

Evaluation of Alvimopan: Is the Outcome Worth the Cost?

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Abstract # 23
IRB Exempt

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Disclosure

- Grace Park
- Potential conflicts of interest: none
- Sponsorship: none
- Proprietary information or results of ongoing research may be subject to different interpretation
- Speaker's presentation is educational in nature and indicates agreement to abide by the non-commercialism guidelines provided

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Learning Objectives

- Review alvimopan and its mechanism of action
- Evaluate the relationship between alvimopan use, length of stay, and hospital costs

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Background

- Postoperative ileus (POI)
 - Impairment of GI motility after abdominal surgery
 - Can vary from few hours to several weeks
 - Multiple factors involved in pathogenesis
 - Exacerbated by use of opioids for surgical pain control
 - Increases length of stay and hospital cost
 - 8.9 days vs. 13.8 days
 - \$16,907 vs. \$25,089

Doorly, M., Senagore, A. Surg Clin N Am 92 (2012) 259-272
Iyer, S., Saunders, W., Stenikowski, S. J. Managed Care Pharm. 2009; 15(6):485-494

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Background

Doorly, M., Senagore, A. Surg Clin N Am 92 (2012) 259-272
https://www.researchgate.net/figure/Proposed-pathway-of-memory-TH1-cell-dissemination-of-postoperative-ileus-POI-the-study_fig1_49662324

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Background

- Alvimopan (Entereg®)
 - Peripheral mu-opioid receptor antagonists
 - Inhibits effect of opioids in GI tract
 - Does not affect opioid analgesic effect
 - Indicated for postoperative ileus to accelerate the time to GI recovery following surgeries

Alvimopan monograph, Lexi-Comp, Inc. (Lexi-Drugs), Lexi-Comp, Inc.; May 1, 2018

Background

- Alvimopan (cont.)
 - For short-term hospital use only (≤ 15 doses)
 - Hospitals required to enroll in REMS program due to potential risk of MI with long-term use
 - Contraindicated in patients taking opioids for > 7 days prior to alvimopan
 - Cost: ~\$190 per dose

Alvimopan monograph. Lexi-Comp, Inc. (Lexi-Drugs). Lexi-Comp, Inc.; May 1, 2018

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Clinical Studies

| | N, type of patients | 1° Outcomes | 2° Outcomes | Notes |
|---|--|--|---|---|
| Wolff, B., et al. Wolff, B., et al. <i>Ann Surg.</i> 2004;240(4): 728-734 | 469 Bowel resection (n=451), total abdominal hysterectomy (n=18) | GI3: 6 mg (n=155; p=0.05) Decrease by 15 hours 12 mg (n=165; p<0.001) Decrease by 22 hours Placebo (n=149) | GI2: 6 mg (p = 0.013) Decrease by 13 hours 12 mg (p<0.001) Decrease by 20 hours Time to discharge: 6 mg (p = 0.07) Decrease by 13 hours 12 mg (p = 0.003) Decrease by 20 hours | Most common side effects nausea/vomiting in treatment group |
| Delaney C., et al Delaney C., et al <i>Dis Col Rectum.</i> 2005;48(6): 1114-1125 | 432 Partial colectomy (n=303), total abdominal hysterectomy (n=129) | GI3: 6 mg (n=152; p=0.003) Decrease by 14.1 hours 12 mg (n=146; p=0.059) Decrease by 13 hours Placebo (n=153) | GI2: 6 mg (p=0.007) Decrease by 15.2 hours 12 mg (p=0.057) Decrease by 10.5 hours Time to discharge: 6mg (p=0.001) Decrease by 14hours 12 mg (0.17) Decrease by 7.2 hours | More vomiting in treatment group vs. placebo |
| GI3: recovery of GI function: 1) toleration of solid food; 2) either first flatus or a BM GI2: recovery of GI function: 1) toleration of solid food; 2) first BM | | | | |

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Clinical Studies

- Morbidity profile by Wolff, B., et. al
- 12 patients need to be treated to prevent one patient from overall post-operative morbidity

| Number Needed to Treat (NNT) to Prevent One Event | |
|---|-------------------------|
| | Alvimopan 12 mg (n=714) |
| Overall post-operative morbidity | 12 |
| Post-operative NGT insertion | 20 |
| Overall complications of POI | 17 |
| Complications of POI resulting in prolonged stay | 21 |
| Complications of POI resulting in readmission | 97 |

Wolff, B., et al. *J Am Col Surg.* 2007; 204:609-616

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Study Design

- Alvimopan removed from institutional formulary in April 2017
- Objective: determine if length of stay and cost changed in patients who underwent bowel surgery since the removal of alvimopan from formulary

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Methods

- Retrospective chart review
 - Group A: January 2015 to December 2016
 - Group B: May 2017 to March 2018
- Inclusion Criteria:
 - Adult patients > 18 years
 - determined by Diagnosis-Related Group (DRG)
 - Major small & large bowel procedure with major complication or comorbidity (MCC)
 - Major small & large bowel procedures with complication or comorbidity (CC)
 - Major small & large bowel procedures without complication or comorbidity/major complication or comorbidity (CC/MCC)

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Methods

- Exclusion Criteria:
 - None planned initially
 - Patients utilizing high cost drugs
- Primary outcomes:
 - Average length of stay to discharge
 - Average drug cost per discharge

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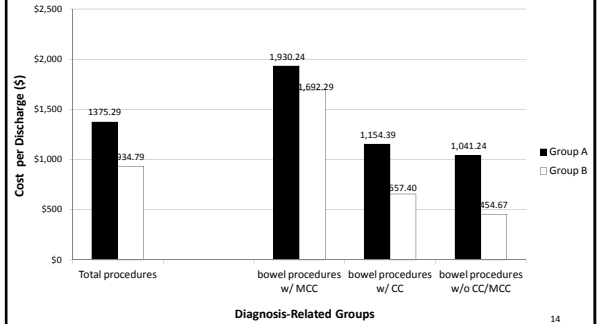
Results

- Total of 274 patients in the study
 - 195 patients in Group A
 - 192 patients received alvimopan
 - 79 patients in Group B

| Patient Population | | |
|-----------------------------|---------|---------|
| DRG | Group A | Group B |
| Bowel procedures w/ MCC | 50 | 21 |
| Bowel procedures w/ CC | 88 | 38 |
| Bowel procedures w/o MCC/CC | 57 | 20 |

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Average Drug Cost per Discharge



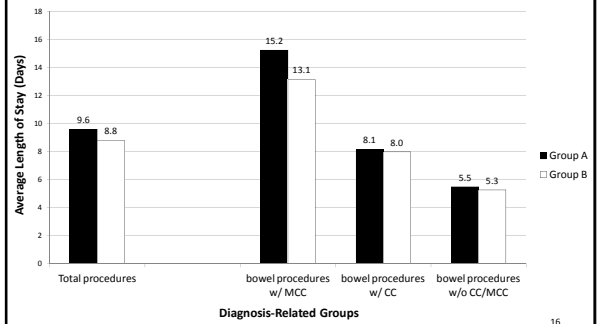
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Results

- Cost per discharge decreased for all DRG groups
- Hospital-wide utilization of other drugs did not change over time

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Average Length of Stay to Discharge



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Results

- Decrease in length of stay observed
 - Statistical analysis pending
- Average length of stay ranged from 6.2 to 7.4 days in 5 clinical trials without alvimopan

Kraft, M., et al. P&T. 2010; 35(1): 44-49

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Conclusion

- Decrease in both average cost per discharge and average length of stay observed since the removal of alvimopan from formulary
 - Decrease in average length of stay not expected
 - Statistical analysis pending

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Study Limitations

- Retrospective pooled data for each DRG
- Included every patients in each DRG
- Sample size difference between the groups

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Assessment

- What is the mechanism of action of alvimopan?
 - a. Inhibits peripheral mu-opioid receptors in the gastrointestinal tract
 - b. Stimulates peristaltic activity of the gastrointestinal tract
 - c. Stimulates cholinergic receptors in the gastrointestinal tract
 - d. Largely unknown
- Why is REMS program required for alvimopan?
 - a. Increased risk of malignancies
 - b. Increased risk of myocardial infarction
 - c. Life-threatening infusion reactions
 - d. Increased risk of pancytopenia

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