Postoperative Pain Management of Total Knee Arthroplasty Using HTX-011 With Multimodal Analgesia: Results From a Phase 3b Open-Label Study

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INTRODUCTION

• Opioids are commonly prescribed for pain relief following orthopaedic surgery but come with the potential for misuse and dependence.1–3
• Although local anesthetics are commonly used for surgical pain, they are limited by their duration of action (6–12 hours); currently approved extended-release (ER) anesthetics provide pain relief for up to 24 hours.4
• HTX-011 is a nonopioid, biodegradable analgesic (DALA) that provides the controlled diffusion of active ingredients over 72 hours.5
• HTX-011 is administered via needle-free application to the surgical site prior to wound closure using a syringe and a Laser-trick applicator (Figure 1).

OBJECTIVE

• To assess pain control, opioid use, safety, and tolerability of HTX-011 when used as the foundation of a scheduled nonopioid MMA regimen in patients undergoing TKA

METHODS

Study Design and Patients

• This phase 3b, open-label study enrolled patients undergoing primary unilateral TKA who met study criteria (Table 1).
• Results are presented as an interim analysis prior to database lock.

RESULTS

Disposition and Baseline Characteristics

• 59 patients received HTX-011
• 61% of patients were female; 95% were white; mean age was 65 years

Pain Intensity

• The mean (SD) AUC last of the VAS was 143.2 (93.5) in patients treated with HTX-011 + MMA.
• Mean pain intensity, measured by VAS, remained in the mild range (VAS 5–44 mm) throughout the 72-hour postoperative period (Figure 3).
• 37% of patients did not experience severe pain at any time during the 72-hour postoperative period

Opioid Use and Discharge Readiness

• Six patients (10.2%) remained opioid-free through the 72-hour postoperative period.
• Median opioid consumption was 22.5 mg morphine morphine equivalents (MME) in 6.5–8.5 mg oxycodone pills per patient throughout 72 hours, approximately one-third the amount consumed by patients that received HTX-011 in the prior phase 2b study (Figure 5).
• Geometric mean (95% CI) of opioid use through 72 hours was 3.7 (2.5–5.6 mg).
• 68.6% of patients (35/51) were deemed ready for discharge within 24 hours using MPADSS, a proportion similar to that observed for HTX-011 in the prior phase 2b study (Figure 4).
• Most patients (74.5%) were discharged without an opioid prescription

DISCUSSION/CONCLUSIONS

• HTX-011, as the foundation of a scheduled, nonopioid MMA regimen, effectively managed postoperative pain relief, maintained mean pain scores in the mild range through 72 hours, and minimized the need for opioid discharge prescriptions following TKA.
• HTX-011, with a scheduled nonopioid MMA regimen, was well-tolerated in patients undergoing TKA.
• In a recent study examining the use of liposomal bupivacaine + hyaluronic acid + MMA at TelK,6–7
• Geometric mean of opioid use through 72 hours was 2.9 mg.
• In this study, HTX-011 + MMA reduced pain and opioid use.
• Geometric mean of opioid use through 72 hours was 3.7 mg.
• 74.5% of patients were discharged without an opioid prescription.
• Using HTX-011 as the foundation of an MMA regimen has the potential to dramatically reduce the number of opioids sent home with following patients that receive TKA (Table 4).

ACKNOWLEDGMENTS

Funding for this manuscript was provided by Pacira Pharmaceuticals, Inc. (San Diego, CA, USA). Medical writing assistance was provided by Flottech Scientific Communications, Inc. (La Jolla, CA, USA). American Society of Anesthesiologists; BMI, body mass index; ER, extended-release; HTX-011, an investigational biodegradable analgesic (DALA) with unique, synergistic mechanism of action containing a bupivacaine and low-dose meloxicam in a proprietary Biochronomer® polymer, which allows for the controlled diffusion of active ingredients over 72 hours.

REFERENCES

4. Developing an individual reference. The PDF should not be altered or reproduced in any form. A fee is required for all copies of this article beyond those reproduced for individual reference.
5. The following table was adapted from the prescribing information. San Diego, CA: Pacira Pharmaceuticals, Inc.; 2018.

Table 1. Summary of AEs

<table>
<thead>
<tr>
<th>AEs (n%)</th>
<th>N = 51</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea</td>
<td>28 (54.9)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>14 (27.5)</td>
</tr>
<tr>
<td>Constipation</td>
<td>10 (19.6)</td>
</tr>
<tr>
<td>Bradycardia</td>
<td>3 (5.9)</td>
</tr>
<tr>
<td>Urinary retention</td>
<td>3 (5.9)</td>
</tr>
<tr>
<td>Dizziness</td>
<td>3 (5.9)</td>
</tr>
</tbody>
</table>

Current practice estimatesa 93,870,000
Potential reduction with HTX-011 + MMA 69,933,150
Potential reduction with MMA 53,936,850

Table 2. Potential Impact of Study3,9

<table>
<thead>
<tr>
<th>Pain</th>
<th>Current practice estimatesa</th>
<th>Pain saved with HTX-011 + MMA</th>
<th>Pain saved with MMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>93,870,000</td>
<td></td>
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1. Grossmont Orthopedic Medical Group, La Mesa, CA, USA
3. Geometric mean of opioid use through 72 hours was 2.9 mg.
4. Geometric mean of opioid use through 72 hours was 3.7 mg.
5. 74.5% of patients were discharged without an opioid prescription.
6. Using HTX-011 as the foundation of an MMA regimen has the potential to dramatically reduce the number of opioids sent home with following patients that receive TKA (Table 4).

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