Patient-Centered Approach in IBS-C Management

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About the Patient

CS is a 40-year-old female internist who was referred to my clinic by a colorectal surgeon in February 2025.

CS had consulted the colorectal surgeon in June 2024 for a colonoscopy following rectal bleeding, which revealed a few polyps and hyperplastic adenomas. Although her hemorrhoids had improved with therapy, she continued to experience constipation. Upon further questioning, she admitted to being constipated for most of her life. As a busy internist, she attempted to manage her condition through lifestyle modifications, but with limited success. These efforts included dietary changes, the use of polyethylene glycol (PEG) solution, drinking plenty of water, taking Metamucil, and maintaining a high-fiber diet (25-35 grams of daily fiber intake).

The surgeon advised CS to consult a gastroenterologist, but her demanding schedule as an internist—dedicated to patient care throughout the day—and reliance on PEG solution and magnesium to manage constipation delayed the appointment. Eventually she was compelled to seek specialized care when these over-the-counter interventions, although effective at facilitating bowel movements, resulted in "overflow diarrhea" associated with urgency. Furthermore, they failed to alleviate her other debilitating symptoms—including a persistent sensation of incomplete evacuation, severe bloating, abdominal pain, and daylong discomfort—all of which severely diminished her quality of life.

CS tried restricting the use of PEG solution and magnesium to weekends, to manage her condition in the relaxed home environment rather than the high-stress work environment. Despite this adjustment, she continued to experience lingering symptoms and found herself spending excessive time in the restroom, and when straining to evacuate, her hemorrhoids became aggravated.

I confirmed a diagnosis of irritable bowel syndrome with constipation (IBS-C) based on her symptom profile and emphasized the importance of using US Food and Drug Administration (FDA)–approved IBS-C medications to address all her symptoms, not just constipation. I initiated treatment with the secretagogue linaclotide at a dose of 145 µg daily, which is the mid-range dosage for this medication. I also explained that diarrhea can be a common side effect.

During the follow-up in April 2025, CS described her experience with linaclotide as "a mixed bag." She noted that although linaclotide was "definitely better" than PEG solution in achieving complete evacuation, the daily dose caused "too much diarrhea with a lot of urgency." She likened this to "a mini bowel prep," describing episodes of urgency and incontinence.

In response, she switched to taking the medication every other day instead of daily. However, there was a marked difference between the days she took the medication and the days she skipped it. On missed days, bothersome symptoms such as bloating, pain, incomplete evacuation, and straining returned and persisted. Furthermore, constant straining may have resulted in what she suspects to be a partial rectal prolapse.

At that point, I considered 2 options. The first was switching to another medication within the same class of secretagogues, such as lubiprostone, which can cause less diarrhea than linaclotide in some patients. The second

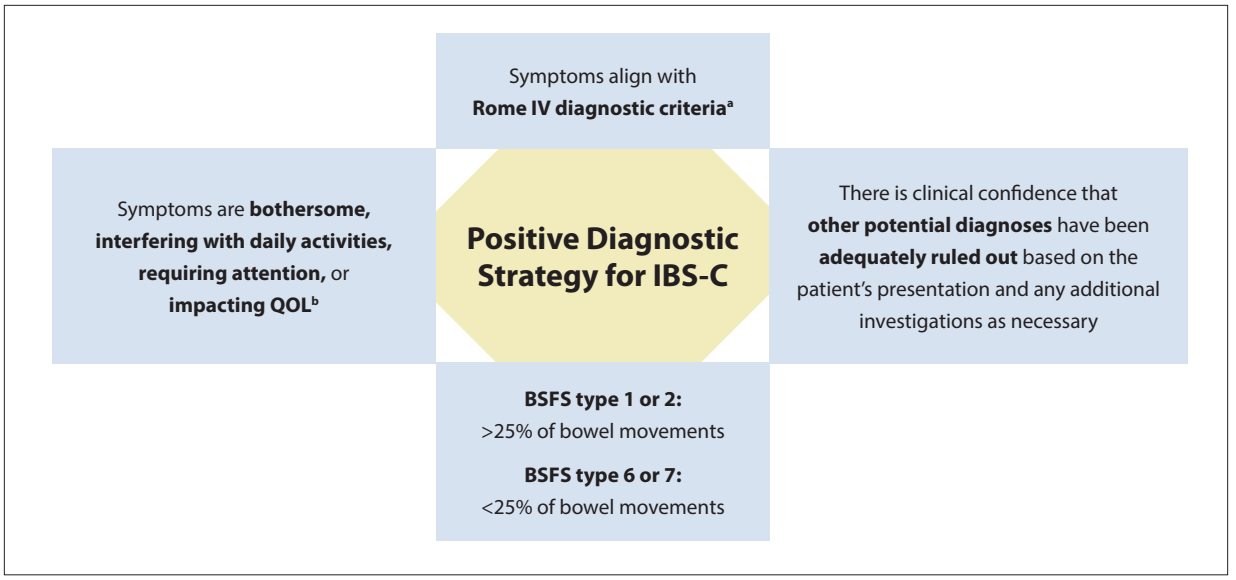

Figure 1. Using a positive diagnostic strategy for IBS-C in the clinic.

BSFS, Bristol Stool Form Scale; IBS-C, irritable bowel syndrome with constipation; QOL, quality of life.

[a]According to the Rome IV criteria, IBS is a disorder of gut-brain interaction in which 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.

[b]Symptoms are present for at least 8 weeks.

option was to use a medication with a different mechanism of action.

After discussing the multifactorial pathophysiology of IBS-C and reviewing the various medication classes available with CS, we opted for the second approach. I prescribed tenapanor 50 mg twice daily and scheduled a follow-up appointment for 8 weeks later to assess her response.

During follow-up, CS stated that she experienced "good control" of her multiple symptoms including abdominal pain, bloating, straining, and constipation. Although on certain days she experienced diarrhea, she could manage it much better. The current plan is to have a regular annual follow-up. Of course, if CS experiences any change in or exacerbation of her symptoms, she should schedule an appointment right away.

In the Clinic . . .

Primary care physicians and colorectal surgeons frequently refer patients to gastroenterologists for issues similar to those experienced by CS. Many patients report experiencing "overflow diarrhea" as a side effect of over-the-counter constipation treatments but often hesitate to share this information because of perceived stigma. This highlights the need for a patient-centered approach to IBS-C management, where building patient–provider trust serves as a crucial foundation.

Building trust requires ensuring that patients fully understand:

- the importance and feasibility of confident IBS-C diagnosis using a positive diagnostic strategy;
- the debilitating impact of both bowel and abdominal symptoms and the importance of addressing both;
- the multifactorial pathophysiology of IBS-C, and that not knowing the exact cause of symptoms does not change the management approach;
- the limited effectiveness of lifestyle modifications and over-the-counter remedies in IBS-C;
- the availability of effective and safe FDA-approved medications for IBS-C with different mechanisms of action;
- the necessity of persisting with treatment to achieve resolution of both abdominal and bowel symptoms;
- the critical role of follow-up appointments in evaluating treatment response;
- the potential for an adequate response with proper management; and
- the option to switch to a medication with a different mechanism of action in case of inadequate response with initial treatment.

The goal of this patient-centered approach is to ensure that patients feel heard at every step and to reassure them that, as providers, we will utilize every tool at our disposal to help them achieve a significantly improved quality of life.

Table 1. IBS Subtypes Based on BSFS[1]

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	

BSFS, Bristol Stool Form Scale; 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.

Table 2. Alarm Features that Suggest an Underlying Organic Gastrointestinal Disorder and Should Prompt Immediate Investigation and Treatment[4,5]

Alarm features that should prompt immediate investigation
• New symptoms in patients over 50 years of age
• Unintended weight loss (more than 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

IBD, inflammatory bowel disease.

Make a Confident IBS-C Diagnosis Using a Positive Diagnostic Strategy

The American College of Gastroenterology (ACG) recommends a positive diagnostic approach utilizing the Rome Diagnostic Criteria for Irritable Bowel Syndrome, fourth iteration (Rome IV criteria), along with a thorough clinical assessment that includes a detailed medical history and physical examination.[1]

According to the Rome IV criteria, IBS is defined by recurrent abdominal pain occurring, on average, at least 1 day per week, accompanied by 2 or more of the following: pain related to defecation, changes in stool frequency, or changes in stool form (appearance).[2] For a diagnosis, these symptoms must have been present for the previous 3 months, with an onset at least 6 months prior. It is important to note that, although these strict criteria are used for clinical research, the Rome Foundation has modified them to ease their application in clinical practice.[3]

In clinical practice, an IBS diagnosis can be made if (Figure 1)[3]:

1. The symptoms align with the Rome IV diagnostic criteria;
2. The symptoms (present for at least 8 weeks) are bothersome, interfering with daily activities, requiring attention, or impacting quality of life; and
3. There is clinical confidence that other potential diagnoses have been adequately ruled out based on the patient's presentation and any additional investigations as necessary.

To diagnose the specific subtype of IBS, the modified Rome IV criteria must be used in conjunction with the Bristol Stool Form Scale (BSFS) (Table 1).[1] In IBS-C, more than 25% of bowel movements are BSFS types 1 and 2 and fewer than 25% are BSFS types 6 and 7.

Although IBS does not affect mortality and is not a precursor to inflammatory bowel disease (IBD), certain alarm features should prompt immediate investigation and treatment, as they may suggest an underlying organic gastrointestinal (GI) disorder (Table 2).[4,5] In the case of CS, there were no alarm features. A colonoscopy following rectal bleeding had revealed a few polyps and hyperplastic adenomas. She had constipation for most of her life. Over the past year, other debilitating symptoms in addition to constipation—including a persistent sensation of incomplete evacuation, severe bloating, abdominal pain, daylong discomfort, and excessive straining—had severely diminished her quality of life. All these were consistent with a diagnosis of IBS-C.

In the Clinic . . .

Use the ACG's Positive Diagnostic Strategy to Make a Diagnosis

There are currently no validated diagnostic tests or biomarkers for IBS-C. Hence a diagnosis of exclusion is unnecessary. It only delays treatment and prolongs the suffering and frustration of your patients, causing them to lose confidence in your diagnosis.

To make a confident diagnosis, rely on the ACG's positive diagnostic strategy. In most cases, the hallmark symptoms of IBS-C—abdominal pain and constipation—are sufficient to meet the Rome IV criteria without the need for additional testing. This positive diagnostic approach reduces unnecessary testing and expedites treatment initiation.

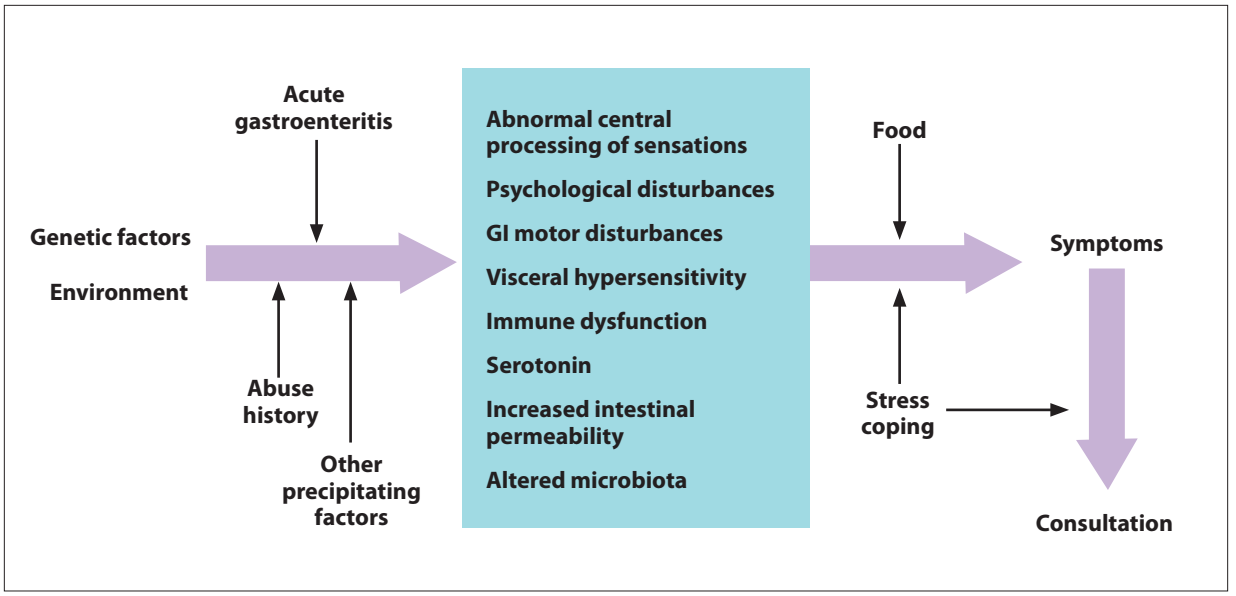

Figure 2. Complex and multifactorial pathophysiology of IBS-C.

GI, gastrointestinal; IBS-C, irritable bowel syndrome with constipation.

Adapted from Lacy BE. *Gastroenterol Hepatol (N Y)*. 2024;20(4):216-226.[18]

Both Bowel and Abdominal Symptoms in IBS-C Are Debilitating

IBS-C is a chronic condition characterized by debilitating symptoms that fluctuate in intensity over time. In the IBS in America 2024 survey, which included 284 respondents with IBS-C, 94% reported additional symptoms beyond constipation.[6] These included bloating (86%), abdominal cramps and pain (85%), abdominal fullness (73%), excessive gas or flatulence (68%), fatigue (64%), tenesmus (57%), and heartburn or gastroesophageal reflux disease (51%). In the case of CS, these additional symptoms included a persistent sensation of incomplete evacuation, severe bloating, abdominal pain, daylong discomfort, and excessive straining.

These debilitating symptoms have a profound impact on the patient's quality of life, as evident not only in this specific case but also in findings from the IBS in America 2024 survey.[7] The majority of survey respondents who experienced abdominal pain described it as either "quite bad" or "very bad," interfering with their day-to-day activities. Furthermore, 90% of respondents reported at least some degree of negative or significantly negative impact of IBS-C on their overall quality of life. Specific areas affected included mental and emotional health (89% of respondents), sexual health and intimacy (64%), employment or education (48%), sense of independence (59%), relationships with friends or family (56%), and household finances (43%).

In the Clinic . . .

Document ALL the IBS-C Symptoms Specific to Each Patient

In addition to abdominal pain and constipation, patients may frequently experience abdominal discomfort, bloating, infrequent bowel movements, straining, and the sensation of incomplete evacuation. When evaluating patients, documenting all these debilitating symptoms is essential, as this provides a valuable baseline for assessing response to treatment. Moreover, recognizing and validating the impact of each symptom on the patient's quality of life can help patients feel heard and thus foster trust, which is the foundation of a patient-centered approach.

Underlying Cause of Each Patient's Symptoms Cannot Be Known

IBS is a functional bowel disorder, now classified as a disorder of gut-brain interaction, with a complex and multifactorial pathophysiology (Figure 2).[8-18] Altered gut motility and water imbalances may contribute to hard stools and decreased defecation. Aberrant microbiome-immune interactions and changes in gut permeability can lead to inflammatory and hyper-visceral responses. IBS is also closely associated with psychiatric and psychological conditions, particularly anxiety and depression. Factors

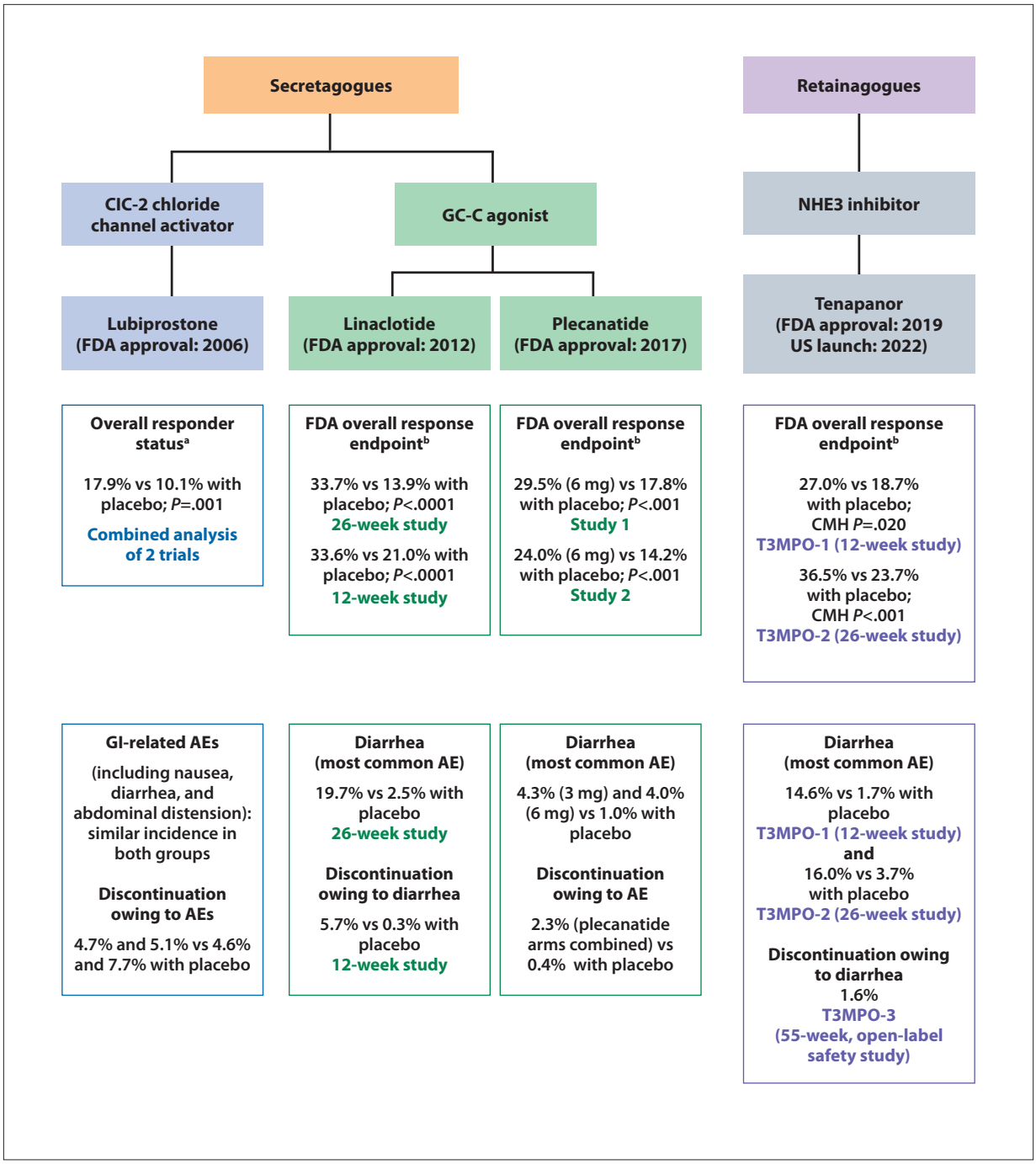

Figure 3. Currently available FDA-approved treatment options for IBS-C and their efficacy and safety data.

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.

[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.

Adapted from Brenner DM. *Gastroenterol Hepatol (N Y)*. 2023;19(12)(suppl 6):749-756.[28]

such as genetic predisposition, adverse early life events, psychological stressors, or GI infections may also play a role.

Why did CS develop IBS-C? Did the stress from IBS-C symptoms in an already high-stress work environment exacerbate her condition? We do not—and cannot—know for certain.

It is important to communicate to patients that pinpointing the exact cause of their symptoms is not possible. Even when 2 patients have identical symptom profiles, the underlying causes may differ. Acknowledging this can help build trust and foster a stronger patient–provider relationship.

In the Clinic . . .

Acknowledge that not knowing the underlying pathophysiology of IBS-C in each patient does not alter your approach to treatment and management.

Lifestyle Modifications and Over-the-Counter Options Have Limited Benefit

The low-fermentable oligo-, di-, monosaccharides, and polyols (FODMAP) diet, widely used for IBS, involves significantly reducing the intake of fermentable foods.[19] However, it is linked to exacerbating constipation and provides no benefit for IBS-C. Adequate fiber intake is often overlooked in IBS-C management and should be considered.[20]

Many patients with IBS-C attempt self-medication with over-the-counter treatments for constipation. However, these medications often do not address abdominal symptoms and, in some cases, exacerbate them. Osmotic and stimulant laxatives have a minimal effect on abdominal pain.[21] Stimulants are associated with worsening abdominal cramps, discomfort, and pain. PEG does not alleviate pain, and guidelines are conflicted regarding its use in IBS-C.[4,22] Fibers such as bran worsen symptoms.[23] Probiotics have a limited effect and do not feature in the American Gastroenterological Association (AGA) guidelines for the management of IBS-C.[22]

In the Clinic . . .

Note that both adequate daily fiber intake and PEG did not have any substantial impact on our patient's global symptoms and likely contributed to her frustration with her condition. Similar results have been reported in the literature as well. Reiterate to your patients that it is important to look beyond over-the-counter options and consider FDA-approved treatment options for IBS-C.

FDA-Approved Medications Can Address All IBS-C Symptoms

The FDA has approved 5 medications for treatment of IBS-C. Among them, tegaserod, a 5-hydroxytryptamine type 4 agonist, was approved in 2002 but is no longer commercially available and hence will not be covered in this discussion.[24] Of the 4 remaining FDA-approved agents (Figure 3), all 3 secretagogues were approved by 2017: lubiprostone in 2006, linaclotide in 2012, and plecanatide in 2017.[25-29] The first-in-class retainagogue, tenapanor, was approved in 2019 and was launched in the United States in 2022.[29] Note that lubiprostone is specifically indicated for the treatment of IBS-C in women at least 18 years of age.

FDA-Approved IBS-C Medications Have Different Mechanisms of Action

Secretagogues increase the secretion of chloride and bicarbonate ions into the intestinal lumen, promoting water secretion. This process accelerates colonic transit, improves stool consistency, and increases the frequency of bowel movements. Among the secretagogues, lubiprostone, a prostaglandin E1 derivative, is a CIC-2 chloride channel activator, whereas linaclotide and plecanatide function as guanylate cyclase-C (GC-C) agonists.[30-33]

The retainagogue tenapanor is a locally acting inhibitor of the sodium/hydrogen exchanger isoform 3 (NHE3).[34-37] The NHE3 antiporter, located on the apical surface of the epithelial cells lining the small intestine and colon, is responsible for the absorption of dietary sodium. NHE3 inhibition results in 3 key effects: (1) reduced absorption of dietary sodium (causing water retention in the intestinal lumen, accelerating intestinal transit); (2) reconstitution of the tight junctions between intestinal epithelial cells (resulting in decreased intestinal permeability); and (3) antagonism of transient receptor potential vanilloid 1 channels. The latter 2 effects, demonstrated in animal models, are hypothesized to be responsible for the reduction in visceral hypersensitivity and improvement in abdominal symptoms.

In the Clinic . . .

Explain to your patients why it is important that there are medications with different mechanisms of action. Because knowing the underlying cause of IBS-C symptoms in each patient is not possible, having medications with different mechanisms of action gives the providers the flexibility to switch treatments to a different class if a medication from one class does not produce the desired outcome.

Large Randomized Trials Have Evaluated Both Bowel and Abdominal Symptoms

The FDA approval of these agents was based on pivotal, large, randomized and placebo-controlled trials.[38-43] The primary endpoints in these trails were: overall response (lubiprostone) and the FDA combined endpoint for IBS-C response (linaclotide, plecanatide, and tenapanor).

Overall responder status was calculated from the weekly assessments of symptom relief. A patient was considered an overall responder if they were a monthly responder for at least 2 of the 3 months of the study. 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. The FDA combined endpoint for IBS-C response was defined as an improvement of at least 30% from baseline in average daily worst abdominal pain score and an increase of at least 1 complete spontaneous bowel movement (CSBM) from baseline, both in the same week for 6 or more out of 12 weeks.

In addition to these primary endpoints, various pivotal trials and follow-up analyses have evaluated many secondary endpoints: abdominal discomfort or pain, bloating, constipation severity, frequency and stool consistency, and straining.[44-47]

In the Clinic . . .

Tell your patients that, unlike over-the-counter remedies for constipation, the FDA-approved medications have been evaluated in large, randomized trials for impact on both bowel and abdominal symptoms.

FDA-Approved IBS-C Medications Are Effective

Lubiprostone: In a combined analysis of two 12-week phase 3 trials, lubiprostone was associated with a significantly higher percentage of overall responders compared with placebo (17.9% vs 10.1%; *P*=.001).[38] These overall responses increased over the first 3 months of treatment for both lubiprostone and placebo (month 1: 10.8% vs 7.5%; month 2: 18.3% vs 11.4%; month 3: 22.0% vs 14.5%). Overall responders also experienced significant improvements in other symptoms compared with nonresponders—abdominal discomfort or pain, bloating, constipation severity, stool consistency, and straining (*P*<.001 for all symptoms).

Linaclotide: Significantly more patients treated with linaclotide achieved the FDA combined endpoint compared with placebo in both a 26-week (33.7% vs 13.9%; *P*<.0001) and a 12-week study (33.6% vs 21.0%; *P*<.0001).[39,40] Linaclotide was also associated with significant improvements compared with placebo across multiple other endpoints: abdominal pain (48.9% vs 34.5%) and CSBM response (47.6% vs 22.6%) for 9 out of 12 weeks in the 26-week study, and reduction in abdominal pain of 30% or greater (50.1% vs 37.5%; *P*=.0003) and an increase of at least 1 CSBM from baseline (48.6% vs 29.6%; *P*<.0001) for at least 6 of the 12 treatment weeks in the 12-week study.

Plecanatide: A significantly higher percentage of patients receiving plecanatide achieved the primary endpoint compared with placebo in both Study 1 (30.2% [3 mg arm] and 29.5% [6 mg arm] vs 17.8%; *P*<.001) and Study 2 (21.5% [3 mg arm] and 24.0% [6 mg arm] vs 14.2%; *P*=.009).[41] Plecanatide was also associated with significantly improved secondary endpoints in both studies, including stool frequency/consistency, straining, and abdominal symptoms.

A reanalysis of data from these studies reported similar results, with significantly more patients in the plecanatide group achieving a novel trisymptom composite endpoint (consisting of abdominal pain, abdominal bloating, and CSBMs) compared with those in the placebo group.[44] In a separate report of patients with IBS-C stratified by bloating intensity, plecanatide significantly reduced bloating severity compared with placebo (least-squares mean change, –1.7 vs –1.3; *P*=.002), reduced abdominal pain (–1.7 vs –1.3; *P*=.006), and increased CSBM frequency (1.4 vs 0.8; *P*<.0001) among patients classified as having moderate-to-severe bloating.[45] In a systemic review and meta-analysis of the efficacy and safety of plecanatide, at the FDA-approved dose of 3 mg once daily, the pooled effect size favored plecanatide compared with placebo across several measures: abdominal pain (pooled effect size, –0.49; 95% CI, –0.88 to –0.09; *P*=.03); change in BSFS score (pooled effect size, 0.82; 95% CI, –0.53 to 2.18; *P*=.12); change in CSBM (pooled effect size, 0.53; 95% CI, –1.77 to 2.83; *P*=.42); and change in straining score outcome (pooled effect size, 0.39; 95% CI, –1.21 to 1.99; *P*=.40).[46]

Tenapanor: Significantly more patients receiving tenapanor compared with placebo met the primary endpoint in both the 12-week T3MPO-1 trial (27.0% vs 18.7%; Cochran-Mantel-Haenszel [CMH] *P*=.020) and the 26-week T3MPO-2 trial (36.5% vs 23.7%; CMH *P*<.001).[42,43] In T3MPO-1, tenapanor was associated with significant improvement in the abdominal pain response (44.0% vs 33.1%; CMH *P*=.008) and in several measures of abdominal symptoms for at least 9 of 12 weeks compared with placebo—abdominal discomfort response

Table 3. Using FDA-Approved IBS-C Medications: What the Guidelines Say[1,22]

FDA-approved IBS-C medication	American College of Gastroenterology	American Gastroenterological Association
Lubiprostone	Strong recommendation	Conditional suggestion
Linaclotide	Strong recommendation	Strong recommendation
Plecanatide	Strong recommendation	Conditional suggestion
Tenapanor	Not reviewed	Conditional suggestion

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

(29.0% vs 17.1% [CMH P<.001]); rate of abdominal bloating response (27.0% vs 16.1% [CMH P=.001]); abdominal cramping response (30.6% vs 23.1% [CMH P=.044]); and abdominal fullness response (27.4% vs 14.4% [CMH P<.001]).[42] In T3MPO-2, tenapanor was associated with significantly greater improvement compared with placebo for both the abdominal pain response (49.8% vs 38.3%; CMH P=.004) and CSBM (47.4% vs 33.3%; CMH P<.001) endpoints.[43] Tenapanor was associated with an improvement in abdominal pain as early as 1 week after treatment initiation and a decrease in other abdominal symptoms including bloating, fullness, discomfort, and cramping.

In a post hoc analysis of pooled data from the T3MPO-1 and T3MPO-2 trials, when compared with placebo, tenapanor was associated with a significantly improved abdominal score (AS; least-squares mean change from baseline: –2.66 vs –2.09; P<.0001) and AS response rate for at least 6 out of 12 weeks (44.4% vs 32.4%; P<.0001) and for at least 9 out of 12 weeks (30.6% vs 20.5%; P<.0001).[47] Note that AS was calculated as the average of weekly scores for abdominal pain, discomfort, and bloating symptoms.

FDA-Approved IBS-C Medications Are Safe

In both lubiprostone studies, GI-related events were the most frequently occurring adverse events and included nausea, diarrhea, and abdominal distension.[38] Diarrhea was the most frequently reported adverse event in linaclotide, plecanatide, and tenapanor studies as well.[39-43] In a 55-week open-label safety study (T3MPO-3), tenapanor was well tolerated with no new safety signals and only 1.6% discontinuation owing to diarrhea.[48] It should be noted that these side effects, which are generally mild or moderate in severity, can be effectively managed.

Direct Comparison Between FDA-Approved IBS-C Medications Is NOT Possible

In the absence of head-to-head trials, the comparative efficacies of the available FDA-approved agents for IBS-C remain unknown. What is certain is that using any of these agents is better than no treatment or over-the-counter treatment. A network meta-analysis of randomized controlled trials of these agents showed similar efficacy across most endpoints and proved their superiority to placebo for the treatment of global IBS-C symptoms.[49] Another network meta-analysis, which compared the efficacy of these agents with respect to abdominal bloating, found all agents superior to placebo and indirect comparisons across agents revealed no significant differences.[50] ACG and AGA guidelines, too, only qualitatively qualify their recommendations without indicating any preference or sequencing algorithm (Table 3).[1,22]

In the Clinic . . .

Initiate Treatment With ANY FDA-Approved Medication for IBS-C

All FDA-approved IBS-C medications have been proven to be both safe and effective in pivotal, large, randomized controlled trials. Treatment with any one of them is better than doing nothing at all.

Setting Patient Expectations

Reiterate to your patients that:

- IBS-C is a chronic disease that requires chronic management.
- The goal of therapy with an FDA-approved IBS-C medication is substantial improvement in both bowel and abdominal symptoms and quality of life.
- In the absence of head-to-head clinical trials, you cannot know if one agent is more effective than another.
- Not knowing the underlying pathophysiology of IBS-C results in a trial-and-error approach to finding the IBS-C medication that addresses the specific root cause of your patient's symptoms.

Persist With Treatment

Patients may notice symptom improvement within the first week of initiating treatment; however, many require longer courses of therapy. Notably, bowel symptoms often improve more rapidly than abdominal symptoms. Two post hoc analyses highlight these dynamics in IBS-C management.

A post hoc analysis of pooled data from 3 tenapanor studies (T3MPO-1, T3MPO-2, and a phase 2b study)

revealed that abdominal symptom relief often lags bowel symptom response.[51] In tenapanor-treated patients, the median time to CSBM response was 2 weeks, whereas abdominal pain and bloating responses took longer—4 weeks and 5 weeks, respectively. In the same analysis, persistence with therapy improved response rates over time. CSBM response probability increased from 52.3% (week 2) to 72.5% (week 8) and 76.7% (week 12). Abdominal pain response probability rose from 54.6% (week 4) to 67.9% (week 8) and 72.3% (week 12). Abdominal bloating response probability increased from 48.1% (week 4) to 61.9% (week 8) and 67.7% (week 12).

A post hoc analysis of linaclotide trials also revealed similar results.[52] Although more than one-half of patients with IBS-C in the linaclotide group experienced responses for abdominal pain, discomfort, bloating, or CSBM frequency within 4 weeks of starting treatment, an additional 8% to 17% showed responses between weeks 5 and 12.

These findings underscore the importance of persisting with treatment for several weeks before assessing response to therapy. The next step in IBS-C management is to evaluate treatment response, which requires understanding what constitutes an "adequate response."

In the Clinic . . .

When to Schedule a Follow-up Visit to Evaluate Response

In my practice, I have observed that IBS-C medications tend to impact bowel symptoms before addressing abdominal bloating and abdominal pain. For this reason, I recommend scheduling a follow-up visit 8 weeks after initiating treatment to assess overall response across all symptom domains. However, patients are encouraged to contact my office sooner if side effects become debilitating. In such cases, I will expedite their visit to evaluate the situation and adjust the treatment plan accordingly.

Conduct a Follow-up Visit to Evaluate Response

In the absence of standardized questionnaires or markers to quantitatively measure treatment response in IBS-C, providers should rely on the patient's initial workup and specific complaints to guide follow-up discussions. For example, if the initial complaints were constipation, straining, and pain, the follow-up should address changes in constipation, including frequency and stool quality as assessed by the BSFS; percentage reduction in straining during bowel movements; and percentage improvement in pain symptoms. Additionally, inquire about any new symptoms, which may be side effects of medication, and assess the patient's overall satisfaction with their current level of response and quality of life.

It is essential to educate patients that the goal of treatment is a substantial improvement in their quality of life and all IBS-C symptoms—that is, achieving an "adequate response." Reassure them that you are committed to exploring different approaches and medications until this goal is accomplished.

In the Clinic . . .

How to Evaluate Response to Treatment

During follow-up visits, ask your patients to:

- Quantify their response as a percentage change across the abdominal and bowel symptoms they initially reported.
- Report any new symptoms, which could indicate potential side effects of the medication.
- Describe any changes in their quality of life.
- Share their expectations for treatment outcomes.

Expect Adequate Response, Tailor Treatment in Case of Inadequate Response

The approach to defining "adequate response" has evolved with the introduction of medications with different mechanisms of action. With the availability of only secretagogues, even mild improvement in some debilitating IBS-C symptoms was deemed an acceptable response. The prevailing mindset at that time was essentially, "this is IBS-C, and there's not much more we can do for our patients."

This approach was owing largely to limited options. After a secretagogue was initiated, the only alternatives were dose adjustments when possible or switching to another agent within the same class. However, if one agent in a given class failed to provide adequate response, another agent with the same mechanism of action was unlikely to deliver substantial improvement. This suggests that the class of agents may not effectively address the patient's unique IBS-C pathophysiology.

The approval of first-in-class tenapanor has expanded what we can do for our patients. As advocates for our patients, we should no longer settle for "some" improvement but strive for truly adequate response—a substantial improvement in both bowel and abdominal symptoms, as well as overall quality of life. This means that if one medication does not provide adequate response, proactively switch to a medication with a different mechanism of action.

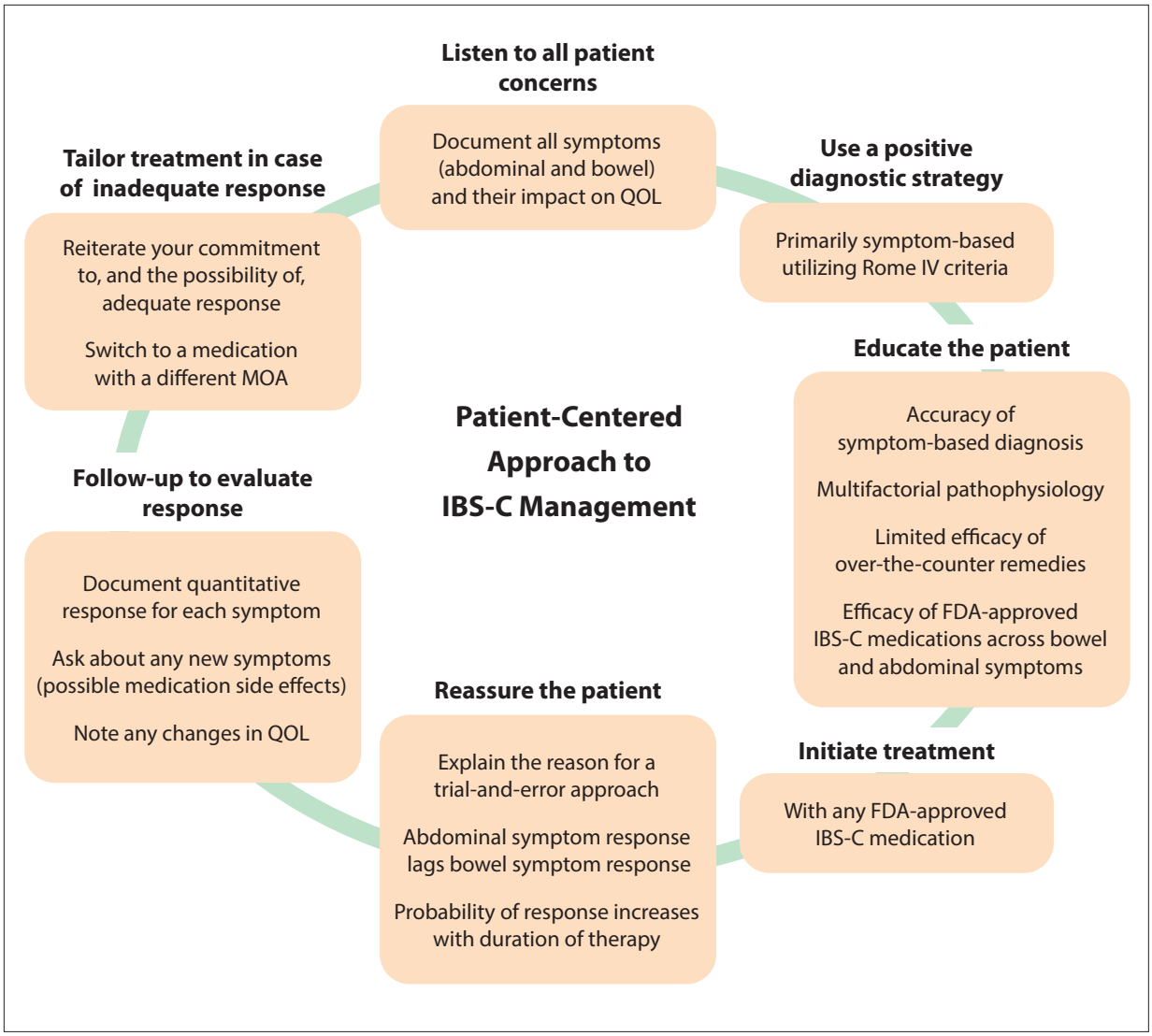

Figure 4. Patient-centered approach to IBS-C management.

FDA, US Food and Drug Administration; IBS-C, irritable bowel syndrome with constipation; MOA, mechanism of action; QOL, quality of life.

In the Clinic . . .

Remember that in case of inadequate response there are other options available.

If I were treating CS 4 years ago, following a poor response to linaclotide, I would have switched to another medication within the same class. Although this might have alleviated some side effects, it would likely have been less effective. Essentially, this approach would have left the patient back at square one. Today, however, because of the availability of another agent with a different mechanism of action, I switched CS to tenapanor, potentially increasing the probability of adequate response.

Bringing It All Together

Patient-centered approach is critical in IBS-C management, as these patients have likely long suffered from a compromised quality of life and debilitating symptoms that wax and wane over time (Figure 4).

Given the multifactorial pathophysiology of IBS-C, predicting which medication will work for a specific patient is impossible. There is no definitive right or wrong choice when selecting the initial FDA-approved IBS-C medication. The key is to evaluate the patient's response to treatment across all aspects of bowel and abdominal symptoms.

If a medication within a particular class proves ineffective, another medication from the same class is highly

unlikely to yield significantly better results. Persisting with a similar treatment may only heighten the patient's suffering and frustration. In such cases, the provider's responsibility is to switch to a medication with a different mechanism of action. Delaying this switch could have unintended consequences.

When I first evaluated CS, there was no evidence of pelvic floor dysfunction during the rectal examination. However, her persistent straining could potentially lead to dyssynergistic and obstructive defecation over time. By proactively switching to a medication with a different mechanism of action—tenapanor in this case—my goal was to help CS achieve adequate relief from both bowel and abdominal symptoms of IBS-C while preventing potential future complications.

Disclosures

Dr Kongara is on the speakers bureau of AbbVie, Ardelyx, Ironwood, Phathom, and Salix; and a consultant/advisor for Sitzmarks.

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