Poster P0809

Tenapanor Improves Abdominal Bloating Symptoms in Patients With IBS-C Experiencing Moderate to Severe Bloating

Kyle Staller,[1] Yang Yang,[2] Suling Zhao,[2] Susan Edelstein[2]

[1]Massachusetts General Hospital, Boston, MA, USA; [2]Ardelyx, Inc., Waltham, MA, USA

Introduction

- Abdominal bloating is one of the most bothersome symptoms of irritable bowel syndrome with constipation (IBS-C),[1] but it is not included in the Rome IV diagnostic criteria.[2]
- Tenapanor is a first-in-class, minimally systemic inhibitor of intestinal sodium/hydrogen exchanger isoform 3 approved by the United States Food and Drug Administration for treatment of IBS-C in adults.[3]
- Previous studies have demonstrated that tenapanor improves abdominal symptoms in IBS-C.[4]
- This post hoc analysis assessed the effect of tenapanor on abdominal bloating in patients with IBS-C with moderate to severe bloating at baseline.

Methods

- Data were pooled from 3 randomized, placebo-controlled clinical trials: a phase 2b study (NCT01923428) and the phase 3 T3MPO-1 (NCT02621892) and T3MPO-2 (NCT02686138) studies, in which patients with IBS-C who met the Rome III criteria were randomized to receive tenapanor or placebo twice a day (bid) for 12 or 26 weeks.[5-7]
  - Study-level data from the tenapanor 50 mg bid and placebo groups of intent-to-treat analysis sets for the first 12 weeks were included in this post hoc analysis.
- A phone diary was used to collect data on daily abdominal bloating on a scale of 0 to 10, which was categorized as <4 (mild), ≥4 to <8 (moderate), and ≥8 (severe).
- This analysis examined patients with moderate to severe bloating at baseline, calculated as the mean of average weekly bloating scores of week −2 and week −1.
  - For a valid study week (ie, a study week with at least 4 days of abdominal bloating reporting), the average weekly bloating score was calculated with the following formula: sum of daily abdominal bloating scores in that study week divided by number of days with abdominal bloating reported in that study week.
- Efficacy endpoints included change from baseline in average weekly bloating score and time to onset of achieving an abdominal bloating response defined as achieving a ≥30% (or ≥50%) reduction from baseline in average weekly bloating score.

Results

Patients

Table 1: Demographics and Baseline Characteristics of Patients With Moderate to Severe Bloating at Baseline (Pooled ITT Analysis Set)[a]

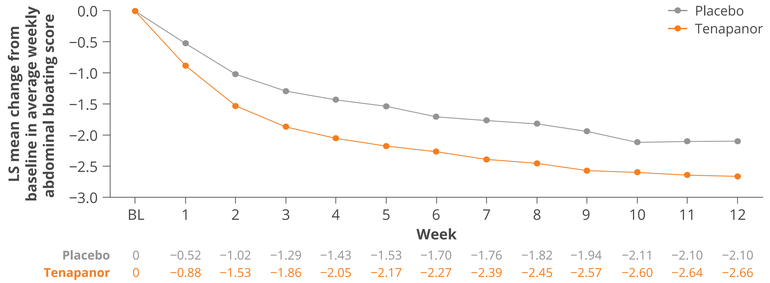
	Placebo bid (N=625)	Tenapanor 50 mg bid (N=628)	Overall (N=1253)
Age at informed consent, mean (SD), y	44.8 (13.5)	45.5 (12.9)	45.2 (13.2)
Sex, n (%)			
Female	523 (83.7)	520 (82.8)	1043 (83.2)
Race, n (%)			
Asian	10 (1.6)	22 (3.5)	32 (2.6)
Black or African American	201 (32.2)	187 (29.8)	388 (31.0)
White	397 (63.5)	407 (64.8)	804 (64.2)
Other[b]	17 (2.7)	12 (1.9)	29 (2.3)
Ethnicity, n (%)			
Hispanic	160 (25.6)	176 (28.0)	336 (26.8)
Non-Hispanic	465 (74.4)	452 (72.0)	917 (73.2)
Body mass index, mean (SD), kg/m²	29.9 (6.8)	30.1 (7.0)	30.0 (6.9)
Duration of IBS-C symptoms before randomization, mean (SD), y[c]	11.6 (11.8)	11.2 (11.5)	11.4 (11.7)
Baseline weekly score for abdominal bloating, mean (SD)	6.92 (1.49)	6.90 (1.53)	6.91 (1.51)

bid, twice a day; IBS-C, irritable bowel syndrome with constipation; ITT, intent to treat.
[a]Average weekly abdominal bloating score ≥4 (N=1253). [b]Includes American Indian or Alaska Native, Multiple, Unknown, and Other. [c]Five patients in the T3MPO-1 study did not report the start date of their IBS-C symptoms; data reported for the following numbers of patients: placebo (N=621), tenapanor (N=627), and overall (N=1248).

Change in Abdominal Bloating Over a 12-Week Treatment Period

- Tenapanor treatment resulted in a consistently greater reduction from baseline in average weekly bloating score compared with placebo over the first 12 weeks (**Figure 1**) (all $P \leq 0.0010$).
- The least-squares (LS) mean change at week 8 was −2.45 for tenapanor and −1.82 for placebo, with an LS mean difference of −0.64 ($P<0.0001$).
- At week 12, the LS mean change was −2.66 for tenapanor and −2.10 for placebo, with an LS mean difference of −0.57 ($P=0.0003$).

Figure 1: LS Mean Change From Baseline in Average Weekly Abdominal Bloating Score in Patients With Moderate to Severe Bloating at Baseline (Pooled Analysis Set)



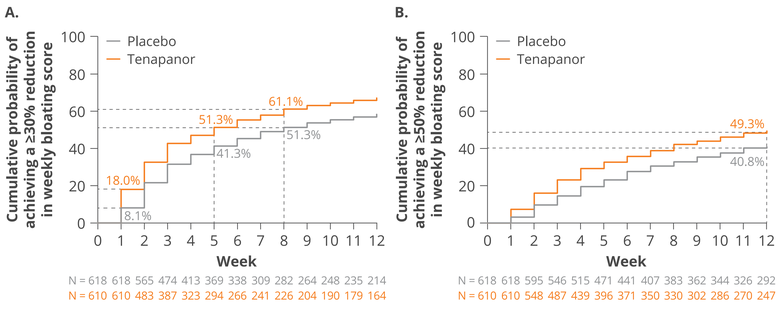
	BL	1	2	3	4	5	6	7	8	9	10	11	12
Placebo	0	−0.52	−1.02	−1.29	−1.43	−1.53	−1.70	−1.76	−1.82	−1.94	−2.11	−2.10	−2.10
Tenapanor	0	−0.88	−1.53	−1.86	−2.05	−2.17	−2.27	−2.39	−2.45	−2.57	−2.60	−2.64	−2.66

BL, baseline; LS, least-squares.

Time to First Abdominal Bloating Response in a 12-Week Treatment Period

- Patients treated with tenapanor had faster improvement in bloating compared with those treated with placebo.
- The median time to onset of achieving a ≥30% reduction in weekly bloating score was 5 weeks (95% CI, 4.0-6.0) for tenapanor-treated patients versus 8 weeks (95% CI, 7.0-10.0) for placebo-treated patients (log-rank test $P<0.0001$; **Figure 2A**).
- By week 1, the cumulative probability of achieving a ≥30% reduction in weekly bloating response was 18.0% with tenapanor versus 8.1% with placebo (**Figure 2A**).
- More patients achieved a weekly ≥50% bloating response by week 12 when treated with tenapanor than patients receiving placebo (log-rank test $P=0.0007$; **Figure 2B**).

Figure 2: Time to Onset of Achieving a (A) ≥30% and (B) ≥50% Reduction in Weekly Bloating Score in Patients With Moderate to Severe Bloating at Baseline (Pooled Analysis Set)



Safety

- The adverse events occurring during the individual studies have been previously reported.[5-7]
- In this population, 37.8% of all patients experienced a treatment-emergent adverse event (TEAE). In the tenapanor group, the most common TEAE related to study drug was diarrhea (**Table 2**).

Table 2: Overview of TEAEs in Patients With Moderate to Severe Bloating at Baseline (Pooled Analysis Set)

TEAEs, n (%)	Placebo bid (N=625)	Tenapanor 50 mg bid (N=628)	Overall (N=1253)
Any TEAE	207 (33.1)	267 (42.5)	474 (37.8)
Study drug–related TEAEs	54 (8.6)	124 (19.7)	178 (14.2)
Serious TEAEs	7 (1.1)	8 (1.3)	15 (1.2)
Deaths	0	0	0
Study drug–related TEAEs by preferred term[a]			
Diarrhea	10 (1.6)	82 (13.1)	92 (7.3)
Flatulence	10 (1.6)	14 (2.2)	24 (1.9)
TEAEs leading to study drug discontinuation by preferred term[b]	7 (1.1)	45 (7.2)	52 (4.2)
Diarrhea	4 (0.6)	37 (5.9)	41 (3.3)

bid, twice a day; TEAE, treatment-emergent adverse event.
[a]TEAEs by the preferred term occurring in ≥2.0% of patients in the tenapanor group and at a higher incidence than in the placebo group. [b]TEAEs leading to study drug discontinuation by the preferred term occurring in ≥2.0% of patients in the tenapanor group and at a higher incidence than in the placebo group.

Limitations

- There is currently no standardized classification for categorizing bloating severity (ie, mild, moderate, or severe).
- This post hoc analysis may not be representative of the real-world population with IBS-C due to the stringent criteria involved in the enrollment of patients with IBS-C into clinical trials.
- Patient drug adherence is usually higher in a clinical setting than in clinical practice.

Conclusions

Tenapanor may be effective in reducing bloating–a persistent and bothersome symptom in a large percentage of patients with IBS-C.

Onset of a clinically meaningful reduction was seen as early as week 1 and was sustained through the duration of treatment.

Disclosures

This study was supported by Ardelyx, Inc. Kyle Staller has received funding from Ardelyx and ReStalsis and served as a consultant for Ardelyx, Anji, Ferring, Gemelli, Laborie, Mahana, Salix, and Takeda. Yang Yang, Suling Zhao, and Susan Edelstein are employees of Ardelyx, Inc.

Acknowledgments

Medical writing support for the development of this poster, under the direction of the authors, was provided by Ashfield MedComms, an Inizio company, and funded by Ardelyx, Inc.

References

1. Neri L et al. *Neurogastroenterol Motil*. 2016;28:581-91.
2. Lacy BE et al. *Gastroenterology*. 2016;150:1393-407.
3. IBSRELA (tenapanor hydrochloride). Prescribing information. Ardelyx Inc.; 2025.
4. Lembo AJ et al. *Am J Gastroenterol*. 2024;119:937-45.
5. Chey WD et al. *Am J Gastroenterol*. 2017;112:763-74.
6. Chey WD et al. *Am J Gastroenterol*. 2020;115:281-93.
7. Chey WD et al. *Am J Gastroenterol*. 2021;116:1294-303.

MED-US--2500493 10/2025

IBSRELA® (tenapanor) is indicated for 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. *[see PI Contraindications (4), Use in Specific Populations (8.4)]*.**
- **Avoid use of IBSRELA in patients 6 years to less than 12 years of age. *[see PI Warnings and Precautions (5.1), Use in Specific Populations (8.4)]*.**
- **The safety and effectiveness of IBSRELA have not been established in pediatric patients less than 18 years of age. *[see PI Use in Specific Populations (8.4)]*.**

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).

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.

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%).

For additional safety information, including the Boxed Warning, please see full Prescribing Information: click here.

IBS-C, irritable bowel syndrome with constipation.

IBSRELA (tenapanor hydrochloride). Prescribing information. Ardelyx, Inc; 2025.
Available at: https://www.ibsrela-hcp.com/PI