

HEALTHCARE RESOURCE UTILIZATION (HRU) ASSOCIATED WITH PREOPERATIVE MELOXICAM IV IN COLORECTAL SURGERY

Delaney, Conor P.⁴; Silinsky, Jennifer D.³; Marcet, Jorge⁵; Anupindi, Vamshi R.²; Karkare, Swapna U.⁶; Shah, Drishti R.²; Mack, Randall J.¹; McCallum, Stewart W.¹; Du, Wei^{7, 1}; Freyer, Alex¹; Galas, Teresa¹; Black, Libby K.¹

1. Baudax Bio, Malvern, PA, United States.
2. IQVIA, Falls Church, NJ, United States.
3. Tulane University, School of Medicine, New Orleans, LA, United States.
4. Cleveland Medical Center, Cleveland, OH, United States.
5. Tampa General Hospital, Tampa, FL, United States.
6. Janssen, Titusville, NJ, United States.
7. Clinical Statistics Consulting, Blue Bell, PA, United States.

Important Safety Information

INDICATION

ANJESO™ (meloxicam) injection is indicated for use in adults for the management of moderate-to-severe pain, alone or in combination with non-NSAID analgesics.

Limitation of Use: Because of delayed onset of analgesia, ANJESO alone is not recommended for use when rapid onset of analgesia is required.

WARNING: RISK OF SERIOUS CARDIOVASCULAR AND GASTROINTESTINAL EVENTS

Cardiovascular Risk

- Non-steroidal anti-inflammatory drugs (NSAIDs) cause an increased risk of serious cardiovascular thrombotic events, including myocardial infarction and stroke, which can be fatal. This risk may occur early in treatment and may increase with duration of use.
- ANJESO™ is contraindicated in the setting of coronary artery bypass graft (CABG) surgery.

Gastrointestinal Risk

- NSAIDs cause an increased risk of serious gastrointestinal (GI) adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients and patients with a prior history of peptic ulcer disease and/or GI bleeding are at greater risk for serious GI events.

Study Overview

- Study Design
 - Prospective economic sub-study of a Phase 3b, randomized, double-blind, placebo-controlled trial in subjects undergoing open or laparoscopic colorectal surgeries.
- Objectives
 - Clinical Study Primary Objective: Evaluate the safety and tolerability of preoperative dosing of meloxicam IV 30mg
 - Economic Sub-study Primary Objective: Evaluate the impact of preoperative dosing of meloxicam IV 30mg on healthcare resource use and healthcare costs.

Methods

- Subjects followed a standardized pre-, peri-, and postoperative ERAS protocol (see following slides)
- Randomization 1:1 to meloxicam IV 30 mg or placebo, with the first dose administered 30 minutes prior to surgery, then Q24 hours thereafter.
- Opioids were used postoperatively for analgesia as required.
- A subject-level database was developed: quantity of service, charges and date of service from UB-04 forms (from admission date to discharge)
- A national cost:charge ratio was applied to convert ‘charges’ to ‘costs’. *
- Total costs and LOS were reported descriptively (mean, median and SD) for each group.
- Comparisons (unadjusted) were made using Wilcoxon rank-sum tests and generalized linear models (adjusted).

*Healthcare Cost and Utilization Project (HCUP). Agency for Healthcare Research and Quality, Rockville, MD. www.hcup-us.ahrq.gov/db/state/costtocharge.jsp. Accessed November 4, 2019

ERAS Protocol – Preoperative and Perioperative

Preoperative

- **Diet:**
 - Encourage Hydration 2 days prior
 - Encourage carbohydrate loading, including ClearFast, Ensure Clear, etc up to 2-6 hours prior to surgery
- **Bowel Prep:**
 - Clear liquids with mechanical bowel prep as indicated by surgery type
 - Antibiotics as indicated by surgeon
- **Motility:**
 - No alvimopan
- **Analgesia:**
 - Gabapentin 300 mg PO once 30-90 min preop
 - APAP 650 PO or IV once 30-90 min preop
 - Study Drug 30 min preop
- **Anxiolysis:**
 - Midazolam 2 mg IV once PRN

Perioperative

- **Epidural:**
 - None allowed
- **Analgesia:**
 - Maintained using IV opioids
- **Nausea Prophylaxis:**
 - Dexamethasone IV up to 4 mg once and ondansetron IV 4 mg once, OR
 - Promethazine IV 25 mg once and a scopolamine transdermal patch 0.5 mg
- **Fluids:**
 - Target 5-7 mL/kg/hr
- **Anesthesia:**
 - Nitrous oxide, isoflurane, sevoflurane or desflurane, OR
 - TIVA
- **Neuromuscular Blockade:**
 - SOC

ERAS Protocol – Postoperative

- Diet:
 - Clear liquids on DOS
 - Advance to solids as tolerated starting on POD1
 - Liquid protein supplements available at each meal
- Ambulation:
 - Out of Bed and ambulating on DOS
 - Out of Bed at least 6 hours with ambulation Q6hr starting on POD1
- Analgesia:
 - APAP 650 PO Q8hr until 24 hours following last study drug dose
 - PCA morphine, 1 mg bolus with 6 minute lockout. Supplement with 1-2 mg IV morphine Q1hr PRN, OR
 - IV morphine bolus PRN, not to exceed 12 mg/hr
 - Convert to oxycodone 5 mg Q4hr PRN, supplement with IV morphine 1-4 mg Q1hr
- Pyrexia:
 - Cooling blankets
- Nausea & Vomiting:
 - Ondansetron PO 4 or 8 mg PRN
- Fluids:
 - Individual needs
- Motility:
 - No alvimopan
 - No gum chewing
- Tube & drains:
 - Orogastric/nasogastric tubes should be removed in the operating room or on DOS.
 - Urinary catheters should be removed on or before POD1.

Results: Subject Disposition and Demographics

Meloxicam IV 30

	mg N = 27	Placebo N = 28	Overall N = 55
Completed Subjects n (%)	26 (96.3)	27 (90.0)	53 (93.0)
Discontinued Subjects n (%)	1 (3.7)	3 (10.0)	4 (7.0)
Study Non-compliance	--	1	2
Subject Decision	1	2	3
Mean Age (yrs)	58.8	60.6	59.7
n (%) ≥ 65 years	9 (33.3)	12 (42.9)	21 (38.2)
n (%) Female	12 (44.4)	11 (39.3)	23 (41.8)
Race, n (%)			
White	22 (81.5)	23 (82.1)	45 (81.8)
Black or African American	4 (14.8)	5 (17.9)	9 (16.4)
Asian	1 (3.7)	--	1 (1.8)
Mean Baseline BMI (kg/m ²)	28.9	27.5	28.2

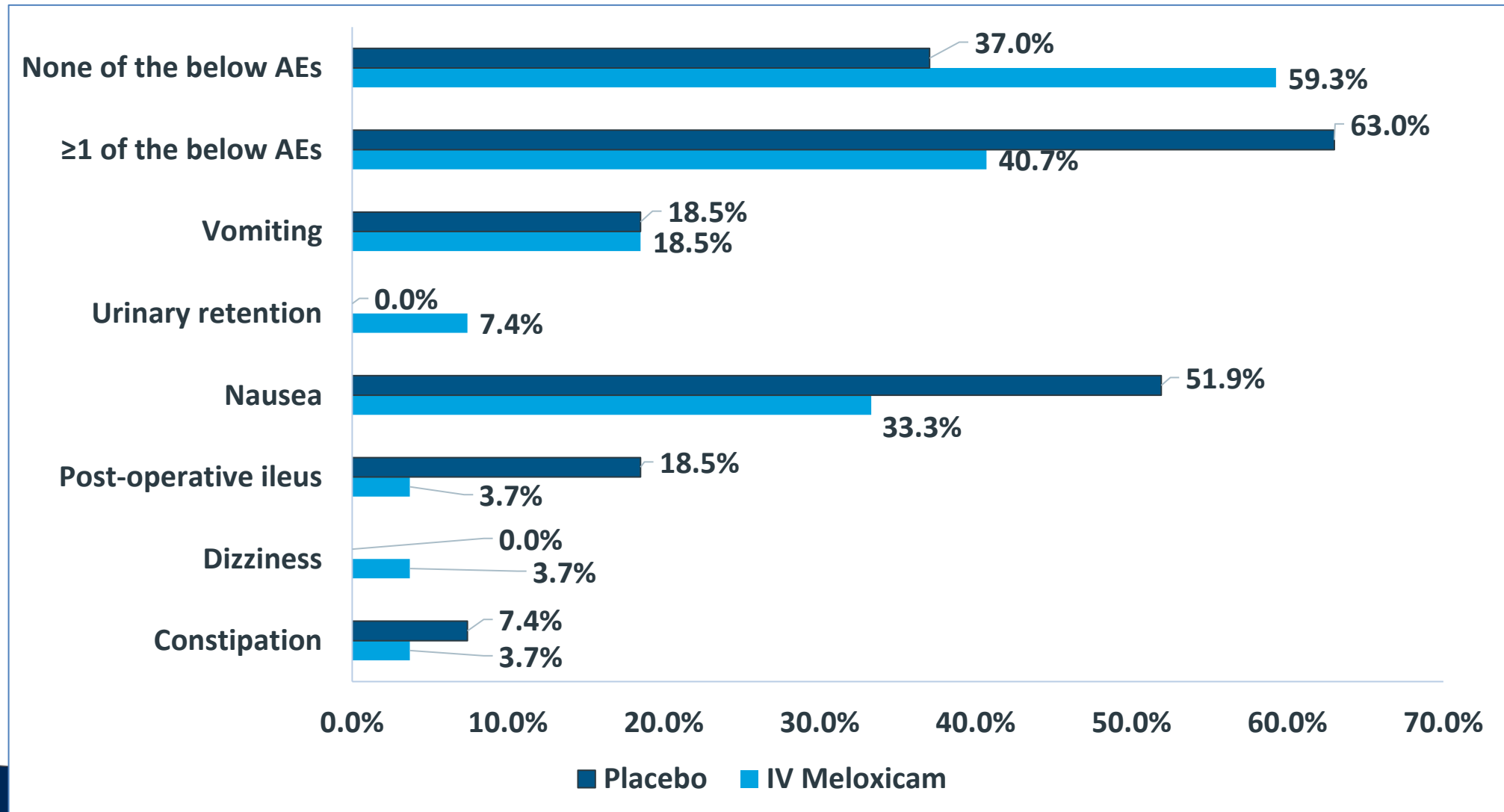
Results: Surgical Characteristics

	Meloxicam IV		Overall
	30 mg N = 27	Placebo N = 28	N = 55
Primary Indication for Surgery: n (%)			
Colon Cancer	13 (48.1)	9 (32.1)	22 (40.0)
Diverticular Disease	4 (14.8)	9 (32.1)	13 (23.6)
Intestinal Polyps	5 (18.5)	1 (3.6)	6 (10.9)
Crohn's Disease	1 (3.7)	1 (3.6)	2 (3.6)
Takedown	1 (3.7)	--	1 (1.8)
Ulcerative Colitis	--	1 (3.6)	1 (1.8)
Other	3 (11.1)	7 (25.0)	10 (18.2)
Actual Incision Type: n (%)			
Open	3 (11.1)	2 (7.1)	5 (9.1)
Laparoscopic	20 (74.1)	23 (82.1)	43 (78.2)
Laparoscopic Converted to Open	4 (14.8)	3 (10.7)	7 (12.7)

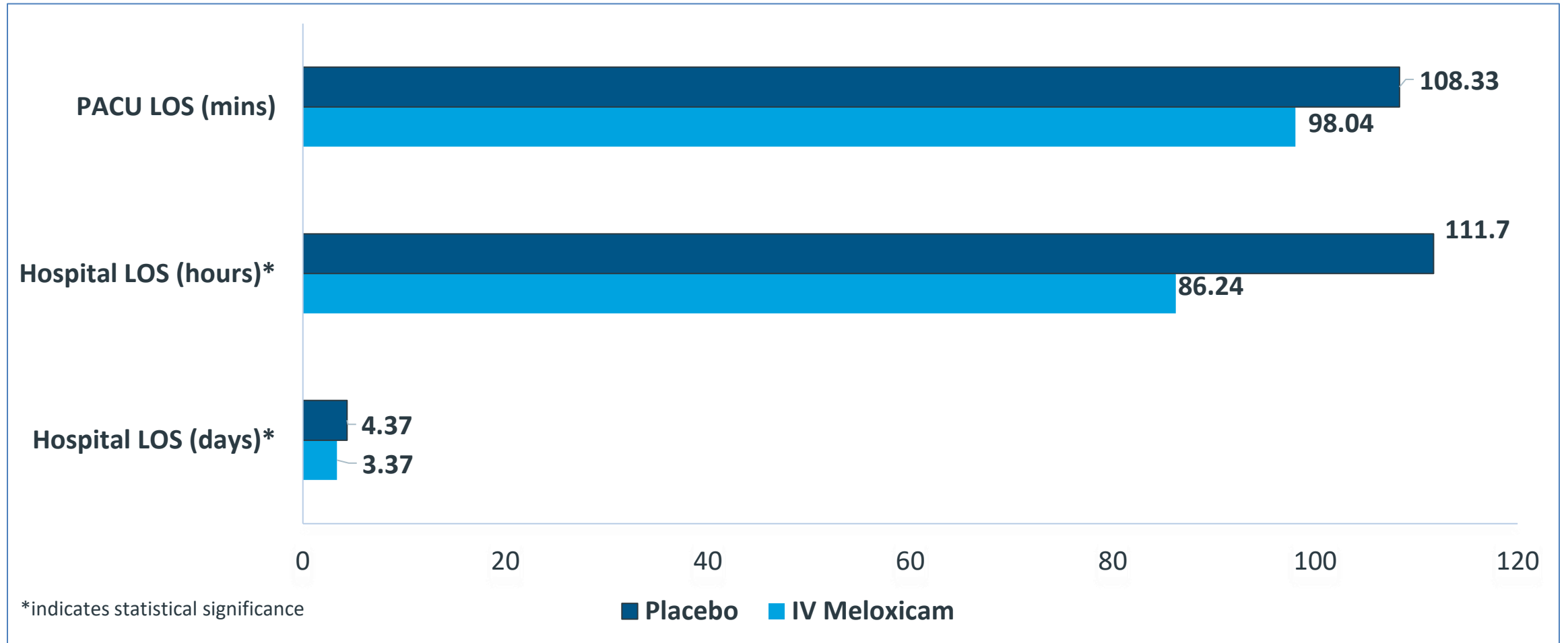
Results: Opioid Consumption (IV Morphine Equivalents-mg)

Parameter	Meloxicam IV 30		Difference
	mg N = 27	Placebo N = 28	
Hour 0-24 – LS Mean (SE)	17.47 (2.513)	19.08 (2.489)	↓ 8.4%
p-value	0.6500		
Hour 24-48 – LS Mean (SE)	6.65 (1.729)	13.06 (1.713)	↓ 49.1%
p-value	0.0106		
Hour 48-72 – LS Mean (SE)	4.32 (1.526)	8.31 (1.337)	↓ 48.0%
p-value	0.0540		
Hour 0-48 – LS Mean (SE)	24.12 (3.817)	32.14 (3.782)	↓ 25.0%
p-value	0.1393		
Hour 0-72 – LS Mean (SE)	27.53 (4.533)	39.89 (4.490)	↓ 31.1%
p-value	0.0567		
Hour 0-EOT – LS Mean (SE)	27.20 (4.466)	38.63 (4.424)	↓ 29.5%
p-value	0.0730		
Hour 0-Discharge – LS Mean (SE)	29.22 (5.237)	45.17 (5.100)	↓ 35.4%
p-value	0.0339		

Results: ORADEs



Results: Mean LOS



Results: Total Hospital Costs

- Total Mean Hospital Costs* were similar between the Meloxicam IV 30mg group compared to the placebo group (\$23,115 vs. \$22,682; $p=0.3370$).
- After removing outliers (top 99th percentile), the total costs of the Meloxicam IV 30mg group decreased whereas the costs for the placebo group remained the same (\$20,492 vs. \$22,682; $p = 0.2196$).
- Mean private room costs for the Meloxicam IV 30mg group were significantly lower compared to the placebo group (\$1,552 vs \$2,512; $p=0.0266$).

*Hospital Costs included charges for: Private room, Drugs, Medical/surgical supplies, Sterile supply, Laboratory, Pathology lab, Operating room, Anesthesia, Recovery room (PACU), Physical therapy, Respiratory therapy, Diagnostic, Occupational therapy, Pulmonary function, Transfusions/blood supply

Conclusions

- This sub-study demonstrated that pre-operative administration of Meloxicam IV 30 mg in subjects undergoing colorectal surgery resulted in reductions in HRU in this sub-study.
- Observed reductions in HRU in this analyses were associated with reductions in opioid use and ORADEs in the Meloxicam IV 30mg group vs. placebo group.