Cost Effectiveness Analysis of Oliceridine Compared with Morphine in The Management of Postoperative Moderate to Severe Acute Pain in a High-Risk Population

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BACKGROUND

- Opioids remain an important component of therapy for the management of moderate to severe acute postoperative pain (*Small and Laycock 2020*).
- However, conventional opioids are associated with adverse events (AEs). The elderly, obese patients, or patients with multiple comorbidities are at increased risk of developing opiod-related adverse events (ORAEs) (*Shafi et al. 2018; Bui et al. 2018; Dahan, Aarts, and Smith 2010*).
- ORAEs can affect patients' health outcomes, compromising optimal postoperative recovery (*Small and Laycock 2020; Shafi et al. 2018*).
- Oliceridine, a new class of IV opioid analgesic acting at μ-opioid receptors, is selective for G-protein signaling (achieving analgesia) with limited recruitment of β-arrestin (associated with ORAEs).

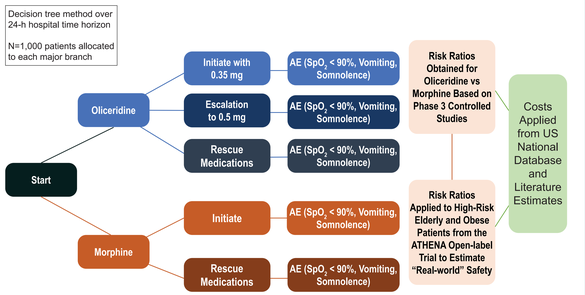
OBJECTIVE

- To estimate cost-effectiveness of oliceridine compared to morphine for postoperative pain in high-risk patients.

METHODS

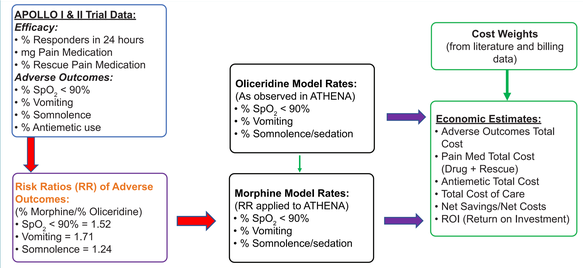
- The overview of the economic model methodology is shown in **Figure 1**.
- We directly compared costs and outcomes of patients managed with demand dosing of oliceridine (0.35 mg and 0.5 mg) to those with morphine (1 mg), using a decision tree with a 24-hour time horizon (with cost estimates across a sample population of 1,000 surgeries treated with either oliceridine or morphine).

Figure 1: Overview of Economic Model Methodology



- Nonresponse to oliceridine 0.35 mg demand dose was assumed to lead to escalation to 0.5 mg demand dose and use of rescue analgesics when 0.5 mg demand dose was inadequate. Nonresponse to morphine was assumed to lead directly to use of rescue analgesics.
- Three common and costly ORAEs, oxygen desaturation (SpO_2 < 90%) as a measure of opioid-induced respiratory depression (OIRD), vomiting, and somnolence were utilized.
- Risk ratios were based on AE rates observed in the two pivotal controlled Phase 3 studies (*Viscusi et al. 2019; Singla et al. 2019*). The pivotal studies used in the model were the basis of FDA approval for oliceridine.
- Risk ratios were then applied to AE rates observed in the elderly (≥ 65 years) and obese (BMI ≥ 30 kg/m^2) patients from the open-label Phase 3 safety study of oliceridine (*Bergese et al. 2019*).
- Costs of analgesics (including rescue) and antiemetics were tabulated based on rates observed in Phase 3 studies. Standard cost weights from National discharge data and literature sources were used to estimate hospital budget impact & costs for each AE.
- Average daily price was set to $100 for oliceridine and $15 for morphine.
- Costs were enumerated as differences in cost of analgesics and differences in resources utilized to manage these AEs in the first 24 hours post-surgery.
- The Analytic Framework of the model is provided in **Figure 2**.

Figure 2: Health Economic Model: Analytic Framework



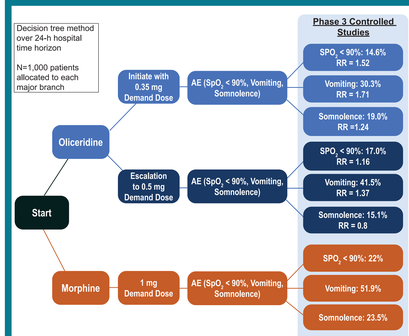
Data Inputs:

Table 1: Summary of Efficacy Outcomes, Rescue Analgesic, and Rescue Antiemetic Medication Use

Input Parameter	Treatment Allocation	Value
Efficacy (% Responder)		
	Oliceridine 0.35 mg demand dose initial responders	66.1%
	Oliceridine 0.5 mg demand dose incremental proportion of responders	19.4%
	Morphine 1 mg demand dose	73.6%
Rescue Analgesic Medication Use (%)		
	Oliceridine 0.35 mg demand dose	17.0%
	Oliceridine 0.5 mg demand dose	14.5%
	Morphine 1 mg demand dose	12.0%
Rescue Antiemetic Medication Use (%)		
	Oliceridine 0.35 mg demand dose	45.3%
	Oliceridine 0.5 mg demand dose	51.1%
	Morphine 1 mg demand dose	62.9%

- AE incidence risk-ratio computation from pooled Phase 3 controlled studies and estimations derived from ATHENA study in high-risk patients is shown in **Figure 3**.

Figure 3: AE Incidence Risk-Ratio Computation from Pooled Phase 3 Controlled Studies and Estimations Derived from ATHENA Study in High-Risk Patients



Estimation of Expected AE Incidence in High-Risk Patients in Real-World Conditions Derived from ATHENA Study

Adverse Event	Treatment Allocation: Oliceridine 0.35 mg demand dose	Oliceridine 0.5 mg demand dose	Morphine 1 mg demand dose
Low O_2 Saturation* Value (%)	13.7%	15.9%	24.2%
Vomitting Value (%)	10.1%	13.8%	23.7%
Somnolence/ Sedation Value (%)	1.9%	1.5%	2.4%

**There was an increase in opioid-induced respiratory depression (OIRD) in high-risk patients*

RESULTS

- Incremental cost of OIRD, vomiting and somnolence was estimated at $3,975, $1,035, and $991, respectively (**Table 2**).

Table 2: Health Economic Model Cost Weights for OIRD, Vomiting, and Somnolence Inflated to 2020 US Dollar Costs

Event Type	2020 Cost Weights Used for Base Model*	± 20% Range for Sensitivity Analysis	Cost in 2017 US Dollars (Low- High)
Respiratory depression (Low O_2 saturation)	**$ 3,975**	$3,180 - $4,770	$4,589 ($3,625 - $5,552)
Vomitting	**$ 1,035**	$828 - $1,242	$1,344 ($972 - $1,716)
Somnolence	**$ 991**	$793 - $1,189	$1,250 ($904 - $6,353)

**2020 costs reflect the inflated cost from the low range of the 2017 cost.*

- Considering cost of analgesics, use of oliceridine resulted in greater medication expenditures ($96,623) for pain medications compared to morphine ($127,181 vs $30,558) (**Table 3**).
- In this high-risk patient group, treatment with oliceridine resulted in 200 fewer AEs, $459,495 lower cost of managing AEs (**Table 3**).
- In a Base Model, assuming substitution of morphine with oliceridine (poster U12 presented in this meeting), the overall cost savings were $228,454 for 1,000 surgeries.
- Use of oliceridine for patients at higher risk for the emergence of ORAEs provides additional overall cost savings by $135,490.

Table 3: Estimates for the Comparative Cost of Care for 1,000 High-Risk Surgical Patients Treated On-Demand with Either Oliceridine or Morphine

	Oliceridine [0.35 mg with escalation to 0.5 mg for nonresponse] (N=1,000)	Morphine 1 mg (N=1,000)	Difference (Oliceridine – Morphine)
Cost of pain medication for 24 hours/patient	$ 108.14	$ 15.00	($ 93.14)
Response rate %	66.1%	73.6%	(7.5%)
% Escalated to 0.5 mg	19.4%	N/A	N/A
Total number of AEs:	309	509	(200)
Respiratory depression (Low O_2 saturation)	157	242	(85)
Vomiting	128	237	(109)
Somnolence	24	30	(6)
Cost of pain medication	$ 127,181	$ 30,558	$ 96,623
Cost of managing AEs	$ 778,764	$ 1,238,259	($ 459,495)
TOTAL COST	$ 907,115	$ 1,271,059	**($ 363,944)**

The model results shown were based on an assumed average daily cost of oliceridine of $100/day for the 0.35 mg dose and $124/day for the 0.5 mg dose, resulting in $108.14 as the weighted cost for day 1.
The total cost also includes the cost of antiemetics: $1,170 in the oliceridine arm and $2,242 in the morphine arm.

CONCLUSIONS

- Among patients at higher risk for the development of opioid-related adverse outcomes, oliceridine has a favorable overall impact on the total cost of postoperative care compared to the use of the conventional opioid morphine, despite a modest increase in pharmacy costs.

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