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HTX-011, a Proprietary, Extended-Release Combination of Bupivacaine and Meloxicam, Reduced Pain Intensity and Opioid Consumption for 96 Hours Following Abdominoplasty

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INTRODUCTION

- After a surgical procedure such as abdominoplasty, pain is most severe within the first 72 hours[1-3]
- Adequate management of pain not only increases patient comfort, it prevents a cascade of adverse clinical outcomes for patients and increased costs for the health care system[4-7]
- Systemic opioids are often relied on for postoperative pain management, increasing the risk of opioid-related adverse events and the potential for drug abuse and addiction[8-10]
- Available local anesthetics, including long-acting formulations, have demonstrated limited effect beyond 24 hours[11,12]
- HTX-011 delivers superior local analgesia by leveraging the anti-inflammatory effect of meloxicam in a unique combination with bupivacaine over 72 hours via sustained release with Biochronomer® technology[13]
- Previous interim results in subjects undergoing inguinal herniorrhaphy[14] and bunionectomy[15] (see Poster 3758) indicated that HTX-011 significantly reduces pain intensity and the need for rescue opioids[14]; efficacy of HTX-011 in abdominoplasty, a procedure involving larger incisions, is currently under investigation

OBJECTIVE

- To assess the safety and efficacy of HTX-011 in reducing pain intensity and opioid consumption after complete abdominoplasty

METHODS

Study Design

- This analysis included a cohort of subjects participating in an ongoing, randomized, multicenter, double-blind, placebo-controlled phase 2 IRB-approved clinical trial (NCT02689258)
  - Based on initial dose-finding cohorts, a 400 mg dose of HTX-011 was selected
- After signing informed consent, subjects were screened to select those who were qualified for complete abdominoplasty
- Subjects were randomly assigned 1:1 to single-dose administration of either:
  - 400 mg HTX-011 (equivalent to 400 mg bupivacaine base) via a combination of injection and instillation
  - Normal saline injection
- Subjects were evaluated postoperatively for their pain and opioid use through 72 hours after study administration during confinement at the study center, and then were discharged. Follow-up visits were scheduled at 96 hours, 10 days, and 28 days after study drug administration

Subjects

- Key inclusion criteria
  - American Society of Anesthesiologists Class I or II adults aged ≥18 years scheduled to undergo elective complete abdominoplasty involving liposuction, umbilical repositioning, or both
  - Body mass index (BMI) <30 kg/m^2
- Key exclusion criteria:
  - Clinically significant renal or hepatic abnormalities (aspartate aminotransferase or alanine aminotransferase ≥3 times upper limit of normal (ULN), creatinine ≥2 times ULN)
  - Current use of analgesics for a chronic pain condition, use of long-acting opioids within 3 days of surgery, or use of any opioids within 24 hours of surgery

Study Assessments

Efficacy End Points

- End points included in this analysis were summed pain intensity score (SPI) during the 0 to 24, 0 to 48, 0 to 72, 0 to 96, 24 to 48, 48 to 72, and 72 to 96 hour time intervals and total opioid rescue medication consumed through 24, 48, 72, and 96 hours after study drug administration
- Pain intensity was assessed on a Visual Analog Scale (100 mm line anchored by "no pain" to "worst pain imaginable") by measuring the distance from 0 (no pain) to the patient's mark
- Rescue pain medication was available as needed; total opioids consumed were converted to milligram morphine equivalents and summed for analysis

Safety End Points

- Safety was evaluated by incidence and assessment of treatment-emergent adverse events (TEAEs) and serious TEAEs as well as changes in vital signs, clinical laboratory evaluations, and electrocardiograms

RESULTS

Baseline Population Characteristics

- A total of 41 women (76% white, mean age 42 years, mean BMI 27) were enrolled and received treatment with either HTX-011 (n = 20) or saline placebo (n = 21) (**Table 1**)
- Demographics were comparable across cohorts (**Table 1**)

Table 1. Demographics and Baseline Characteristics

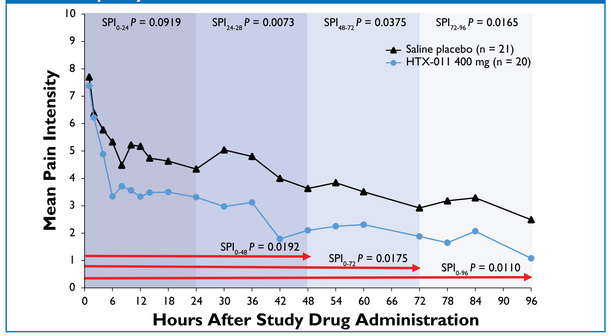
	HTX-011 n = 20	Saline Placebo n = 21
Mean age, years (SD)	41.4 (9.25)	43.0 (7.84)
Mean BMI, kg/m^2 (SD)	26.95 (2.10)	27.51 (1.67)
Race, n (%)		
Black or African American	5 (25.0)	5 (23.8)
White	15 (75.0)	16 (76.2)
Ethnicity, n (%)		
Hispanic or Latino	7 (35.0)	5 (23.8)
Not Hispanic or Latino	13 (65.0)	16 (76.2)

BMI, body mass index.

Efficacy

- Subjects treated with HTX-011 trended toward lower mean SPI scores for the first 24 hours and reported significantly lower mean SPI scores through 48, 72, and 96 hours after treatment than saline placebo recipients. Subjects treated with HTX-011 also demonstrated significantly lower mean SPI scores in the 24 to 48, 48 to 72, and 72 to 96 hour time intervals (**Figure 1**)

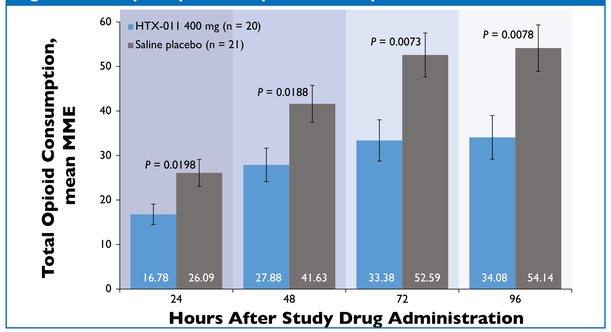
Figure 1. Mean pain intensity over time following complete abdominoplasty.



SPI, summed pain intensity.
Last observation carried forward method used to account for missing data; no adjustment for opioid rescue medication administered.

- HTX-011 subjects required significantly less opioid administration through 24, 48, 72, and 96 hours after dose (35.7%, 33.0%, 36.5%, and 37.1% decrease compared with saline placebo, respectively) (**Figure 2**)

Figure 2. Total postoperative opioid consumption over time.



MME, milligram morphine equivalent.

Safety

- The incidence of treatment-related adverse events in subjects treated with HTX-011 and with saline placebo are presented in **Table 2**

Table 2. Treatment-Related Adverse Events[a]

TRAE, n (%)	HTX-011 400 mg n = 20	Saline Placebo n = 21
Nausea	3 (15.0)	2 (9.5)
Pruritus	0 (0.0)	3 (14.3)
Headache	2 (10.0)	0 (0.0)

TRAE, treatment-related adverse event.
[a]TEAEs occurring in >1 subject.

- No deaths, serious TEAEs, or TEAEs leading to premature discontinuation were reported

CONCLUSIONS

- HTX-011, a novel combination of bupivacaine and meloxicam, was well tolerated and significantly reduced pain intensity and opioid consumption through 96 hours after complete abdominoplasty when compared with saline placebo
- These results confirm the versatility of HTX-011, which has previously demonstrated efficacy in both herniorrhaphy[14] and bunionectomy[15] (see Poster 3758) and now in abdominoplasty, which has a much larger incision
- HTX-011 represents a significant advance in postoperative pain management

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