Poster #5166

Phase 3 Study of the Efficacy and Safety of Meloxicam IV in Subjects with Moderate to Severe Pain following Abdominoplasty

Matthew Bindewald, MD[1]; Sonia Singla, DO[2]; David Leiman, MD[3]; Barr Baynton, MD[4]; Harold Minkowitz, MD[5]; Stewart McCallum, MD[6]; Randall Mack[6]; Alex Freyer, PharmD[6]; Wei Du, PhD[7]

[1] MGB Plastic Surgery Associates of San Antonio, San Antonio, TX, USA; [2] Lotus Clinical Research, Pasadena, CA, USA; [3] HD Research, Bellaire, TX, USA ; [4] Endeavor Clinical Trials, San Antonio, TX, USA; [5] Research Concepts, Bellaire, TX, USA; [6] Recro Pharma, Inc., Malvern, PA, USA; [7] Clinical Statistics Consulting, Blue Bell, PA, USA

2018 World Congress on Regional Anesthesia & Pain Medicine
April 19-21, 2018 | New York Marriott Marquis, New York City, USA
www.asra.com/world-congress | #ASRAWorld18

INTRODUCTION

Intravenous (IV) meloxicam (Meloxicam IV) is a novel formulation of NanoCrystal Colloidal Dispersion® meloxicam, being developed for the management of moderate to severe pain. Meloxicam IV has been evaluated across a range of dose levels and patient populations during Phase 2 clinical studies. The meloxicam IV Phase 3 program included 2 randomized, placebo-controlled efficacy studies in subjects with moderate to severe pain following hard and soft tissue surgeries, as well as a large placebo controlled safety study in subjects undergoing various major surgeries. The presented Phase 3 study was designed to evaluate the efficacy and safety of daily dosing with meloxicam IV 30 mg in an adequate and well controlled trial in a soft tissue model of moderate to severe pain.

OBJECTIVES

The primary objective of this study was to demonstrate the analgesic efficacy of meloxicam IV 30 mg compared with placebo, using the summed pain intensity difference over the first 24 hours ($SPID_{24}$) in subjects with moderate to severe pain following abdominoplasty surgery.

Secondary objectives of this study included:

- Evaluating the analgesic effects of meloxicam IV 30 mg versus placebo at various time points using a series of secondary efficacy endpoints for pain intensity, pain relief, and use of rescue medication
- Determine the safety and tolerability of meloxicam IV 30 mg as evaluated with physical examination, vital signs, clinical laboratory tests, ECGs, wound evaluation, and incidence of Adverse Events (AEs) and Serious AEs (SAEs).

METHODS

Subjects

This study was conducted under an FDA IND, IRB approval was obtained prior to study conduct, and all subjects provided written informed consent.

Selected inclusion criteria:

- Healthy males and females aged 18 to 75 years undergoing abdominoplasty surgery without collateral procedures.
- Moderate to severe pain within 3 hours of the end of surgery (last suture), with a numeric pain rating scale (NPRS) score ≥ 4 out of 10.

Selected exclusion criteria:

- Known bleeding disorder or taking agents affecting coagulation.
- Taking or had taken an opioid chronically (more than one month of routine use) for pain in the past year
- Major surgery within previous 3 months or another painful condition that could interfere with pain assessments

Study Design

- Multi-center, randomized, double-blind, placebo controlled study at 4 US sites
- Participation consisted of a screening visit, surgery and inpatient evaluation, and 2 follow-up visits, 7 and 28 days after last study dose.
- Following abdominoplasty, subjects could be maintained using IV fentanyl until eligible to randomize to treatment
- Randomized 1:1 to meloxicam IV 30 mg or placebo
- Study doses were administered every 24 hours for up to 3 doses.

Statistical Analysis

Efficacy analyses were performed using the Intent-to-Treat (ITT) analysis set, which included all randomized subjects. The safety analysis set includes all subjects treated with study drug. All randomized subjects received study drug, therefore the efficacy and safety populations were the same. Analysis of covariance (ANCOVA) was used to assess the difference between treatment groups for SPID, including main effects of treatment and investigational site and a covariate of baseline pain intensity score.

RESULTS

Demographics

- A total of 219 subjects were enrolled in this study; all enrolled subjects were randomized and treated with study drug, and included in the safety and efficacy analyses.

Table 1: Summary of Subject Demographics

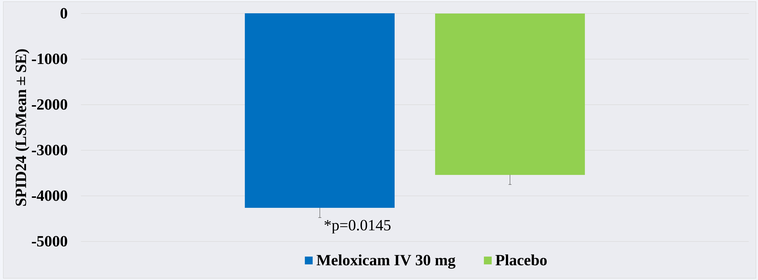
Variable	Meloxicam IV 30 mg (N=110)	Placebo (N=109)	Overall (N=219)
Age (yrs) – mean ± SD	38.9 ± 8.40	41.0 ± 9.63	40.0 ± 9.08
Sex, Male/Female; n (%)	1 (0.9) / 109 (99.1)	3 (2.8) / 106 (97.2)	4 (1.8) / 215 (98.2)
Race, n (%)			
White	69 (62.7)	69 (63.3)	138 (63.0)
Black or African American	37 (33.6)	36 (33.0)	73 (33.3)
Other	4 (3.7)	4 (3.7)	8 (3.7)
Surgery Duration (hr) – mean ± SD	1.3 ± 0.48	1.4 ± 0.44	1.4 ± 0.46
Time (hr) End of Surgery to First Dose – mean±SD	0.85 ± 0.57	0.86 ± 0.53	0.85 ± 0.55
Baseline PI (0-10) – mean ± SD	7.2 ± 1.57	7.4 ± 1.68	-

Efficacy

Primary Efficacy Endpoint – $SPID_{24}$

- Statistically significant difference in $SPID_{24}$ favoring meloxicam IV 30 mg over placebo (p=0.0145).

Figure 1: $SPID_{24}$



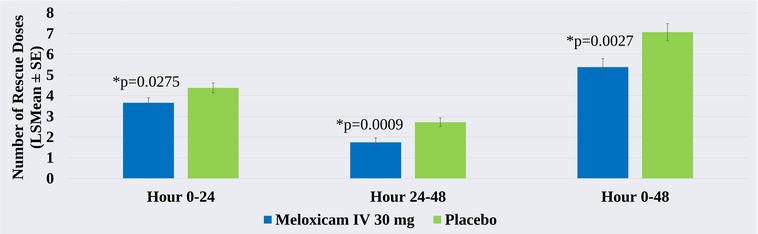
SPID At Other Intervals

- SPID assessed at other postdose intervals ($SPID_6$, $SPID_{12}$, $SPID_{48}$, and $SPID_{24-48}$) favored meloxicam IV at all intervals, and reached statistical significance at all but the $SPID_6$ interval (p<0.05).

Rescue Analgesia Use

- Rescue analgesia (oxycodone 5 mg PO) was available for inadequately controlled pain during the treatment phase.
- The number of rescue doses utilized per subject was significantly lower in each assessed study interval (Hour 0-24, Hour 24-48, and Hour 0-48) in the meloxicam IV 30 mg group compared with placebo (p<0.05).
- No difference was observed in the time to first rescue use.

Figure 2: Summary of Rescue Analgesia Use



Safety

- Doses of meloxicam IV 30 mg were well tolerated in the study, the majority of subjects received 3 study doses (79.1%).
- AEs of special interest (including hepatic, renal, cardiovascular, bleeding, wound healing, and injection site events) were infrequent, with a greater incidence overall in the placebo group.
- No trends for changes in vital signs or ECGs were observed.

Table 2: Overview of Adverse Events

AE Parameter	Meloxicam IV 30 mg (N=110)	Placebo (N=109)
TEAEs By Intensity Assessment, n (%)		
Mild	53 (48.2)	69 (63.3)
Moderate	13 (11.8)	26 (23.9)
Severe	0	1 (0.9)
SAEs, n (%)	1 (0.9)	3 (2.8)
Discontinuations Due to TEAE, n (%)	0	1 (0.9)
Deaths	0	0

Table 3: Summary of Treatment-Emergent AEs in ≥ 3% of Subjects - Number of Subjects (%)

Preferred Term	Meloxicam IV 30 mg (N=110)	Placebo (N=109)
Any AE	58 (52.7)	80 (73.4)
Nausea	30 (27.3)	41 (37.6)
Headache	13 (11.8)	18 (16.5)
Vomiting	5 (4.5)	10 (9.2)
Dizziness	4 (3.6)	10 (9.2)
Back Pain	1 (0.9)	4 (3.7)

Wound Healing Assessment

- Surgical wounds were assessed for investigator satisfaction rated using a 0-10 scale (0=completely unsatisfied; 10=completely satisfied), along with assessing various characteristics including erythema, drainage, edema, induration, and hematoma.
- Overall, satisfaction was similar between meloxicam IV 30 mg and placebo at all assessments.
- Clinically significant wound assessment parameters were more common in the placebo group vs. meloxicam IV 30 mg.

Table 4: Investigator Satisfaction with Surgical Wound Healing (0-10 NRS)

Time Point	Meloxicam IV 30 mg (N= 110)	Placebo (N=109)
Hour 48	9.1 ± 1.08	9.2 ± 0.99
Last Study Dose +7 Days	9.4 ± 0.77	9.4 ± 1.03
Last Study Dose +28 Days	9.7 ± 0.74	9.6 ± 0.90

CONCLUSIONS

- Meloxicam IV 30 mg administered as an IV push once daily, was well tolerated with a low incidence of AEs, SAEs, and infusion events.
- Dosing with meloxicam IV 30 mg was demonstrated to provide a significant reduction in pain, as evidenced by $SPID_{24}$ results, and the reduction in opioid rescue use.
- Once daily dosing with meloxicam IV maintained analgesia over the 24-hour dosing interval
- Assessment of wound healing demonstrated no differences between meloxicam IV and placebo treated subjects
- The study supported the efficacy and safety of meloxicam IV 30 mg administered IV once daily in subjects with moderate to severe pain following abdominoplasty surgery.