ADVANCING GI PATIENT CARE

APRIL 28–30, 2023

Frisco, Texas

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GI Alliance

What's New in GI Pharmacotherapy

Philip Schoenfeld, MD, MSEd, MSc (Epi)
Editor-in-Chief
Evidence-Based GI: An ACG Publication
Chief (Emeritus)-GI Section, John D. Dingell VAMC

Disclosures

- Advisory Board:
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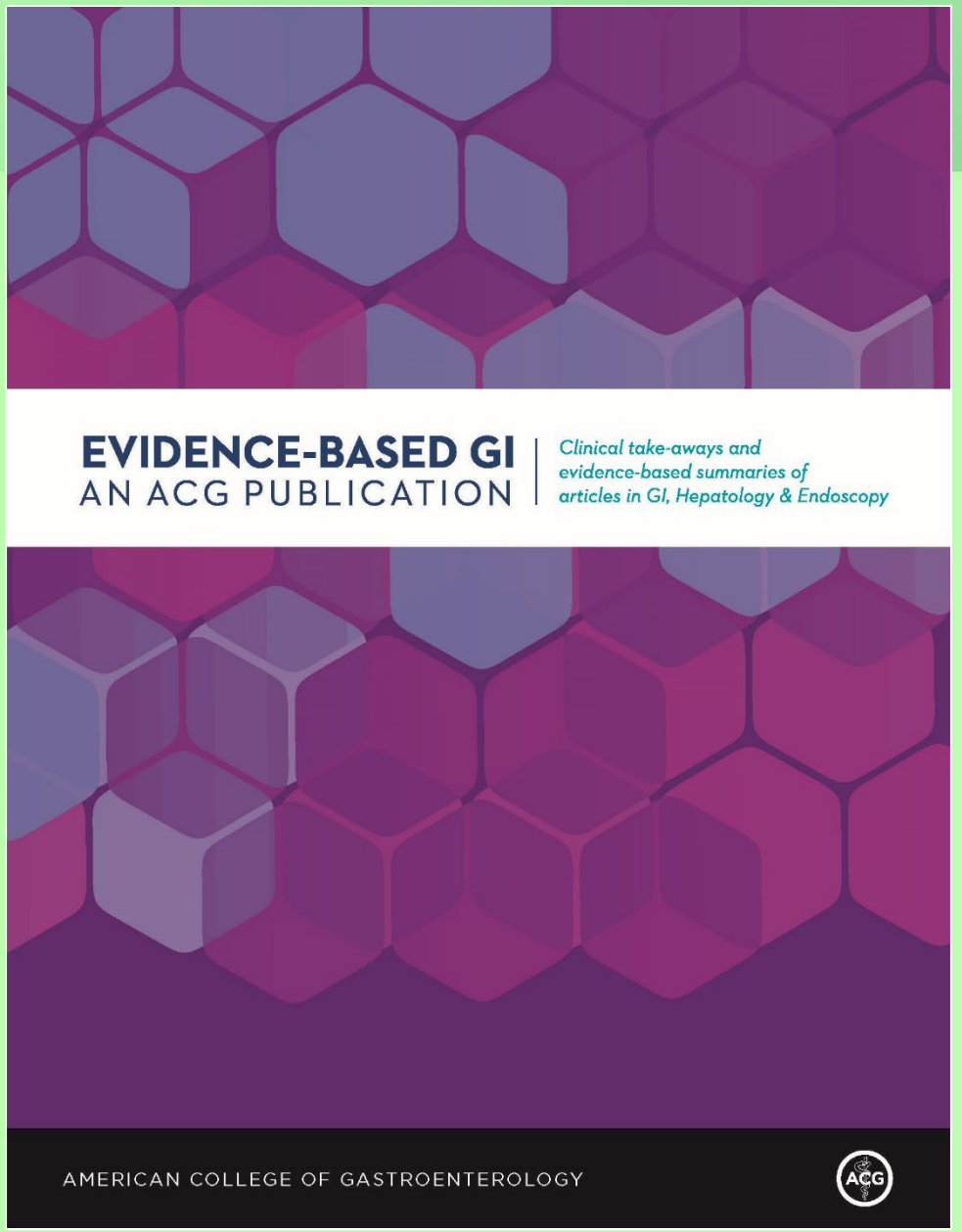
  - AbbVie, Iroonwood, Salix
- Speaker:
  - AbbVie, Ardelyx, Exact Sciences, Ironwood, Phathom


EVIDENCE-BASED GI
AN ACG PUBLICATION
Clinical take-aways and evidence-based summaries of articles in GI, Hepatology & Endoscopy
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Tenapanor (IBSRELA) for Treatment of IBS-C: Effective Over 26 Weeks

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Philip Schoenfeld, MD, MSEd, MSc (Epi)
Editor-in-Chief

This article reviews Chey WD, Lembo A, Yang Y, Rosenbaum DP. Efficacy of Tenapanor in Treating Patients With Irritable Bowel Syndrome with Constipation: A 26-Week, Placebo-Controlled Phase 3 Trial (T3MPO-2). Am J Gastroenterol 2021; 116: 1294-1303. https://doi.org/10.14309/ajg.0000000000001056

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Adapted from:
Chey, W; Lembo, A. J.; Yang, Y; Rosenbaum, D.P. Efficacy of Tenapanor in Treating Patients With Irritable Bowel Syndrome With Constipation: A 26-Week, Placebo-Controlled Phase 3 Trial (T3MPO-2), The American Journal of Gastroenterology: June 2021 - Volume 116 - Issue 6 - p 1294-1303
doi:10.14309/ajg.0000000000001056

Key Study Definitions

👉 Weekly combined response :

⬇ in average weekly worst abdominal pain of ≥30.0% from baseline

+

⬆ of ≥1 weekly complete spontaneous bowel movements (CSBM) from baseline

👉 6/12-week combined responder rate:

% of pts who had a weekly combined response (defined 👆) for at least 6 out of the first 12 txt weeks.

Key Study Endpoints

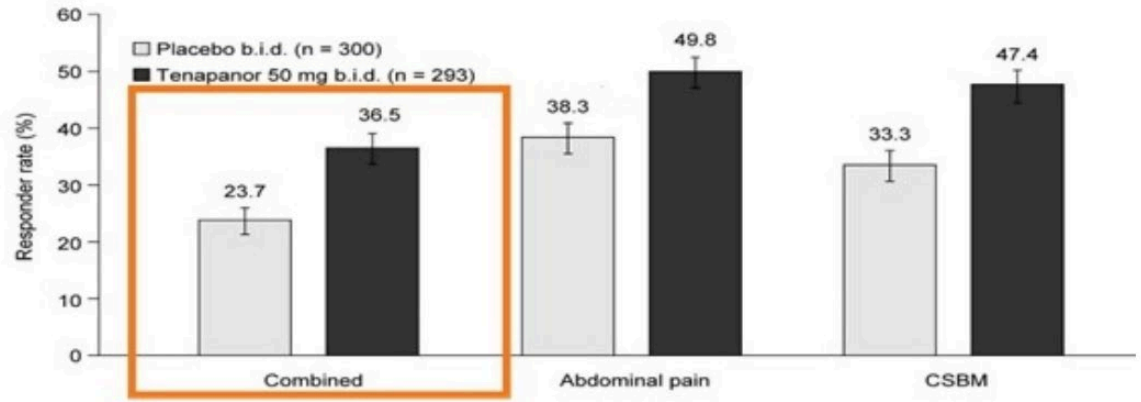
🥇 **Primary Endpoint:**

- The 6/12-week combined rate.

🥈 **Key Secondary Endpoint:**

- 6/12-week CSBM and abdominal pain responder rates
- 9/12-week combined responder rate
- 13/26-week combined responder rate

Adapted from:
Chey, W; Lembo, A. J.; Yang, Y; Rosenbaum, D.P. Efficacy of Tenapanor in Treating Patients With Irritable Bowel Syndrome With Constipation: A 26-Week, Placebo-Controlled Phase 3 Trial (T3MPO-2), The American Journal of Gastroenterology: June 2021 - Volume 116 - Issue 6 - p 1294-1303 doi: 10.14309/ajg.0000000000001056



Risk difference versus placebo, % (95% CI)	12.9 (5.5, 20.2)	11.5 (3.6, 19.4)	14.1 (6.3, 21.9)
P value	<0.001	0.004	<0.001

Figure 1. ≥ 6/12 week responders for FDA-combined endpoint, abdominal pain endpoint, and CSBM endpoint.

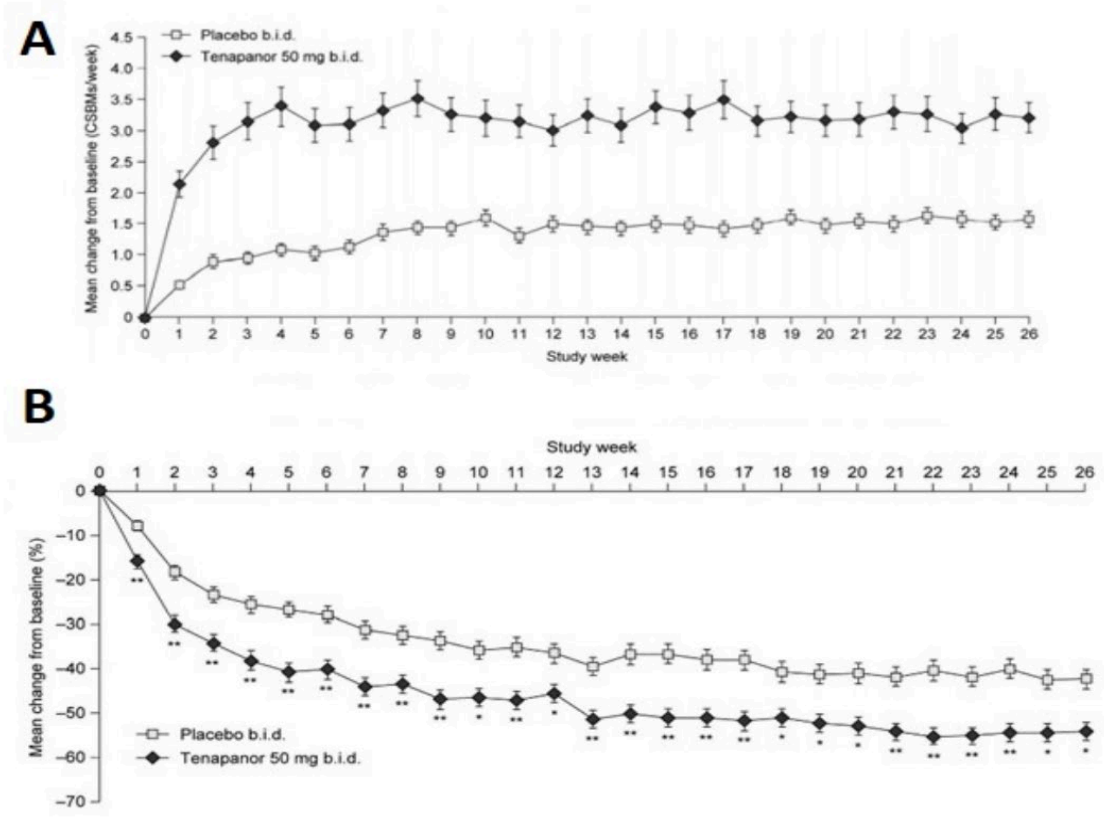


Figure 2. Weekly change in CSBMs (A) and abdominal pain (B).

Dr. Schoenfeld's My Practice To the Use of Tenapanor

✗ adequate relief w/ **initial** course of a guanylate cyclase-C agonist (linaclotide or plecanatide)

Tenapanor

Tips:

- Can combine Tenapanor + peppermint oil capsules as PRN
- Can add daily anti-spasmodic tx
- Can add neuromodulator (e.g. duloxetine 30-60mg daily)
- Can refer to dietician for instruction in low-FODMAP diets

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Semaglutide Produces Mean Weight Loss of 34 Pounds over 68 Weeks in Obese and Overweight Individuals-A Huge "STEP" in Medical Management of Obesity

Sonali Paul, MD, MS [1] and Philip Schoenfeld, MD, MSED, MSc (Epi), FACG [2]

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Editor-in-Chief, Philip Schoenfeld, MD, MSEd, MSc (Epi), FACG

Associate Editor, Sonali Paul, MD, MS

This article reviews Wilding JPH, et al. for the Semaglutide Treatment Effect in People with Obesity (STEP) Investigators. Once-Weekly Semaglutide in Adults with Overweight or Obesity. N Engl J Med 2021; 384: 989-1002. https://www.nejm.org/doi/10.1056/NEJMoa2032183

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FDA NEWS RELEASE
June 04, 2021

FDA Approves New Drug Treatment for Chronic Weight Management, First Since 2014

Current indications for use per FDA in chronic weight management:

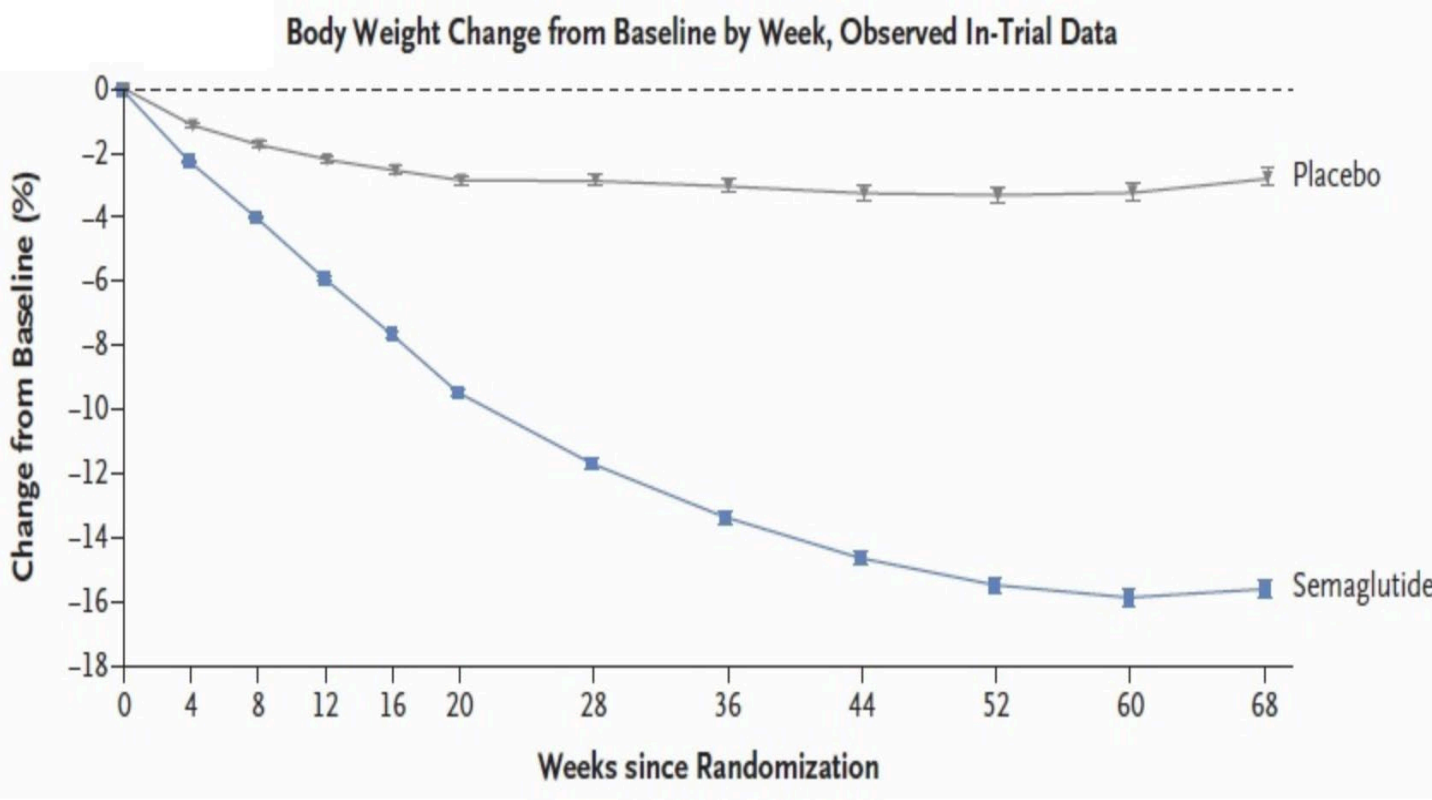
- In patients with BMI of 30 kg/m2 or greater.
- In patients with BMI of 27 kg/m2 or greater who have at least one weight-related ailment (HTN, DM, HLD, etc.)

	Semaglutide group	Placebo group
Participants	1306	655
Received rescue interventions	7	13
Age (yrs)	46 +/- 13	47 +/-12
Mean body weight (kgs)	105.4±22.1	105.2±21.5
Mean BMI	37.8±6.7	38.0±6.5

Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med. 2021;384(11):989–1002

RESULTS

Semaglutide	Placebo
14.9% weight loss	2.4%weight loss
33.7 pounds wt loss at 68 weeks	5.7 pounds wt loss at 68 weeks
Nausea 44.2%	Nausea 17.4%
Diarrhea 31.5%	Diarrhea 15.9%



Wilding JPH, Batterham RL, Calanna S, et al. Once-weekly semaglutide in adults with overweight or obesity. N Engl J Med. 2021;384(11):989–1002

Dr Paul's "My Practice"

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- Includes many NASH patients
- Most obese and overweight patients with one additional risk factor are prescribed semaglutide.
- As this practice is becoming popular, be conscious of shortages occurring at some pharmacies
- Educate patients on possible mild Nausea/diarrhea with dose escalation and discontinue dx for severe symptoms.
- All of our patients must also see a dietitian for counseling.

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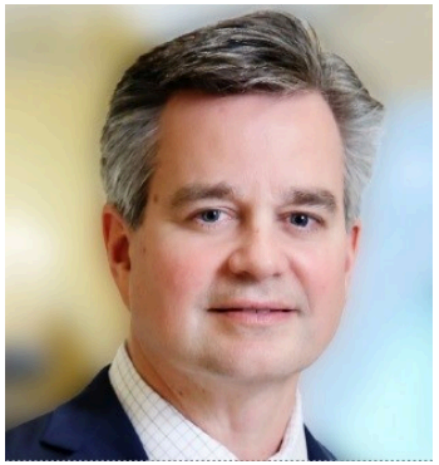
Treating *Helicobacter pylori* Infection With Vonoprazan, A Potassium-Competitive Acid Blocker: A New Paradigm



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Tweetorial provided by:

Romy Chamoun, MD
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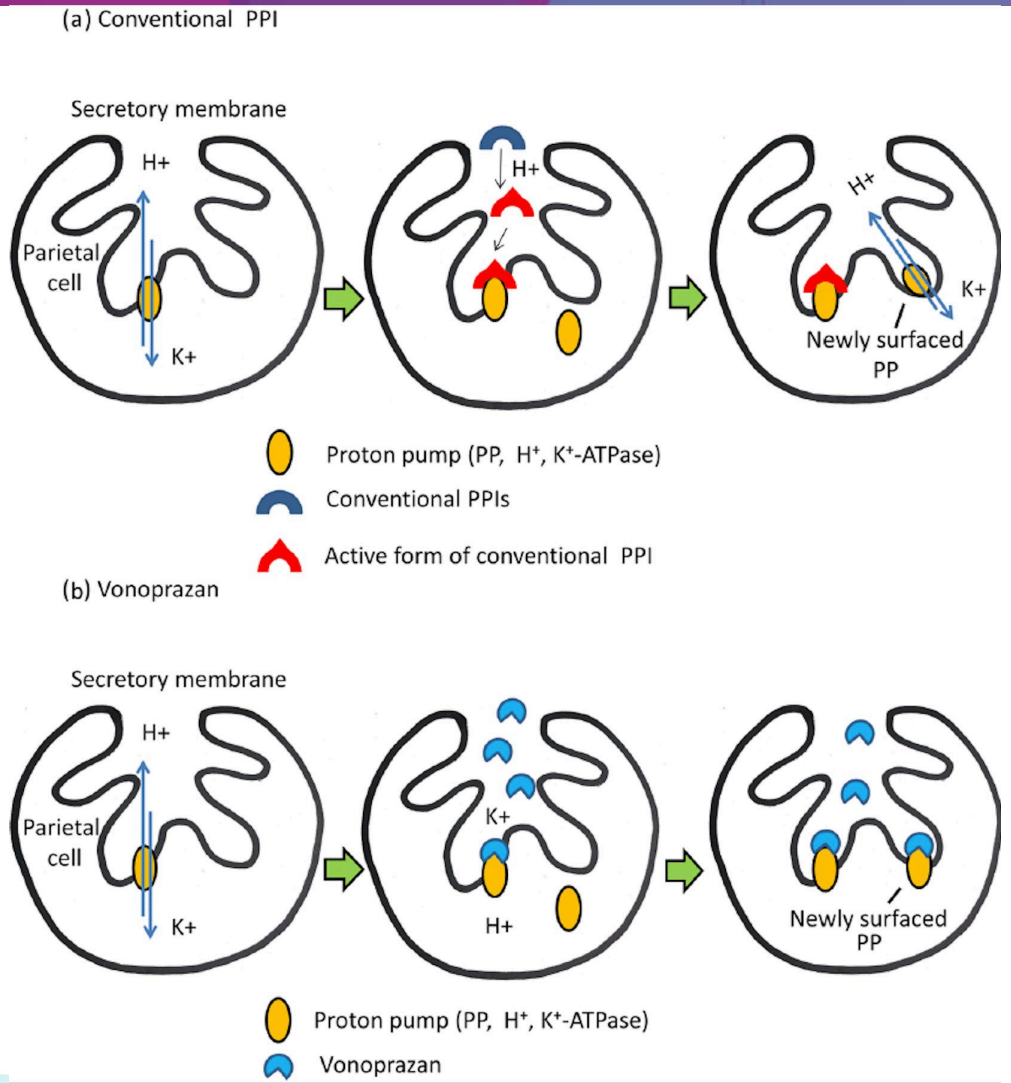
EBGI Ambassador

PGY-3, Lankenau Medical Center

Adapted from:
Akazawa et al. Vonoprazan-based therapy for Helicobacter pylori eradication: experience and clinical evidence. Therapeutic Advances in gastroenterology. 2017. 9 (6) 845-852



Conventional PPIs are
- unstable in canaliculi
- rapidly degraded
- not able to inhibit new proton pumps (PPs) that surface after administration of the drug.

→ require a few days to reach their maximum effect

Vonoprazan, a potassium-competitive acid blocker acts differently:
✓ does not require acid activation
✓ rapidly absorbed in the small intestine
✓ binding to H+/K+-ATPase in a K+-competitive manner
✓ more stable than conventional PPIs in the canaliculi

→ fast and stable inhibition of gastric acid secretion

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Adapted from: Chey WD, Megraud F, Laine L, et al. Vonoprazan Triple and Dual Therapy for *Helicobacter* pylori Infection in the US and Europe: A Randomized Controlled Trial. Gastroenterology 2022 Jun 6;S0016-5085(22)00609-6.

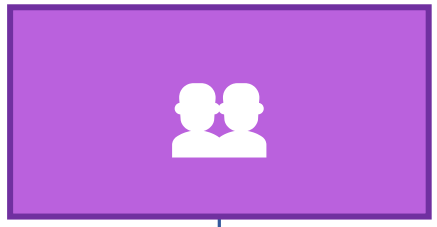
Inclusion Criteria

A - > 18 years old

B - 1 of the following:

- Dyspepsia
- Recent/New diag of non- PUD
- Hx of PU not prev tx for *H.pylori*
- Requirement for long-term NSAIDs drug tx at a stable dose.

C - They were tx-naïve + had *H.pylori* confirmed with a positive ^{13}C-urea breath test



Vonoprazan dual therapy:
- Vonoprazan 20 mg b.i.d.
+
-Amoxicillin 1g t.i.d X 14 days)

Double-blind Vonoprazan triple therapy:
-Vonoprazan 20 mg b.i.d.
+
-Amoxicillin 1 g b.i.d.
+
-Clarithromycin 500 mg b.i.d. X 14 days

Lansoprazole triple therapy :
-Lansoprazole 30 mg b.i.d.
+
-Amoxicillin 1 gm b.i.d.
+
- Clarithromycin 500 mg b.i.d. X 14 days).

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Adapted from: Chey WD, Megraud F, Laine L, et al. Vonoprazan Triple and Dual Therapy for *Helicobacter* pylori Infection in the US and Europe: A Randomized Controlled Trial. Gastroenterology 2022 Jun 6;S0016-5085(22)00609-6.

US and European phase 3 RCT comparing vonoprazan- and lansoprazole-based regimens

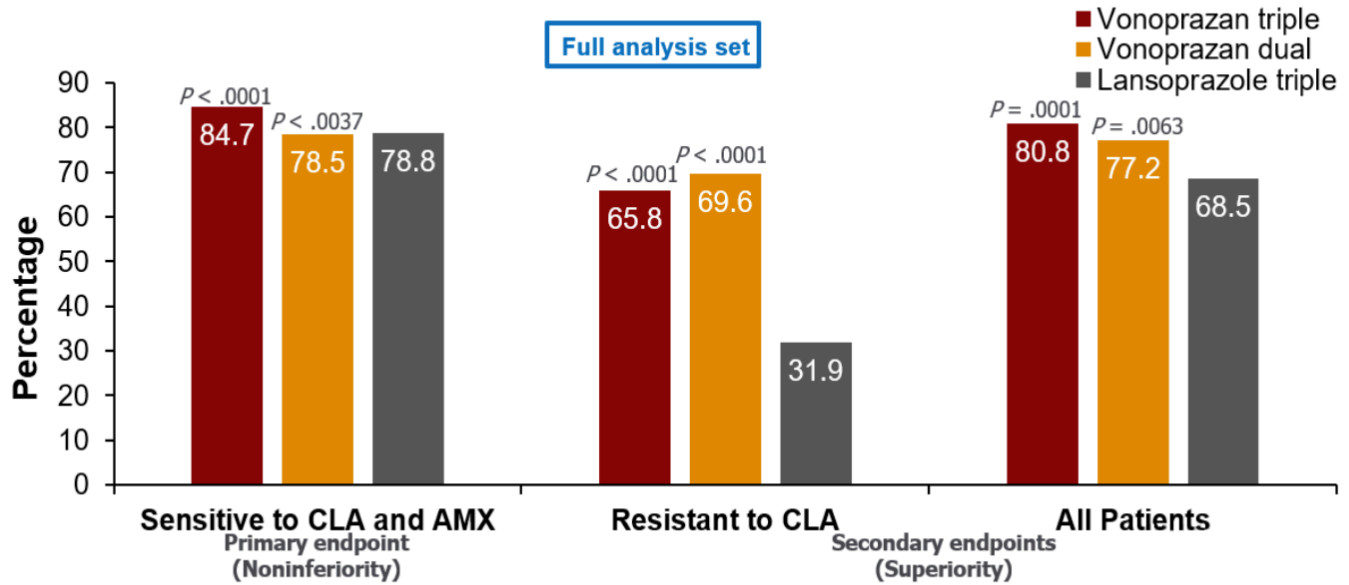

Figure 1: *Helicobacter pylori* eradication rates.
AMX, amoxicillin ; CLA, clarithromycin; RCT, randomized controlled trial.

If 💵 **& availability** can be addressed

⬇

🥇 Vonoprazan-based dual therapy with amoxicillin

ACG rec: post-tx testing should be performed 👉 ☑ eradication.

📣 ***Dr Schoenfeld recs:***

🔎 💩 ***Antigens for H. pylori with the specimen collected :***

👂 ***at least 4 wks after completing antibiotics***

👂 ***2 weeks after discontinuing PPI***

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It's a Bad "Prep" Even Though the Patient Took It Correctly: Consider 15 mg Bisacodyl plus 4-Liter PEG Split Prep Before Next Colonoscopy

Philip Schoenfeld, MD, MSEd, MSc (Epi)

Chief (Emeritus)-Gastroenterology Section, John D. Dingell VA Medical Center, Detroit, MI

This article reviews Sey MSL, Von Renteln D, Sultanian R, et al. A Multicenter Randomized Controlled Trial Comparing Bowel Cleansing Regimens for Colonoscopy After Failed Bowel Preparation. Clin Gastroenterol Hepatol 2022; In Press.

Philip Schoenfeld, MD, MSEd, MSc (Epi)
Editor-in-Chief

Tweetorial provided by:

Zubair Khan, MD
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Our first EBGI Ambassador

PGY-6, University of Texas at Houston

❖ **Risk Factors for colonic dysmotility and inadequate bowel preparation despite compliance**

- Obesity
- Current opioid use
- Diabetes mellitus
- History of using constipation treatments
- Current use of anticholinergics (including TCA)

❖ **In non-compliant patient**

- Additional patient education is more helpful than prescribing supratherapeutic regimen.

Prior Trials with Bowel Preparations

Gimeno-Garcia et al. *Am J Gastroenterol 2017; 112: 951-58.*

- 10 mg bisacodyl on the day before the procedure + a low-residue diet for 3 days pre-procedure.
- 4L PEG-3350 as split-prep vs 2L PEG + ascorbic acid as split-prep
- 4L PEG-3350-superior for adequate bowel cleansing (81.1% vs 67.4%, P< 0.01, ITT analysis)

→ Does not answer if supratherapeutic purgative regimens are more effective!

❖ **In current trial:** Sey MSL et al. *Clin Gastroenterol Hepatol. 2021 Jul 10:S1542-3565(21)00746-1*

- 36.7% obese, 40.8% with history of constipation or IBS-C, approximately 10% using opioids

❖ **Main Discussion points:**

- Low-Dose is noninferior to High-Dose Split-prep for providing adequate bowel preparation.
- Low-Dose Split-Prep results in fewer symptoms, with greater willingness to repeat the bowel preparation.
- The overall impact of diet was modest.

It's a Bad "Prep" Even Though the Patient Took It Correctly: Consider 15 mg Bisacodyl plus 4-Liter PEG Split Prep Before Next Colonoscopy

Outcome		Split-dose 4L + bisacodyl (n = 97)	Split-dose 6L + bisacodyl (n = 99)	*P*-value
Adequate cleansing	Defined as BBPS ≥ 6	83 (91.2%)	78 (87.6%)	0.44
	Defined as adequate to identify polyps > 5mm	82 (91.1%)	76 (85.4%)	0.24
Secondary endpoints	Cecal intubation rate, n (%)	87 (96.7%)	82 (92.1%)	0.19
	Adenoma detection rate, n (%)	34 (37.4%)	28 (31.5%)	0.41
Adherence	Diet + consumed 100% of prep	67 (81.7%)	53 (68.0%)	0.05
	Diet + consumed 80% of prep	71 (86.6%)	57 (73.1%)	0.03

Adapted by Sey MSL et al. Clin Gastroenterol Hepatol. 2021 Jul 10:S1542-3565(21)00746-1.

It's a Bad "Prep" Even Though the Patient Took It Correctly: Consider 15 mg Bisacodyl plus 4-Liter PEG Split Prep Before Next Colonoscopy

Dr. Schoenfeld's My Practice To avoid Inadequate Bowel Prep	
Reactive prescription: prior inadequate bowel cleansing	**Proactive Prescription:** any patient with 2 or more risk factors for inadequate bowel cleansing
6L PEG-3350 split-prep with 4L PEG consumed between 6 and 10 PM on the night before the procedure, and 2L consumed 4-6 hours before colonoscopy.	
Adequate cleansing Successes per BBPS	
87.7%	91.5%
Remember, patient education is the preferred intervention in non-compliant patients.	