Trust your gut: Effect of a pharmacist-driven pilot project to decrease alvimopan use past gastrointestinal recovery in postsurgical patients

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Purpose. Alvimopan is a peripherally acting opioid receptor antagonist indicated to accelerate gastrointestinal (GI) recovery following surgery, but its benefits past GI recovery are unknown and evidence suggests that it may increase risk for myocardial infarction. The purpose of this study was to evaluate the efficacy of a pilot alvimopan stewardship program aimed at intervening to discontinue alvimopan use following GI recovery.

Methods. This was a retrospective, observational study examining the first 5 months of the alvimopan stewardship pilot program. During this initial period, a pharmacy resident assessed whether each patient met criteria for GI recovery, defined as solid food toleration and first bowel movement or flatus. If a patient met the criteria for GI recovery, the resident intervened and recommended that the primary team discontinue alvimopan. Primary outcomes were the percentage of patients with alvimopan continued past GI recovery and the percentage of patients for whom alvimopan ordered past GI recovery was discontinued following intervention by stewardship. Secondary outcomes included the percentage of accepted recommendations to discontinue alvimopan following GI recovery and the number of alvimopan doses ordered following GI recovery.

Results. In total, 73 patients were included in the study analysis, all of whom underwent abdominal and/or urologic surgery. Alvimopan was ordered to be administered in 35.6% (26/73) of patients after GI recovery. The stewardship program intervened and recommended discontinuation on 50% (13/26) of the alvimopan doses ordered past GI recovery. Recommendations were accepted by the primary team for 92.3% (12/13) of the patients. A total of 51 doses of alvimopan were ordered for administration past GI recovery, with an average of 2 doses per patient.

Conclusion. A pilot pharmacy-driven alvimopan stewardship program was able to identify and intervene on alvimopan orders continued past GI recovery. Interventions decreasing alvimopan use past GI recovery could be of benefit by minimizing potential risk and decreasing potential costs without a negative impact on patient outcomes.

Keywords: XXX

Alvimopan (Entereg; Adolor Corporation, Exton, PA) is a peripherally acting opioid receptor antagonist indicated to accelerate gastrointestinal (GI) recovery following bowel resection with opioid use and primary anastomosis.[1] Enhanced Recovery After Surgery (ERAS) pathways are designed to reduce surgical stress and hasten recovery using a multimodal approach after surgery. Several ERAS pathways now recommend alvimopan to hasten GI recovery after off-label procedures with opioid use, including cystectomy, pancreatoduodenectomy, and gynecologic surgery.[2-5] Alvimopan is dosed as 12 mg by mouth before surgery, followed by 12 mg by mouth twice daily after surgery for up to 15 total doses, until GI recovery or until hospital discharge, whichever comes first.[1,6,7] GI recovery was defined in clinical trials as solid food toleration and first bowel movement or solid food toleration and first bowel movement or flatus.[8-11]

In 2018, we suspected that alvimopan might be continued past GI recovery in some of our postsurgical patients. We performed a retrospective medication use analysis of a convenience sample including 68 adults ordered alvimopan via an ERAS pathway from January 2018 to August 2018. GI recovery was defined as solid food toleration and first bowel movement or flatus. At least 1 alvimopan dose was administered after GI recovery in 57.4% of patients (39/68). Additionally, 30.8% (110/357) of alvimopan doses were ordered to be administered following GI recovery.

The benefit of alvimopan following GI recovery is unclear, and we are unaware of any evidence suggesting improved outcomes when continuing alvimopan past GI recovery. There are, however, potential risks, as alvimopan carries a boxed warning due to evidence suggesting increased incidence of myocardial infarction vs absence of treatment.[1] The Entereg access support and education (E.A.S.E.) risk evaluation and mitigation strategy (REMS) was created alongside alvimopan's Food and Drug Administration approval given the

concerning findings of a higher incidence of ischemic cardiovascular events in patients receiving alvimopan.[12] It is important to note, however, that the study prompting the creation of E.A.S.E. was 12 months in length and assessed patients using opioids for chronic pain, for which alvimopan is not indicated. Per the REMS program, overall length of therapy with alvimopan is limited to 15 doses and alvimopan is not to be used in the outpatient setting. Additionally, alvimopan is also expensive, costing more than $3,000 per 15-dose treatment course, according to a tertiary drug reference.[13] Interventions decreasing alvimopan use past GI recovery could be of benefit by minimizing potential risk and decreasing potential costs without worsening patient outcomes.

In 2019, our institution implemented a pilot stewardship program to decrease alvimopan use past GI recovery. This program was developed, implemented, and administrated by a single postgraduate year 1 (PGY1) pharmacy resident, who reviewed all patients with active alvimopan orders on scheduled working days. Other pharmacists did not review alvimopan orders for the stewardship program on days when the pharmacy resident was not working. The pharmacy resident assessed whether each patient met criteria for GI recovery. This was defined as solid food toleration and first bowel movement or flatus to align with previous clinical trials.[8-11] If a patient met criteria for GI recovery, the resident intervened and recommended the primary team discontinue alvimopan. The final decision to discontinue alvimopan was left to the discretion of the primary team.

The purpose of this study was to evaluate the first 5 months of our pilot alvimopan stewardship program. Primary outcomes were the percentage of patients with alvimopan continued past GI recovery and the percentage of patients for whom stewardship intervened to discontinue alvimopan following GI recovery. Secondary outcomes included the percentage of accepted recommendations to discontinue alvimopan following GI

recovery and the number of alvimopan doses ordered for administration following GI recovery.

Methods

This retrospective, observational study was completed at a single academic medical center and was deemed exempt by the institutional review board. Consecutive adult patients ordered alvimopan as part of an ERAS pathway from October 1, 2019, to March 1, 2020, were identified via a query of the electronic medical record. Patients on opioids for 7 or more days immediately before alvimopan administration were excluded, as alvimopan use in this scenario is contraindicated by the package insert.[1] Unfortunately, there was no easy way to identify such patients using the medical record. Opioid usage was therefore assessed through a query of the New York State Prescription Monitoring Registry. Patients who had filled a prescription for a 30-day opioid supply within 30 days of alvimopan administration were thought to have a high probability of meeting the exclusion criterion and were therefore excluded from the study. GI recovery was defined as solid food toleration and first bowel movement or flatus to align with previous trials.

All data were collected by a single investigator trained in data collection using a standardized data collection form. Collected data were intermittently reviewed by a second investigator for quality and accuracy. Collected data included demographics, surgery type, days of postoperative opioid use, postoperative bowel regimen, time until first bowel movement or flatus, time until solid food toleration, total number of ordered alvimopan doses, total number of alvimopan doses ordered after GI recovery, total postoperative length of stay, pharmacist intervention, and acceptance of pharmacist intervention. All data are presented using descriptive statistics, including the number (%), mean (SD), and median

(interquartile range, IQR). All statistical analyses were performed using Excel 16.0 (Microsoft Corporation, Redmond, WA).

Results

During the study period, alvimopan was ordered for 83 patients via an ERAS pathway. Ten patients were excluded due to opioid use for 7 or more consecutive days immediately before alvimopan administration. In total, 73 patients were included in the study analysis. Mean (SD) age was 58.4 (17.1) years, mean (SD) weight was 86.9 (24.3) kg, and 54.8% (40/73) of patients were male. All patients underwent abdominal and/or urologic surgery, and most surgeries were open (50/73, 68.5%). The median (IQR) number of days of postoperative opioid use was 2 (0-3) days, and the median (IQR) postoperative length of stay was 4 (2-7) days. A postoperative bowel regimen was ordered in only a few patients (19/73, 26%). The mean (SD) time to postoperative solid food toleration was 2.5 (2.0) days, and the mean (SD) time to postoperative bowel movement or flatus was 1.1 (1.0) days; overall, the mean (SD) time to postoperative GI recovery was 2.6 (2.0) days. Alvimopan was ordered to be administered in 35.6% (26/73) of patients after GI recovery, totaling 51 orders for alvimopan administration past GI recovery. The mean (SD) number of doses ordered for these 26 patients after GI recovery was 2.0 (1.2) doses. The stewardship program intervened and recommended discontinuation for 50% (13/26) of the alvimopan doses ordered past GI recovery. The mean (SD) time at which discontinuation was recommended was 3.2 (1.8) days after surgery, and the recommendations were accepted by the primary team 92.3% (12/13) of the time.

Discussion

This report, to our knowledge, represents the first description of an alvimopan stewardship program. Other institutions have described continuing alvimopan until first stool or return of bowel function, but it is unclear whether or how these institutions address alvimopan continuation past these endpoints.[7,8] Over our 5-month study period, 35.6% of patients were continued on alvimopan past GI recovery, totaling 51 orders for alvimopan administration past GI recovery. These results indicate a significant opportunity for alvimopan stewardship, and our pilot program demonstrates that a pharmacist can monitor and intervene on postsurgical alvimopan use. Our stewardship program was able to intervene in 50% of postsurgical patients who had alvimopan orders past GI recovery. Although this finding may not seem impressive, it is important to remember that our pilot program was operated by a single PGY1 pharmacy resident during their normal staffing days. With increased pharmacist involvement, we likely could have monitored and intervened in all alvimopan orders continued past GI recovery. Additionally, providers appeared receptive to pharmacy recommendations to discontinue alvimopan after GI recovery, as evidenced by the 92.3% acceptance rate of recommendations. This percentage may vary at other institutions where provider-pharmacist relationships are different, especially when considering that this medication is not typically a target for pharmacist intervention.

The value of an alvimopan stewardship program is unclear, but there is no evidence suggesting further benefit when continuing alvimopan past GI recovery. Conversely, there is evidence suggesting potential risk, and the medication carries a boxed warning for myocardial infarction vs absence of treatment.[1] This risk, however, is reported to occur with long-term alvimopan use, and it is uncertain whether decreasing alvimopan use by a few

doses will confer lower risk to the patient.[14] Therefore, we recognize that it is unlikely that our program has a large safety benefit. However, it is our opinion that an alvimopan stewardship program could have a significant financial benefit. Over the 5-month study period, there were 51 orders for alvimopan administration after GI recovery, which extrapolates to 122 orders over a 12-month period. Alvimopan costs $207.82 per capsule, according to a common tertiary drug reference.[13] This means our health system could spend greater than $25,000 per year on alvimopan orders following GI recovery. Our results suggest that an alvimopan stewardship program could potentially decrease alvimopan utilization following GI recovery and could also decrease associated costs. The American Society of Health-System Pharmacists states that a cost-saving strategy should have a systematic approach that is mindful of patient safety and quality care.[15] We believe that our alvimopan stewardship program meets these standards, and pharmacy management has decided to expand our alvimopan stewardship program to all pharmacists so that we can obtain maximum program benefit.

There are a few limitations to our study besides its small sample and retrospective design. First, the most recent ERAS guidelines for colorectal surgery reference a systematic review assessing alvimopan benefit after major abdominal surgery, in which 6 studies were found to show benefit while 2 did not. These studies were determined to be of moderate to low quality, leading to a weak ERAS recommendation for alvimopan, and the guidelines do not explicitly argue for or against alvimopan use.[5] This has raised questions about alvimopan use, and decisions to utilize this medication will be institution specific. Our results will only apply to institutions using alvimopan. Second, during the 5-month study period, our providers discontinued alvimopan before GI recovery in 64.4% (47/73) of patients. We cannot exclude the possibility that our providers may have eventually discontinued

alvimopan orders continuing past GI recovery without pharmacist intervention. Although we recognize this possibility, this does not discount the opportunity for pharmacist intervention, and we believe that our results demonstrate that pharmacist stewardship could decrease alvimopan use after GI recovery. Finally, our alvimopan stewardship program was exclusively performed by a single PGY1 pharmacy resident. This was done owing to staffing limitations as we were unsure of the benefit of the pilot program. As stated previously, we have since expanded our alvimopan stewardship program to include all pharmacists, but we recognize that other hospital pharmacies may have difficulty implementing a similar program if they do not have similar staffing capabilities.

Conclusion

We found that alvimopan was continued past GI recovery in many postsurgery patients for whom the medication was ordered through an ERAS pathway. A pilot pharmacy-driven alvimopan stewardship program was able to identify and intervene on alvimopan orders continued past GI recovery. Providers accepted 92.3% of pharmacist recommendations to discontinue alvimopan orders continued past GI recovery.

Disclosures

The authors have declared no potential conflicts of interest.

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