Treatment of Postoperative Pain in Shoulder Surgery With SABER®-Bupivacaine

INTRODUCTION

• Early postsurgical pain typically peaks on the first postoperative day with limited improvement in the first 72 hours.
• Therefore, many surgical procedures performed under general anesthesia require complex postoperative pain management involving opioids, but up to 80% of patients experience an opioid-related adverse event (4).
• Local anesthetics can significantly reduce pain after surgery, but the short duration (4-24 hours) of most provides little relief past the first postoperative day (1,2).
• SABER-Bupivacaine (lysoeucel catechol lysoeucel tetradecyl gelseeducel-bupivacaine) is a semiliminary solution that contains the active ingredient bupivacaine (152 mg/mL) in a delivery platform composed of a biodegradable organic matrix and the solvent benzyl alcohol (3).
• On instillation, the solvent diffuses leaving an extended-release, in situ depot that delivers the local anesthetic at the surgical site throughout the first 72 postoperative hours.
• SABER-Bupivacaine is intended to prolong pain relief after surgery, reduce reliance on opioid analgesic medications, and improve postoperative recovery by slowly releasing bupivacaine for 72 hours (3).
• The trial presented was conducted to evaluate SABER-Bupivacaine treatment for postoperative pain in patients undergoing arthroscopic subacromial decompression.

METHODS

Study Design and Treatment

• This was an international, parallel-group, randomized, double-blind, active-placebo-controlled phase 2 trial in 107 adult patients (>18 years of age) undergoing elective arthroscopic shoulder surgery.
• Patients were randomly assigned in a 2:1:1 allocation ratio to the following treatment arms:
  - 5 mL SABER-Bupivacaine (660 mg bupivacaine; n = 53)
  - 5 mL SABER-placebo (n = 25)
• Arthroscopic subacromial decompression was performed on day 0, entry to the subacromial space was through 3 to 4 standard portals under general anesthesia.
• On completion of the shoulder surgery, a single dose of treatment medication was deposited subacromially under direct vision with the arthroscope.
• All patients received paracetamol (4 g/day) as background treatment. If pain was not sufficiently relieved, patients were allowed rescue medication in the form of morphine (oral or intravenous [IV]) from day 0 to 72 hours after surgery.

Study End Points

• The co-primary end point of mean pain intensity on movement AUC for the time period 1 hour to 72 hours after surgery was 5.16 (±1.94 SD) for the standard bupivacaine group, 4.83 (±1.77 SD) for the SABER-placebo group, and 5.16 (±2.38 SD) for the standard bupivacaine group (Figure 1).
• Median time to first opioid use (hours) with SABER-placebo throughout the first 72 hours after surgery.
• Rescue medication use was significantly reduced in patients treated with SABER-Bupivacaine compared with SABER-placebo (Wilcoxon P = .013), with median morphine equivalents of 4 mg for SABER-placebo and 12 mg for SABER-placebo over 72 hours (Figure 3).

RESULTS

Study Patients

Table 1. Patient Demographics and Baseline Characteristics (ITT population).

<table>
<thead>
<tr>
<th>Age, years, mean (SD)</th>
<th>Male</th>
<th>Female</th>
<th>White</th>
<th>Hispanic</th>
<th>Asian</th>
<th>Other</th>
<th>Mean BMI (range)</th>
<th>Placebo</th>
<th>SABER-Bupivacaine</th>
<th>SABER-placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>50.1 (9.5)</td>
<td>26.77 (20.3-35.3)</td>
<td>33.62 (17.8-56.6)</td>
<td>50.94 (3.3)</td>
<td>2 (3.8)</td>
<td>0</td>
<td>0</td>
<td>25.38 (19.3-34.5)</td>
<td>25.52</td>
<td>25.77</td>
<td>25.60</td>
</tr>
</tbody>
</table>

Table 2. Summary of TEAEs Occurring in ≥2% of Total Patients (safety population).

<table>
<thead>
<tr>
<th>TEAEs</th>
<th>Placebo</th>
<th>SABER-Bupivacaine</th>
<th>SABER-placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>3 (5.7)</td>
<td>1 (1.9)</td>
<td>1 (0.9)</td>
</tr>
<tr>
<td>Nausea</td>
<td>1 (1.9)</td>
<td>1 (2.4)</td>
<td>1 (3.4)</td>
</tr>
<tr>
<td>Musculoskeletal pain</td>
<td>2 (3.8)</td>
<td>2 (6.5)</td>
<td>2 (5.7)</td>
</tr>
</tbody>
</table>

All patients completed the trial normally (no discontinuations/withdrawals), and the incidence of treatment-emergent AEs (TEAEs) was similar between treatment groups.

• The most frequent TEAEs were headache, nausea, and musculoskeletal pain (4.7% of total patients for each) (Table 2).
• Most TEAEs were reported as mild or moderate in intensity (no notable differences between treatment groups with regard to intensity).

CONCLUSIONS

• SABER-Bupivacaine significantly reduces pain intensity compared with SABER-placebo throughout the first 72 hours after surgery.
• Additionally, SABER-Bupivacaine was shown to be statistically superior to standard bupivacaine HC and SABER-placebo in a repeated-measures pain intensity on movement analysis for the period of 1 to 24 hours after surgery.
• SABER-Bupivacaine was shown to significantly reduce rescue opioid use and prolonged median time to first opioid rescue medication compared with SABER-placebo for 0 to 72 hours after surgery.
• SABER-Bupivacaine, standard bupivacaine HC, and SABER-placebo were generally safe and well tolerated.
• Taken together, these results indicate that patients treated with SABER-Bupivacaine experienced significantly less pain and required significantly less rescue medication throughout the first 72 hours after shoulder surgery than did those who received SABER-placebo.

REFERENCES


Figure 2. Repeated-measures pain intensity on movement (ITT population).

Figure 3. Rescue opioid medication use (based on nonparametric test; ITT population).

Figure 4. Median time to first opioid rescue medication (log-rank test; ITT population).