EDUCATIONAL PROGRAM

Recognizing the Growing Burden of OIC

Bill H. McCarberg, MD
Founder, Chronic Pain Management Program
Kaiser Permanente San Diego
Adjunct Assistant Clinical Professor
University of California San Diego
San Diego, CA

Opioid Use in Palliative Care

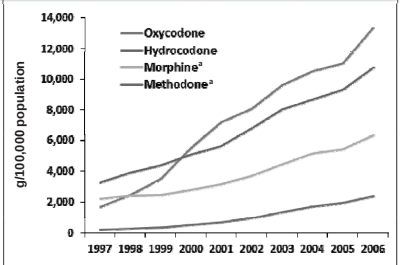
- Relief of pain is one of the core components of palliative care[1,2]
  - Up to 69% of patients with advanced cancer experience pain[3]
  - ~65% of patients dying from nonmalignant disease experience pain[4]
- Opioids are a mainstay of therapy for pain in palliative care[1,2]
  - Primarily used for moderate-to-severe pain[1,2]
  - Recommended for treatment of pain by World Health Organization[1]

1. World Health Organization. http://www.who.int/cancer/palliative/painladder/en/. Accessed November 7, 2013.
2. Swarm R, et al. NCCN adult cancer pain clinical practice guidelines in oncology 2011. http://nccn.org/professionals/physician_gls/default.asp. Accessed November 7, 2013.
3. van den Beuken-van Everdingen MHJ, et al. *Ann Oncol.* 2007;18:1437-1449.
4. Colvin L, et al. *BMJ*. 2006;332:1081-1083.

Opioid Use for Chronic Noncancer Pain

- Opioids are increasingly prescribed to treat moderate-to-severe pain in patients with nonmalignant diseases[1,2]
- Common conditions treated with opioids include back pain, osteoarthritis, fibromyalgia, and headache[2]

Therapeutic Opioid Use in US (g/100,000 population)[1]



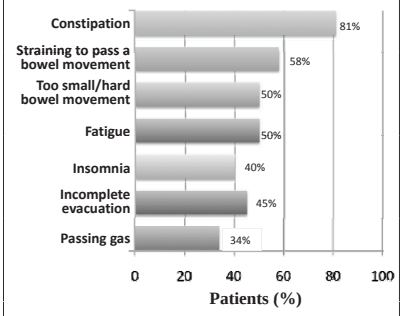
[a]For year 2000, data is not available, the average of 1999 and 2001 was taken.
Used with permission.

1. Manchikanti L, Singh A. *Pain Physician*. 2008;11(suppl):S63-S88.
2. Chou R, et al. *J Pain*. 2009;10:113-130.

Opioid-Induced Constipation

- Opioid-induced constipation (OIC) is one of the most common and troublesome adverse events (AEs) with opioid therapies[1-2]
  - Reported in 95% of patients with cancer pain and up to 80% of patients with nonmalignant pain[1,2]
- Tolerance to OIC rarely develops[2,3]
- Prevalence of constipation increased with duration of opioid treatment in patients with chronic, non-cancer pain[4]

Opioid-induced GI AEs That Patients With Chronic Pain Find Most Bothersome[2]*



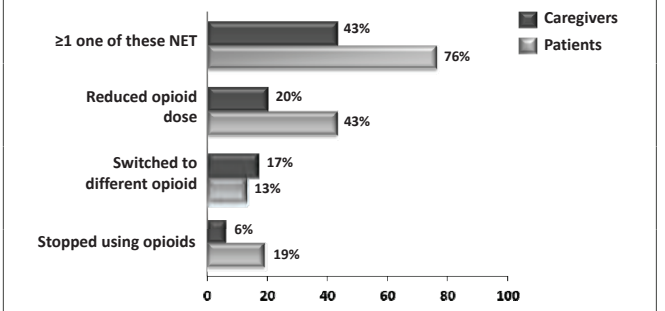
Data from PROBE 1 Survey. 4% of respondents suffered from cancer-related pain.
*AEs reported by ≥20% of patients.

PROBE, Patient Reports of Opioid-related Bothersome Effects.

1. Robinson CB, et al. *Clin J Oncol Nurs*. 2000;4:79-84.
2. Bell TJ, et al. *Pain Med*. 2009;10:35-42.
3. Panchal SJ, et al. *Int J Clin Pract*. 2007;61:1181-1187.
4. Tuteja AK, et al. *Neurogastroenterol Motil*. 2010;22:424-430.

OIC Can Compromise Pain Management in Patients With Cancer

Change in Opioid Use Due to OIC

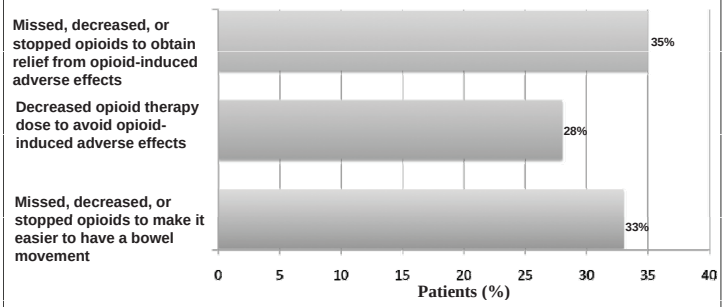


Data from survey of end-stage cancer patients (n=310).
Adapted with permission.

The Compassion Compromise: Trade-offs in pain management for patients with terminal illness. Executive Summary. April 2008. http://www.hpna.org/PicView.aspx?ID=726. Accessed November 7, 2013.

OIC Can Compromise Pain Management in Patients With Chronic, Non-cancer Pain

Results From the PROBE 1 Survey*



92% of patients who decreased or stopped opioids experienced pain.

Bell TJ, et al. *Pain Med*. 2009;10:35-42.

*4% of survey respondents suffered from cancer-related pain.
PROBE=Patient Reports of Opioid-related Bothersome Effects.

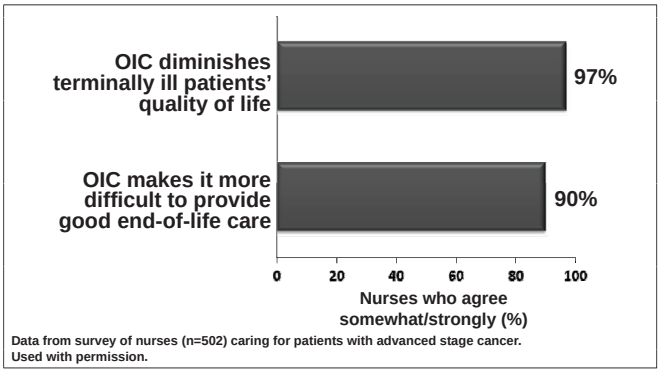
OIC Increases Use of Health Care Resources for Patients With Chronic, Non-cancer Pain

	Mean Number of Visits in Last 6 Months	
	OIC (n=359)	No OIC (n=2071)
Emergency room visits	0.5	0.5
Number of days hospitalized	1.6	1.6
Physician visits	13.5*	9.7
Alternative case visits	6.2*	4.4

Data from International Health and Wellness Survey 2004 from persons aged ≥18 years taking opioids for ≥6 months.
**P<.05.*

Bell T, et al. *J Opioid Manag*. 2009;5:137-144.

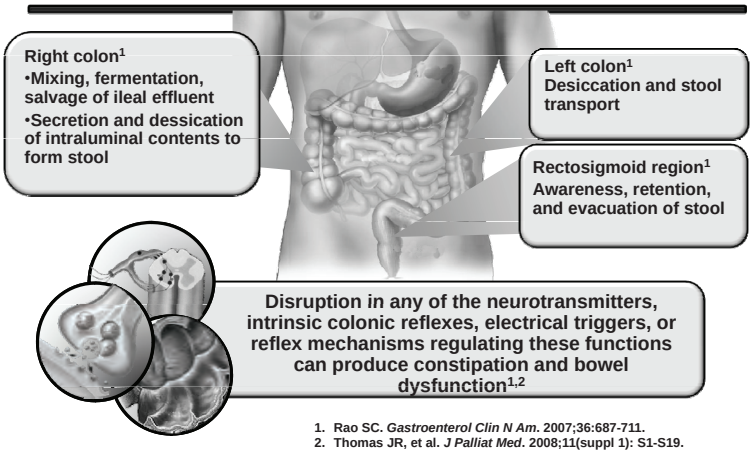
OIC Reduces Quality of Life in Patients With Cancer



Data from survey of nurses (n=502) caring for patients with advanced stage cancer. Used with permission.

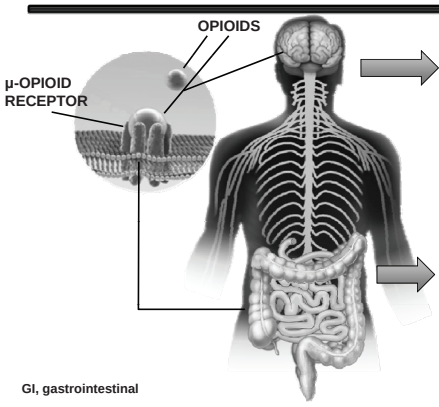
The Compassion Compromise: Trade-offs in pain management for patients with terminal illness. Executive Summary. April 2008. http://www.hpna.org/PicView.aspx?ID=726. Accessed November 7, 2013.

Normal Colorectal Functional Processes



1. Rao SC. *Gastroenterol Clin N Am*. 2007;36:687-711.
2. Thomas JR, et al. *J Palliat Med*. 2008;11(suppl 1): S1-S19.

Pathophysiology of OIC



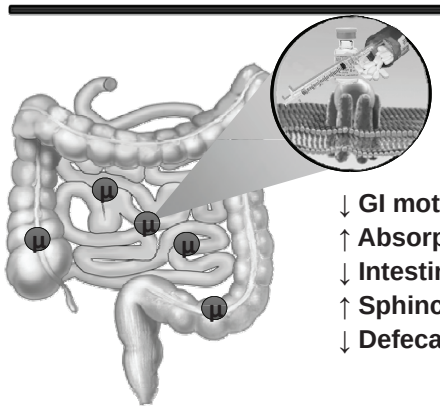
Opioids primarily exert analgesic effects via central μ-opioid receptors[1]

OIC is largely mediated by opioid actions on μ-opioid receptors in the GI tract[1-3]

GI, gastrointestinal

1. Thomas JR, et al. *J Palliat Med.* 2008;11(suppl 1):S1-S19.
2. Diego L. *Expert Opin Investig Drugs*. 2011;8:1047-1056.
3. Leppert W. *Adv Ther*. 2010;27:714-730.

Opioid Effects on the Gastrointestinal Tract

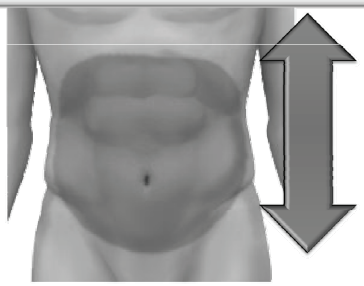


↓ GI motility
↑ Absorption of fluid from gut
↓ Intestinal secretion
↑ Sphincter tone
↓ Defecation reflex

1. Leppert W. *Adv Ther*. 2010;27:714-730.
2. Kurz A, Sessler DI. *Drugs*. 2003;63:649-671.

The Spectrum of Opioid-induced Bowel Dysfunction

Opioids Affect the Entire GI Tract[1,2]



- Reflux/heartburn
- Abdominal cramping
- Abdominal spasms
- Bloating
- Decreased appetite
- Nausea/vomiting
- Hard and dry stools
- Painful/incomplete defecation
- Constipation

1. Thomas JR, et al. *J Palliat Med*. 2008;11(suppl 1): S1-S19.
2. Kurz A, et al. *Drugs*. 2003;63:649-671.

Defining Constipation

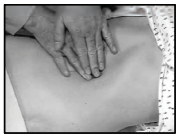
Daily ⟷ 3 bowel movements ⟷ Weekly

- A wide range of bowel movement frequencies is considered normal[1]
- Definition of constipation depends on more than the daily number of bowel movements[1,2]
- Should address other symptoms such as passage of hard stools, excessive straining, and feeling of incomplete evacuation[1,2]

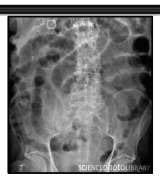
1. McMillan SC. *Cancer Control*. 2004;11(suppl 1):3-9.
2. Rao SSC. *Gastroenterol Clin North Am*. 2007;36:687-711.

Assessment of OIC

Patient interview[1-3]
- **Bowel habit**
- **Activity level**
- **Medical history**
- **Drug history**
- **Cancer history**



Physical exam[1-3]
- **Abdominal**
- **Neurologic**
- **Anorectal**



Diagnostic imaging[2,3]
- **R/O obstruction**

Signs That May Indicate Insufficient Laxative Response[3,4]
- **Hard stools**
- **Infrequent stools (<3 per week)**
- **Excessive straining**
- **Sense of incomplete evacuation**
- **Excessive time spent on toilet**
- **Unsuccessful defecation**

R/O, rule out

1. McMillan SC. *Cancer Control*. 2004;11(suppl 1):1-9.
2. Leppert W. *Adv Ther*. 2010;27:714-730.
3. Rao SSC. *Gastroenterol Clin N Am*. 2007;36:687-711.
4. Lembo A, Camilleri M. *N Engl J Med*. 2003;349:1360-1368.

The Patient History: Asking the Right Questions

- **Previous bowel pattern prior to starting opioids[1,2]**
- **Current pattern while taking opioids[1,2]**
  - **Stool frequency, consistency, and size**
  - **Degree of straining during defection**
  - **History of ignoring call to stool**

- **Fiber intake[1]**
- **Fluid intake[1]**
- **Number and timing of meals (particularly breakfast because colonic motility increases 2-3 times after waking and after a meal)[1]**

- **Laxative use (frequency and types)[1,2]**
- **Other medications (anticholinergics, calcium channel antagonists, iron supplements, calcium supplements)[1,2]**

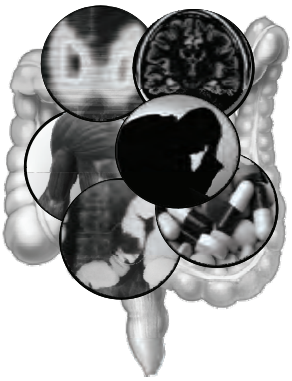
1. Peppin JF. *Practical Pain Management*. 2012 Apr:59-65.
2. Rao SSC. *Gastroenterol Clin N Am*. 2007;36:687-711.

Differential Diagnosis of OIC: Secondary Causes of Constipation

Endocrine/metabolic
Diabetes mellitus
Hypercalcemia
Hyperparathyroidism
Hypothyroidism
Uremia

Myopathic
Amyloidosis
Myotonic dystrophy
Scleroderma

Mechanical/structural
Anal dyssynergia
Anal fissures, strictures, hemorrhoids
Inflammatory bowel disorder
Obstructive colonic lesions



Neurologic diseases
Autonomic neuropathy
Cerebrovascular disease
Multiple sclerosis
Parkinson's disease
Spinal cord injury, tumors

Psychological
Anxiety
Depression
Somatization

Medications
Antacids
Anticholinergic agents
Calcium channel blockers
Clonidine
Iron
Levodopa
Nonsteroidal anti-inflammatory drugs

Thomas JR, et al. *J Palliat Med.* 2008;11(suppl 1): S1-S19.
McMillan SC. *Cancer Control*. 2004;11(suppl 3):3-9.

The Pharmacist's Role in Preventing and Managing OIC: A Case-based Approach to Care

Gregory L. Holmquist, PharmD, CPE
Pain and Palliative Care Specialist
Certified Pain Educator
Palliative Care Strategies
Seattle, WA

OIC – Issues for Patients

- Feared by many patients as much as the symptom of pain[1]
- Patients may refuse higher doses of opioid or may discontinue opioid therapy because of GI effects of opioid analgesics[2]
- Patients with OIC have more opioid-related adverse events[3]
- Can lead to a vicious cycle in which patients take more opioids to relieve pain associated with constipation, which exacerbates OIC[4]

1. Clemens KE, Klaschik E. *Ther Clin Risk Manag.* 2010;6:77-82.
2. Thomas JR, et al. *J Palliat Med.* 2008;11(suppl 1):S1-S19.
3. Candrilli SD, et al. *J Pain Palliat Care Pharmacother.* 2009;23:231-241.
4. Fallon M, O'Neill B. *BMJ.* 1997;315:1293-1296.

Laxatives for OIC

- Laxatives are the current standard of care[1]
- No consensus-based guidelines exist for use of laxatives for OIC in patients in palliative care[1]
- Laxatives can result in substantial medication burden[2]
- Typical approach:
  - Stool softener and stimulant laxative for patients[1]
    - Must be titrated[2]
  - If ineffective, osmotic laxatives or rectal agents may be added[1]

1. Thomas JR, et al. *J Palliat Med*. 2008;11:S1-S19.
2. Thomas JR. *J Support Oncol*. 2006;4:220-223.

Oral Laxatives Used for Prevention and Treatment of OIC[1-3]

Laxative class	Agent	Time to efficacy/Limitation
Bulking agents	Dietary fiber Bran Psyllium Methylcellulose Calcium polycarbophil	• 1-3 days • Fiber may not be appropriate in palliative care[1,2]
Surfactant laxatives/Stool softeners	Docusate	• 1-3 days • Water required for ingestion of capsules
Stimulant laxatives	Senna Bisacodyl	• 6-12 hours • Water required for ingestion of capsules
Osmotic agents	Lactulose	• 1-2 days • Sweet taste may be intolerable[3]
Saline laxatives	Magnesium hydroxide Magnesium citrate Magnesium sulfate	• 1-6 hours • Magnesium hydroxide should be used as last resort[3]
Macrogols	Polyethylene glycol	• 1-4 days

OIC, opioid-induced constipation
1. Librach SL, et al. *J Pain Symptom Manage*. 2010;40:761-773. 2. Larkin PJ, et al. *Palliat Med*. 2008;22:796-807.
3. Economou. In: Ferrell and Coyle, eds. *Oxford Textbook of Palliative Nursing*. 3rd ed. 2010:269-290.

Laxative Mechanisms of Action

Laxative class	Mechanism of action[1-3]
Bulking agents	↑ Fecal bulk and luminal fluid retention ↑ Colonic transit time
Surfactant laxatives/Stool softeners	↑ Water and electrolyte secretion in jejunum and colon ↓ Water and electrolyte reabsorption in small and large intestines ↑ Peristalsis at high doses
Stimulant laxatives	↑ Gut motility by stimulation of peristalsis ↓ Water absorption from gut by altering intestinal mucosal permeability
Osmotic agents	↑ Water in intestinal lumen ↑ Fecal weight ↑ Peristalsis by mechanical distention
Saline laxatives	↑ Water secretion in intestine ↑ Peristalsis
Macrogols	↑ Stool water content and stool volume Trigger direct colonic propulsion and defecation

1. Librach SL, et al. *J Pain Symptom Manage*. 2010;40:761-773. 2. Larkin PJ, et al. *Palliat Med*. 2008;22:796-807.
3. Economou. In: Ferrell and Coyle, eds. *Oxford Textbook of Palliative Nursing*. 3rd ed. 2010:269-290.

Insufficient Response to Standard Laxative Therapy Marked by Symptoms of Chronic Constipation

Signs That May Indicate Insufficient Response
• Hard stools
• Infrequent stools (<3 per week)
• Excessive straining
• Sense of incomplete evacuation
• Excessive time spent on toilet
• Unsuccessful defecation

OIC, opioid-induced constipation
Lembo A, Camilleri M. *N Engl J Med.* 2003;349:1360-1368.

Non-Laxative Alternatives to Treat OIC

- Targeting the mu-opioid receptor
  - Methylnaltrexone
    - Available as subcutaneous injection
    - Oral formulation under development
- Type 2 chloride channel activator
  - Lubiprostone
    - Available in oral formulation
    - Methadone use can interfere with efficacy

Practice Case 1

- A 45-year-old female patient has just been diagnosed with stage IV metastatic breast cancer with metastases to the bone
- Patient presents a prescription for hydrocodone-acetaminophen 1–2 tablets po prn for pain

Audience Question

Is this patient at risk for becoming constipated?

1. Yes
2. No
3. Maybe

Audience Question

Which laxative(s) would you recommend for this patient?

1. High fiber diet/bulking agents
2. Stool softener (e.g., docusate)
3. Stimulant laxative (e.g. senna)
4. Macrogol
5. Combination of above

Practice Case 1 – questions?

What counseling tips should you give this patient with regards to constipation?

OIC Counseling Tips

- Even very low doses of pain medications can lead to constipation.
- Better to prevent constipation than to react to it after the fact.
- Constipation can be prevented and does not have to affect patient's life or pain regimen.
- High fiber diet alone will not be helpful and may be harmful.
- Watch for early signs of constipation getting worse:
  - Infrequent stools
  - Feeling bloated or full
  - Not feeling that bowels completely empty
  - Straining
- Consider other causes of constipation
- Consider other medication options for constipation caused by pain medications

Practice Case 2

- A 60-year-old male with severe back pain has been taking methadone for several months.
- He was initially prescribed docusate and senna to manage constipation.
- Despite treatment with these laxatives, the patient continues to experience infrequent stools that are hard and difficult to pass.
- He also complains that he spends excessive time on the toilet and frequently feels that he has failed to completely evacuate his stools.

Audience Question

Should this patient be classified as constipated?

1. Yes
2. No
3. Maybe

Audience Question

Which next steps are most appropriate for this patient?

1. Change the opioid to oxycodone
2. Increase the dose of senna and docusate
3. Add in a magrogol
4. Change regimen to methylnaltrexone
5. Make no changes

OIC Counseling Tips

- All opioids can be constipating
- Patients do not build up a tolerance to the constipating effects of opioids
- Constipation is often a constellation and progression of symptoms. PREVENTION IS KEY TO PREVENTING SEVERE COMPLICATIONS.
- Higher dosages of ineffective agents often do not provide relief.
- Consider non-laxative alternatives

Practice Case 3

- A 53-year-old male with advanced lung cancer with bone metastases receiving palliative care has been an inpatient for over a week.
- He has been receiving morphine and fentanyl for severe pain.
- The patient now complains of abdominal pain, and the medical chart indicates no bowel movement for several days.
- Malignant causes for the pain and bowel obstruction have been ruled out.
- The medical team determines the patient has OIC.

Audience Question

Which next steps are most appropriate for this patient?

1. Administer enemas
2. Advance dose of current laxatives and continue to monitor the patient
3. Add in a magrogol
4. Change regimen to non-laxative alternative
5. Make no changes

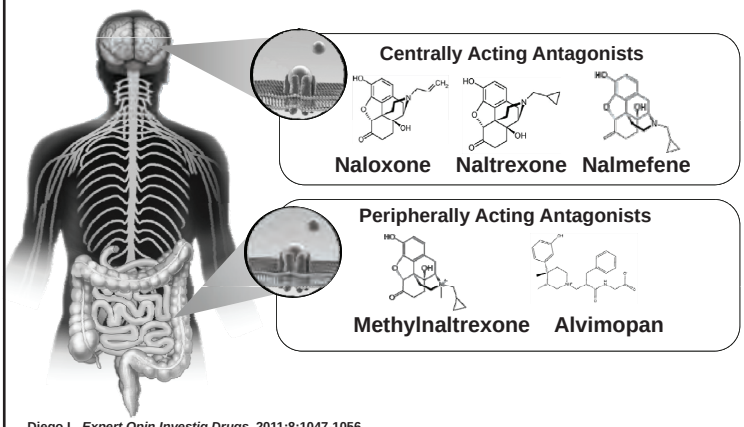
OIC Counseling Tips

- Constipation in this patient is a serious health issue and could lead to serious morbidity if not dealt with rapidly.
- Patient appears to be resistant to current regimen of laxatives and an alternative approach should be explored.
- Enemas and disimpaction are time-consuming and costly and will most likely not improve the patient in the short- or long-term.
- Consider alternatives (e.g., methylnaltrexone or lubiprostone) to treat OIC.
- Upon discharge, consider outpatient use of alternative treatment.

New Approaches to Treating OIC: Taking Advantage of the Latest Advances

Bill H. McCarberg, MD
Founder, Chronic Pain Management Program
Kaiser Permanente San Diego
Adjunct Assistant Clinical Professor
University of California San Diego
San Diego, CA

μ-Opioid Receptor Antagonists for OIC



Diego L. *Expert Opin Investig Drugs*. 2011;8:1047-1056.

Oral Naloxone for OIC

- Low (2%) systemic bioavailability due to extensive first-pass effect[1,2]
  - Oral administration of the IV formulation results in local action on opioid receptors in GI tract
- Clinical use limited by narrow therapeutic index[1-3]
  - Doses that reverse OIC often cause reversal of analgesia or symptoms of opioid withdrawal (eg, yawning, sweating, shivering)[1-3]

IV, intravenous

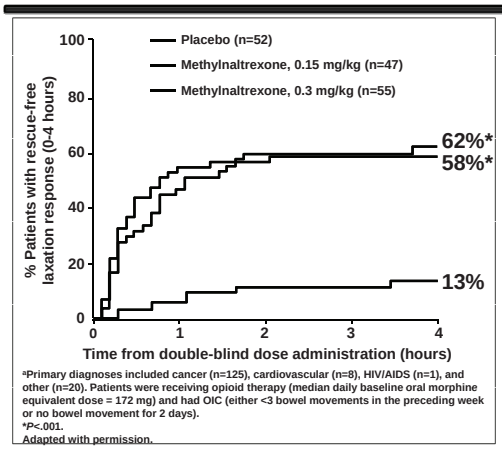
1. Camilleri M. *Am J Gastroenterol*. 2011;106:835-842.
2. Diego L. *Expert Opin Investig Drugs*. 2011;8:1047-1056.
3. Liu M, Wittbrodt E. *J Pain Symptom Manage*. 2002;23:48-53.

Methylnaltrexone

- Approved for OIC in advanced illness who are receiving palliative care
- Currently available for subcutaneous administration

1. Diego L. *Expert Opin Investig Drugs*. 2011;8:1047-1056.
2. Camilleri M. *Am J Gastroenterol*. 2011;106:835-842.

Single-Dose Methylnaltrexone for OIC in Patients With Advanced Illness[a]



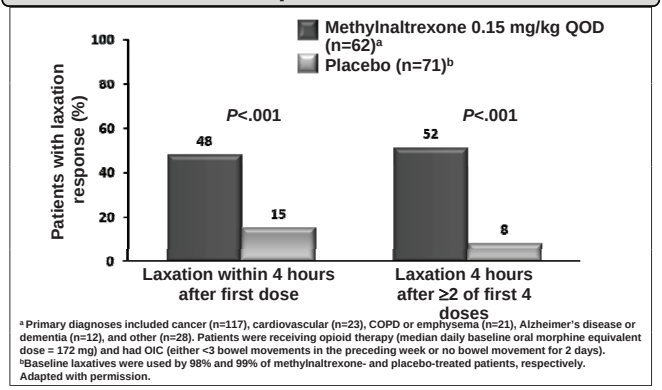
[a]Primary diagnoses included cancer (n=125), cardiovascular (n=8), HIV/AIDS (n=1), and other (n=20). Patients were receiving opioid therapy (median daily baseline oral morphine equivalent dose = 172 mg) and had OIC (either <3 bowel movements in the preceding week or no bowel movement for 2 days).
*P<.001.
Adapted with permission.

No difference in baseline pain or opioid withdrawal scores were noted between treatment groups

Slatkin N, et al. *J Support Oncol*. 2009;7:39-46.

Repeated Dosing of Methylnaltrexone for OIC in Patients With Advanced Illness*

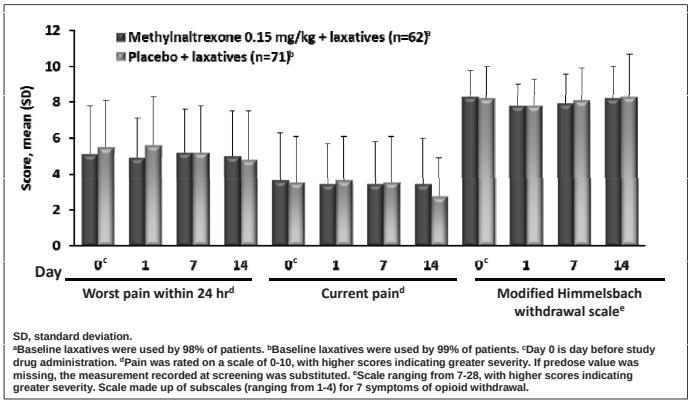
Laxation Response Within 4 Hours



[a] Primary diagnoses included cancer (n=117), cardiovascular (n=23), COPD or emphysema (n=21), Alzheimer's disease or dementia (n=12), and other (n=28). Patients were receiving opioid therapy (median daily baseline oral morphine equivalent dose = 172 mg) and had OIC (either <3 bowel movements in the preceding week or no bowel movement for 2 days).
[b]Baseline laxatives were used by 98% and 99% of methylnaltrexone- and placebo-treated patients, respectively.
Adapted with permission.

Thomas J, et al. *N Engl J Med*. 2008;358:2332-2343.

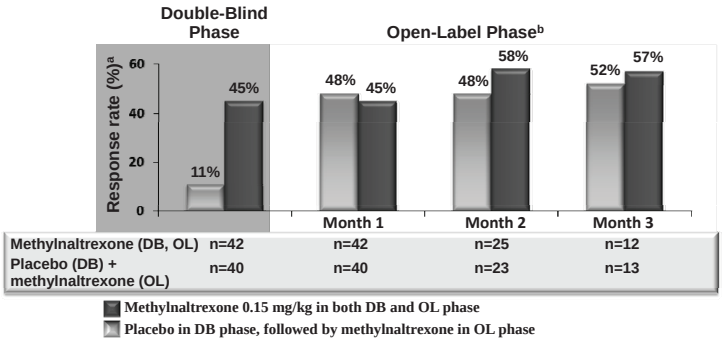
Effect of Methylnaltrexone on Central Analgesia and Opioid Withdrawal



SD, standard deviation.
[a]Baseline laxatives were used by 98% of patients. [b]Baseline laxatives were used by 99% of patients. [c]Day 0 is day before study drug administration. [d]Pain was rated on a scale of 0-10, with higher scores indicating greater severity. If predose value was missing, the measurement recorded at screening was substituted. [e]Scale ranging from 7-28, with higher scores indicating greater severity. Scale made up of subscales (ranging from 1-4) for 7 symptoms of opioid withdrawal.

Thomas J, et al. *N Engl J Med*. 2008;358:2332-2343.

Durability of Methylnaltrexone Response in OIC



DB, double-blind; OL, open-label
[a]Response rate = number of doses for which there was rescue-free laxation divided by total number of doses.
[b]Patients who completed DB phase could enter OL phase and received subcutaneous methylnaltrexone 0.15 mg/kg as often as every 24 hr as needed.
First dose of OL methylnaltrexone was >14 days after first DB dose and >24 hr after last DB dose. Dose could be reduced to 0.075 mg/kg if drug-related AEs occurred or could be increased to 0.3 mg/kg after 4 hr if no laxation occurred.

Thomas J, et al. *N Engl J Med*. 2008;358:2332-2343.

Methylnaltrexone AEs in Controlled Trials

Adverse Event	Methylnaltrexone 0.075, 0.15, 0.30 mg/kg (n=165)	Placebo (n=123)
Abdominal pain	47 (28.5%)	12 (9.8%)
Flatulence	22 (13.3%)	7 (5.7%)
Nausea	19 (11.5%)	6 (4.9%)
Dizziness	12 (7.3%)	3 (2.4%)
Diarrhea	9 (5.5%)	3 (2.4%)
Hyperhidrosis	11 (6.7%)	8 (6.5%)

Relistor® [package insert]. Raleigh, NC: Salix Pharmaceuticals, Inc.; 2012.

Methylnaltrexone Dosing for OIC

- Usual schedule is one dose every other day as needed, but not more frequently than a 24-hour period
- Dose should be reduced by half in patients with severe renal impairment (CrCl <30 mL/min)

Methylnaltrexone Dosing

Patient Weight		Injection Volume	Dose
lb	kg		
<84	<38	Calculated[a]	0.15 mg/kg
84 to <136	38 to <62	0.4 mL	8 mg
136 to 251	62 to 114	0.6 mL	12 mg
>251	>114	Calculated[a]	0.15 mg/kg

[a]Injection volume calculated by multiplying patient weight in lb by 0.0034 or in kg by 0.0075 and rounding up the volume to the nearest 0.1 mL.

Relistor® [package insert]. Raleigh, NC: Salix Pharmaceuticals, Inc.; 2012.

Alvimopan in OIC

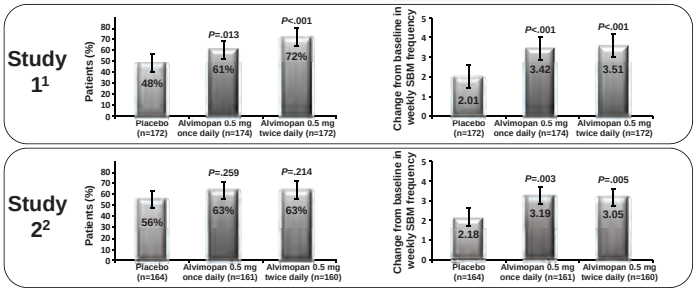
- Approved for GI recovery following bowel resection surgery[1]
  - Maximum of 15 doses
- Available in oral formulation[1,2]
  - Distribution limited to hospitals that have enrolled in the alvimopan Risk Evaluation Mitigation Strategy (REMS) program
- Contraindicated in patients taking opioid medications for more than 7 days

Alvimopan is restricted to short-term hospital use due to association with increased risk of myocardial infarction[1,2]

1. Diego L. *Expert Opin Investig Drugs*. 2011;8:1047-1056.
2. Camilleri M. *Am J Gastroenterol*. 2011;106:835-842.

Alvimopan for OIC in Patients With Chronic, Noncancer Pain

Mean Proportion of SBM Responders[a] | **Change From Baseline in SBM Frequency**



SBM, spontaneous bowel movement
Most common primary pain conditions were back pain (59-60%) and arthritis (9-12%).
[a]Defined as the proportion of patients experiencing ≥3 SBMs per week over the treatment period and an average increase from baseline of ≥1 SBM per week.
Used with permission.

1. Jansen JP, et al. *J Pain*. 2011;12:185-193.
2. Irving G, et al. *J Pain*. 2011;12:175-184.

Alvimopan AEs in Patients With Chronic, Noncancer Pain

	Study 1[1]		Study 2[2]	
Adverse Event	Alvimopan 0.5 mg BID (n=172)	Placebo (n=172)	Alvimopan 0.5 mg BID (n=160)	Placebo (n=164)
Abdominal pain	15 (9%)	11 (6%)	19 (12%)	14 (9%)
Headache	17 (10%)	13 (8%)	12 (8%)	8 (5%)
Diarrhea	13 (8%)	9 (5%)	8 (5%)	9 (5%)
Nausea	9 (5%)	12 (7%)	10 (6%)	7 (4%)
Vomiting	9 (5%)	12 (7%)	9 (6%)	6 (4%)

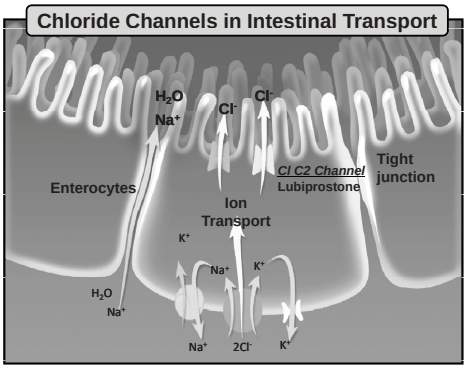
Alvimopan did not antagonize opioid analgesia[2] (based on pain intensity scores and opioid consumption)

BID, twice daily.
Adapted with permission.

1. Jansen JP, et al. *J Pain*. 2011;12:185-193.
2. Irving G, et al. *J Pain*. 2011;12:175-184.

Lubiprostone

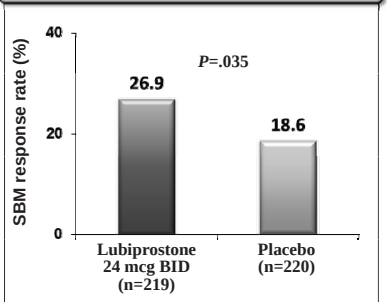
- Lubiprostone is a chloride channel activator that induces intestinal secretion
- Approved for chronic idiopathic constipation and IBS-C in women
- Available in oral formulation



IBS-C, constipation-predominant irritable bowel syndrome.
Adapted from Rome Foundation, Inc. Computer-Based Learning Program for Functional GI Disorders [CD-ROM]; 2009. http://www.romecriteria.org/pdfs/AllSlides_Pictures.pdf. Accessed November 7, 2013.
Wong BS, Camilleri M. *Expert Opin Pharmacother*. 2011;12:983-990.

Lubiprostone for Non-Methadone OIC in Chronic, Noncancer Pain: Results of 12-Week Controlled Trial

SBM Responder Rate[a]



[a]Defined as patients who experienced ≥1 SBM improvement over baseline SBM frequency for all treatment weeks for which observed data were available, and full response (≥3 SBMs per week) for ≥9 of the 12 treatment weeks.

Most Common (>5%) Treatment-Related AEs

Adverse Events	Lubiprostone (n=219) %	Placebo (n=220) %
Diarrhea	9.6	1.4
Nausea	8.2	2.7
Abdominal pain	5.5	0

Jamal MM, et al. *Gastroenterology*. 2012;142(5 Suppl 1):S144-5.

Investigational Therapies for OIC

Drug	Description	Development Phase 1	2	3
Prucalopride[1]	5-HT_4 agonist			
NKTR-118[1-3] (naloxegol)	Peripheral μ-opioid receptor antagonist			
TD-1211[1,2]	Peripheral μ-opioid receptor antagonist			
ADL-7445[2]	Peripheral μ-opioid receptor antagonist			
ADL-5945[2]	Peripheral μ-opioid receptor antagonist			

1. Camilleri M. *Am J Gastroenterol*. 2011;106:835-842.
2. Diego L. *Expert Opin Investig Drugs*. 2011;8:1047-1056.
3. Nektar Therapeutics. Naloxegol (NKTR-118) and NKTR-119. http://www.nektar.com/product_pipeline/cns_pain_oral_nktr-118and119.html Accessed October 23, 2013.

Conclusions

- OIC constipation is an increasingly common problem for patients with chronic pain that can compromise patient quality of life and pain management
- Laxatives are a mainstay of therapy for prevention and management of OIC
  - Usefulness may be limited by poor efficacy and side effects
- Peripheral μ-opioid receptor antagonists improve OIC without reversing analgesia
  - Methylnaltrexone rapidly induces laxation in patients with advanced illness without inducing opioid withdrawal or affecting central analgesic effects
  - New formulations under development
- Preliminary data suggest benefit of lubiprostone in OIC
  - Methadone use can decrease effectiveness

Notes

Continuing Professional Development (CPD): Reflect | Plan | Do | Evaluate

Opioid-Induced Constipation: Update on Prevention and Management

Center for Independent Healthcare Education is committed to supporting pharmacists in their Continuing Professional Development (CPD) and lifelong learning. Please use this form to incorporate the learning from this educational activity into your everyday practice.

Continuing Professional Development: a self-directed, ongoing, systematic and outcomes-focused approach to learning and professional development that assists individuals in developing and maintaining continuing competence, enhancing their professional practice, and supporting achievement of their career goals.

CPD Value Statement:

"Pharmacists who adopt a CPD approach accept the responsibility to fully engage in and document their learning through reflecting on their practice, assessing and identifying professional learning needs and opportunities, developing and implementing a personal learning plan, and evaluating their learning outcomes with the goal of enhancing the knowledge, skills, attitudes and values required for their pharmacy practice."

REFLECT

Consider my current knowledge and skills in managing OIC, and self-assess my professional development needs and goals.

PLAN

Develop a "Personal Learning Plan" to achieve intended outcomes, based on what and how I want or need to learn.

Develop objectives that are specific for you, measurable, achievable, relevant to the learning/practice topic, and define the time frame to achieve them.

DO

Implement my learning plan utilizing an appropriate range of learning activities and methods.

List learning activities that you will engage in to meet your goals.
List resources (e.g. materials, other people) that you might use to help achieve your goal.

EVALUATE

Consider the outcomes and effectiveness of each learning activity and my overall plan, and what (if anything) I want or need to do next.

Monitor progress regularly toward achievement of your goal.