Pilot Study of Vocacapsaicin for Treatment of Pain Following Open Laparotomy Repair of Ventral Hernia

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ABSTRACT

Introduction: Vocacapsaicin is a novel, nonopioid therapeutic that provides long-lasting postsurgical pain relief after a single intraoperative administration.

Methods: This was a Phase 2, randomized, double-blind, placebo-controlled, parallel group design, pilot study of the safety, pharmacokinetics, and preliminary efficacy study of vocacapsaicin in patients undergoing open laparotomy ventral hernia repair (VHR). Patients were randomized to placebo or 24 mg of vocacapsaicin delivered during surgery in 80 mL (0.3 mg/mL) of aqueous solution. All groups received full standard-of-care that included administration of long-acting local anesthetic. Postoperative pain and opioid consumption were recorded in hospital for 4 days, then after hospital discharge for up to 15 days after surgery.

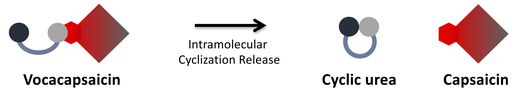
Results: In the VHR surgical model, vocacapsaicin 24 mg produced safe, durable and clinically meaningful pain reduction when added to a standard of care analgesic regimen. The safety profile was benign and mostly indistinguishable from saline placebo.

Conclusion: When combined with study results from the use of vocacapsaicin in total knee arthroplasty and bunionectomy, these results suggest that vocacapsaicin may be useful for both soft-tissue and orthopedic surgery.

INTRODUCTION

Managing multi-day postoperative pain following ventral hernia repair (VHR) and other open laparotomy procedures remains an important unmet medical need. Increased focus on postoperative mobilization requires effective management of pain with movement. Vocacapsaicin (formerly CA-008) is a water-soluble prodrug of capsaicin that provides c-fiber mediated analgesia without numbness or motor weakness (Figure 1). A single intraoperative administration of vocacapsaicin has been shown to provide post-operative analgesia and reduce opioid consumption for two weeks following total knee arthroplasty[1] and bunionectomy[2]. We evaluated the safety and efficacy of vocacapsaicin in a randomized, double-blind, pilot study of patients undergoing open laparotomy for VHR.

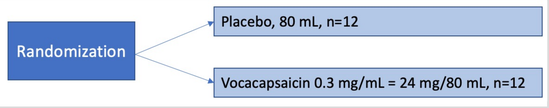
Figure 1: Vocacapsaicin, a pH-labile, water-soluble prodrug of capsaicin



METHODS

The study was conducted in patients undergoing elective, open VHR with mesh (Rives-Stoppa technique or equivalent) under general anesthesia with full standard-of-care perioperative analgesia including a bilateral rectus block with bupivacaine 75 mg, plus peri-incisional, local anesthetic infiltration with bupivacaine 100 mg and preoperative acetaminophen and celecoxib. (ClinicalTrials.gov NCT04774328) Eligible patients were aged 18-80 years with BMI up to 40 kg/m^2. Patients were excluded if opioid tolerant, allergic to capsaicin, or had a concurrent painful condition. Following IRB approval and written informed consent, patients were randomized 1:1 to placebo or 24 mg of vocacapsaicin delivered in 80 mL (0.3 mg/mL) of aqueous solution (Figure 2). Prior to surgical closure, the test article was infiltrated into (a) the deep midline, peritoneal layer, (b) the mesh/fascia layer (including the virtual space created for the mesh) and (c) the anterior layer. Patients remained in the hospital for 4 days for assessments and collection of blood samples for pharmacokinetic analysis. After discharge, all patients received celecoxib twice daily and acetaminophen or acetaminophen with oxycodone as needed.

Figure 2: Study Design



The primary outcome measures were pain and opioid consumption. Pain was measured using a numerical rating score (NRS) with activity (coughing and ambulation) and at rest. NRS scores were integrated over 96 hours and over 8 days. Safety endpoints were measured until post-operative day 28, and included vital signs, physical examination, surgical site assessments, neurosensory testing, adverse events, and clinical laboratory evaluations.

RESULTS

A total of 24 patients (mean age 45 years, 71% men, mean BMI 31 kg/m^2) were enrolled. Groups were well-matched at baseline. Over the first 4 days, vocacapsaicin 24 mg reduced pain on coughing by 46% (p=0.02) and pain on ambulation by 35% (p=0.08) compared to placebo (Figure 3). Pain at rest was reduced by 21% and cumulative opioid consumption was reduced 26% compared to placebo, but neither approached statistical significance. There was a trend toward improved analgesia through Day 8 in patients receiving vocacapsaicin, but this did not reach statistical significance (Figure 4). After Day 9, pain in the control group was recorded as mild (NRS ~1). There was no difference between vocacapsaicin and saline placebo in the safety analysis through day 29.

Figure 3: Endpoints of Pain and Opioid Consumption Through 96 Hours

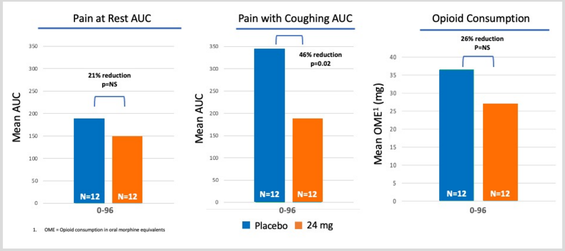
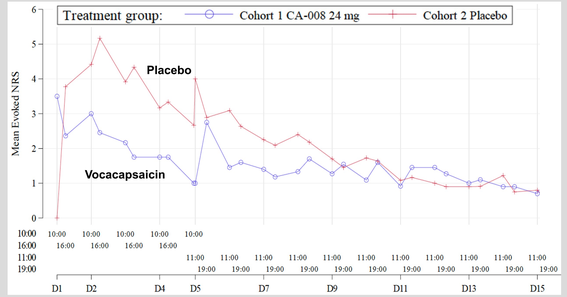


Figure 4: Pain on Coughing Through Day 15



DISCUSSION

This pilot study suggests that a single intraoperative administration of vocacapsaicin during abdominal surgery provides durable and clinically meaningful pain reduction when added to a standard of care analgesic regimen that includes a regional block and local anesthetic infiltration with bupivacaine. The results are consistent with previous results in total knee arthroplasty[1] and bunionectomy[2], suggesting that the prolonged analgesic effects of vocacapsaicin may prove useful in both soft-tissue and orthopedic surgery. These results also provide guidance for additional studies of vocacapsaicin for postoperative analgesia after open laparotomy and other soft-tissue procedures.

Acknowledgements:

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References:

1) Teichman, SL, Leiman D, Minkowitz H, et al. Vocacapsaicin Reduces Pain and Opioid Consumption for Two Weeks Following a Single Administration During Total Knee Arthroplasty. Presented at ASRA 2021. (https://epostersonline.com/ASRASPRING21/node/942?view=true)

2) Gottlieb IJ, Beaton A, Solanki D, et al. A randomized, placebo-controlled trial of intraoperative administration of CA-008 for post-operative analgesia after bunionectomy. Presented at ASRA 2019. (https://epostersonline.com/ASRASPRING19/node/1194?view=true)