzed for Safety based on Treated Population: 96 (49 lidocaine, 47 celecoxib)</p>	

<b>Diagnosis and Main Criteria for Inclusion:</b> Patients 18 years of age or older who were in generally good health and had axial LBP with or without radiation present for at least 3 months and had daily moderate to severe LBP as the primary source of pain.
<b>Test Product, Dose and Mode of Administration, Batch Number(s):</b> Lidocaine patch 5% (Lidoderm <sup>®</sup> , Endo Pharmaceuticals Inc.), 2 patches applied once daily (q24h) directly to the most painful area of the low back, lot number 5321.
<b>Reference Therapy, Dose and Mode of Administration, Batch Number(s):</b> Celecoxib (Celebrex <sup>®</sup> , G.D. Searle & Co., Chicago, IL), one 200 mg oral capsule QD, lot number C300608.
<b>Duration of Treatment:</b> 12 weeks
<b>Criteria for Safety and Tolerability Evaluation:</b> <ul style="list-style-type: none"><li>• AEs, including discontinuations due to AEs</li><li>• Dermal assessment (lidocaine group only)</li><li>• Skin sensory testing (lidocaine group only)</li><li>• Clinical laboratory test results, including urinalysis</li><li>• Vital signs measurements</li><li>• Physical and neurological examinations</li><li>• Body weight</li><li>• Plasma lidocaine concentrations (lidocaine group only)</li></ul>
<b>Statistical Methods:</b> <p>The frequency of treatment-emergent AEs (TEAEs), treatment-related TEAEs, and TEAEs by intensity were tabulated by Medical Dictionary for Regulatory Activities (MedDRA) preferred term and system organ class (SOC). Serious adverse events (SAEs) and discontinuations due to AEs were summarized separately. All clinical laboratory measurements were summarized by mean values, changes from baseline, and shift changes. Vital signs, body weight, physical and neurological examinations, dermal/sensory assessments, and plasma lidocaine concentrations were summarized.</p>
<b>SUMMARY:</b> <p>A total of 96 patients (49 lidocaine and 47 celecoxib) received at least one dose of study medication. Of the 96 patients, only 13 patients completed the full 12-week course of treatment due to the early termination of the study. At least one TEAE was reported by 32.7% (16/49) of patients in the lidocaine group and by 42.6% (20/47) of patients in the celecoxib group. Nausea was the only treatment-related AE occurring in at least two patients in either treatment group. Three lidocaine-treated patients discontinued prematurely as a result of AEs (back pain; application site anesthesia and tenderness; and application site burning, rash, and edema); four celecoxib-treated patients discontinued prematurely as a result of AEs (upper abdominal pain; anasarca, muscle spasms, and headaches). There were no deaths or non-fatal SAEs reported in this study. There were no clinically notable changes in laboratory test results, vital signs, and neurological and physical examinations.</p> <p>There was little systemic absorption of lidocaine with plasma concentrations maintained well below the levels associated with cardiac activity (1500 ng/mL) or toxicity (5000 ng/mL). The lidocaine patch was well tolerated. There were no reports of moderate or severe erythema, edema, or papules; vesicular reaction was reported in only one patient.</p>