UPMC PALLIATIVE AND SUPPORTIVE INSTITUTE

THE TABLET: PALLIATIVE CARE PHARMACY TIPS

January 10, 2024 Vol. 5, No. 1

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If you have a topic you would like the pharmacy team to answer, please send your suggestions to: lowrymf@upmc.edu

TODAY'S TOPIC:

UPMC Research: Evaluating opioid induced constipation management: naloxegol use in the inpatient setting

Kelly Frank, Anneliese Harp, Alexis Gaggini, PharmD, BCACP, BC-ADM, DipACLM, Maria Felton Lowry, PharmD, BCPS, BCGP

Results presented at American Society of Health-System Pharmacists (ASHP) Midyear Meeting 2024

Background:

- Opioid receptors are widely distributed throughout the gastrointestinal (GI) tract
- Opioid analgesics bind to these receptors, causing delayed gastric emptying and peristalsis: opioid-induced constipation (OIC)
- OIC accounts for 40-60% of constipation in patients with cancer-related pain treated with opioids[1]
- First line treatment for OIC: scheduled stimulant and/or osmotic laxatives[2]
- Peripherally acting μ-opioid receptor antagonists (PAMORAs) act on the GI μ-opioid receptors, mitigating OIC without affecting opioid analgesia
- PAMORAs effectively treat OIC refractory to standard laxatives in cancer and non-cancer patients (they are recommended as second-line therapy)[2]
- Naloxegol is FDA-approved for OIC in adults with chronic non-cancer pain and is used off-label for OIC caused by cancer-related pain
- All laxative medications are recommended to be discontinued before naloxegol initiation[3]
- Literature is limited for use of oral PAMORAs in the inpatient setting

Importance:

Naloxegol is being used by our palliative care teams for opioid-induced constipation. It is important to review our internal prescribing practices, efficacy and safety to compare to other palliative care (limited) evidence.

The Research:

Primary Objective: Determine the rate at which bowel movement occurs within one calendar day of PAMORA administration in an inpatient population

Secondary Objectives: Quantify the incidence of scheduled bowel regimen utilization prior to PAMORA administration, quantify incidence of adverse reactions (abdominal cramping, diarrhea, dose reduction for intolerance) following PAMORA administration

Subgroups analyzed:

- Cancer versus non-cancer population
- Naloxegol doses
- Palliative care consultation

Methods:

- An IRB-approved retrospective chart review was conducted among adult (>18 years old) inpatients who received naloxegol for OIC while on opioid therapy at UPMC Shadyside or UPMC Horizon from August 1, 2022 to July 31, 2023
- **Exclusion Criteria:** Prior use of a PAMORA, discharged within 1 calendar day of receiving first dose of oral naloxegol
- Descriptive statistics utilized for analysis

Results:

- N=92 received naloxegol, mean age: 61, 57% female, 49% active cancer diagnosis

49 patients (53%) had a documented bowel movement within one calendar day after naloxegol administration

Table 1. Doses and Adverse Events

Subgroup	N	Adverse Event N (%)
12.5mg	75	17 (22.7%)
Diarrhea		14 (18.7%)
Cramping		3 (4%)
25mg	17	4 (23.5%)
Diarrhea		4 (23.5%)
Cramping		0 (0%)

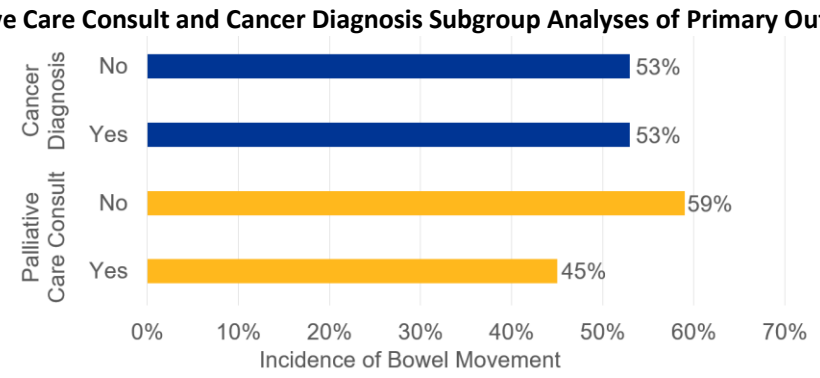
Table 2. Incidence of Adverse Events

Adverse Event	N	%
Diarrhea	18	19.6
Cramping	3	3.2

Table 3. Doses and Incidence of Bowel Movements

Subgroup	N	Primary Outcome (%)
12.5mg	75	37 (49%)
25mg	17	12 (71%)

Figure 1. Palliative Care Consult and Cancer Diagnosis Subgroup Analyses of Primary Outcome



Discussion:

- This retrospective chart review found that oral naloxegol for OIC can lead to bowel movement within one calendar day in the inpatient setting, consistent with efficacy data in the outpatient setting
- Diarrhea is a more common adverse effect from oral naloxegol than abdominal cramping
- Naloxegol can be efficacious for OIC even when patients have a primary diagnosis of cancer despite only being FDA-approved for OIC in adults with chronic noncancer pain
- The 25 mg dose led to bowel movements at a higher rate than 12.5 mg, suggesting that patients should be started at 25 mg as package insert suggests (unless renal function inhibits this)
- It's possible that patients being followed by palliative care may have higher incidence of refractory symptoms, making symptom management more challenging
- **Limitations**:
  - Small patient population
  - Retrospective
  - Variability in documentation/clinical notes where much of our information was obtained

References:

1. Coyne KS. Opioid-induced constipation among patients with chronic noncancer pain in the united states, canada, germany, and the united kingdom: laxative use, response, and symptom burden over time. 2015 Aug.
2. Squeo F, Celiberto F, Lerardi E, *et al*. Opioid-induced constipation: old and new concepts in diagnosis and treatment. *J Neurogastroenterol Motil.* 2024;30:131-142.
3. Naloxegol (Movantik) prescribing information. Wilmington, DE: AstraZeneca Pharmaceuticals; 2018 Feb.

CLINICAL PEARL: Naloxegol can be effective for an inpatient population. Would recommend starting at package-insert recommended dose of 25mg, rather than dose-reducing to 12.5mg, unless otherwise indicated.