

Safety and Tolerability of Tenapanor in Pediatric Patients With Irritable Bowel Syndrome With Constipation: An Analysis of Blinded Safety Data From a Phase 3 Study and Its Open-Label Extension

Thomas Wallach,¹ Mihaela Ringheanu,² Ana Roig Cantisano,³ Yang Yang,⁴ Karishma Raju,⁴ Jocelyn Tabora,⁴ Susan Edelstein⁵

¹SUNY Downstate Health Sciences University, Brooklyn, NY, USA; ²Texas Digestive Specialists, Harlingen, TX, USA; ³Florida Pharmaceutical Research & Associates, Miami, FL, USA; ⁴Ardelyx, Inc., Newark, CA, USA; ⁵Ardelyx, Inc., Waltham, MA, USA

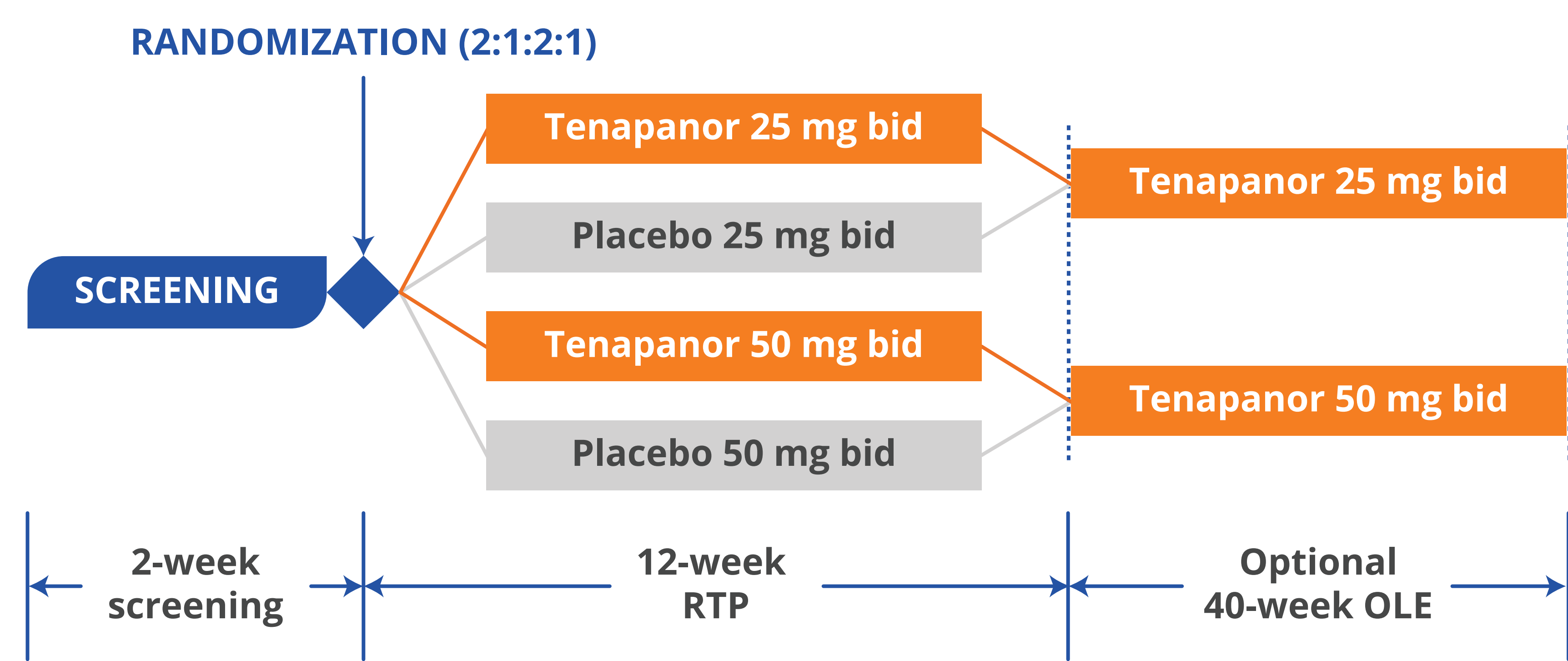
Introduction

- Irritable bowel syndrome (IBS) is a gastrointestinal disorder that affects approximately 5% of children in the United States, with IBS with constipation (IBS-C) being the most common subtype.^{1,2}
- Tenapanor is a first-in-class, minimally absorbed inhibitor of intestinal sodium/hydrogen exchanger isoform 3 approved for the treatment of IBS-C in adults.³
- Tenapanor improves symptoms of IBS-C by increasing sodium and water retention in the gut, which facilitates softer stool consistency and faster transit. It also decreases intestinal permeability to macromolecules and reduces visceral hypersensitivity and abdominal pain in animal models.³
- In adult clinical trials, tenapanor demonstrated efficacy and was generally well tolerated, with diarrhea being the most commonly reported adverse event (AE).³
- The phase 3 R-ALLY (NCT05643534) study is ongoing and plans to enroll approximately 180 patients with the goal of evaluating the efficacy, safety, and tolerability of tenapanor in pediatric patients aged ≥12 and <18 years.⁴
- Patients who complete the 12-week R-ALLY randomized treatment period (RTP) may be able to enter a 40-week open-label safety extension (OLE) study (NCT05905926).⁵
- Here, we present preliminary, blinded, interim safety data from R-ALLY and its OLE.

Methods

- R-ALLY (TEN-01-304) is a randomized, double-blind, placebo-controlled study in patients (aged ≥12 to <18 years) meeting the Rome IV criteria for child/adolescent diagnosis of IBS-C (**Figure 1**).
 - During the 12-week RTP, patients are assessed on site every 2 or 4 weeks for safety.
- Patients who complete the 12-week RTP may enter a 40-week OLE study (TEN-01-306) (**Figure 1**).
 - Titrations are allowed between 25 mg bid and 50 mg bid during the OLE.
 - Patients are assessed on site approximately every 6 weeks for safety.

Figure 1: Study Design for Phase 3 R-ALLY and Optional 40-Week OLE Study



bid, twice daily; OLE, open-label extension; RTP, randomized treatment period.

Results

12-Week RTP

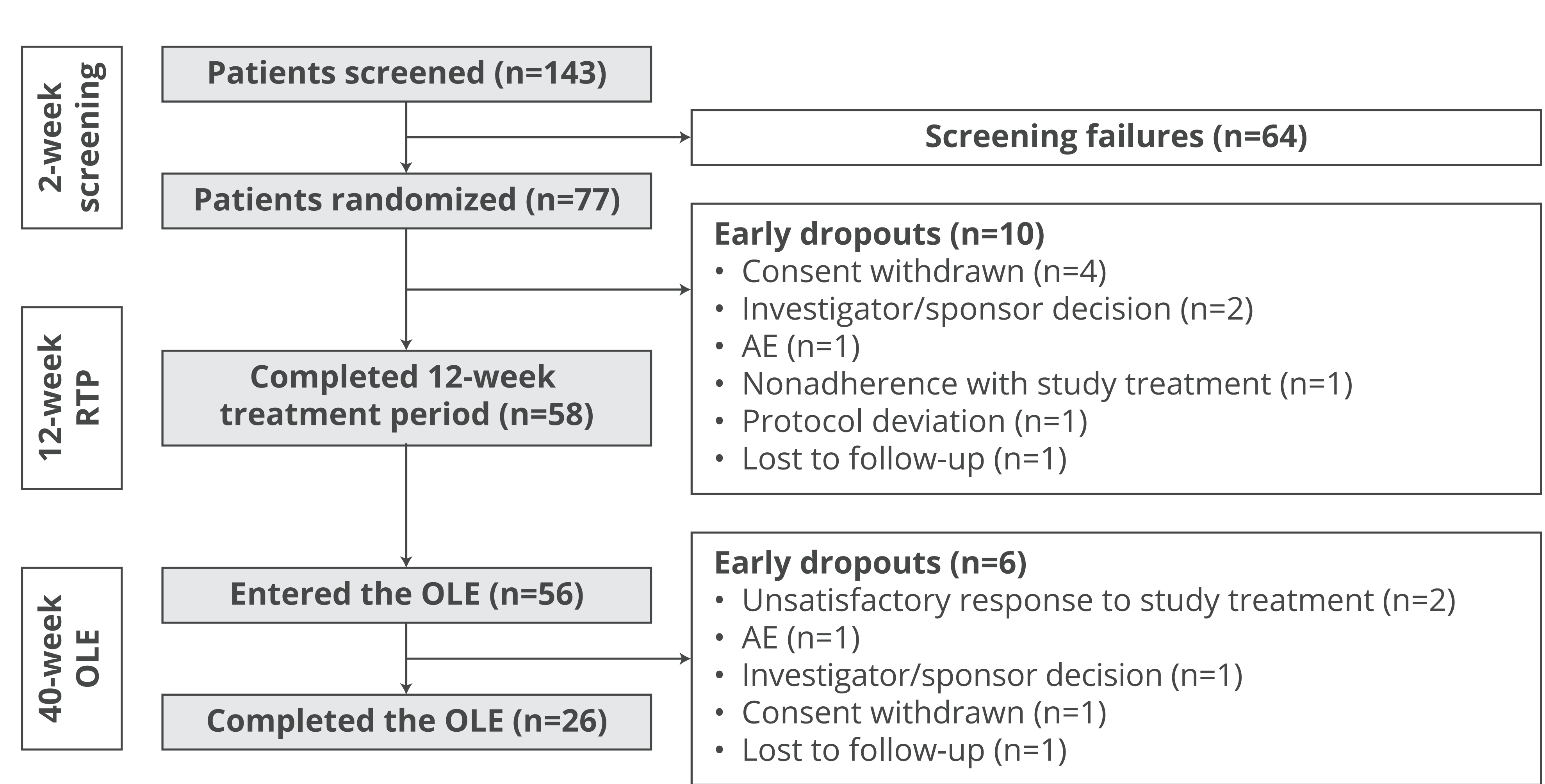
- Table 1** summarizes the interim baseline demographics and treatment-emergent AEs (TEAEs) for the safety analysis set (SAS), which included 77 randomized and treated patients (**Figure 2**).
- All TEAEs were resolved or resolving and considered unrelated to study drug, except diarrhea.
 - One TEAE of severe diarrhea led to study drug discontinuation.

Table 1: R-ALLY Baseline Demographics and Blinded Data on TEAEs (Safety Analysis Set)

Baseline demographics (N=77)	
Age at informed consent, mean (SD), y	14.2 (1.71)
Female, n (%)	48 (62.3)
Race, n (%)	
White	54 (70.1)
Asian	11 (14.3)
Black or African American	9 (11.7)
Other	2 (2.6)
Multiple	1 (1.3)
Not Hispanic or Latino, n (%)	37 (48.1)
IBS-C duration at randomization, median (range), y	2.940 (0.05–17.26)
TEAEs (N=77) - all groups combined	
Patients with any..., n (%)	
TEAE	23 (29.9)
Serious TEAE	0
Severe TEAE	3 (3.9)
Drug-related TEAE	11 (14.3)
Severe, drug-related TEAE	1 ^a (1.3)
TEAE leading to study drug discontinuation	1 ^a (1.3)
Reported term	
Diarrhea/loose stool	12 (15.6)
Cold	4 (5.2)
Nausea	2 (2.6)
Worsening in IBS-C symptoms	2 (2.6)
Abdominal pain	1 (1.3)
Anal irritation	1 (1.3)
Anorexia	1 (1.3)
Bacterial vaginosis	1 (1.3)
Chest pain	1 (1.3)
Elevated protein	1 (1.3)
Gastroenteritis	1 (1.3)
Headache	1 (1.3)
Runny nose	1 (1.3)
Urinary tract infection	1 (1.3)
Vomiting	1 (1.3)

^aFrom the same patient, who reported a TEAE of severe diarrhea that led to study drug discontinuation. IBS-C, irritable bowel syndrome with constipation; TEAE, treatment-emergent adverse event.

Figure 2: Overview of Patient Flow Through the Study as of November 1, 2024



AE, adverse event; OLE, open-label extension; RTP, randomized treatment period.

40-Week OLE

- Table 2** summarizes the interim baseline demographics and TEAEs for the SAS, which included 56 enrolled and treated patients (**Figure 2**).
- All TEAEs were resolved except 2 mild events: 1 overflow incontinence and 1 diarrhea.
- All TEAEs were considered unrelated to study drug except diarrhea.

Table 2: TEN-01-306 Baseline Demographics and TEAEs (Safety Analysis Set)

Baseline demographics (N=56)	
Age at 306 informed consent, mean (SD), y	14.8 (1.64)
Female, n (%)	35 (62.5)
Race, n (%)	
White	44 (78.6)
Asian	7 (12.5)
Black or African American	4 (7.1)
Other	1 (1.8)
Not Hispanic or Latino, n (%)	25 (44.6)
IBS-C duration at 306 enrollment, median (range), y	4.050 (0.28–15.41)
TEAEs (N=56)	
Patients with any..., n (%)	
TEAE	16 (28.6)
Serious TEAE	0
Severe TEAE	1 (1.8)
Drug-related TEAE ^a	3 (5.4)
TEAE leading to study drug discontinuation	1 (1.8)
Reported term	
Diarrhea/loose stool	4 (7.1)
Influenza	4 (7.1)
Headache	2 (3.6)
Abrasions, left lower leg	1 (1.8)
Cough	1 (1.8)
COVID-19	1 (1.8)
Dysmenorrhea (menstrual cramps)	1 (1.8)
Epistaxis	1 (1.8)
Fever	1 (1.8)
Labial abscess	1 (1.8)
Nausea	1 (1.8)
Overflow incontinence	1 (1.8)
Worsening in IBS-C symptoms	1 (1.8)
Yeast infection	1 (1.8)

^aNo patients reported a severe, drug-related TEAE in TEN-01-306. IBS-C, irritable bowel syndrome with constipation; TEAE, treatment-emergent adverse event.

Limitation

- Phase 3 safety data are from a blinded, pooled data set that included placebo and tenapanor.

Conclusions

Preliminary blinded safety results of the R-ALLY study in pediatric patients with IBS-C and its open-label safety extension are consistent with those from previous studies of tenapanor in adult patients with IBS-C.

Diarrhea was the only AE related to study drug.

As of November 1, 2024, no unexpected safety concerns have been observed.

References

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Disclosures

Thomas Wallach is a consultant for Nutricia and has ownership interest in Kiwi Bioscience. Mihaela Ringheanu is a speaker for Nutricia. Ana Cantisano has nothing to disclose. Yang Yang, Karishma Raju, Jocelyn Tabora, and Susan Edelstein are full-time employees of Ardelyx, Inc.



Dr. Wallach can be contacted for further information at Thomas.Wallach@downstate.edu

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