Management of Elderly Patients with Chronic Constipation

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Learning Objectives

- Recognize the impact of chronic idiopathic constipation in the elderly
- Differentiate newer agents for the treatment of chronic constipation in terms of safety, efficacy and the patient populations for which they are approved
- Apply treatment strategies utilizing newer agents after the failure of laxatives or as first line agents for the management of chronic constipation when appropriate
- Utilize appropriate outcome measures to determine treatment response and impact on quality of life in order to guide treatment decisions

Note: Due to space constraints, study limitations are not addressed for the studies presented. Participants are directed to the cited references for information on individual study limitations.
Demographic Question 1

Please indicate your profession

1. Gastroenterologists
2. Gerontologists
3. Primary Care Physician
4. Physician Assistant
5. Nurse Practitioner
6. Nurse
7. Other
Demographic Question 2

Which best describes your work environment?

1. Academic
2. Staff-model health maintenance organization
3. Single-specialty practice
4. Multispecialty practice
5. Community hospital
6. Fellowship/training
7. Other
Demographic Question 3

How many years have you been in practice?

1. 1-5
2. 6-10
3. 11-15
4. 16-20
5. 21+
6. N/A
Demographic Question 4

How many patients with chronic constipation do you see each week?

1. 1-5
2. 6-10
3. 11-15
4. 16-20
5. 21+
6. N/A
Studies have suggested that the prevalence of chronic constipation in the elderly community may be greater than...

1. 40%
2. 50%
3. 60%
4. 70%
Chronic Constipation has been demonstrated to have a significant impact on quality of life (QoL). In which of the following QoL measurement tools was chronic constipation shown to have the greatest impact as compared to other GI symptoms, such as abdominal bloating, abdominal pain, or chronic diarrhea?

1. Activity impairment score
2. Overall work impairment score
3. SF-12 mental component summary score
4. SF-12 physical component summary score
5. A and B
6. All of the above
According to the American Gastroenterological Association, the initial treatment for chronic constipation should be fiber supplementation and/or osmotic or stimulant laxatives. However, studies have shown that these approaches are not effective or suitable in all patients. More than 40% of patients have reported dissatisfaction with laxatives, mainly for reasons of efficacy, in which of the following patient populations?

1. Chronic idiopathic constipation (CIC)
2. Opioid induced constipation (OIC)
3. Irritable bowel syndrome with constipation (IBS-C)
4. A and B
5. All of the above
According to the American Gastroenterological Association’s Medical Position Statement on Constipation, “A newer agent should be considered when symptoms do not respond to laxatives.” Which of the following is/are approved for the treatment of opioid induced constipation in patients unresponsive to laxatives.

1. Lubiprostone
2. Naloxegol
3. Plecanitide
4. Linaclotide
5. A and B
6. All of the above
What is Chronic Constipation: Rome III Criteria*

Must include ≥2 of the following (>25% of defecations):

- Straining
- Lumpy / hard stools
- Sensation of incomplete evacuation
- Sensation of anorectal obstruction
- Manual maneuvers
- <3 defecations per week

Loose stools rarely present without laxative use insufficient criteria for IBS

*Criteria fulfilled for the last 3 months with symptom onset at least 6 months prior to diagnosis

Longstreth et al, Gastroenterology 2006; 130: 1480–91
The Key Questions

- How common is it?
- What is the burden of illness?
- What causes constipation?
- What tests can be used to assess chronic constipation?
- What are the treatments?
Prevalence of Chronic Idiopathic Constipation According to Country

Pooled prevalence of CIC According to Age

<table>
<thead>
<tr>
<th>Age band</th>
<th>Number of subjects</th>
<th>Pooled prevalence of CIC (95% confidence interval)</th>
<th>Odds ratio for CIC (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 29 years</td>
<td>7,153</td>
<td>12.0 (10.0 - 14.0)</td>
<td>1</td>
</tr>
<tr>
<td>30 - 44 years</td>
<td>7,092</td>
<td>15.0 (12.0 - 19.0)</td>
<td>1.20 (1.09 - 1.33)</td>
</tr>
<tr>
<td>45 - 59 years</td>
<td>5,314</td>
<td>16.0 (11.0 - 21.0)</td>
<td>1.31 (1.09 - 1.58)</td>
</tr>
<tr>
<td>≥60 years</td>
<td>3,443</td>
<td>17.0 (13.0 - 22.0)</td>
<td>1.41 (1.17 - 1.70)</td>
</tr>
</tbody>
</table>

CIC, chronic idiopathic constipation.

Chronic Constipation in an Aging Population

- U.S. individuals ≥ 65 years of age in 2010 was 40.2 million - projected to rise to 88.5 million in 2050 ¹

- Constipation prevalence in an elderly community setting was 40.1% in individuals with a mean age of 76 years ²

- Studies report that chronic constipation affects the majority of long-term patients in hospitals and residents in nursing homes ³,⁴

The Key Questions

• *How common is it?*

• *What is the burden of illness?*

• *What causes constipation?*

• *What tests can be used to assess chronic constipation?*

• *What are the treatments?*
Leading GI Symptoms Prompting an Outpatient Visit

<table>
<thead>
<tr>
<th>Rank</th>
<th>Symptom</th>
<th>Estimated visits</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Abdominal pain</td>
<td>15,863,956</td>
</tr>
<tr>
<td>2</td>
<td>Diarrhea</td>
<td>4,236,051</td>
</tr>
<tr>
<td>3</td>
<td>Constipation</td>
<td>3,175,842</td>
</tr>
<tr>
<td>4</td>
<td>Vomiting</td>
<td>2,861,790</td>
</tr>
<tr>
<td>5</td>
<td>Nausea</td>
<td>2,814,364</td>
</tr>
<tr>
<td>6</td>
<td>Heartburn and indigestion</td>
<td>1,982,517</td>
</tr>
<tr>
<td>7</td>
<td>Rectal bleeding</td>
<td>1,702,331</td>
</tr>
</tbody>
</table>

Peery AF, et al. Gastroenterology 2012;143:1179
## Impact of Select GI Diseases and Symptoms on QOL, Activity and Work Productivity

<table>
<thead>
<tr>
<th>Gastrointestinal Symptoms</th>
<th>SF-12 mental component summary score Mean (SD)(^a)</th>
<th>SF-12 physical component summary score Mean (SD)(^a)</th>
<th>Activity impairment score Mean (SD)(^b)</th>
<th>Overall work impairment score Mean (SD)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal bloating</td>
<td>43 (12)</td>
<td>46 (12)</td>
<td>35 (31)</td>
<td>26 (29)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>42 (12)</td>
<td>45 (12)</td>
<td>38 (32)</td>
<td>28 (30)</td>
</tr>
<tr>
<td>Chronic constipation</td>
<td>41 (13)</td>
<td>39 (13)</td>
<td>51 (32)</td>
<td>37 (33)</td>
</tr>
<tr>
<td>Chronic diarrhea</td>
<td>42 (12)</td>
<td>43 (12)</td>
<td>42 (32)</td>
<td>31 (30)</td>
</tr>
<tr>
<td>Heartburn</td>
<td>46 (12)</td>
<td>46 (11)</td>
<td>30 (30)</td>
<td>21 (27)</td>
</tr>
<tr>
<td>Other references</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Population norm</td>
<td>50 (10)</td>
<td>50 (10)</td>
<td>24 (29)</td>
<td>16 (25)</td>
</tr>
</tbody>
</table>

\(^a\) A lower score is associated with worse quality of life;  
\(^b\) A higher percentage is associated with greater impairment

Peery AF, et al. Gastroenterology 2012;143:1179
The Key Questions

• How common is it?
• What is the burden of illness?
• What causes constipation?
• What tests can be used to assess chronic constipation?
• What are the treatments?
## Factors Associated with Constipation Among US Men and Women from NHANES, 2005-06 & 2007-08

<table>
<thead>
<tr>
<th></th>
<th>Women(^a) POR (95% CI), (N=3,841)</th>
<th>Men(^a) POR (95% CI), (N=3,561)</th>
</tr>
</thead>
<tbody>
<tr>
<td>African-American race/ethnicity</td>
<td>1.39 (1.00, 1.93)</td>
<td>1.40 (0.82, 2.41)</td>
</tr>
<tr>
<td>Living above poverty income</td>
<td>0.93 (0.72, 1.20)</td>
<td>0.71 (0.48, 1.04)</td>
</tr>
<tr>
<td>Higher education</td>
<td>0.82 (0.71, 0.94)</td>
<td>0.92 (0.69, 1.21)</td>
</tr>
<tr>
<td>Comorbidity</td>
<td>1.00 (0.87, 1.15)</td>
<td>0.97 (0.79, 1.19)</td>
</tr>
<tr>
<td>Body mass index (obese)</td>
<td>0.65 (0.49, 0.88)</td>
<td>0.91 (0.55, 1.52)</td>
</tr>
<tr>
<td>Poor/fair self-rated health</td>
<td>1.24 (0.86, 1.78)</td>
<td>1.31 (0.83, 2.05)</td>
</tr>
<tr>
<td>Vigorous physical activity</td>
<td>0.96 (0.68, 1.36)</td>
<td>0.74 (0.45, 1.20)</td>
</tr>
<tr>
<td>Low fiber intake (lowest quartile)</td>
<td>1.07 (0.84, 1.36)</td>
<td>1.40 (0.88, 2.20)</td>
</tr>
<tr>
<td>Low dietary liquid intake (lowest quartile)</td>
<td><strong>1.29 (1.02, 1.64)</strong></td>
<td><strong>2.42 (1.51, 3.88)</strong></td>
</tr>
</tbody>
</table>

CI, confidence interval; NHANES, National Health and Nutrition Examination Surveys; POR, prevalence odds ratio

\(^a\)All multivariable models controlled for age (in decades) and included appropriate sampling weight. Bolded items represent significant POR (95% CI), \(P<0.05\).

Issues in the Elderly that might contribute to Constipation

- **Physiological Changes**?
- **Dietary Changes**
  - *Reduced fiber intake, increased fat & protein*
  - *Reduced fluid intake*
  - *Smaller meals*
- **Reduced Physical Activity/Mobility**
- **Cognitive impairment/Neurological Diseases**
- **Depression**
Consultation rates with healthcare providers for patients meeting the diagnostic criteria for IBS rise progressively with increasing patient age.

Although the prevalence of IBS does not increase in the elderly population, clinicians may actually see more elderly patients with IBS (and constipation associated with IBS) than they do younger patients.

Chronic pain – 45% to 85% of elderly patients report moderate-to-severe chronic pain ¹

The American Geriatric Society (AGS) recommendation: opioids preferred over NSAIDs for management of moderate-to-severe chronic pain among older adults ²

Opioid prescriptions significantly increased in patients aged ≥65 years between 1995 to 2010, compared to younger aged patients (OR = 8.85) ³

Opioid treatment for moderate-to-severe chronic pain is associated with bowel dysfunction leading to constipation in the majority of patients ⁴

Medications Are a Common Cause of Constipation in the Elderly

- Asa/NSAIDs
- Opioids
- Anticholinergics
- Antidepressants
- Antihistamines
- Antihypertensives
- Anti-parkinsonian drugs
- Diuretics
- Calcium & Iron supplements

Risk of Colorectal Cancer in Patients with or without Constipation (Cross-Sectional Surveys)

**Odds ratio meta-analysis plot (random effects)**

- Tate and Royle, 1988: 0.210 (0.000, 1.841)
- de bossett et al., 2002: 0.254 (0.006, 1.556)
- Selvachandran et al., 2002: 0.290 (0.077, 0.778)
- Panzuto et al., 2003: 1.171 (0.571, 2.406)
- Bersani et al., 2005: 0.250 (0.050, 0.777)
- Adler et al., 2007: 0.464 (0.000, 3.959)
- Bafandeh et al., 2008: 1.298 (0.139, 5.930)
- Huang et al., 2010: 0.594 (0.421, 0.825)
- Combined (random): 0.563 (0.358, 0.885)

Subtypes of Constipation

- Slow transit and IBS-C overlap in half of each group
- Recent SR found prevalence of STC to be 38-80%

## Causes of Outlet Obstruction

### Constipation

Dyssynergic Defecation

<table>
<thead>
<tr>
<th>Condition</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anal fissure</td>
</tr>
<tr>
<td>Anal stricture</td>
</tr>
<tr>
<td>Intussusception</td>
</tr>
<tr>
<td>Pelvic floor descent (impaired or excessive)</td>
</tr>
<tr>
<td>Proctitis</td>
</tr>
<tr>
<td>Rectal prolapse</td>
</tr>
<tr>
<td>Rectocele/Enterocoele</td>
</tr>
<tr>
<td>Thrombosed hemorrhoids</td>
</tr>
<tr>
<td>Urogynecologic dysfunction</td>
</tr>
</tbody>
</table>

The Key Questions

• How common is it?
• What is the burden of illness?
• What causes constipation?
• What tests can be used to assess chronic constipation?
• What are the treatments?
Chronic Constipation

1. Patient with infrequent and/or hard stool and/or difficult to pass stools when not on laxatives

2. History and physical examination

3. Alarm features?
   - yes
   - no

4. Investigations as indicated, eg. colonoscopy, metabolic screen

5. Any abnormality identified?
   - yes
   - no

6. Colorectal cancer or other obstructing lesion, anorectal disease, hypothyroidism, hypercalcemia

7. Constipating drugs
   - yes
   - no

8. Stop drugs where possible

9. Symptom improvement?
   - yes
   - no

10. Drug-induced constipation

11. Functional constipation

12. Explanation physiology, modify lifestyle and diet, discuss bulking agents, simple laxatives

13. Symptom improvement?
   - yes
   - no

14. Formulate longer term management plan

15. Refer for consideration of physiological assessment (anorectal function, colonic transit), see ‘refractory constipation and difficult defecation’ algorithm

Available at: http://www.romecriteria.org/education/algorithm/pdfs/Chronic_constipation.pdf
Alarm Features for Chronic Constipation

- Age >50 years; >45 years if African-American
- New onset constipation in elderly
- Severe symptoms not investigated
- Rectal bleeding
- Fever
- Weight loss
- Family history of organic GI disease
- Palpable abdominal / rectal mass

Investigate and treat appropriately; colonoscopy may be indicated.
Chronic Constipation

Available at: http://www.romecriteria.org/education/algorithmpdfs/Chronic_constipation.pdf
Bristol Stool Form Scale

Slow gut transit

Type 1: Separate hard lumps
Type 2: Sausage-like but lumpy
Type 3: Sausage-like but with cracks in the surface
Type 4: Smooth and soft
Type 5: Soft blobs with clear-cut edges
Type 6: Fluffy pieces with ragged edges, a mushy stool
Type 7: Watery, no solid pieces

Rapid gut transit

Normal Anorectal Physiology

At Rest

Defecation

- Anorectal Angle ~90°
- Sphincter relaxes
- Pelvic floor descends

Angle more Obtuse

For patients with alarm features; lack of response to treatment consider:

- **Balloon expulsion**: Suspected outlet problems / dyssynergia
- **Anorectal manometry**: Suspected dyssynergia; Hirschsprung’s disease
- **Defecography**: Suspected outlet problems / pelvic floor dysfunction
- **Colonic transit** (Sitz markers or Wireless pH-motility capsule testing): Identify slow colon transit

Lacy, MedGenMed 2005; 7: 19
Cash et al, Rev Gastroenterol Disord 2007; 7: 116–33
The Key Questions

• **How common is it?**
• **What is the burden of illness?**
• **What causes constipation?**
• **What tests can be used to assess chronic constipation?**
• **What are the treatments?**
Graded Treatment of Chronic Constipation

- Psychological treatments
- Continuing care
- Improve functioning

- Follow-up visit
- Manage stress
- Pharmacotherapy

- Diet, lifestyle, advice
- Positive diagnosis
- Explain, reassure

Colon Transit Time According to Physical Activity Level

<table>
<thead>
<tr>
<th>Physical Activity Level</th>
<th>Male (n = 24)</th>
<th>Female (n = 25)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low</td>
<td>9.2</td>
<td>35.4</td>
</tr>
<tr>
<td>Moderate</td>
<td>7.6</td>
<td>30.5</td>
</tr>
<tr>
<td>High</td>
<td>5.2</td>
<td>2.8</td>
</tr>
<tr>
<td>Total</td>
<td></td>
<td>25.8</td>
</tr>
</tbody>
</table>

P-values:
- Male vs. Female: P = 0.002
- Male vs. Low: P = 0.022
- Male vs. Moderate: P = 0.026
- Male vs. High: P = 0.002

Pharmacological Treatments for Chronic Constipation:

- **Bulking Agents**
  - Psyllium/Isphagula

- **Osmotic Laxatives**
  - PEG 3350
  - Magnesium salts

- **Stool Softeners**
  - Ducosate sodium

- **Stimulant Laxatives**
  - Picosulfate
  - Bisacodyl
  - Senna

- **Prokinetic Agents**
  - Prucalopride
  - Tegaserod

- **Prosecretory Agents**
  - Lubiprostone
  - Linaclotide, Plecanatide
  - A3309

ACG Functional GI Disorders Task Force. Am J Gastroenterol. 2005;100(suppl 1):S1-21
Prevalence of Constipation According to Intake of Dietary Fiber & Total Dietary Moisture

Fiber and Stool Softeners

- Fiber and stool softeners (Ducosate) are most useful in patients with mild, infrequent constipation
  - Best evidence for psyllium up to 25 gr/d

- Their role in patients with significantly delayed colon transit or dyssynergia is limited
  - Fiber may worsen symptoms in patients with significantly delayed colon transit or DD

Osmotic Laxatives: Sugars and Sugar Alcohols

- These laxatives are metabolized by bacteria in the colon to short-chain fatty acids which create an osmotic load and decrease the pH

Lactulose  (Cephulac, Chronulac) 10-40 grams (15-60 mls) per day
Sorbitol  30-150 mls (70% solution) per day

Main side effects: dose dependent cramping, bloating, diarrhea

Ramkumar D, Rao SS. Am J Gastroenterol. 2005; 100:936
Osmotic Laxatives: Saline Laxatives

- **Magnesium (MOM, Mg Citrate) or PEG (Miralax) laxatives**
  - Milk of Magnesia  20-30 cc per day
  - Magnesium Citrate  240 ml once daily as a purgative
  - Polyethylene Glycol  17-51 grams per day
  - Main side effects: bloating, gas, borborygmi diarrhea. Pts with significant heart/kidney disease should use magnesium laxatives with caution

- Loosens & softens stool
- Increased fecal mass stimulates peristalsis

PEG* for Chronic Constipation

- US multicenter, double-blind, randomized placebo-controlled trial of PEG vs. placebo for 6 months

*PEG = polyethylene glycol 3350 ***p<0.01 vs placebo
**treatment response = ≥3 BMs/week and no more than 1 of the remaining 3 Rome symptoms in the absence of rescue medications = ≥ 50% of the time

- Adverse events not different between PEG and placebo

Stimulant Laxatives: Classification and Mechanism of Action

- Anthraquinones (sennosides, cascara, aloe)
- Bisacodyl, Picosulfate
- Castor oil

Senna (Ex-Lax, Sennekeot, various laxative teas) 15-30 mg per day
Bisacodyl (Carters, Correctol, Dulcolax, Magic Bullet) 5-20 mg per day

Main side effects: cramping, bloating, borborygmi, diarrhea

Locke GR III et al. Gastroenterology 2000; 119:1766
Randomized, Placebo-controlled Trial of Bisacodyl for Chronic Constipation

- **RCT, 27 centers in UK**
  - 368 adults with CC (Rome III), 75% female
  - Bisacodyl 10mg/d x 4 wks (n=247) vs. placebo (n=121)

<table>
<thead>
<tr>
<th></th>
<th>Bisacodyl</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSBM/wk (1.1)</td>
<td>5.2 ± 0.3</td>
<td>1.9 ± 0.3</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>SBM/wk (4)</td>
<td>12-8</td>
<td>unchanged</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Global assessment*</td>
<td>79.5%</td>
<td>49.6%</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>QOL</td>
<td></td>
<td></td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Bisacodyl superior to placebo for straining, sense of anorectal blockage and stool form (p < 0.001)

AEs 72% vs. 37%, SAEs 6.5% vs. 1.7%

* "good or "satisfactory"

Unmet Needs

• Stool softeners, stimulant laxatives, osmotic agents, and lubricants are not effective or suitable in all patients.

• Up to 47% of patients with CIC using laxatives were not completely satisfied with their treatment, mainly for reasons of efficacy.

• In patients with opioid induced constipation who required laxative therapy, only 46% reported achieving the desired treatment results more than 50% of the time.

• A 2009 survey among patients with IBS found that 34% of patients were not satisfied with IBS medications & remedies available at the time.

Recently Approved Pharmacologic Agents For The Management of Constipation

• “A newer agent should be considered when symptoms do not respond to laxatives.” (American Gastroenterological Association)
  – Lubiprostone and linaclotide are newer agents approved in the United States for chronic idiopathic constipation and IBS-C
  – Lubiprostone is also approved for the treatment of opioid-induced constipation in adults with chronic, non-cancer pain
Chloride Channels in Intestinal Transport

Dose: IBS-C 8 mcg twice daily
CC 24 mcg twice daily
Dose with food

Main side effects: Nausea, headache, diarrhea
Rare cases of shortness of breath

Lubiprostone for CC: Results from Phase III

Lubiprostone 24 mcg bid vs. placebo x 4 weeks
242 adults with CC (Modified Rome II)

Johanson et al. 2008; Am J Gastroenterol; 103:170
Lubiprostone for IBS-C: Data from 2 Phase III Trials

- Overall responder: monthly responder for at least 2 of 3 months
- Monthly responder: at least moderate relief for 4/4 weeks or significant relief for 2/4 weeks

Comparison:
- Lubiprostone 8 mcg bid: n=780
- Placebo: n=387

Significance: *P=0.001

Drossman DA et al. Gastroenterology 2007; 132:639f
Lubiprostone for Opiate Induced Constipation

Primary Endpoint: ≥3 SBM and increase of ≥1 SBM per week for 9/12 weeks

Study 1
- Lubri 24 mcg bid: 27.1%
- Placebo: 18.9%

Study 2
- Lubri 24 mcg bid: 24.3%
- Placebo: 15.4%

Study 3
- Lubri 24 mcg bid: 15.3%
- Placebo: 13%

Medical Letter 2013
1Cryer et al. DDW 2010;906; 2US FDA CDER. Amitiza NDA 021908 Label 4/19/13; 3Mazen Jamal et al. DDW 2012;848a
### Incidence of Nausea with Lubiprostone in Clinical Trials

- **Chronic idiopathic constipation**: 24 mcg bid with food
- **Irritable bowel syndrome with constipation**: 8 mcg bid with food

#### Phase II & III Trials in Chronic Constipation
- 24-mcg-bid

#### Phase III Trials in OIC
- 24-mcg-bid

#### Phase III Trials in IBS-C
- 8-mcg-bid

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Linaclotide for Chronic Constipation: Primary Results from 2 Phase III Clinical Trials

Responder = ≥3 CSBM/wk & increase of ≥1 CSBM/wk for ≥ 9/12 wks

Study 01

- L 145 mcg, n=430: 16%
- L 290 mcg, n=418: 21%
- Placebo, n=424: 6%

Study 303

- L 145 mcg, n=430: 21%
- L 290 mcg, n=418: 19%
- Placebo, n=424: 3%

* p≤0.0012

Most common AE diarrhea (14-16% vs. 4.7%)
Discontinuation (4% vs. 0.5%)

CSMB, complete spontaneous bowel movement
Linaclotide Phase 3 IBS-C Trial

6/12 Week Responder Primary Endpoint

**Composite Responder** (FDA Interim Endpoint)

≥30% abdominal pain reduction + increase ≥1 CSBM from baseline; **in the same week**

Most common AE: Diarrhea 18%

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>Lin 266 µg</th>
</tr>
</thead>
<tbody>
<tr>
<td>% Responders</td>
<td>13.9%</td>
<td><strong>33.7%</strong></td>
</tr>
<tr>
<td>N=403</td>
<td></td>
<td>N=401</td>
</tr>
</tbody>
</table>

**p< 0.0001, ITT Population (266 µg vs. placebo, CMH test)**

Emerging Therapies for IBS-C and Chronic Constipation (CC)

- **Luminally Acting Drugs**
  - *Prosecretory Drugs:*
    - Plecanatide (phase III)
    - RDX5791 (phase IIb)
  - *Bile Acid Modulators*
    - Elobixibat (phase III)

- **Systemic Drugs**
  - *Prokinetics*
    - 5-HT₄ Agonists (various drugs)

Concluding Remarks

- Constipation is a multi symptom condition
- The main causes of constipation are slow colon transit and/or disordered defecation
- Diet and lifestyle changes can help with mild or intermittent constipation symptoms
- Laxatives including osmotics, stimulants, and prosecretory agents improve many patients
- When patients fail to respond to laxatives, diagnostic testing should be pursued to determine the etiology of constipation symptoms
  - A multi-disciplinary approach is optimal for severely affected patients
  - Biofeedback and PT are the preferred treatments for dyssynergic defecation
Posttest Question 1

Studies have suggested that the prevalence of chronic constipation in the elderly community may be greater than...

1. 40%
2. 50%
3. 60%
4. 70%
Posttest Question 2

Chronic Constipation has been demonstrated to have a significant impact on quality of life (QoL). In which of the following QoL measurement tools was chronic constipation shown to have the greatest impact as compared to other GI symptoms, such as abdominal bloating, abdominal pain, or chronic diarrhea?

1. Activity impairment score
2. Overall work impairment score
3. SF-12 mental component summary score
4. SF-12 physical component summary score
5. A and B
6. All of the above
According to the American Gastroenterological Association, the initial treatment for chronic constipation should be fiber supplementation and/or osmotic or stimulant laxatives. However, studies have shown that these approaches are not effective or suitable in all patients. More than 40% of patients have reported dissatisfaction with laxatives, mainly for reasons of efficacy, in which of the following patient populations?

1. Chronic idiopathic constipation (CIC)
2. Opioid induced constipation (OIC)
3. Irritable bowel syndrome with constipation (IBS-C)
4. A and B
5. All of the above
According to the American Gastroenterological Association’s Medical Position Statement on Constipation, “A newer agent should be considered when symptoms do not respond to laxatives.” Which of the following is/are approved for the treatment of opioid induced constipation in patients unresponsive to laxatives.

1. Lubiprostone
2. Naloxegol
3. Plecanitide
4. Linaclotide
5. A and B
6. All of the above
References


References


References


References


References


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