ASA 2010 Annual Meeting

Title: EXPAREL™, A Liposomal Bupivacaine Local Analgesic, Extends Pain Relief and Decreases Opioid Use

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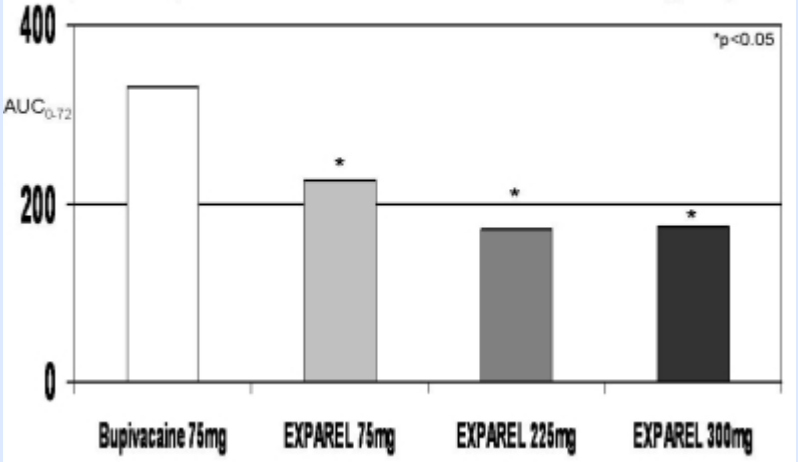
Background: Liposomal drug-containing formulations can provide for controlled drug release over an extended period of time. This FDA-approved, Phase 2 clinical trial compared EXPAREL, an experimental liposomal bupivacaine-based analgesic, to plain bupivacaine for the prevention of pain after hemorrhoidectomy procedures.

Methods: After obtaining IRB approval, 100 consenting patients undergoing hemorrhoidectomy were randomly assigned to receive either a single injection of bupivacaine (75mg; n=26) or EXPAREL (75mg, 225mg, or 300mg; n=24, 25, and 25) at the conclusion of the surgical procedure. The severity of pain was assessed after surgery at specific time points using a numeric rating scale (NRS) at rest for pain with 0 = no pain and 10 = worst possible pain. The NRS scores were used to calculate the area under the curve (AUC) through multiple postoperative time points. Other endpoints included number of patients who required no parenteral opioid analgesic medications, median time to first opioid use (rescue), total opioid analgesic requirement, and an integrated analysis of pain score and opioid usage.

Results: The AUC for the NRS pain scores from the start of study drug injection through 72 hours after surgery demonstrated a statistically significant advantage to EXPAREL over bupivacaine at all doses tested ($p=0.03$ for 75mg; $p<0.01$ for 225mg; $p<0.01$ for 300mg; as shown in figure 1). These results maintained significance through 96 hours ($p=0.02$, <0.01, and <0.001, respectively). A larger percentage of EXPAREL-treated patients avoided opioid rescue medication during the first 72 hours after surgery (16% for 75mg, 24% for 225mg, and 32% for 300mg of EXPAREL compared to only 8% for bupivacaine). The total opioid dosage requirement and median time to first opioid use were significantly different between the EXPAREL 300mg group and the plain bupivacaine group (6mg vs 20mg; $p<0.01$ and 19 hours vs 8 hours; $p<0.01$). An integrated analysis accounting for both pain scores and opioid usage further supported the advantages of EXPAREL in reducing postoperative pain and the need for opioid rescue analgesic therapy. Treatment emergent adverse events (TEAEs) were reported by 20% of EXPAREL-treated patients compared to 42% in the plain bupivacaine group; however, there were no deaths or discontinuations due to TEAEs in either group.

Figure 1: The dose-dependency of the AUC for the postoperative NRS pain scores from 0-72 hr in the plain bupivacaine and EXPAREL treatment groups



Conclusion: EXPAREL, an investigational long-acting local analgesic, appears to offer clinically significant advantages over plain bupivacaine in preventing pain by increasing duration of analgesia and decreasing the need for opioid analgesic drugs after hemorrhoidectomy procedures.

Funding: There are no external funding sources for this abstract.

Summary: EXPAREL, a liposomal bupivacaine based analgesic, resulted in significant decreases in postoperative pain and opioid usage compared to plain bupivacaine.