Connecting the Dots Between Theory and Practice: Speaking With Your Patients About IBS-C Management

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About the Patient

MB is a 32-year-old woman with symptoms of constipation dating back to college. She notes that these symptoms have worsened over the past 4 years. She reports that stools are hard and can be difficult to evacuate. She may experience 1 to 2 days without having a bowel movement. She does not use any manual maneuvers to assist with having a bowel movement. Pain and discomfort are present in her lower abdomen on more days than not. The abdominal pain generally improves after having a bowel movement. She feels bloated and distended and jokes that she "must be pregnant again."

To help with constipation symptoms she used a fiber supplement for 3 weeks, but this worsened her bloating and distension. Her gynecologist suggested that she use stool softeners (twice daily) but this did not help constipation symptoms. She tried using magnesium citrate each night but this caused urgent diarrhea and did not help with the abdominal pain or bloating. A 4-week trial of polyethylene glycol (PEG) helped soften her stool but sometimes caused unpredictable urgent diarrhea, which made her morning commute on the subway difficult. The PEG formulation did not improve the abdominal pain or bloating.

Her primary care provider suggested a diet low in FODMAPs (fermentable oligo-, di-, monosaccharides and polyols). This helped her bloating but left her even more constipated. She notes having tried generic lubiprostone but with limited benefit.

She states that her life is stressful, as she works full-time and is responsible for most childcare activities for her 2 young children. She sleeps poorly and never feels rested. Her weight has been stable over the past few years (body mass index=23 kg/m^2).

A recent complete blood count was normal. Serologic testing for celiac disease was negative while eating gluten. Her gynecology examination was normal as was a pregnancy test. Her only medication is an oral contraceptive. She has not had any abdominal surgeries. No family member has inflammatory bowel disease, celiac disease, or any type of gastrointestinal malignancy. Her physical examination is normal other than mild left lower quadrant discomfort. A rectal examination, with a chaperone present, is normal without evidence of dyssynergia. She asks what her diagnosis is and whether other treatment options are available.

A definitive diagnosis of irritable bowel syndrome with constipation (IBS-C) is confirmed, consistent with the symptom-based diagnostic approach endorsed by the American College of Gastroenterology (ACG) and after sharing the Bristol Stool Form Scale (BSFS) chart with MB to aid her in qualifying her bowel movements. The inadequacy of fiber, stool softeners, osmotic agents, and low-FODMAP diet in addressing the constellation of symptoms MB is experiencing is explained. The efficacy and safety data of 4 medications approved by the US Food and Drug Administration (FDA) for IBS-C are discussed along with the differences in the mechanisms of action (MOA) and their relevance to the multifactorial pathophysiology of IBS-C.

Making a Confident Symptom-Based IBS-C Diagnosis

1. Take a careful patient history

Note the chief complaints prompting consultation and the impact of what the patient has tried in the past.

- Presenting symptoms and timeline
- Potential triggers (eg, infection, stress)
- Diet
- Medications
- Comorbid conditions (fibromyalgia, interstitial cystitis, migraine headaches, chronic pain syndrome)

2. Perform a thorough physical examination, including a digital rectal examination *(always in the presence of a chaperone)*

- Patient appearance
- Vital signs
- Abdominal examination
- Signs of systemic and local diseases that might cause constipation
- Assess the anorectum and pelvic floor muscles
- Other relevant abnormalities

3. Rule out alarm features that are suggestive of an underlying organic gastrointestinal disorder

- New symptoms in patients over 50 years of age
- Unintended weight loss (>10% within 3 months)
- Hematochezia (unrelated to hemorrhoids or anal fissures)
- Symptoms that disrupt sleep or awaken the patient at night
- Fever, anemia, or rapidly progressing or acute symptoms
- A palpable mass, ascites, or lymphadenopathy
- A family history of colorectal cancer, polyposis syndrome, celiac disease, or IBD

4. Apply symptom-based Rome IV criteria for clinical practice

- Abdominal pain recurs on average at least 1 day per week and is associated with at least 2 of the following symptoms: related to defecation, associated with a change in the frequency of stool, or associated with a change in the form (appearance) of stool.
- Symptoms are bothersome, interfering with daily activities, requiring attention, or impacting QOL are present for at least 8 weeks.

5. Classify the appropriate IBS subtype using the BSFS

IBS subtype	Bowel movements	
	BSFS types 1 and 2	BSFS types 6 and 7
IBS-C	More than 25%	Less than 25%
IBS-D	Less than 25%	More than 25%
IBS-M	More than 25%	More than 25%
IBS-U	Cannot be determined	

Figure 1. Making a positive IBS diagnosis: 5 key features.

BSFS, Bristol Stool Form Scale; IBD, inflammatory bowel disease; IBS, irritable bowel syndrome; IBS-C, IBS with constipation; IBS-D, IBS with diarrhea; IBS-M, IBS with mixed or alternating bowel habits; IBS-U, IBS without a significant pattern of abnormal stool or unclassified; QOL, quality of life.

At this point, MB asks the following questions:

- "If you do not know for sure what is causing my symptoms, how can you know which medication will work for me?"
- "How will I know that the medication is working?"
- "How long will I have to wait to experience any improvement?"
- "Can you do anything for me if this approach does not work?"

IBS-C management is explained as a trial-and-error approach because of 2 unknown factors: comparative efficacy of FDA-approved medications and the exact underlying pathophysiology of the patient's symptoms. Therefore, the patient could be started on any one of the 4 available FDA-approved IBS-C medications. In some cases, access barriers such as insurance denials might shape real-world treatment pathways. The importance of follow-up to assess response and adapt treatment (eg, change to a medication with a different MOA) in case of inadequate response is stressed.

Because MB has already tried lubiprostone with limited benefit in the past, she is started on tenapanor 50 mg

twice daily. She is asked to report her experience in 3 to 4 weeks via her online portal; an in-person follow-up visit is scheduled for 8 weeks later.

After 3 weeks of trialing the medication, MB reports marked improvement in constipation with having a bowel movement every day but still experiences some abdominal pain and bloating. MB is reassured that abdominal symptoms typically take longer to resolve than constipation symptoms and she should continue the medication as directed and monitor her IBS symptoms for a careful review at the time of her scheduled 8-week follow-up.

At her scheduled 8-week follow-up, MB reports a marked improvement in all her symptom domains and improved quality of life (QOL). She reports that for the first time in a long time she has not had to constantly worry about her pain, bloating, and constipation, which has led to significantly reduced stress at work and at home. MB then inquires, "Since I am feeling a lot better now, can I discontinue my medication?"

At that point, the chronic nature of IBS-C is reiterated. MB is told categorically that, as with any chronic condition (such as hypertension), current therapies cannot offer a cure but only successful long-term symptom management with continued treatment. MB is told that her symptoms would return if she discontinued her medication.

The following sections discuss this case in the form of answers to typical patient questions and strategies that physicians can use to bridge the gap between theory and practice to effectively help patients manage IBS-C.

Reassure the Patient That a Confident Definitive Symptom-Based IBS-C Diagnosis Is Possible

IBS-C is not a diagnosis of exclusion; rather, in the absence of validated tests or biomarkers, it is diagnosed clinically using a positive, symptom-based approach endorsed by the ACG.[1-5] Physicians can make a confident IBS diagnosis using the following stepwise approach (Figure 1).[6]

- **Step 1.** Take a careful patient history *(Note the chief complaints prompting consultation and the impact of what the patient has tried in the past.)*
- **Step 2.** Perform a thorough physical examination, including a digital rectal examination *(always in the presence of a chaperone)*
- **Step 3.** Rule out alarm features that are suggestive of an underlying organic gastrointestinal disorder
- **Step 4.** Apply symptom-based Rome IV criteria for clinical practice
- **Step 5.** Classify the appropriate subtype using the BSFS

Reassure the patient that in the absence of alarm features, symptom-based Rome IV criteria for clinical practice are associated with a high predictive value of IBS diagnosis. In MB's case, her physical examination was unremarkable, there were no alarm features, her symptoms fit the Rome IV criteria for IBS, and she could qualify the form of her bowel movements using the BSFS chart, leading to a confident IBS-C diagnosis.

Educate the Patient That IBS Is a Common Disorder of Visceral Hypersensitivity Involving the Gut-Brain Axis

Emphasize that IBS is a common chronic condition. In a population-based survey of adults in the United States, Canada, and United Kingdom (5931 valid responders), 4.6% met the Rome IV criteria for IBS.[7] Normalizing the prevalence thus helps counter the patient's belief that "I am the only one with this problem."

IBS is best understood as a disorder of visceral hypersensitivity in which the gut perceives and responds to sensations more intensely than in individuals without IBS. Explaining the gut-brain axis further reinforces this concept. This bidirectional system means that stress, anxiety, and sleep disruption can heighten gut sensitivity, just as gut distress can influence mood. Even brief sleep loss lowers sensory thresholds, which patients recognize from everyday experiences such as being more "on edge" after a sleepless night with a child or after an extended oncall shift.

Together, these points reassure patients that their symptoms reflect a common, physiologic sensitivity pattern rather than structural disease.

Teaching Point

Explaining Visceral Hypersensitivity to the Patient

I often ask patients whether they are sensitive to medications, touch, sound, or environmental stimuli. Mentioning well-recognized sensitivity disorders like migraine headaches or fibromyalgia, and drawing parallels to these common conditions, helps frame IBS within a broader pattern of altered sensory processing and assists patients in understanding that their symptoms fit within a broader pattern of sensitivity rather than representing something mysterious or dangerous.

Acknowledge That the Exact Cause of Your Patient's Symptoms Cannot Be Determined

Explain to patients that IBS has a complex, multifactorial pathophysiology.[8-15] Visceral hypersensitivity, gastrointestinal motility, increased intestinal permeability, diet, gut microbiome changes, immune activation, genetic factors, infection, and psychosocial factors/stress have all been implicated in IBS. It is impossible to know the exact underlying reasons for each patient's symptoms. Identical

symptoms in 2 separate patients could be the result of entirely different underlying mechanisms.

Don't Reinvent the Wheel

The most common mistake physicians make during their first consultation is to recommend what the patient has already tried with an unsuccessful outcome.

Patients with IBS-C often reach a gastroenterologist's clinic after cycling through several common first-line strategies with limited benefit.[16-19] Many have tried increasing dietary fiber intake, although this may worsen bloating without reliably improving constipation. Others use PEG, which can help stool frequency but often lacks predictability—an important limitation for patients with long commutes or rigid morning schedules. In addition, PEG does not improve abdominal pain. Dietary modification, such as the low-FODMAP diet, may reduce bloating but can exacerbate constipation. Some patients also experience diarrhea or intolerance with other agents.

Our patient MB had a similar experience with a fiber supplement, stool softeners, magnesium citrate, PEG, and a low-FODMAP diet. It is therefore prudent to recognize the inadequacy of these options and educate the patient about the 4 available FDA-approved medications for IBS-C. These medications have been proven to address the constellation of symptoms associated with IBS-C in various large randomized trials and follow-up analyses.

Teaching Point

Over-the-Counter Options and Diet Have Limited Benefit in IBS-C

1. Fiber can worsen bloating and does not help abdominal pain.
2. There are no data to support stool softeners for the treatment of IBS-C.
3. Osmotic agents may address constipation but will not address abdominal pain, which is the cornerstone symptom of IBS.
4. A low-FODMAP diet may help bloating but can worsen constipation (and most studies demonstrating benefits are in patients with IBS-D, not IBS-C).

Explain the Benefit of Different MOAs of FDA-Approved IBS-C Medications

One of the most common follow-up concerns that patients express is uncertainty about how clinicians can select an effective medication when the exact cause of their symptoms cannot be definitively identified. This is an opportunity to discuss the MOA of different FDA-approved medications and the fact that if one medication does not address all patient symptoms, another with a different MOA could. Therefore, in case of inadequate response, patients would be switched to an agent with a different MOA.

The FDA has approved 3 secretagogues—lubiprostone (in 2006), linaclotide (in 2012), and plecanatide (in 2017)—and one first-in-class retainagogue, tenapanor (in 2019; launched in the United States in 2022).[20-23]

Secretagogues increase chloride and bicarbonate ion secretion into the intestinal lumen. This promotes water secretion, accelerating colonic transit, improving stool consistency, and increasing the frequency of bowel movements.

Tenapanor, commonly referred to as a retainagogue, is a locally acting inhibitor of sodium/hydrogen exchanger isoform 3 (NHE3).[24-27] Tenapanor-mediated NHE3 inhibition decreases the absorption of dietary sodium. By reducing the absorption of dietary sodium, it causes water retention in the intestinal lumen and accelerates intestinal transit. NHE3 inhibition in animal models has been shown to reduce visceral hypersensitivity and improve abdominal symptoms by reconstituting tight junctions between intestinal epithelial cells (decreasing intestinal permeability) and causing antagonism of transient receptor potential vanilloid 1 channels.

Teaching Point

Explaining Complex MOA to the Patient

Some IBS-C medications such as lubiprostone, plecanatide, and linaclotide help your gut pull more fluid into the intestines and hence are often called secretagogues. Tenapanor, on the other hand, helps your gut hold onto the fluid that's already there. That is why it is often referred to as a retainagogue (because it retains fluids in the lumen of the gastrointestinal tract).

Beyond helping with stool and transit, these medications also help with the nerve sensitivity that many people with IBS-C experience. Your gut is more sensitive than the average person's, and these treatments can help lower that sensitivity so the gut doesn't overreact to normal signals.

The goal is not only to get things moving, but also to help calm down that hypersensitive gut.

Reiterate That All FDA-Approved IBS-C Medications Are Safe and Effective and Start the Patient on Any One of Them

The 4 available FDA-approved IBS-C medications have been evaluated in pivotal, large, randomized, and placebo-controlled clinical trials and follow-up analyses and have consistently shown improvement compared with placebo across a range of abdominal and bowel symptoms (Figure 2).[28-39]

All 4 medications are associated with generally mild

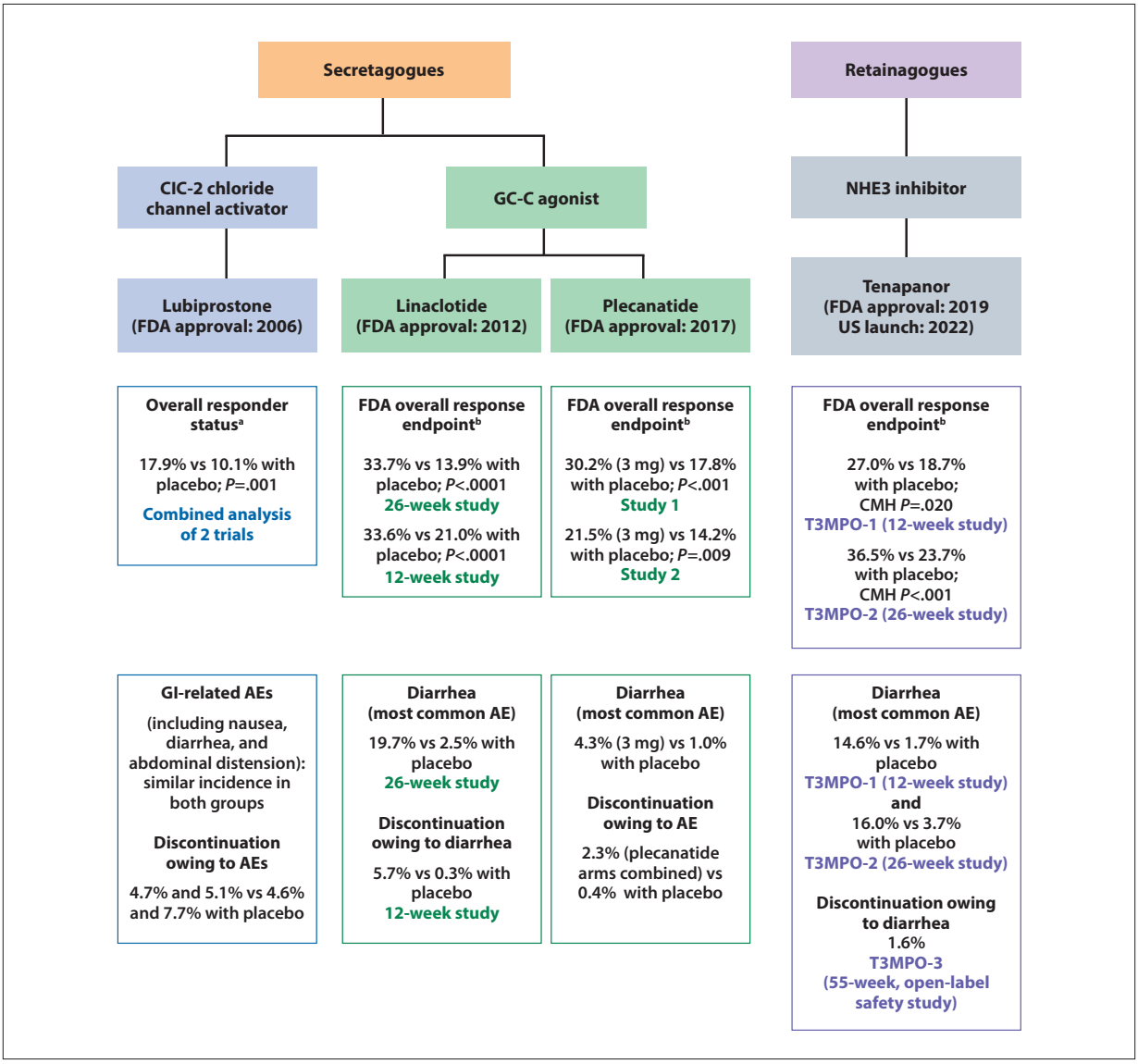

Figure 2. Currently available FDA-approved treatment options for IBS-C and their efficacy and safety data.

[a]Overall responder status was calculated from the weekly assessments of symptom relief. Monthly responders were defined as patients who rated their IBS symptoms as being at least moderately relieved for all 4 weeks of the month or significantly relieved for at least 2 weeks of the month, with no ratings of moderately or severely worse. A patient was considered an overall responder if they were monthly responders for at least 2 of the 3 months of the study.

[b]Defined as an improvement of at least 30% from baseline in average daily worst abdominal pain score and an increase of at least 1 CSBM from baseline, both in the same week for 6 or more out of 12 weeks.

AE, adverse event; CMH, Cochran-Mantel-Haenszel; CSBM, complete spontaneous bowel movement; FDA, US Food and Drug Administration; GC-C, guanylate cyclase-C; IBS-C, irritable bowel syndrome with constipation; NHE3, sodium/hydrogen exchanger isoform 3.

Adapted from Brenner DM. *Gastroenterol Hepatol* (N Y). 2023;19(12)(suppl 6):749-756.[31]

or moderately severe side effects. Whereas lubiprostone was associated with gastrointestinal-related events like nausea, diarrhea, and abdominal distension in pivotal studies, linaclotide, plecanatide, and tenapanor were most frequently associated with diarrhea. In a 55-week open-label safety study (T3MPO-3), tenapanor was well tolerated with no new safety signals and only a 1.6% discontinuation rate owing to diarrhea.[34]

Because there are no head-to-head trials, the comparative efficacy of these medications cannot be determined. Indirect comparisons in 2 network meta-analyses reveal their superiority to placebo when treating global IBS-C

Table. Indication, Dosage, and Administration of Currently Available FDA-Approved IBS-C Medications

FDA-approved agent	FDA-approved indication for	Dosage	Administration
Lubiprostone	Women >18 years of age	8 µg orally twice daily	With food and water
Linaclotide	Adults	290 µg orally once daily	On empty stomach at least 30 minutes prior to a meal at approximately the same time each day
Plecanatide	Adults	3 mg orally once daily	With or without food
Tenapanor	Adults	50 mg orally twice daily	Immediately prior to breakfast or the first meal of the day and immediately prior to dinner

FDA, US Food and Drug Administration; IBS-C, irritable bowel syndrome with constipation.

Adapted from: Orleck K. *Gastroenterol Hepatol* (N Y). 2025;21(11)(suppl 7):1-14.[6]

symptoms and similar efficacy across most endpoints including abdominal bloating.[40,41]

Against the backdrop of unknown comparative efficacy and the exact underlying pathophysiology for the patient's symptoms, IBS-C management is a trial-and-error approach. Start the patient on any one of the 4 available FDA-approved IBS-C medications per the recommended dosage and administration guidelines (Table).[20-23] In some cases, access barriers such as insurance denials might shape real-world treatment pathways.

Evaluate the patient's response in 8 weeks. In cases of an inadequate response, treatment should be modified by either using augmentation therapy, if there was a partial response, or trying another therapeutic agent with a different MOA.

Teaching Point

Unknowns in IBS-C DO NOT Alter Your Management Approach

Reiterate to the patient that you are dealing with **2 unknowns** that make IBS-C management a trial-and-error approach: exact pathophysiology responsible for your patient's symptoms and comparative efficacy of available FDA-approved IBS-C medications. These unknowns, however, do not alter the management approach. Start the patient on any FDA-approved medication and, in case of inadequate response, adapt treatment and switch to a medication with a different MOA.

Educate the Patient on Adequate Trial and Plan a Follow-up

Setting appropriate expectations is essential when initiating therapy for IBS-C, as this supports adherence, reduces frustration, and aligns treatment decisions with the natural trajectory of symptom response. Patients should understand both when they might expect improvement and which symptoms are most likely to improve first.

Explain to the patient what an adequate treatment trial is. Most individuals experience improvement in constipation within the first week, consistent with both clinical trial findings and real-world observations. However, improvements in abdominal symptoms typically happen more gradually with approximately one-third of patients who ultimately experience meaningful improvement in abdominal pain do so only after several additional weeks of therapy.[42,43] Recent data reinforce this point.

According to a recently published post hoc analysis of 1372 patients with IBS-C (684 treated with tenapanor and 688 with placebo), tenapanor was associated with earlier and sustained symptom relief in IBS-C compared with placebo.[43] Median time to first response was 2 weeks vs 4 weeks for a complete spontaneous bowel movement, and 4 to 5 weeks vs 6 to 8 weeks for abdominal pain, discomfort, bloating, or AS3 (3-item abdominal score) response with tenapanor vs placebo. Moreover, 67.8% to 76.7% of tenapanor-treated patients vs 59.1% to 69.4% of placebo-treated patients achieved first responses by week 12. Furthermore, tenapanor was also associated with higher weekly response rates for all endpoints in each week of the 12-week treatment period (Figure 3).

Premature discontinuation may therefore lead to missed clinical benefit. For this reason, patients should be encouraged to complete at least a 6- to 8-week therapeutic trial before determining overall benefit.

Follow-up planning should also be explicit. After initiating treatment, I typically ask patients to send an update after 3 to 4 weeks to assess early response, which is often improvement in constipation and evolving changes in abdominal pain. A formal follow-up visit is usually scheduled around 8 weeks.

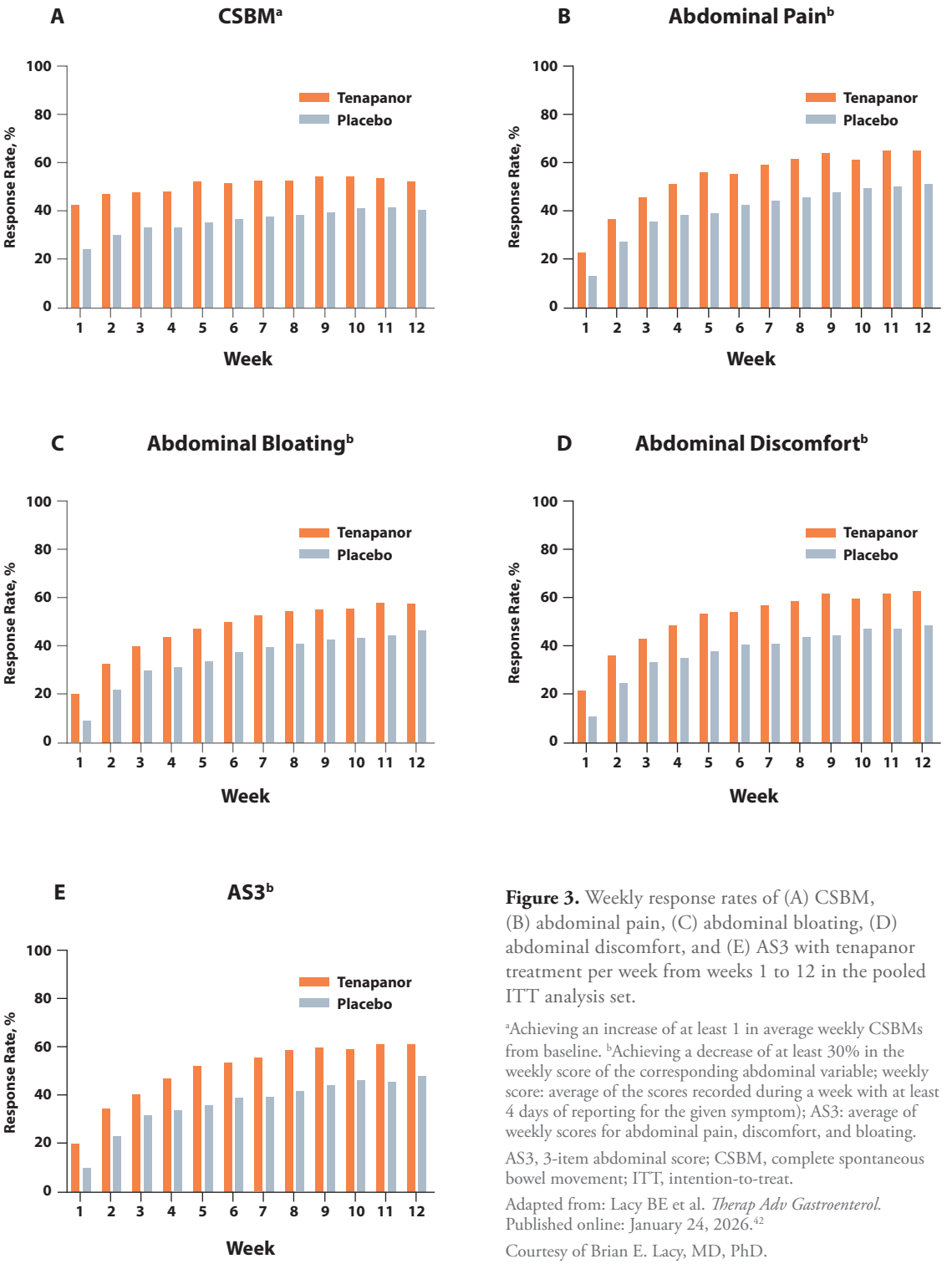

Figure 3. Weekly response rates of (A) CSBM, (B) abdominal pain, (C) abdominal bloating, (D) abdominal discomfort, and (E) AS3 with tenapanor treatment per week from weeks 1 to 12 in the pooled ITT analysis set.

[a]Achieving an increase of at least 1 in average weekly CSBMs from baseline. [b]Achieving a decrease of at least 30% in the weekly score of the corresponding abdominal variable; weekly score: average of the scores recorded during a week with at least 4 days of reporting for the given symptom); AS3: average of weekly scores for abdominal pain, discomfort, and bloating.

AS3, 3-item abdominal score; CSBM, complete spontaneous bowel movement; ITT, intention-to-treat.

Adapted from: Lacy BE et al. *Therap Adv Gastroenterol.* Published online: January 24, 2026.[42]

Courtesy of Brian E. Lacy, MD, PhD.

Teaching Point

What Is an Adequate Trial of an IBS-C Medication?

An adequate trial of an FDA-approved IBS-C medication generally requires a minimum of 8 weeks of therapy, unless side effects necessitate earlier discontinuation and treatment adaptation.

Evaluate Response and Expect Adequate Response as the Only Acceptable Outcome

In research trials, standardized questionnaires such as the Irritable Bowel Syndrome–Symptom Severity Scale can be used to assess treatment response. However, in clinical practice, a practical approach is to anchor follow-up discussions to the baseline evaluation and assess change across 3 domains: abdominal symptoms (abdominal pain, discomfort, bloating), bowel function (ie, constipation), and QOL.

Guide the patient to provide quantitative (percentage change) rather than vague qualitative descriptions of improvement like "somewhat better." Open-ended questions are also essential, as they elicit richer detail and avoid the limitations of yes/no responses.

If a patient has shown inadequate response (not improved across all 3 domains: abdominal symptoms, bowel function, and QOL) at the 8-week follow-up, then consider changing the medication to one with a different MOA. If a patient is doing well across all 3 domains, then reiterating the nature of long-term management of IBS-C is critical.

Avoid Common Traps and Pitfalls in Long-Term IBS-C Management

Patients often question why ongoing therapy is necessary after symptoms improve, especially when they have experienced symptoms for many years prior to diagnosis. At this point, avoiding common pitfalls is critical.

Discontinuing therapy as soon as a patient reports improvement (often around 8 weeks) will result in symptom recurrence. Reiterate to the patients that IBS-C, like many other medical disorders such as hypertension, hyperlipidemia, and thyroid disease, is a chronic disorder, and symptom relapse after stopping treatment is expected.

However, management can be individualized over time. For patients who have been stable for several months, considering dose reduction may be reasonable. Such strategies are used with other chronic medications. For example, although the recommended dose of tenapanor is 50 mg twice daily, some patients may maintain symptom control with 50 mg once daily. Any such adjustments are off-label and should be accompanied by close symptom monitoring.

Dose tapering also may be successful in patients who make concurrent lifestyle changes that support symptom improvement. These include enhancements in sleep quality, stress reduction practices, and modest improvements in fiber intake. For some individuals whose mornings were previously chaotic or irregular, adopting a structured routine—waking at the same time, consuming coffee or tea to stimulate colonic motility, eating breakfast to activate the gastrocolic reflex, and taking medications at appropriate times—can meaningfully improve overall symptom management.

Teaching Point

Reiterate to the Patient That Discontinuing Therapy Will Result in Symptom Recurrence and Treatment Adherence Is Critical for Sustained Response

Use familiar analogies to explain the chronic nature of IBS-C. Chronic conditions like gastroesophageal reflux disease, hypertension, hyperlipidemia, or thyroid disease often require ongoing therapy to maintain control. In this regard IBS-C is more akin to these chronic conditions rather than to an acute infection like bronchitis or a urinary tract infection for which medication is required for only a few days. As with other chronic conditions, available treatments do not "cure" IBS-C; rather, they manage symptoms and improve the patient's QOL. When presented in this context, patients are more likely to understand the rationale for continued therapy.

Conclusion

MB's case demonstrates the importance of a confident, symptom-based IBS-C diagnosis, paired with patient education about its multifactorial pathophysiology and chronic nature, the inadequacy of over-the-counter options, and the effectiveness of FDA-approved therapies with distinct MOAs in addressing the constellation of symptoms associated with IBS-C.

The absence of comparative efficacies and unknown pathophysiology responsible for each patient's symptoms necessitates a trial-and-error approach. Physicians should start treatment with any one of the available FDA-approved medications; access barriers such as insurance denials might shape real-world treatment pathways.

Schedule a follow-up visit to assess response across 3 domains: abdominal symptoms, bowel function, and QOL. In case of inadequate response, consider switching to an agent with a different MOA.

Furthermore, physicians should set clear expectations about treatment timelines and define an adequate thera-

peutic trial. Early improvement in constipation followed by more gradual relief of abdominal pain and bloating mirrors findings from clinical trials and follow-up analyses. This is also seen in the case of MB, who achieved meaningful improvement across bowel, abdominal, and QOL domains with sustained tenapanor therapy. Tenapanor has been anecdotally associated with adequate response when abdominal pain and bloating are reported as main concerns in IBS-C.

Long-term successful IBS-C management requires periodic reassessment and clear communication that symptom control, not cure, is the achievable therapeutic goal with ongoing therapy.

Disclosures

Dr Lacy is a consultant/advisor for Gemelli Biotech; Ironwood Pharmaceuticals, Inc.; Salix Pharmaceuticals, Inc.; Sanofi; Takeda Pharmaceuticals North America, Inc.; and has received research funding from Bausch Health.

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