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A SPECIAL MEETING REVIEW EDITION

Highlights in IBS-C From Digestive Disease Week 2024

A Review of Selected Posters and CME Symposium From DDW 2024

May 18-21, 2024 • Washington, DC

Special Reporting on:

- Efficacy of Tenapanor in Patients With IBS-C: A Post Hoc Analysis of Patients With and Without Prior Use of Other IBS-C Prescription Medications From the Phase 3 T3MPO-1 and T3MPO-2 Studies
- Comparing the Efficacy of Tenapanor in IBS-C in Hispanic Versus Non-Hispanic Patients: A Post Hoc Analysis of Patients in the Phase 3 T3MPO-1 and T3MPO-2 Studies
- Efficacy, Safety, and Time to Response of Linaclotide in Patients ≥65 With IBS-C

PLUS Meeting Abstract Summaries

PLUS Interview With Darren M. Brenner, MD, on the CME Symposium "One Size Does NOT Fit All: Improving Patient Care in IBS-C"

With Expert Comments by:

Darren M. Brenner, MD
Professor of Medicine (Gastroenterology and Hepatology) and Surgery
Northwestern Medicine
Northwestern University
Feinberg School of Medicine
Chicago, Illinois

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Efficacy of Tenapanor in Patients With IBS-C: A Post Hoc Analysis of Patients With and Without Prior Use of Other IBS-C Prescription Medications From the Phase 3 T3MPO-1 and T3MPO-2 Studies

Irritable bowel syndrome (IBS) is commonly accompanied by diarrhea but may instead be marked by constipation (IBS-C).[1] IBS-C affects approximately 29% of the population and can cause severe deterioration in quality of life. Tenapanor is a first-in-class locally acting inhibitor of the sodium/hydrogen exchanger isoform 3 (NHE3).[2] The drug received approval by the US Food and Drug Administration (FDA) for the treatment of patients with IBS-C, based on the double-blind, multicenter, phase 3 T3MPO-1 and T3MPO-2 trials.[3-5] T3MPO-1 enrolled 1599 adults for a 12-week treatment period, and T3MPO-2 enrolled 1461 adults for a 26-week treatment period. Patients in both trials were evenly randomized to receive tenapanor (50 mg, twice daily) versus placebo. The trials demonstrated improvements in IBS symptoms, including significant increases in the frequency of complete spontaneous bowel movements (CSBM) and decreased pain compared with baseline values.

Both the T3MPO-1 and T3MPO-2 trials allowed the enrollment of patients who had previously used other prescription medications, as long as their use had stopped within

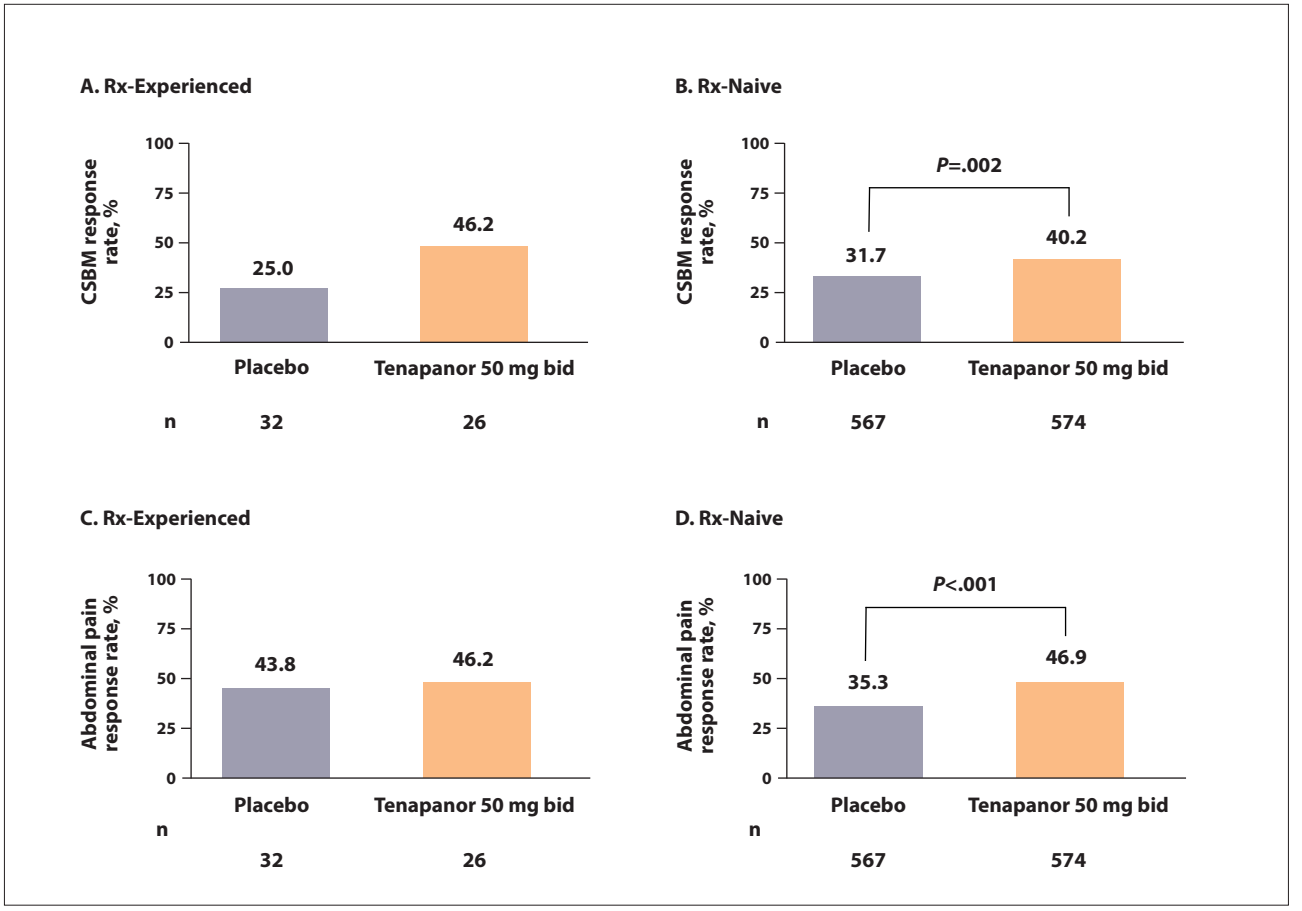

Figure 1. CSBM and abdominal pain response rates in patients with (A, C) and without (B, D) prior IBS-C prescription medication use in the pooled population from T3MPO-1 and T3MPO-2 studies.[a,b,c]

bid, twice a day; CSBM, complete spontaneous bowel movement; IBS-C, irritable bowel syndrome with constipation; Rx, treatment.

[a]A CSBM responder was defined as a patient with an increase of ≥1 weekly CSBM from baseline.

[b]The sample size of the subgroup of patients with prior IBS-C prescription medication use (Rx-Experienced; n=58) was too small to yield a statistically significant *P* value for the treatment comparison of the CSBM response endpoint.

[c]An abdominal pain responder is defined as a patient with ≥30% decrease in average weekly worst abdominal pain from baseline.

Adapted from Shah et al. Poster Tu1658. Presented at DDW 2024; May 18-21, 2024; Washington, DC.

The consideration of whether a patient is treatment-naive or has prior treatment experience is important when prescribing therapies. However, findings from this post hoc analysis revealed that regardless of treatment history, patients were more likely to respond to tenapanor than to placebo. Interestingly, patients who were not treatment-naive exhibited a higher likelihood of response to tenapanor, but it is important to note that this assessment was based on a very small percentage of the overall population (<5%).

Another unexpected observation from this analysis was that the vast majority of patients (95%) enrolled in these phase 3 trials were treatment-naive. This finding contrasts with expectations, considering that tenapanor, the most recently marketed therapeutic for IBS-C management, was introduced to the US market in 2022, approximately 20 years after FDA approval of the first therapeutic for IBS-C management (tegaserod in 2002, now discontinued).

—Darren M. Brenner, MD

30 days of trial enrollment. Therefore, a post hoc analysis was performed to evaluate the effect of prior medication use on the clinical response to tenapanor, using pooled patient data from the 2 trials.[6] A CSBM response was defined as an increase of 1 or more weekly CSBM from baseline, and abdominal pain response was defined as a decrease of at least 30% in average weekly worst abdominal pain from baseline. The FDA composite response was defined as having both a CSBM response and an abdominal pain response in the same week for at least 6 of the 12 weeks of study treatment. The post hoc analysis included 58 patients with prior prescription medication use for their IBS-C (tenapanor, n=26; placebo, n=32) and 1145 patients with no prior prescription medication use for their IBS-C (tenapanor, n=576; placebo, n=569). The most common prior prescription medication was linaclotide (61.5%-59.4%), followed by lubiprostone (38.5%-37.5%). Both linaclotide and lubiprostone had been previously used by 3.1% of patients in the placebo cohort versus 0% in the tenapanor cohort.

Among patients with prior exposure to prescription medication for their IBS-C, the composite response rate was significantly higher with tenapanor versus placebo (42.3% vs 18.8%; *P*=.038). The composite response rate was also higher with tenapanor versus placebo among patients without prior exposure to prescription medication for their IBS-C (31.2% vs 21.3%; *P*<.0001). Among patients with prior exposure to prescription medication for IBS-C, tenapanor was associated with a higher rate of CSBM response versus placebo (46.2% vs 25.0%; Figure 1), whereas the abdominal pain response was similar for tenapanor and placebo (46.2% vs 43.8%, respectively). Among the cohort of patients without prior exposure to prescription medication for their IBS-C, tenapanor was superior to placebo based on both the CSBM rate (40.2% vs 31.7%; *P*=.002) and reduction in abdominal pain (46.9% vs 35.3%; *P*<.001).

Tenapanor was generally well tolerated. Treatment-emergent adverse events (AEs) were more common among patients with prior exposure to prescription medication for their IBS-C compared with patients without (59% vs 36%). During the randomized treatment period, the most common treatment-emergent AE was diarrhea, in patients with (26.9%) and those without (14.8%) prior IBS-C prescription medication use.

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Comparing the Efficacy of Tenapanor in IBS-C in Hispanic Versus Non-Hispanic Patients: A Post Hoc Analysis of Patients in the Phase 3 T3MPO-1 and T3MPO-2 Studies

Studies suggest that there may be differences between Hispanic and non-Hispanic adults with IBS, in terms of health-care–seeking behaviors, internalized stigma, and the time spent attending to bowel function.[1-3] Hispanic people comprise the second largest ethnic population in the United States, at approximately 65 million or nearly 20% of the entire US population; however, Hispanic patients only represent approximately 11% of clinical trial participants.[3-5] A post hoc study evaluated outcomes in Hispanic versus non-Hispanic patients in the T3MPO-1 and T3MPO-2 studies, whose study populations included 28% Hispanic patients.[6-8]

The multicenter, double-blind, phase 3 T3MPO-1 and T3MPO-2 studies enrolled adults with IBS-C. Patients were randomized to treatment with tenapanor (50 mg, twice daily) versus placebo for 12 weeks (T3MPO-1) or 26 weeks (T3MPO-2).[9] The pooled analysis of the current study included 600 patients who were treated with tenapanor (175 Hispanic and 425 non-Hispanic patients) and 599 patients who received placebo (161 Hispanic and 438 non-Hispanic) from the intention-to-treat population.

The response to tenapanor versus placebo was defined as follows. A 6- of 12-week overall response was defined as achieving a CSBM response and an abdominal pain response in the same week for at least 6 of the first 12 weeks of treatment. A 9- of 12-week overall response was defined as achieving a CSBM response, an abdominal pain response, plus at least 3 CSBMs in the same week for at least 9 of the first 12 weeks of treatment. A 9- of 12-week durable overall response was defined as achieving a CSBM response, an abdominal pain response, and at least 3 CSBM in the same week for at least 9 of the 12 weeks of treatment plus 3 of the 4 final weeks of treatment (during weeks 9-12 of treatment).

All three of the efficacy outcomes showed superior results with tenapanor versus placebo in both the Hispanic and non-Hispanic cohorts from the pooled analysis, and outcomes were generally comparable between the 2 ethnic subgroups of patients. The 6- of 12-week overall response rate was 30.86% with tenapanor versus 18.01% with placebo (Δ=12.84%; *P*=.006) in the Hispanic cohort and was 32.00% versus 22.37%, respectively, in the non-Hispanic cohort (Δ=9.63%; *P*=.002; Figure 2). The 9- of 12-week overall response rate was 18.29% with tenapanor versus 6.21% with placebo in the Hispanic cohort (Δ=12.07%; *P*<.001) and was 15.06% versus 3.65%, respectively, in the non-Hispanic cohort (Δ=11.41%; *P*<.001). The 9- of 12-week durable overall response rate was 17.71% with tenapanor versus 6.21% with placebo in the Hispanic cohort (Δ=11.50%; *P*<.001) and was 14.59% versus 3.42% in the non-Hispanic cohort (Δ=11.16%; *P*<.001).

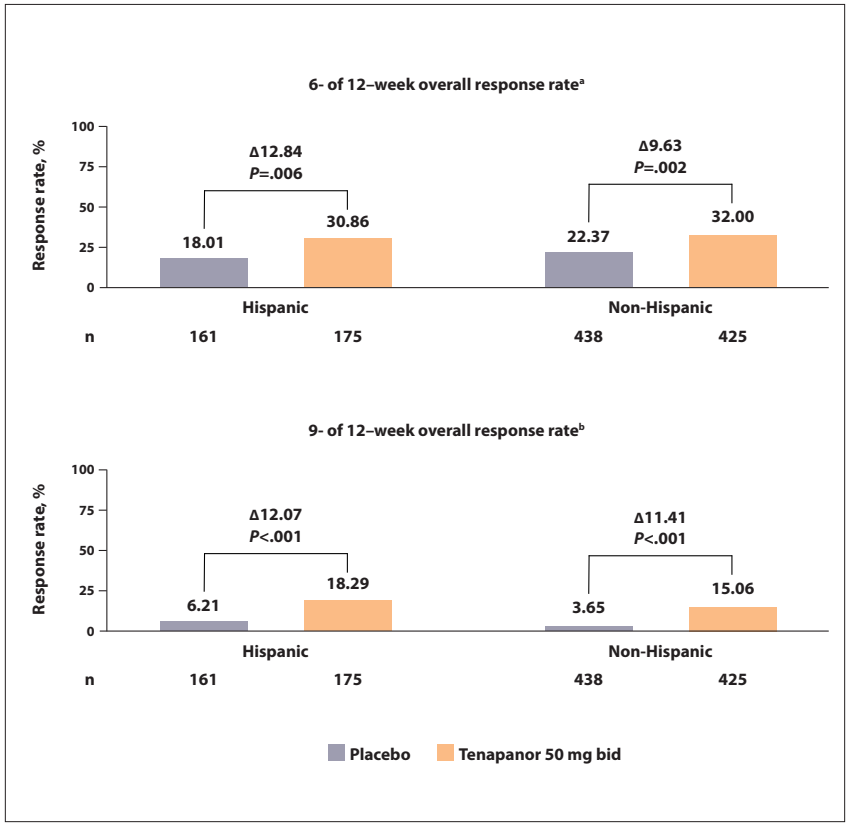

Figure 2. Overall response rates in Hispanic and non-Hispanic patients in the pooled population from T3MPO-1 and T3MPO-2 studies (ITT analysis set).

bid, twice a day; CSBM, complete spontaneous bowel movement; ITT, intention to treat.

[a]A 6 of 12-week overall response was defined as achieving a CSBM response and an abdominal pain response in the same week for ≥6 of the first 12 treatment weeks.

[b]A 9 of 12-week overall response was defined as achieving a CSBM response, an abdominal pain response, and ≥3 CSBMs in the same week for ≥9 of the first 12 treatment weeks.

Adapted from Frazier et al. Poster Tu1663. Presented at DDW 2024; May 18-21, 2024; Washington, DC.

Hispanic individuals represent a significant percentage of the American population, yet data specifically assessing the efficacy of FDA-approved therapeutics for treating IBS-C in this population are lacking. This post hoc analysis addressed this gap and revealed that tenapanor was significantly more effective than placebo for improving global symptoms in individuals of Hispanic descent with IBS-C, with response rates comparable to those in non-Hispanic patients. Tenapanor should, therefore, be considered an effective and appropriate therapeutic for treating Hispanic patients with IBS-C.

—Darren M. Brenner, MD

Treatment-related AEs were reported by 26.9% of Hispanic patients versus 48.2% of non-Hispanic patients; however, the difference between the 2 cohorts was attributed to random factors. Diarrhea was the most common treatment-emergent AE of any grade in both the Hispanic (8.6%) and non-Hispanic (18.0%) cohorts. Other treatment-emergent AEs included nausea, nasopharyngitis, flatulence, headache, and urinary tract infection.

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Efficacy, Safety, and Time to Response of Linaclotide in Patients ≥65 With IBS-C

Linaclotide is a guanylate cyclase-C agonist that is approved by the FDA for the treatment of adults with IBS-C.[1] Despite the high incidence of IBS-C in the overall population, few studies have focused specifically on elderly patients. A Japanese study suggested that IBS-C symptoms may differ among patients in different age groups.[2] To evaluate the effects of linaclotide therapy in older patients, a post hoc analysis evaluated the safety, efficacy, and time to response in patients with IBS-C based on age.[3] Patient data were pooled from 3 phase 3 trials that compared daily linaclotide (290 µg) versus placebo for 12 weeks: LIN-MD-31, MCP-103-302, and MCP-103-312.[4-6] All of the trials included patients who met the modified Rome II or Rome III criteria for IBS-C and had a mean baseline abdominal pain score of at least 3.

The post hoc subgroup analysis included 2044 patients aged less than 65 years (linaclotide, n=1028; placebo, n=1016) and 152 patients aged 65 years or greater (linaclotide, n=73; placebo, n=79). Patients in the younger subgroup had a mean age of 42.8±11.8 years and 89% were female. Patients in the older subgroup had a mean age of 70.6±5.2 years and 72% were female. Baseline characteristics were similar across the 4 subgroups, including mean body mass index (27.7-28.5 kg/m^2), abdominal pain score (5.3-5.8), and CSBM frequency (0.2-0.4). In both the younger and older subgroups, linaclotide yielded significant improvements in IBS-C–related symptoms compared with placebo, based on abdominal pain, abdominal discomfort, abdominal bloating, and CSBM frequency (Figure 3).

Linaclotide also yielded a superior median time to response compared with placebo based on abdominal symptoms and CSBM frequency in both cohorts based on age. In the older subgroup of patients, linaclotide significantly improved the median time to response based on abdominal pain (3 vs 6 weeks; *P*=.0106), abdominal discomfort (3 vs 8 weeks; *P*=.0054), abdominal bloating (3 vs 9 weeks; *P*=.0005), and CSBM frequency (2 vs 3 weeks; *P*=.0165). In the younger subgroup of patients, linaclotide again showed a significant improvement in

time to response based on abdominal pain (3 vs 6 weeks; *P*<.0001), abdominal discomfort (3 vs 7 weeks; *P*<.0001), abdominal bloating (4 vs 8 weeks; *P*<.0001), and CSBM frequency (2 vs 4 months; *P*<.0001).

The most common treatment-emergent AE in both linaclotide-treated subgroups was diarrhea of any grade, affecting 15% to 16% of patients. The majority of treatment-emergent diarrhea was mild to moderate in severity. In patients aged 65 years or greater, treatment-emergent diarrhea led to discontinuation in 5.3% of patients; in patients less than 65 years of age, treatment-emergent diarrhea led to discontinuation in 3.9% of patients. Among patients treated with placebo, the rate of treatment discontinuation owing to treatment-emergent diarrhea was 2.5% in the older versus 0% in the younger patients. In summary, linaclotide demonstrated acceptable safety and efficacy outcomes for the treatment of IBS-C in both younger and older patient subgroups from 3 phase 3 trials.

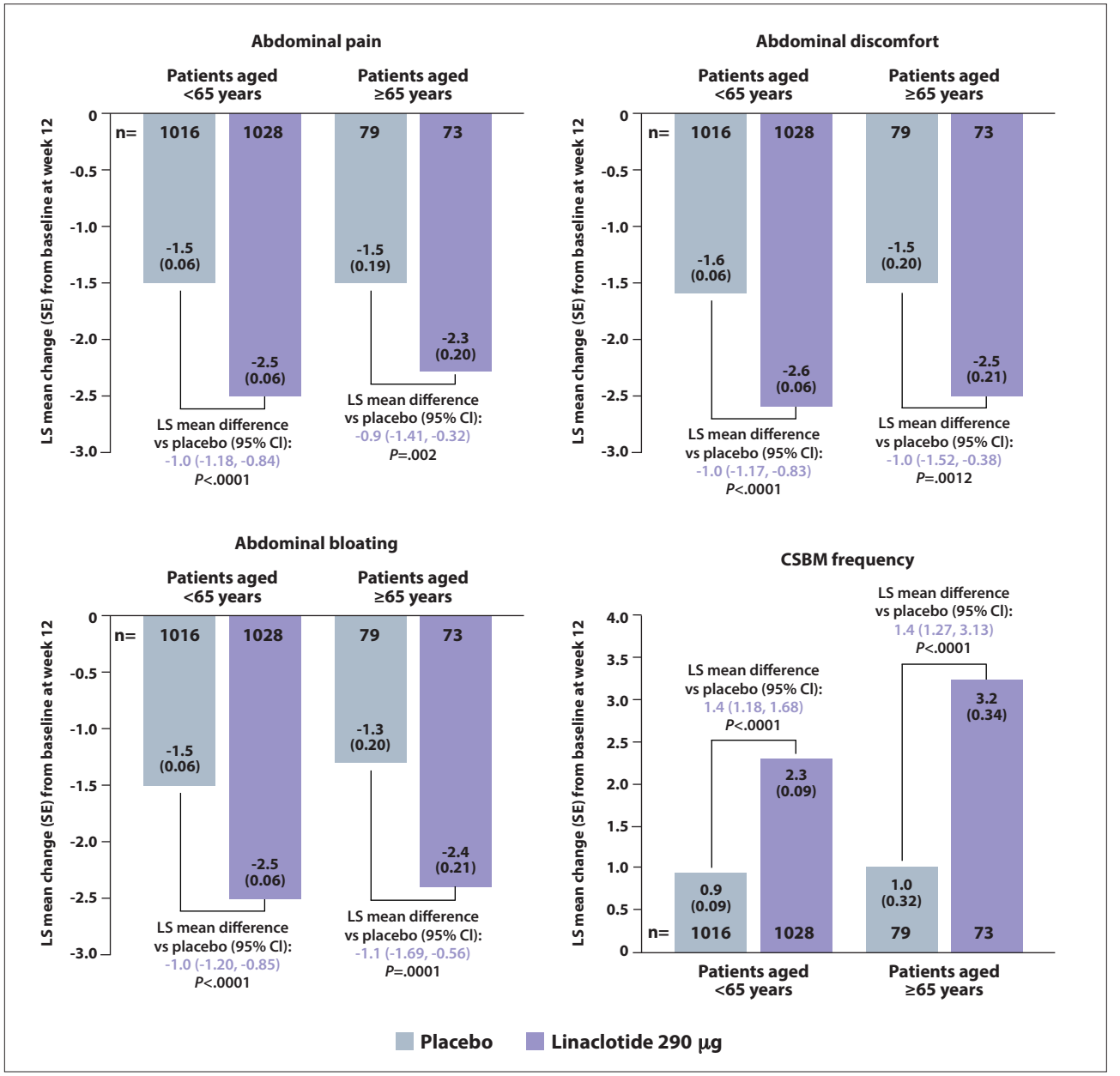

Figure 3. Linaclotide treatment significantly improved abdominal pain, abdominal discomfort, and abdominal bloating scores, and increased CSBM frequency compared with placebo in both age groups (integrated efficacy population).

CI, confidence interval; CSBM, complete spontaneous bowel movement; LS, least-squares; SE, standard error.

n is the number of patients with ≥1 post-baseline assessment and with baseline scores for abdominal pain, abdominal discomfort, and abdominal bloating of ≥3. *P* values are based on t tests.

Adapted from Chang et al. Poster Tu1653. Presented at DDW 2024; May 18-21, 2024; Washington, DC.

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Age-related factors are often a concern among clinicians when prescribing therapies. Linaclotide was proven to be effective across the age spectrum for patients with IBS-C with a plethora of abdominal and bowel symptoms. Analysis of time to response for both abdominal and bowel symptoms also reveals that, irrespective of age, an individual is more likely to respond faster to linaclotide than to placebo. Age-related factors should, therefore, not be a concern when using linaclotide for treating patients with IBS-C.

—Darren M. Brenner, MD

ABSTRACT SUMMARY Comparison of Bowel Habits Characterized by Bowel Diaries and Questionnaires in Persons With Normal Bowel Movement and Patients With Constipation

Questionnaires that are commonly used to assess bowel habits are limited by patient recall bias and the inability to account for day-to-day changes in bowel habits.[1] A study was conducted to compare information on patient bowel habits recorded by means of a questionnaire versus daily bowel diaries in people with or without bowel disorders.[2] The study enrolled 230 people without bowel dysfunction and 219 patients with constipation based on Rome II criteria. Each patient completed a validated questionnaire pertaining to bowel function as well as a 2-week diary with questions regarding bowel symptoms. Dietary fiber supplements and rescue therapy were allowed, but bowel modifiers were excluded. Some symptoms were only assessed in 323 community members in order to avoid referral bias.

A significant association was observed between bowel habits recorded by means of a questionnaire versus with a diary; however, some discrepancies were noted. For the stool frequency category of 0 to 2 per week on the questionnaire, the diaries recorded a mean weekly stool frequency of 5.6±3.6 per week, and for the stool frequency category of 3 to 4 per week on the questionnaire, the diaries showed a mean weekly stool frequency of 7.1±3.0 per week. Discrepancies were also observed regarding a sense of incomplete evacuation after defecation. The questionnaires accounted for 12% of the variance pertaining to hard stools and anal digitation and accounted for 42% of the variance pertaining to stool frequency versus the same variable recorded in the bowel diary. R2 values were calculated using either a univariate model, in which the only variable was based on a query in the questionnaire, or a bivariate model, in which constipation status was included as a variable. For the sense of incomplete evacuation, the variance explained increased from 0.41 with the univariate model to 0.48 with the bivariate model ($P<.0001$). Other variables that showed a significant change in R2 with the univariate versus the bivariate model included frequency of hard stools, excessive straining, and anal digitation. Thus the bowel diaries were seen to provide additional information that was lacking in the questionnaires. More frequent symptoms were associated with a reduction in quality of life, even after adjusting for somatic symptoms.

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ABSTRACT SUMMARY Brain-Gut-Microbiota Analysis of Abdominal Bloating in IBS-C

A prospective study was conducted to characterize the gut microbiota in IBS-C patients with bloating versus without bloating.[1,2] Patients with IBS-C were assessed based on the Rome III criteria. From among 1373 patients who were screened, the study included 13 IBS-C patients with bloating, 13 IBS-C patients without bloating, and 13 healthy controls. Baseline characteristics were balanced among the 3 arms. Nearly all of the study participants (95%) were female. The median age ranged from 38 to 46 years (P=.39) and the median body mass index ranged from 20.6 kg/m^2 to 22.1 kg/m^2 (P=.276). Gut microbiota was analyzed using next-generation sequencing and their function was determined using the Kyoto Encyclopedia of Genes and Genomes. Magnetic resonance imaging with voxel-based morphometry was used to evaluate volume changes of specific regions of the brain.

Comparison of the gut microbiota in 26 patients with IBS-C versus 13 healthy controls showed significantly different levels of p_TM7 (P=.03), g_*Dorea* (P=.02), and g_*Turicibacter* (P=.02). Based on the unweighted unique fraction distance, β diversity was not significantly different between IBS-C patients with versus without bloating (P=.251) nor between IBS-C patients without bloating versus healthy controls (P=.074). However, the β diversity was significantly different between IBS-C patients with bloating versus healthy controls (P=.013). The population of g_*Dorea* was significantly greater in IBS-C patients with bloating versus healthy controls (P<.01). The population of g_*Turicibacter* was significantly greater in IBS-C patients without bloating versus healthy controls. And the population of g_*Rothia* was significantly greater in IBS-C patients with bloating versus those without bloating (P=.02). No difference in gray matter volume was observed among the 3 cohorts. However, the abundance of g_*Turicibacter* was negatively correlated with the gray matter volume of Brodmann area 6. Other variables that were evaluated included bloating, constipation, *Staphylococcus aureus* infection, age, sex, and whole brain volume, and the genuses *Akkermansia*, *Dorea*, *Parvimonas*, *Rothia*, *Ruminococcus*, and *Veillonella*.

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One Size Does NOT Fit All: Improving Patient Care in IBS-C An Interview With Darren M. Brenner, MD

This interview is based on the presentations and discussion at the CME symposium "One Size Does NOT Fit All: Improving Patient Care in IBS-C," which was planned and implemented by Medical Education Resources and GI Health Foundation. Presenters at the symposium included Darren M. Brenner, MD, Christina Hansen, FNP-C, and Gregory Sayuk, MD.

G&H What are the typical symptoms that patients with IBS-C experience?

DMB In clinical practice, there is often a convergence of symptoms between IBS-C and chronic idiopathic constipation (CIC). IBS-C manifests with abdominal pain along with symptoms of constipation. Additionally, many patients with IBS-C also experience abdominal discomfort and bloating, hence the importance of assessing each of these symptoms in clinical trials. Regarding bowel symptoms, patients commonly report decreased stool frequency and/or the passage of hard stools (Bristol Stool Form Scale [BSFS] 1-2) as well as sensations of straining and/or incomplete evacuation. When evaluating a patient with IBS-C, it is crucial to thoroughly investigate all functional constipation symptoms.

G&H What are the social and economic burdens associated with IBS-C?

DMB IBS-C imposes substantial economic burdens, estimated in the billions per annum in the United States alone. These costs encompass both direct expenses and indirect losses, with the latter stemming from reduced work productivity in the forms of absenteeism and presenteeism, and the excessive utilization of unnecessary diagnostic procedures. Surprisingly, despite both the American Gastroenterological Association (AGA) and American College of Gastroenterology (ACG) advocating for the use of a positive diagnostic strategy minimizing testing, extensive testing remains the norm.

Beyond financial ramifications,

IBS-C profoundly affects patients' quality of life, with the majority experiencing significant distress from their symptoms. Depression and anxiety rates are elevated among patients along with constraints on physical and social activities. One study revealed the staggering extent of this impact, with patients expressing a willingness to sacrifice one-quarter of their remaining life expectancy (averaging 15 years) for a treatment guaranteeing symptom relief.

Despite its debilitating nature, a troubling 75% of individuals with IBS remain undiagnosed. Early, accurate diagnosis is thus paramount to initiating timely treatment interventions.

G&H Why is making an IBS-C diagnosis important?

DMB Making a definitive diagnosis of IBS-C is important for many reasons. First, it validates the patient's symptoms and acknowledges that their condition is real. This is crucial for fostering open communication between the patient and the health care provider, enabling a more effective dialogue regarding treatment strategies.

Moreover, a formal diagnosis reduces unnecessary testing and increases the likelihood of the patient being offered evidence-based treatment options tailored to address the spectrum of symptoms associated with IBS-C. By acknowledging the multifaceted nature of the condition, health care providers can offer comprehensive treatment plans aimed at alleviating the various symptoms that contribute to its debilitating impact on patients' lives.

G&H Do the AGA and the ACG guidelines recommend any particular diagnostic strategy?

DMB Both the AGA and ACG guidelines emphasize the adoption of a positive diagnostic strategy for IBS, which stands in contrast to a diagnostic approach of exclusion involving extensive testing. Several studies have compared these 2 approaches, consistently demonstrating that extensive testing only leads to increased costs. Importantly, increased testing has not correlated with improved symptomatic or quality of life outcomes for individuals with IBS-C. In essence, the positive IBS diagnostic strategy has been proven to be noninferior to the diagnostic approach of exclusion.

G&H How can clinicians make a positive IBS-C diagnosis?

DMB Because of the absence of validated diagnostic tests or biomarkers for IBS-C, clinicians rely on a comprehensive assessment involving medical history, physical examination, and adherence to diagnostic criteria. The Rome IV criteria, established in 2016, serve as a cornerstone for diagnosis, supplemented by the BSFS.

According to the Rome IV criteria, a definitive diagnosis of IBS requires recurrent abdominal pain occurring at least once weekly along with 2 or more of the following criteria: association with defecation, altered stool frequency, or changes in stool appearance. Furthermore, the presence of more than 25% of bowel movements categorized as BSFS types 1 or 2, and less than 25% as types 6 or 7, supports the diagnosis of IBS-C.

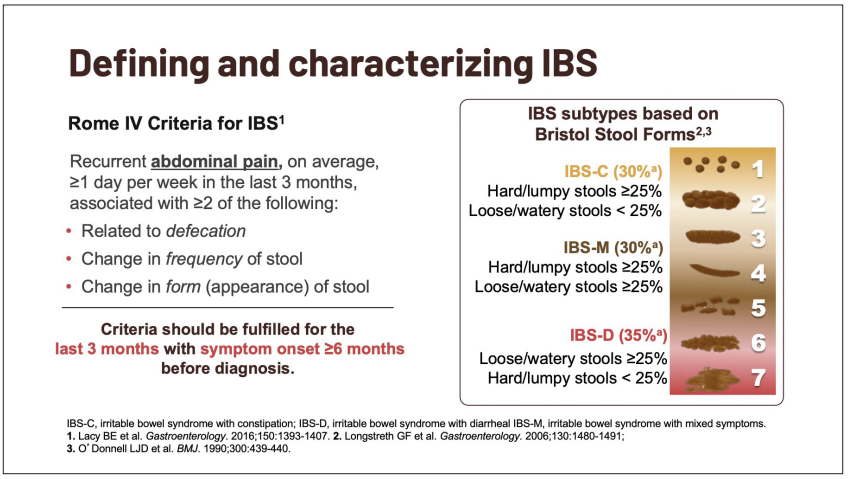
Recognizing the challenges in applying stringent criteria in clinical practice, the Rome Foundation has modified these diagnostic criteria to enhance clinical utility. These modifications allow for a clinical diagnosis of IBS if symptoms align with Rome IV criteria and significantly impact daily activities or quality of life, and alternative diagnoses have been reasonably ruled out by the practitioner.

G&H How accurate is this positive diagnostic strategy? When is additional testing warranted?

DMB The reliability of the Rome criteria alongside limited diagnostic testing has been extensively validated, dating back to the utilization of Rome II criteria nearly 3 decades ago. Remarkably, diagnosis based solely on symptoms has demonstrated accuracy in up to 98% of patients.

However, the presence of alarm signs, such as new symptoms in patients over 50 years old, unintended weight loss, hematochezia, nocturnal awakening owing to symptoms, acute or rapidly progressing symptoms, and a family history of colorectal cancer, celiac disease, or inflammatory bowel disease, indicates a need for further investigation to rule out alternative diagnoses.

To ensure accuracy in diagnosis, I adhere to 8 straightforward rules, which help guide clinical decision-making and ensure comprehensive evaluation when necessary.

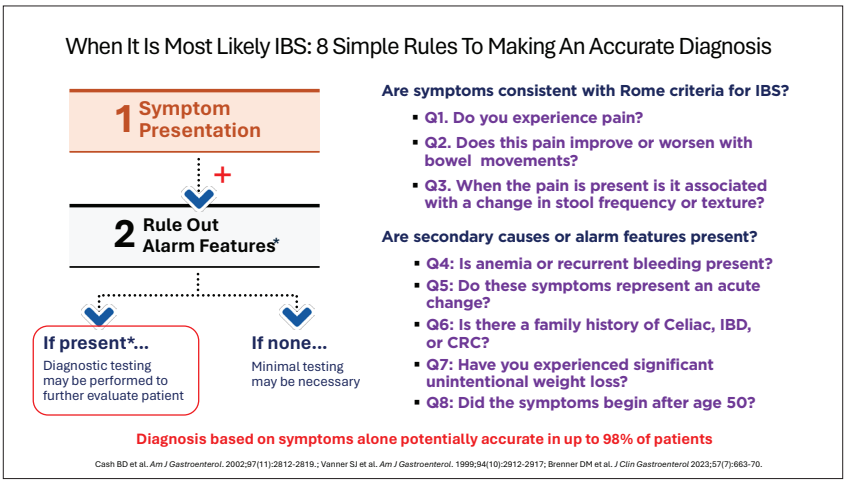


Courtesy of Darren M. Brenner, MD

G&H Why is treating IBS-C a "one size does not fit all" approach?

DMB The symptom profile of IBS-C can arise from various underlying etiopathogenic mechanisms, including disruptions in guanylate cyclase-C receptors, chloride channels, or sodium hydrogen exchangers. However, pinpointing the specific cause for an individual patient is challenging, given the complexity and variability of these mechanisms. Consequently, recommending therapy often relies on an empirical approach.

Owing to the multifactorial pathophysiology of IBS-C, treatment response can vary among patients. Thus, if a patient proves unresponsive to one therapy, there is potential for positive outcomes with an alternative approach. This underscores the importance of flexibility and adaptability in treatment strategies, tailoring interventions to each patient's unique presentation and response.



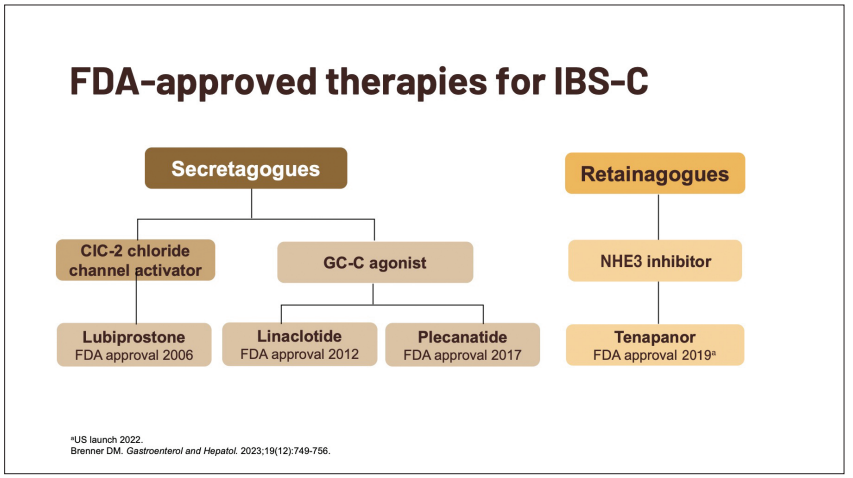
Courtesy of Darren M. Brenner, MD

G&H What are the available FDA-approved therapies and how do their mechanisms of action differ?

DMB There are currently 4 FDA-approved options available for treating IBS-C: the secretagogues lubiprostone, linaclotide, and plecanatide, as well as the retainagogue tenapanor. Lubiprostone gained FDA approval in 2006, followed by linaclotide in 2012, plecanatide in 2017, and tenapanor in 2019 (with its US market launch in 2022).

Secretagogues function by increasing luminal fluid secretion and promoting intestinal transit. Tenapanor is a first-in-class locally acting inhibitor of the sodium/hydrogen exchanger isoform 3 (NHE3). Tenapanor-mediated NHE3 inhibition results in several effects: reduced dietary sodium absorption, leading to water retention in the intestinal lumen and accelerated intestinal transit; decreased intestinal permeability; and diminished visceral hypersensitivity.

Although all 4 therapies accelerate intestinal transit, their distinct mechanisms of action play a crucial role in addressing abdominal sensory symptoms such as pain, discomfort, and bloating. These differences are particularly significant in tailoring treatment to individual needs. Given the multifaceted nature of IBS-C, it is essential to target both abdominal and bowel symptoms comprehensively. Should one class of agents fail to address both abdominal and bowel symptoms, utilizing a therapeutic agent from an alternative class is advisable.



Courtesy of GI Health Foundation

G&H How effective and safe are these therapies in managing both the bowel and abdominal symptoms?

DMB All 4 currently available FDA-approved agents were evaluated in large, pivotal, phase 3 randomized controlled trials. All 4 agents significantly outperformed placebo in terms of overall response and improvement in individual symptoms.

For lubiprostone, an overall responder was defined as a monthly responder for at least 2 of 3 months, with monthly responder defined as a patient 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. For linaclotide, plecanatide, and tenapanor, overall response was defined as at least a 30% improvement from baseline in average daily worst abdominal pain score plus an increase of at least 1 CSBM from

baseline, both in the same week for 6 or more of 12 weeks of treatment.

All 4 agents are associated with common gastrointestinal adverse effects. For lubiprostone, the most common side effect was nausea. For linaclotide, plecanatide, and tenapanor, it was diarrhea.

G&H Are there any predictors of therapy discontinuation/continuation?

DMB A recent study by Shah and colleagues examined the predictors for discontinuation of drug therapy in individuals with IBS-C. Multiple factors were assessed, and overall women and individuals with at least 1 chronic pain condition were less likely to discontinue linaclotide.

G&H Do the AGA and ACG agree on treatment recommendations for IBS-C?

DMB In general, both guidelines align on the use of therapies for IBS-C, but differences arise in the strength of their recommendations. Notably, discrepancies exist regarding PEG laxatives and antispasmodics, with the ACG advising against their use.

The variance in recommendations stems from the methodologies employed in guideline development. The ACG guidelines rely on global symptom response assessments, whereas the AGA guidelines base recommendations on comparisons with no pharmaceutical treatment intervention.

G&H What makes the choice of treatment difficult?

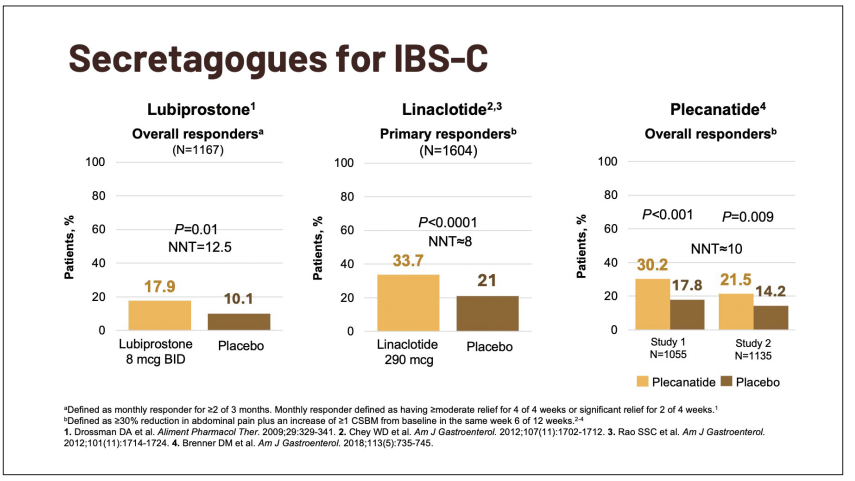
DMB Choosing the right treatment for IBS-C presents numerous challenges owing to several factors. First, our current understanding of IBS-C does not allow for precise targeting of patient symptoms, making it difficult to predict the most effective treatment. Additionally, the lack of head-to-head trials comparing available therapies means we have limited knowledge of their comparative efficacies.

Although network meta-analyses have demonstrated the superiority of all agents over placebo for treating global IBS-C symptoms and abdominal bloating, indirect comparisons have not revealed significant differences between drugs. When treating individual patients, factors such as time to response and side effect profiles must be carefully considered.

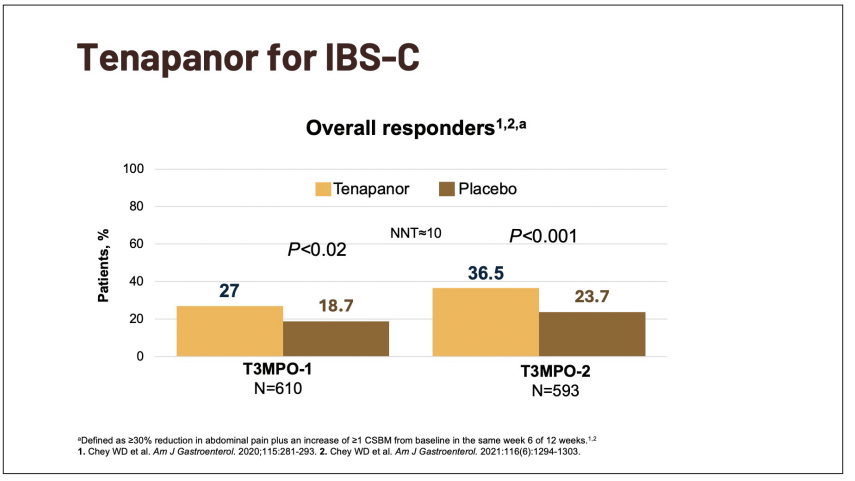
Furthermore, personalized treatment plans should take into account the patient's preferences and biases. Some patients may prefer food-based interventions, behavior-based therapies, alternative medicine approaches, or pharmaceutical treatments. Considering these preferences alongside clinical evidence is crucial for developing effective and patient-centered management plans for IBS-C.

G&H We are seeing increasing incorporation of APPs (advanced practice providers) in provision of care for patients with IBS. What are the drivers of this growth?

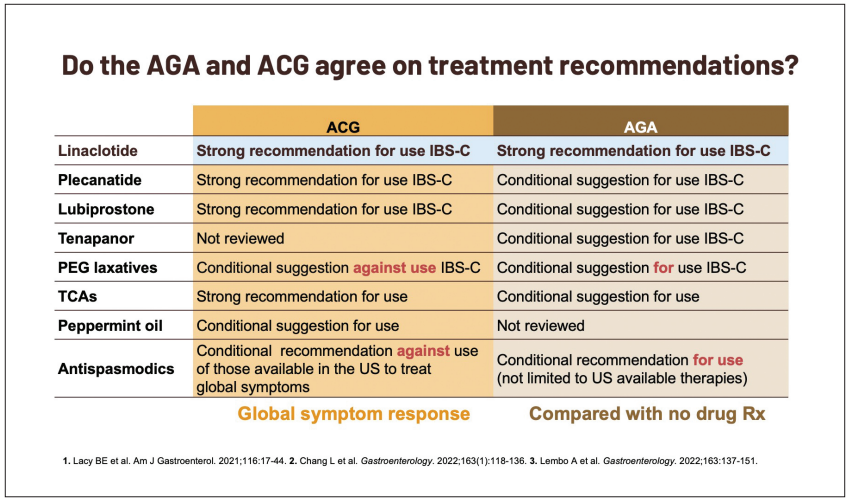
DMB The increased demand for services from APPs in providing care for patients with IBS can be attributed to several factors. These include a shortage of physicians, the rising prevalence of gastrointestinal diseases, an aging population with multiple comorbidities, the introduction of new therapies, procedures, and medications, and a greater number of insured patients seeking health care services.



Courtesy of GI Health Foundation



Courtesy of GI Health Foundation



Courtesy of GI Health Foundation

G&H How can integrating APPs in clinical practice improve the care of patients with IBS?

DMB Multidisciplinary care involving APPs has demonstrated significant benefits for individuals with IBS, driven by several key factors. First, patients with IBS often require dedicated time and compassionate listening, especially when discussing social situations and factors that may exacerbate their anxiety. APPs, with their ability to spend more time with individual patients compared with gastroenterologists, are well suited to provide this personalized attention and support.

Moreover, involving APPs in the care of patients with IBS enhances access to care, improves continuity of care, and reduces wait times for consultations and follow-up visits. This streamlined approach not only ensures that patients receive timely and comprehensive care but also alleviates the burden on gastroenterologists, allowing them to focus on procedures and more complex cases.

By enabling APPs to take on a greater role in patient management, physicians can better meet the increasing demands for endoscopic procedures while also reducing burnout among the entire health care team. This collaborative model of care not only improves patient outcomes but also enhances overall health care delivery by maximizing resources and promoting a more efficient health care system.

G&H Are there any APP collaborative models that can be employed in the clinic?

DMB APPs can play various roles in team-based care for patients with IBS, depending on the clinic or practice model and the needs of the patient population. Some potential roles include follow-up visits, collaborative consultations, and independent consultations.

APPs can conduct follow-up visits with patients after the initial diagnosis is made by a physician. These visits can involve monitoring treatment progress, addressing any concerns or questions the patient may have, and making adjustments to the treatment plan as needed.

APPs and physicians can work together to meet with patients during appointments. This collaborative approach allows for comprehensive assessments and treatment discussions, drawing on the expertise of both health care providers.

Experienced APPs may be capable of conducting initial consultations and follow-up visits independently, assessing patient symptoms, providing education, and implementing treatment plans. They can determine if a referral to a physician is necessary based on the patient's clinical presentation.

The specific model of care may vary between community-based and academic-based institutions, as well as among individual clinics or practices. Each entity should define a model that aligns with their resources, patient population, and organizational goals.

G&H How can we successfully integrate APPs in our clinical practice?

DMB Successful integration of APPs into clinical practice requires comprehensive training and experience. This includes exposure to various aspects of patient care, interdisciplinary collaboration, and opportunities for professional development.

Upfront training for APPs should encompass not only patient interaction skills but also exposure to different specialties involved in the care of patients with IBS. This may include spending time in clinics with gastroenterologists, dieticians, and behavioral therapists to gain a deeper understanding of their roles and how they contribute to patient care.

APPs should have opportunities to collaborate with other health care professionals involved in the management of IBS. This collaboration allows them to better understand the roles of each practitioner, the tools they utilize, and how they approach patient care. This knowledge enables APPs to effectively communicate with patients about what to expect during consultations with different practitioners and to make appropriate referrals based on patient needs.

Engaging APPs in academic settings, such as through organizations like Gastroenterology and Hepatology Advanced Practice Provider (GHAPP), provides opportunities for professional growth and development. This may include participating in lectures, advisory committees, and collaborative research projects with physicians. By contributing to

ABSTRACT SUMMARY Real-World Prescribing Patterns for Pediatric Patients With Functional Constipation and IBS-C

In the United States, IBS-C and functional constipation (FC) are commonly observed in children.[1,2] The most recent guidelines, published in 2014, recommend polyethylene glycol 3350 (PEG) as first-line therapy for pediatric FC; however, there are no such guidelines for pediatric IBS-C. Recently, linaclotide garnered FDA approval for pediatric patients with FC.[3] A retrospective, observational study used a large US claims database to investigate real-world prescribing patterns of health care providers for the treatment of pediatric patients with FC or IBS-C.[4] Eligible patients identified in the Komodo Healthcare Map database were less than 18 years of age and had an ICD-10 code for FC or IBS-C between January 1, 2018 and June 11, 2023.

The study identified 5,149,698 patients with FC and 94,459 patients with IBS-C, of whom 36.0% and 26.3%, respectively, received at least 1 prescription medication for their constipation. PEG was the most commonly prescribed medication for both patients with FC (83.4%) and patients with IBS-C (77.4%), followed by lactulose (20.9% vs 15.2%, respectively), and docusate (5.4% vs 14.8%, respectively). PEG therapy was discontinued in favor of a different prescription medication in 4.9% of patients with FC and 13.9% of patients with IBS-C. The most commonly prescribed second-line medication was lactulose (63.4%) in patients with FC and docusate (33.9%) in patients with IBS-C. Before switching from PEG to the second-line medication, PEG was prescribed for a median 60 days for patients with FC and 84 days for patients with IBS-C.

For pediatric patients with FC, the most common prescribers were pediatricians (39.3%), nurse practitioners or physician assistants (29.0%), and pediatric gastrointestinal specialists (7.9%). For pediatric patients with IBS-C, the most common prescribers were pediatric gastrointestinal specialists (31.0%), nurse practitioners or physician assistants (29.9%), and pediatricians (24.5%).

Limitations of the study include that only prescription information was available from the claims database, and therefore over-the-counter remedies were not included; the data reflect prescriptions that were issued and not necessarily usage by the patient; and the ICD-10 codes could have included patients with occasional constipation, but this was considered unlikely based on sensitivity analysis.

References

1. Robin SG, Keller C, Zwiener R, et al. Prevalence of pediatric functional gastrointestinal disorders utilizing the Rome IV criteria. *J Pediatr.* 2018;195:134-139.
2. Saps M, Nurko S, Benninga MA, et al. A collaborative effort to advance drug development in pediatric constipation and irritable bowel syndrome. *J Pediatr Gastroenterol Nutr.* 2021;73(2):145-149.
3. Linzess (linaclotide) [package insert]. North Chicago, IL: AbbVie, Inc.; June2023.
4. Khlevner J, Liu J, Shakhnovich V, Kosch KJ, Chumpitazi BP, Sanghavi RM. Real-world prescribing patterns for pediatric patients with functional constipation and irritable bowel syndrome with constipation [DDW abstract Su2047]. *Gastroenterol.* 2024;166(6 [suppl 1]).

presentations and publications, APPs can enhance their understanding of IBS and contribute to advancements in the field.

G&H Do you have any overall take-home message from this symposium for clinicians?

DMB Interdisciplinary and integrative care is essential for optimizing outcomes in patients with IBS-C, benefiting both the patients and the health care system as a whole. IBS-C management is inherently complex and multifaceted, requiring a personalized approach tailored to each individual's unique needs and preferences.

Given the multifactorial pathophysiology of IBS-C and the variability in patient presentations, a one-size-fits-all approach is not effective. Instead, a comprehensive care plan that integrates dietary, behavioral, and pharmaceutical interventions offers a more holistic and effective approach to managing symptoms and improving quality of life for patients with IBS-C. This approach not only maximizes treatment efficacy but also enhances patient satisfaction and engagement in their care.

Disclosures

Dr Brenner is a speaker, advisor, and consultant and has participated in educational programs for American Gastroenterological Association (AGA), Anji Pharmaceuticals, Ardelyx, Inc., Continuing Education Alliance, LLC, Continuing Education Company, Inc., Elsevier, Inc., Enova International, Focus Medical Communications, LLC, GI Health Foundation, Gemelli Biotech, Ironwood Pharmaceuticals, Inc., Mahana Therapeutics, Inc., MedForce, Inc., Meetings & Events International, Pri-Med Institute, LLC, Primary Care Education Consortium, RedHill Biopharma Ltd, Salix Pharmaceuticals, Inc., Tactical Advantage Group, University of California, Los Angeles (UCLA), and WebMD, LLC.

IBSRELA (tenapanor) tablets, for oral use

Brief Summary of Full Prescribing Information

WARNING: RISK OF SERIOUS DEHYDRATION IN PEDIATRIC PATIENTS

- **IBSRELA is contraindicated in patients less than 6 years of age; in nonclinical studies in young juvenile rats administration of tenapanor caused deaths presumed to be due to dehydration [*see Contraindications (4), Use in Specific Populations (8.4)*].**
- **Avoid use of IBSRELA in patients 6 years to less than 12 years of age [*see Warnings and Precautions (5.1), Use in Specific Populations (8.4)*].**
- **The safety and effectiveness of IBSRELA have not been established in patients less than 18 years of age [*see Use in Specific Populations (8.4)*].**

1 INDICATIONS AND USAGE

IBSRELA is indicated for treatment of irritable bowel syndrome with constipation (IBS-C) in adults.

4 CONTRAINDICATIONS

IBSRELA is contraindicated in:

- Patients less than 6 years of age due to the risk of serious dehydration [*see Warnings and Precautions (5.1), Use in Specific Populations (8.4)*].
- Patients with known or suspected mechanical gastrointestinal obstruction.

5 WARNINGS AND PRECAUTIONS

5.1 Risk of Serious Dehydration in Pediatric Patients

IBSRELA is contraindicated in patients below 6 years of age. The safety and effectiveness of IBSRELA in patients less than 18 years of age have not been established. In young juvenile rats (less than 1 week old; approximate human age equivalent of less than 2 years of age), decreased body weight and deaths occurred, presumed to be due to dehydration, following oral administration of tenapanor. There are no data available in older juvenile rats (human age equivalent 2 years to less than 12 years).

Avoid the use of IBSRELA in patients 6 years to less than 12 years of age. Although there are no data in older juvenile rats, given the deaths in younger rats and the lack of clinical safety and efficacy data in pediatric patients, avoid the use of IBSRELA in patients 6 years to less than 12 years of age [*see Contraindications (4), Warnings and Precautions (5.2), Use in Specific Populations (8.4)*].

5.2 Diarrhea

Diarrhea was the most common adverse reaction in two randomized, double-blind, placebo-controlled trials of IBS-C. Severe diarrhea was reported in 2.5% of IBSRELA-treated patients [*see Adverse Reactions (6.1)*]. If severe diarrhea occurs, suspend dosing and rehydrate patient.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared with rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety data described below reflect data from 1203 adult patients with IBS-C in two randomized, double-blind, placebo-controlled clinical trials (Trial 1 and Trial 2). Patients were randomized to receive placebo or IBSRELA 50 mg twice daily for up to 52 weeks. Demographic characteristics were comparable between treatment groups in the two trials [*see Clinical Studies (14)*].

Most Common Adverse Reactions

The most common adverse reactions reported in at least 2% of patients in IBSRELA-treated patients and at an incidence greater than placebo during the 26-week double-blind placebo-controlled treatment period of Trial 1 are shown in Table 1.

Table 1: Most Common Adverse Reactions* in Patients With IBS-C in Trial 1 (26 Weeks)

Adverse Reactions	IBSRELA N=293 %	Placebo N=300 %
Diarrhea	16	4
Abdominal Distension	3	<1
Flatulence	3	1
Dizziness	2	<1

*Reported in at least 2% of patients in IBSRELA-treated patients and at an incidence greater than placebo.

The adverse reaction profile was similar during the 12-week double-blind placebo-controlled treatment period of Trial 2 (610 patients: 309 IBSRELA-treated and 301 placebo-treated) with diarrhea (15% with IBSRELA vs 2% with placebo) and abdominal distension (2% with IBSRELA vs 0% with placebo) as the most common adverse reactions.

Adverse Reaction of Special Interest – Severe Diarrhea

Severe diarrhea was reported in 2.5% of IBSRELA-treated patients compared to 0.2% of placebo-treated patients during the 26 weeks of Trial 1 and the 12 weeks of Trial 2 [*see Warnings and Precautions (5.2)*].

Patients with Renal Impairment

In Trials 1 and 2, there were 368 patients (31%) with baseline renal impairment (defined as eGFR less than 90 mL/min/1.73m^2). In patients with renal impairment, diarrhea, including severe diarrhea, was reported in 20% (39/194) of IBSRELA-treated patients and 0.6% (1/174) of placebo-treated patients. In patients with normal renal function at baseline, diarrhea, including severe diarrhea, was reported in 13% (53/407) of IBSRELA-treated patients and 3.5% (15/426) of placebo-treated patients. No other differences in the safety profile were reported in the renally impaired subgroup.

The incidence of diarrhea and severe diarrhea in IBSRELA-treated patients did not correspond to the severity of renal impairment.

Adverse Reactions Leading to Discontinuation

Discontinuations due to adverse reactions occurred in 7.6% of IBSRELA-treated patients and 0.8% of placebo-treated patients during the 26 weeks of Trial 1 and the 12 weeks of Trial 2. The most common adverse reaction leading to discontinuation was diarrhea: 6.5% of IBSRELA-treated patients compared to 0.7% of placebo-treated patients.

Less Common Adverse Reactions

Adverse reactions reported in less than 2% of IBSRELA-treated patients and at an incidence greater than placebo during the 26 weeks of Trial 1 and the 12 weeks of Trial 2 were: rectal bleeding and abnormal gastrointestinal sounds.

Hyperkalemia

In a trial of another patient population with chronic kidney disease (defined by eGFR from 25 to 70 mL/min/1.73m^2) and Type 2 diabetes mellitus, three serious adverse reactions of hyperkalemia resulting in hospitalization were reported in 3 patients (2 IBSRELA-treated patients and 1 placebo-treated patient).

7 DRUG INTERACTIONS

7.1 OATP2B1 Substrates

Tenapanor is an inhibitor of intestinal uptake transporter, OATP2B1 [*see Clinical Pharmacology (12.3)*]. Drugs which are substrates of OATP2B1 may have reduced exposures when concomitantly taken with IBSRELA. Monitor for signs related to loss of efficacy and adjust the dosage of concomitantly administered drug as needed.

Enalapril is a substrate of OATP2B1. When enalapril was coadministered with tenapanor (30 mg twice daily for five days, a dosage 0.6 times the recommended dosage), the peak exposure (C_{max}) of enalapril and its active metabolite, enalaprilat, decreased by approximately 70% and total systemic exposures (AUC) decreased by approximately 50% to 65% compared to when enalapril was administered alone [*see Clinical Pharmacology (12.3)*].

Monitor blood pressure and increase the dosage of enalapril, if needed, when IBSRELA is coadministered with enalapril.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

Tenapanor is minimally absorbed systemically, with plasma concentrations below the limit of quantification (less than 0.5 ng/mL) following oral administration [*see Clinical Pharmacology (12.3)*]. Therefore, maternal use is not expected to result in fetal exposure to the drug. The available data on IBSRELA exposure from a small number of pregnant women have not identified any drug associated risk for major birth defects, miscarriage, or adverse maternal or fetal outcomes. In reproduction studies with tenapanor in pregnant rats and rabbits, no adverse fetal effects were observed in rats at 0.1 times the maximum recommended human dose and in rabbits at doses up to 8.8 times the maximum recommended human dose (based on body surface area).

Data

Animal Data

In an embryofetal development study in rats, tenapanor was administered orally to pregnant rats during the period of organogenesis at dose levels of 1, 10 and 30 mg/kg/day. Tenapanor doses of 10 and 30 mg/kg/day were not tolerated by the pregnant rats and was associated with mortality and moribundity with body weight loss. The 10 and 30 mg/kg dose group animals were sacrificed early, and the fetuses were not examined for intrauterine parameters and fetal morphology. No adverse fetal effects were observed in rats at 1 mg/kg/day (approximately 0.1 times the maximum recommended human dose) and in rabbits at doses up to 45 mg/kg/day (approximately 8.8 times the maximum recommended human dose, based on body surface area).

In a pre- and post-natal developmental study in mice, tenapanor at doses up to 200 mg/kg/day (approximately 9.7 times the maximum recommended human dose, based on body surface area) had no effect on pre- and post-natal development.

8.2 Lactation

Risk Summary

There are no data available on the presence of tenapanor in either human or animal milk, its effects on milk production or its effects on the breastfed infant. Tenapanor is minimally absorbed systemically, with plasma concentrations below the limit of quantification (less than 0.5 ng/mL) following oral administration [*see Clinical Pharmacology (12.3)*]. The minimal systemic absorption of tenapanor will not result in a clinically relevant exposure to breastfed infants. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for IBSRELA and any potential adverse effects on the breastfed infant from IBSRELA or from the underlying maternal condition.

8.4 Pediatric Use

IBSRELA is contraindicated in patients less than 6 years of age. Avoid IBSRELA in patients 6 years to less than 12 years of age [*see Contraindications (4), Warnings and Precautions (5.1)*].

The safety and effectiveness of IBSRELA in patients less than 18 years of age have not been established.

In nonclinical studies, deaths occurred in young juvenile rats (less than 1-week-old rats approximate human age equivalent of less than 2 years of age) following oral administration of tenapanor, as described below in Juvenile Animal Toxicity Data.

Juvenile Animal Toxicity Data

In a 21-day oral dose range finding toxicity study in juvenile rats, tenapanor was administered to neonatal rats [post-natal day (PND) 5] at doses of 5 and 10 mg/kg/day. Tenapanor was not tolerated in male and female pups and the study was terminated on PND 16 due to mortalities and decreased body weight (24% to 29% reduction in females at the respective dose groups and 33% reduction in males in the 10 mg/kg/day group, compared to control).

In a second dose range finding study, tenapanor doses of 0.1, 0.5, 2.5, or 5 mg/kg/day were administered to neonatal rats from PND 5 through PND 24. Treatment-related mortalities were observed at 0.5, 2.5, and 5 mg/kg/day doses. These premature deaths were observed as early as PND 8, with majority of deaths occurring between PND 15 and 25. In the 5 mg/kg/day group, mean body weights were 47% lower for males on PND 23 and 35% lower for females on PND 22 when compared to the controls. Slightly lower mean tibial lengths (5% to 11%) were noted in males and females in the 0.5, 2.5, and 5 mg/kg/day dose groups on PND 25 and correlated with the decrements in body weight noted in these groups. Lower spleen, thymus, and/or ovarian weights were noted at the 0.5, 2.5, and 5 mg/kg/day doses. Tenapanor-related gastrointestinal distension and microscopic bone findings of increased osteoclasts, eroded bone, and/or decreased bone in sternum and/or femorotibial joint were noted in males and females in the 0.5, 2.5, and 5 mg/kg/day dose groups [*see Contraindications (4), Warnings and Precautions (5.1)*].

8.5 Geriatric Use

Of the 1203 patients in placebo-controlled clinical trials of IBSRELA, 100 (8%) were 65 years of age and older. No overall differences in safety or effectiveness were observed between elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

10 OVERDOSAGE

Based on nonclinical data, overdose of IBSRELA may result in gastrointestinal adverse effects such as diarrhea as a result of exaggerated pharmacology with a risk for dehydration if diarrhea is severe or prolonged [*see Warnings and Precautions (5.1)*].

17 PATIENT COUNSELING INFORMATION

Advise the patients to read the FDA-approved patient labeling (Medication Guide).

Diarrhea

Instruct patients to stop IBSRELA and contact their healthcare provider if they experience severe diarrhea [*see Warnings and Precautions (5.2)*].

Accidental Ingestion

Accidental ingestion of IBSRELA in children, especially children less than 6 years of age, may result in severe diarrhea and dehydration. Instruct patients to store IBSRELA securely and out of reach of children [*see Contraindications (4), Warnings and Precautions (5.1)*].

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A Therapy With a Different Mechanism of Action for Adults With IBS-C

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INDICATION

IBSRELA (tenapanor) is indicated for the treatment of Irritable Bowel Syndrome with Constipation (IBS-C) in adults.

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF SERIOUS DEHYDRATION IN PEDIATRIC PATIENTS

IBSRELA is contraindicated in patients less than 6 years of age; in nonclinical studies in young juvenile rats administration of tenapanor caused deaths presumed to be due to dehydration. Avoid use of IBSRELA in patients 6 years to less than 12 years of age. The safety and effectiveness of IBSRELA have not been established in patients less than 18 years of age.

CONTRAINDICATIONS

- IBSRELA is contraindicated in patients less than 6 years of age due to the risk of serious dehydration.
- IBSRELA is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction.

WARNINGS AND PRECAUTIONS

Risk of Serious Dehydration in Pediatric Patients

- IBSRELA is contraindicated in patients below 6 years of age. The safety and effectiveness of IBSRELA in patients less than 18 years of age have not been established. In young juvenile rats (less than 1 week old; approximate human age equivalent of less than 2 years of age), decreased body weight and deaths occurred, presumed to be due to dehydration, following oral administration of tenapanor. There are no data available in older juvenile rats (human age equivalent 2 years to less than 12 years).
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Diarrhea

Diarrhea was the most common adverse reaction in two randomized, double-blind, placebo-controlled trials of IBS-C. Severe diarrhea was reported in 2.5% of IBSRELA-treated patients. If severe diarrhea occurs, suspend dosing and rehydrate patient.

MOST COMMON ADVERSE REACTIONS

The most common adverse reactions in IBSRELA-treated patients (incidence ≥2% and greater than placebo) were: diarrhea (16% vs 4% placebo), abdominal distension (3% vs <1%), flatulence (3% vs 1%) and dizziness (2% vs <1%).

Reference: IBSRELA [prescribing information]. Waltham, MA: Ardelyx, Inc.; 2022.

Please see Brief Summary of full Prescribing Information on the following page.

ardelyx