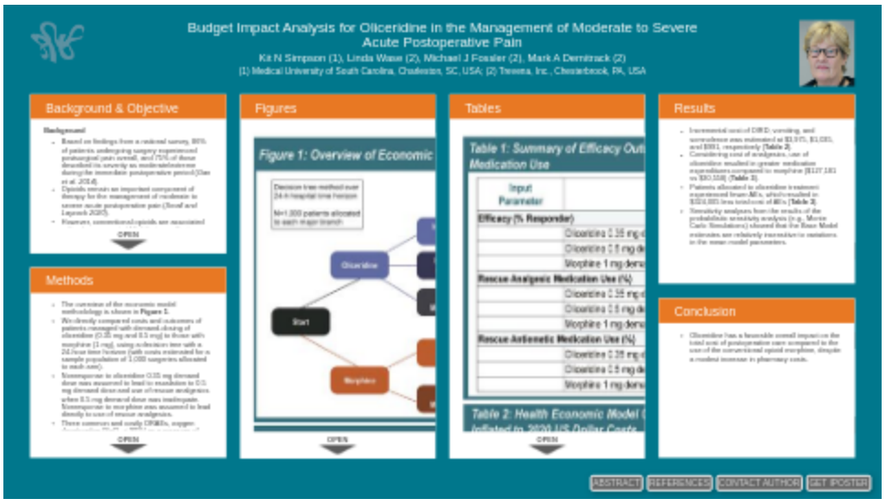
Budget Impact Analysis for Oliceridine in the Management of Moderate to Severe Acute Postoperative Pain



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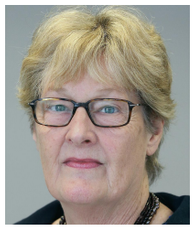


PRESENTED AT:

BACKGROUND & OBJECTIVE

Background

- Based on findings from a national survey, 86% of patients undergoing surgery experienced postsurgical pain overall, and 75% of those described its severity as moderate/extreme during the immediate postoperative period (*Gan et al. 2014*).
- 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) that 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 opioid-related adverse events (ORAEs)].

Objective

- To estimate budget impact of oliceridine compared to morphine for postoperative pain.

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 costs estimated for a sample population of 1,000 surgeries allocated to each arm).
- 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 adverse event (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.
- The risk ratios were then applied to AE rates observed in an open-label Phase 3 safety study of oliceridine (*Bergese et al. 2019*) to estimate the expected AE incidence in a real-world patient sample.
- Costs of analgesics (including rescue) and antiemetics were tabulated based on rates of utilization 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**.
- A summary of the data input related to efficacy outcomes and rescue analgesic and rescue antiemetic medication use is provided in **Table 1**.

- 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**.

FIGURES

Figure 1: Overview of Economic Model Methodology

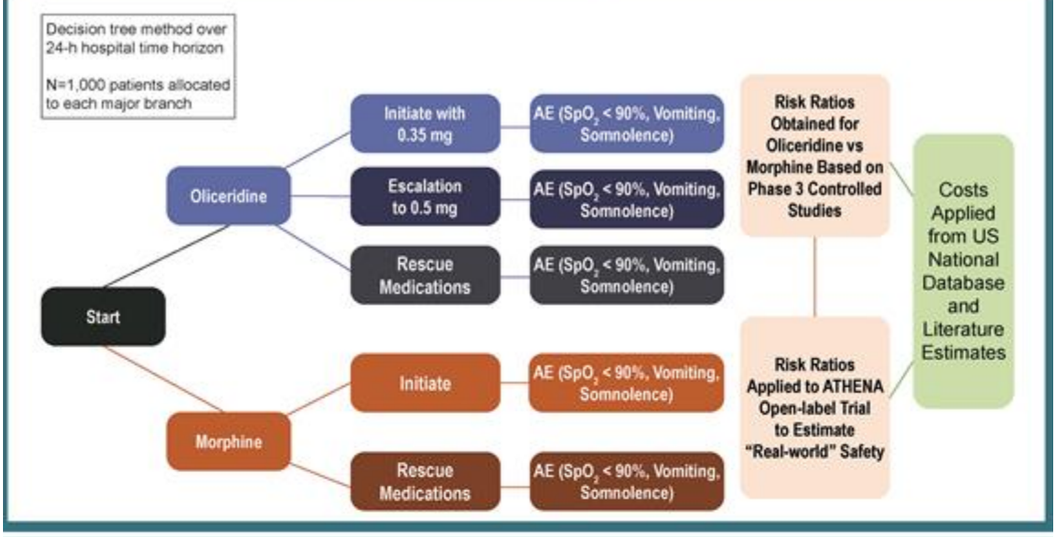


Figure 2: Health Economic Model: Analytic Framework

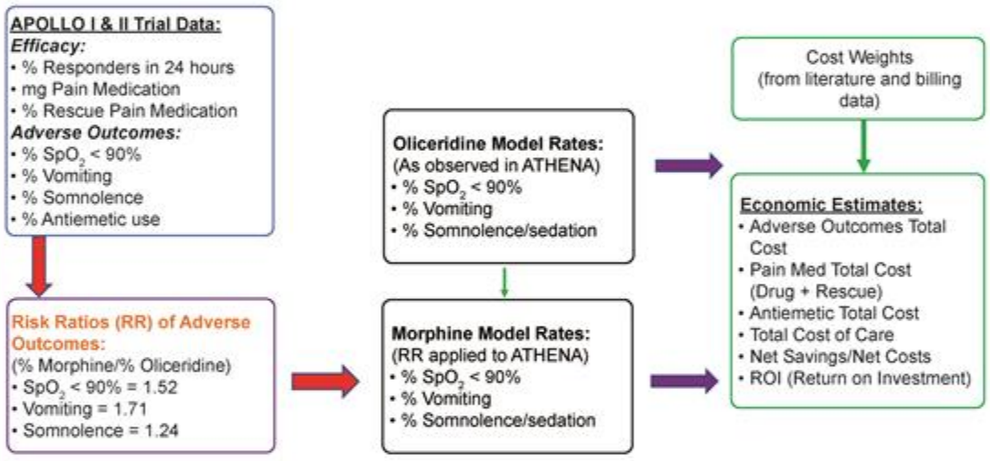
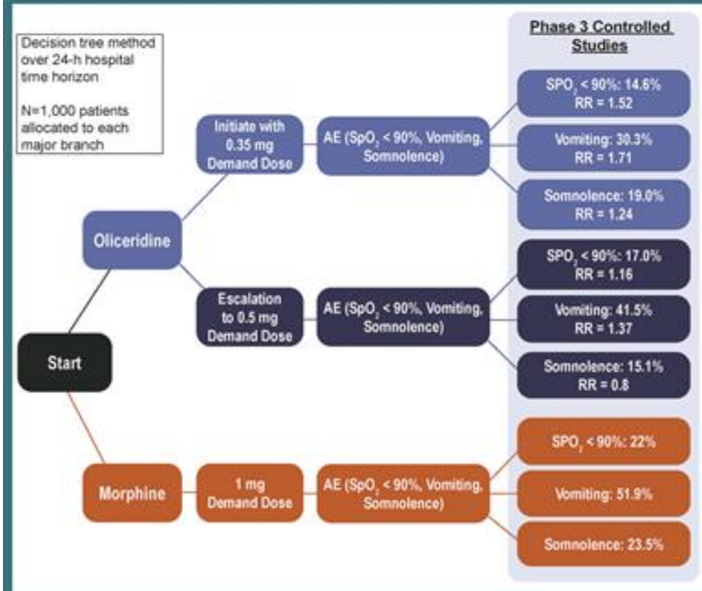


Figure 3: AE Incidence Risk-Ratio Computation from Pooled Phase 3 Controlled Studies and Estimations Derived from ATHENA Study



Estimation of Expected AE Incidence 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 (%)	8.3%	9.7%	14.7%
Vomitting Value (%)	10.1%	13.8%	23.7%
Somnolence/ Sedation Value (%)	1.9%	1.5%	2.4%

RR=Risk Ratio applied

TABLES

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%

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.*

Table 3: Estimates for the Comparative Cost of Care for 1,000 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:	242	408	(166)
Respiratory depression (Low O_2 saturation)	95	147	(52)
Vomiting	128	237	(109)
Somnolence	19	24	(5)
Cost of pain medication	$127,181	$30,558	$96,623
Cost of managing AEs	$528,424	$852,429	($324,005)
TOTAL COST	$656,775	$885,229	**($228,454)**

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.

RESULTS

- Incremental cost of OIRD, vomiting, and somnolence was estimated at $3,975, $1,035, and $991, respectively (**Table 2**).
- Considering cost of analgesics, use of oliceridine resulted in greater medication expenditures compared to morphine ($127,181 vs $30,558) (**Table 3**).
- Patients allocated to oliceridine treatment experienced fewer AEs, which resulted in $324,005 less total cost of AEs (**Table 3**).
- Sensitivity analyses from the results of the probabilistic sensitivity analysis (e.g., Monte Carlo Simulations) showed that the Base Model estimates are relatively insensitive to variations in the mean model parameters.

CONCLUSION

- 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.

ABSTRACT

OBJECTIVES:
Use of conventional opioids for postoperative pain are associated with adverse events (ORAEs) that can affect health outcomes, compromising analgesia. Oliceridine, a new class of μ-opioid receptor IV agonist , is selective for G-protein signaling (achieving analgesia) with limited recruitment of β-arrestin (associated with ORAEs). Here we estimate the budget impact of oliceridine vs morphine for postoperative pain.

METHODS:
We compared costs & outcomes of patients managed with demand dosing (DD) of oliceridine (0.35mg and 0.5mg) to those with morphine (1mg), using a decision tree with a 24-hour time horizon and sample population of 1,000 surgeries for each arm. Three common and costly ORAEs; respiratory depression (SpO_2 <90%, RD), vomiting, and somnolence were utilized. Costs were enumerated as differences in cost ofanalgesics and resources utilized to manage the 3 ORAEs within 24 hours post-surgery. Risk ratios (RR) were based on AE rates observed in two controlled Phase-3 studies. RRs were then applied to AE rates observed in an open-label Phase-3 study of oliceridine to estimate AE incidence in real-world sample. Costs of all analgesics 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 price was set to $100/day for oliceridine and $15/day for morphine.

RESULTS:
Incremental cost of RD, vomiting and somnolence was estimated at $3,975, $1,035 and $991, respectively. Use of oliceridine resulted in greater medication expenditures vs. morphine ($127,181 vs $30,558). However, overall hospital costs resulting from resources for managing AEs were lower for oliceridine vs morphine ($528,424 vs $852, 429), with net savings of $324,005 for each 1,000 treated patients.

CONCLUSIONS:
Use of oliceridine vs morphine for postoperative pain is expected to increase pharmacy costs but have a favorable overall budget impact.

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