

# SABER®-Bupivacaine Concurrently Reduces Postoperative Pain Intensity and Opioid Use for 72 Hours: Evaluation of CROPIRS Scores

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## INTRODUCTION

- Early postsurgical pain generally peaks within 24 hours after surgery and continues for a period of 72 hours<sup>1,2</sup>
- Inadequate postoperative pain relief may lead to chronic pain, resulting in prolonged recovery and reduced patient satisfaction<sup>3</sup>
- In addition, the use of opioids for postsurgical pain can result in the development of opioid-related adverse events (AEs) in up to 80% of patients<sup>4</sup>
  - Opioid-related AEs can extend the length of hospital stay, increase the cost of care, and increase the risk of readmission
  - Postoperative opioid use represents a common gateway to opioid addiction<sup>5</sup>
- A multimodal regimen should effectively manage pain and reduce opioid use
  - Local anesthetics are a key component of multimodal approaches, but their duration of action is 24 hours at most; hence, they provide little pain relief beyond the first postoperative day<sup>6,7</sup>
  - This highlights the unmet need for a simple-to-use, nonopioid treatment option that provides reliable pain relief over the 72-hour postsurgical period, regardless of surgery type
  - Furthermore, it is important that the efficacy of local anesthetics is evaluated based on a combination of pain intensity and reduction in opioid use
- SABER-Bupivacaine is an extended-release formulation of bupivacaine designed to provide prolonged postsurgical local analgesia and reduced reliance on opioid analgesic medications for up to 72 hours following a single-dose administration<sup>8</sup>

## OBJECTIVE

- To evaluate the combination of reduction in postsurgical pain intensity and reduction in opioid use and corresponding AEs in patients receiving SABER-Bupivacaine by using the Combined Relative Opioid and Pain Intensity Reduction Scale (CROPIRS)

## METHODS

### Study Designs

- This analysis evaluated data from 2 randomized, double-blind, placebo-controlled trials that enrolled patients undergoing either soft-tissue (unilateral tension-free inguinal hernia repair) or bony (arthroscopic subacromial decompression [ASD]) surgery<sup>8,9</sup>

### Inguinal Hernia Repair Study (CLIN006-0006)

- Eligible patients were undergoing inguinal hernia repair using standard tension-free Lichtenstein technique<sup>1</sup> under general anesthesia<sup>9</sup>
- All patients were randomly assigned (3:3:2) to receive 1 of the following<sup>9</sup>:
  - 2.5 mL of SABER-Bupivacaine (12% wt/wt, 132 mg/mL bupivacaine)
  - 5 mL of SABER-Bupivacaine
  - 2.5 or 5 mL of SABER-placebo
- Half the treatment dose was instilled into the wound; after closure of the aponeurosis, the next half was instilled into the wound<sup>9</sup>
- Rescue medication was allowed for all patients<sup>9</sup>

- For moderate to severe pain: intravenous (IV) or oral tramadol 50 to 100 mg (maximum, 500 mg per day)
- For mild to moderate pain: acetaminophen 1 g 4× per day
- All opioid medications were converted to morphine-equivalent doses
- Primary efficacy end points were mean pain intensity on movement-time-normalized area under the curve (AUC) during the first 72 hours after surgery and the proportion of patients receiving opioid rescue medication<sup>9</sup>

### ASD Surgery Study

- Patients were randomly assigned in a 2:1:1 allocation ratio to 5 mL of SABER-Bupivacaine (660 mg bupivacaine), 5 mL of SABER-placebo, or 20 mL of standard Bupivacaine HCl (50 mg bupivacaine)<sup>8</sup>
- Arthroscopic subacromial decompression was performed on day 0; entry to the subacromial space was through 2 to 3 standard portals under general anesthesia<sup>8</sup>
  - On completion of the shoulder surgery, a single dose of treatment medication was deposited subacromially
- All patients received acetaminophen (4 g/day) as background treatment
  - Patients were allowed rescue medication in the form of morphine (oral or IV) from day 0 to 72 hours after surgery, if pain was not sufficiently relieved<sup>8</sup>
- The coprimary end points were pain intensity on shoulder movement AUC during the period 1 to 72 hours after surgery (AUC<sub>1-72</sub>) and total use of opioid rescue analgesia 0 to 72 hours after surgery<sup>8</sup>

## CROPIRS

- CROPIRS combines proportional reductions in opioid use and pain intensity into a single, scaled, relative-improvement score
  - This score represents the relative improvement in efficacy of a treatment (i.e., SABER-Bupivacaine) compared with the comparator (e.g., SABER-placebo)
- The CROPIRS score is determined by calculating the relative distance in 2 dimensions, where:
  - *a* represents the mean percentage reduction in pain intensity
  - *b* represents the mean percentage reduction in opioid use
  - *c* represents the CROPIRS improvement score

$$a^2 + b^2 = c^2$$

- As a result, the CROPIRS improvement score can be calculated as follows:

$$c = \sqrt{a^2 + b^2}$$

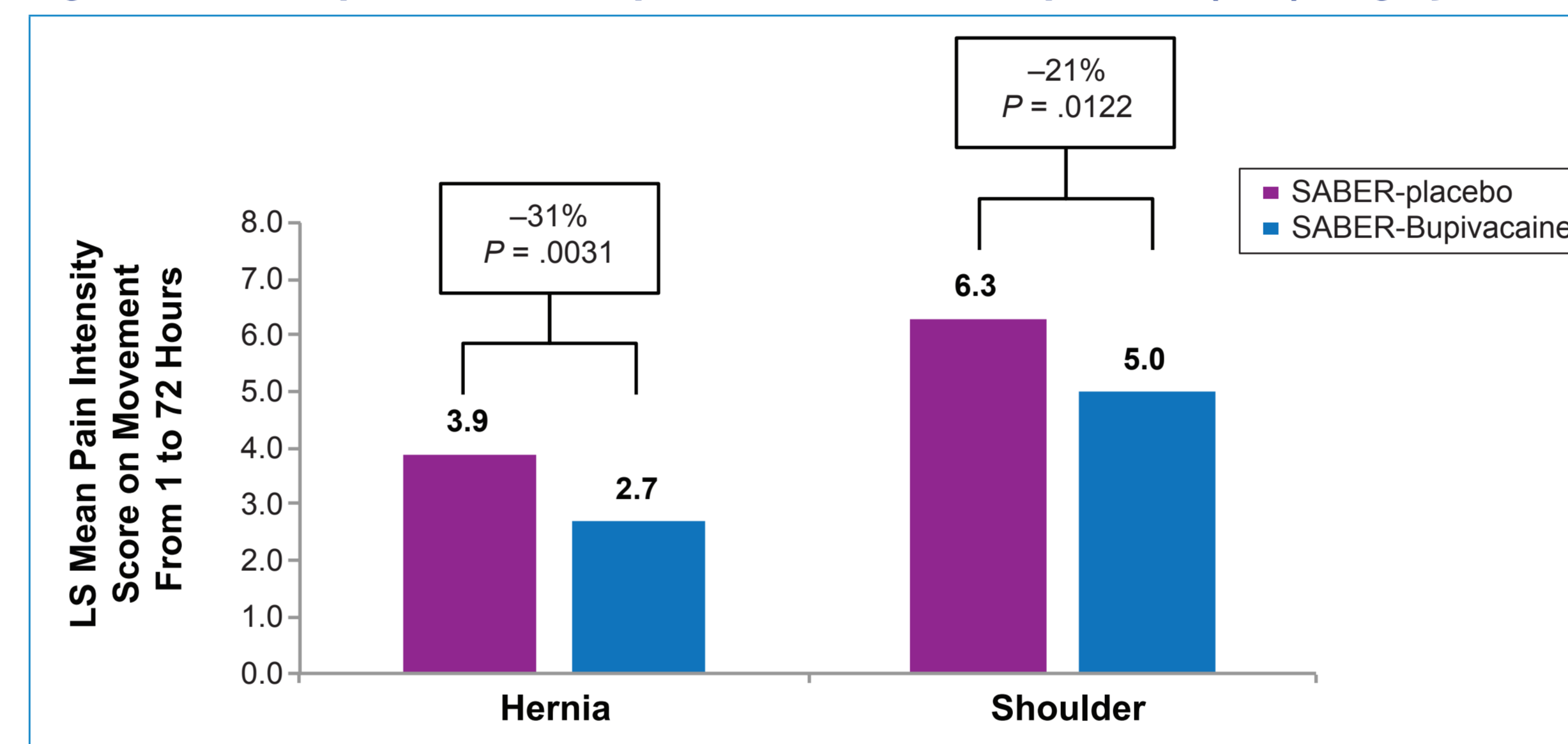
- In the current analysis, CROPIRS improvement scores were calculated for SABER-Bupivacaine versus SABER-placebo in patients undergoing inguinal hernia repair or ASD surgery

## RESULTS

### Pain Intensity on Movement

- In 79 patients undergoing inguinal hernia repair surgery, least squares (LS) mean pain intensity scores on movement were lower for SABER-Bupivacaine versus SABER-placebo, with an overall reduction of 31% in pain intensity on movement during the 72-hour postoperative period (**Figure 1**)
- In 107 patients undergoing ASD surgery, LS mean pain intensity scores on movement were 21% lower for SABER-Bupivacaine versus SABER-placebo during the 72-hour postoperative period (**Figure 1**)

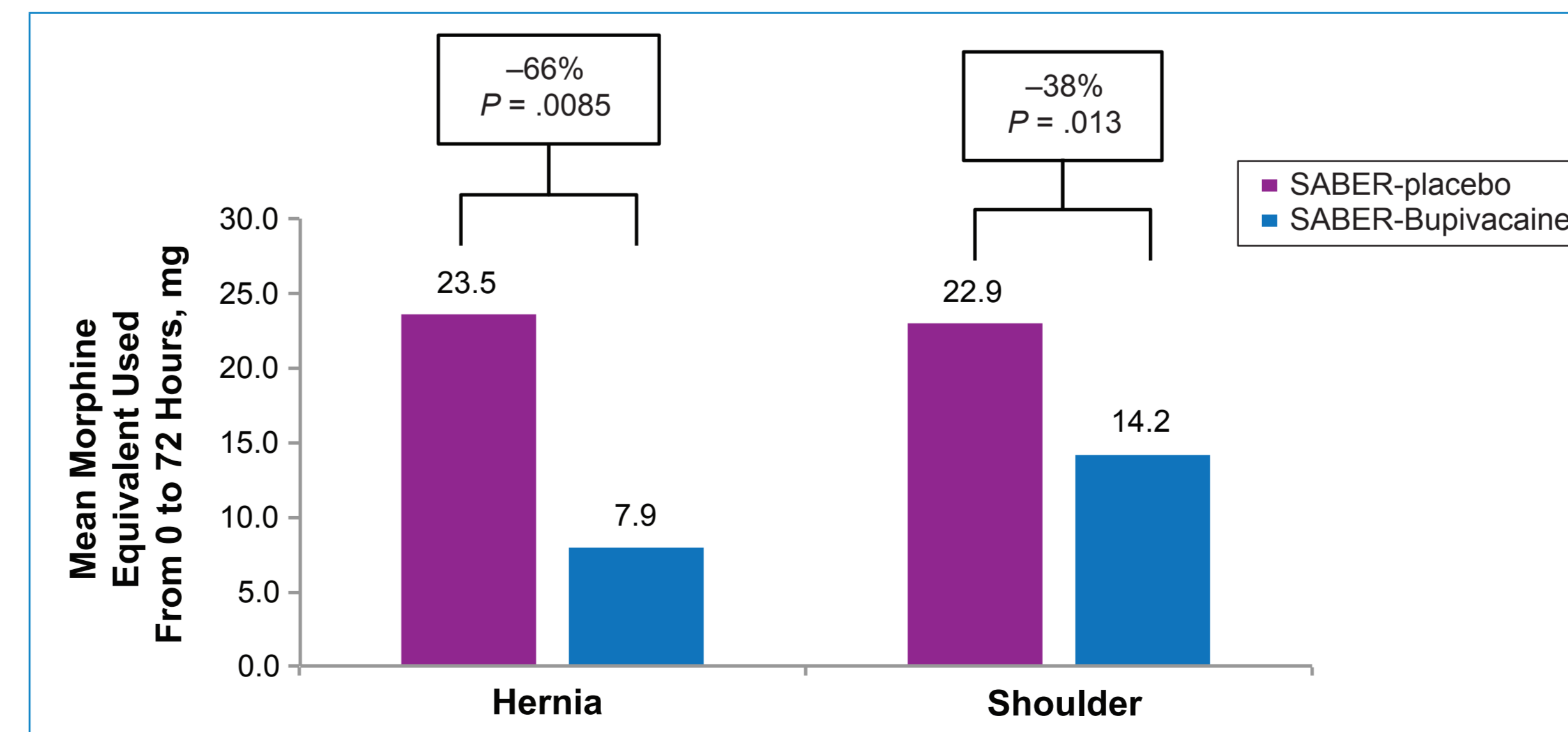
**Figure 1. Least squares (LS) mean pain intensity scores on movement for SABER-Bupivacaine versus SABER-placebo from 1 to 72 hours after surgery in patients undergoing inguinal hernia repair or arthroscopic subacromial decompression (ASD) surgery.**



### Opioid Use

- In patients undergoing inguinal hernia repair surgery, mean morphine equivalent used was lower for SABER-Bupivacaine versus SABER-placebo, with an overall reduction of 66% in opioid use during the 72-hour postoperative period (**Figure 2**)
- In patients undergoing ASD surgery, mean morphine equivalent used was 38% lower for SABER-Bupivacaine versus SABER-placebo during the 72-hour postoperative period (**Figure 2**)

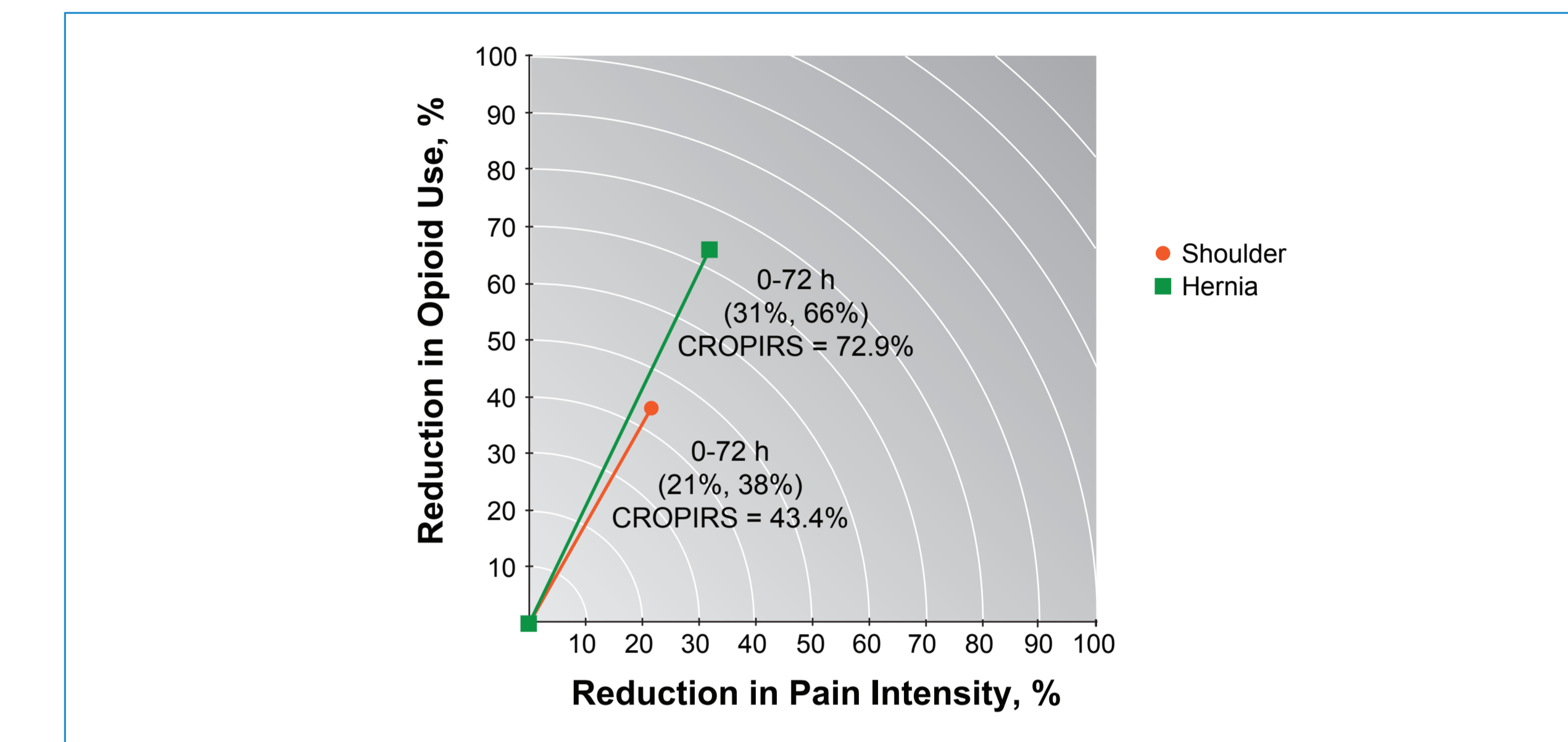
**Figure 2. Mean morphine equivalent used (i.e., opioid use) for SABER-Bupivacaine versus SABER-placebo from 0 to 72 hours after surgery in patients undergoing inguinal hernia repair or arthroscopic subacromial decompression (ASD) surgery.**



## CROPIRS Improvement Scores

- By combining percentage reductions in pain intensity and opioid use, CROPIRS demonstrated that SABER-Bupivacaine was associated with improvements in efficacy of 72.9% and 43.4% in patients undergoing inguinal hernia repair and ASD surgery, respectively (**Figure 3**)

**Figure 3. CROPIRS improvement scores in patients undergoing inguinal hernia repair or ASD surgery.**



## CONCLUSIONS

- SABER-Bupivacaine effectively decreased pain intensity on movement versus SABER-placebo for 72 hours after surgery in patients undergoing inguinal hernia repair and ASD surgery
- SABER-Bupivacaine also effectively reduced opioid use versus SABER-placebo for the first 72 hours after surgery in patients undergoing inguinal hernia repair and ASD surgery
- Combining these 2 end points using CROPIRS enabled the overall efficacy of SABER-Bupivacaine to be evaluated
- A number of possible limitations are associated with the current analysis:
  - CROPIRS is not a validated measure
  - Use of CROPIRS assumes equal weighting between the 2 end points (i.e., reduction in pain intensity and opioid use)
  - Other methods of combining the data may provide a better reflection of overall efficacy
- These findings suggest that SABER-Bupivacaine has the potential to act as the foundation of a multimodal pain management regimen, which should concurrently reduce pain intensity and opioid use during the first 72 hours after surgery

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### Financial Disclosure

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