

**Title:**

**Reduced Incidence of Opioid-Induced Respiratory Depression with Oliceridine Compared to Morphine As Measured By The Frequency And Average Cumulative Duration of Dosing Interruption In Patients Treated For Acute Postoperative Pain**

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**Multicenter, randomized, double-blind, placebo-and active-controlled phase 3 studies**

- Age  $\geq 18$  and  $\leq 75$  years at screening
- $\geq 40$  kg in body weight or a body mass index (BMI) of  $\leq 35$  kg/m<sup>2</sup>
- Scheduled to undergo primary surgery with no additional collateral procedures

	Hard Tissue (Bunionectomy)	Soft Tissue (Abdominoplasty)
Sample size, N (randomized and treated)	389	401
Treatment period	48 hours	24 hours
Anesthesia	Regional (popliteal sciatic nerve block)	General
Pain entry criteria	NRS* $\geq 4$ within 9 hours after discontinuation of regional anesthesia	NRS* $\geq 5$ within 4 hours from end of surgery

**Key exclusion criteria:** sleep apnea, evidence of hemodynamic instability or respiratory insufficiency, or surgical/anesthetic complications  
 \*NRS= numeric rating scale for pain score

Treatment	Clinician-administered Loading Dose	Patient-administered Demand Dose	Clinician-administered Supplemental Dose
<b>Oliceridine</b>	1.5 mg	0.1 mg	0.75 mg q1h PRN
		0.35 mg	
		0.5 mg	
<b>Morphine</b>	4 mg	1 mg	2 mg q1h PRN
<b>Placebo</b>	Volume-matched solution	Volume-matched solution	Volume-matched solution

*Multimodal therapy was not permitted; Rescue pain medication (etodolac 200 mg PO q6h PRN) was permitted during the treatment period if study medication was inadequate*

*Certified nurse anesthetists blinded to treatment monitored each patient and may have withheld study medication according to patient's respiratory status*