

# Rifaximin Improves Both Fecal Urgency and Stool Consistency in Adults With Irritable Bowel Syndrome With Diarrhea: A Composite Endpoint Analysis of Two Randomized, Phase 3 Trials

Brooks D. Cash, MD<sup>1</sup>; Kyle Staller, MD<sup>2</sup>; Leila Neshatian, MD, MSc<sup>3</sup>; Christopher Allen, MS<sup>4</sup>; Zeev Heimanson, PharmD<sup>4</sup>; Ali Rezaie, MD, MSc<sup>5</sup>

<sup>1</sup>University of Texas Health Science Center, Houston, TX; <sup>2</sup>Massachusetts General Hospital, Boston, MA; <sup>3</sup>Stanford University School of Medicine, Stanford, CA; <sup>4</sup>Salix Pharmaceuticals, Bridgewater, NJ; <sup>5</sup>Cedars-Sinai Medical Center, Los Angeles, CA

## BACKGROUND

- Irritable bowel syndrome (IBS) is a chronic disorder of gut-brain interaction characterized by recurrent abdominal pain and altered bowel habits<sup>1,2</sup>
- In patients with IBS with diarrhea (IBS-D), fecal urgency and loose stools are common, bothersome symptoms<sup>3,4</sup>
- Fecal urgency in patients with IBS-D is associated with more frequent and looser bowel movements,<sup>5</sup> and is an independent predictor of patient-reported IBS severity<sup>6</sup>
- Rifaximin (Xifaxan®, Salix Pharmaceuticals, Bridgewater, NJ) is indicated in the United States for the treatment of adults with IBS-D<sup>7</sup> and has demonstrated efficacy versus placebo for improvement of abdominal and bowel symptoms, including fecal urgency and stool consistency<sup>8,9</sup>

## AIM

- To evaluate rifaximin treatment for simultaneously improving IBS-D symptoms of fecal urgency and loose/watery stool consistency as a unique composite bowel symptom endpoint

## METHODS

- Pooled post hoc analysis of 2 identically designed, phase 3, randomized, double-blind, placebo-controlled trials<sup>8</sup>
- Patient population included adults with IBS-D with a daily mean stool consistency score of  $\geq 3.5$  (Table 1) and mean daily abdominal pain/discomfort and bloating scores of 2 to 4.5 (range: 0 ["not at all"] to 6 ["a very great deal"]) during a screening period of  $\geq 7$  days (prior to treatment initiation)
  - Additional symptom assessment included fecal urgency, based on patient response to the daily question "Have you felt or experienced a sense of urgency today?"

**Table 1. Stool Consistency Score Scale**

Score	Description
1	Very hard
2	Hard
3	Formed
4	Loose
5	Watery

- Patients were treated with rifaximin 550 mg three times daily or placebo for 2 weeks, followed by a 4-week treatment-free phase to assess response and an additional 6 weeks of treatment-free follow-up (ie, 10 weeks of post-treatment follow-up)

- Composite bowel symptom responders were defined as patients who simultaneously achieved a  $\geq 30\%$  decrease from baseline in the percentage of days with fecal urgency and had a mean weekly stool consistency score of  $< 4$  on a 5-point scale (Table 1)
  - Response was assessed weekly
- Sustained composite responders were defined as responders in the initial 4-week post-treatment period who also maintained the composite response for  $\geq 3$  of 6 additional treatment-free weeks of follow-up
- Data were analyzed using last observation carried forward
- P values were calculated using the Cochran-Mantel-Haenszel method, adjusting for analysis center

## RESULTS

- A total of 1258 adults with IBS-D (rifaximin [n=624]; placebo [n=634]) were included in the analysis
- Similar values at baseline were observed for rifaximin and placebo groups for the percentage of days with fecal urgency (82%), mean daily stool consistency score (3.9), and mean number of daily bowel movements (3.0; Table 2)

**Table 2. Demographic and Baseline Characteristics**

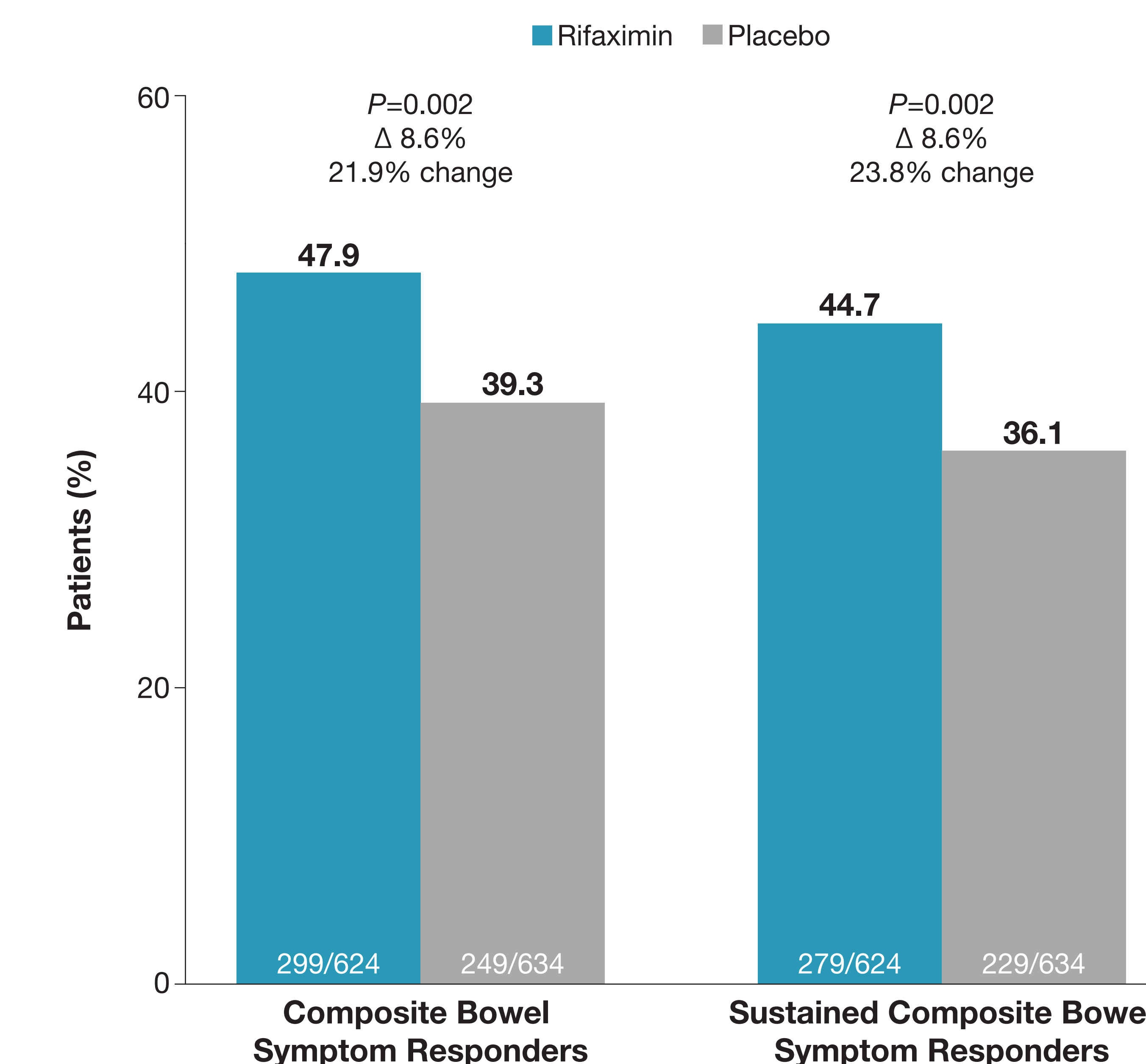
Characteristic	Rifaximin 550 mg TID (n=624)	Placebo (n=634)
Age, y, mean (SD)	46.0 (14.4)	45.9 (14.6)
Female, n (%)	462 (74.0)	447 (70.5)
Race, n (%)		
White	563 (90.2)	582 (91.8)
Black	45 (7.2)	44 (6.9)
Other	16 (2.6)	8 (1.3)
BMI, kg/m <sup>2</sup> , mean (SD)	29.2 (6.9)	28.8 (6.7)
Days with fecal urgency, %*	81.6	82.5
Daily stool consistency score, mean (SD) <sup>†</sup>	3.9 (0.3)	3.9 (0.3)
Daily bowel movements, mean (SD)	3.0 (1.5)	3.0 (1.5)
Daily abdominal pain/discomfort score, mean (SD) <sup>‡</sup>	3.2 (0.7)	3.3 (0.7)
Daily bloating score, mean (SD) <sup>‡</sup>	3.3 (0.8)	3.3 (0.7)

\*Calculated using the following formula:  $100 \times (\text{number of days with a sense of urgency with any bowel movement} \div \text{number of days with bowel movements})$ .  
<sup>†</sup>5-point scale (1 = "very hard"; 2 = "hard"; 3 = "formed"; 4 = "loose"; 5 = "watery").  
<sup>‡</sup>7-point scale (0 = "not at all"; 2 = "somewhat"; 3 = "moderately"; 4 = "a good deal"; 5 = "a great deal"; 6 = "a very great deal").  
 BMI = body mass index; TID = three times daily.

## RESULTS

- A significantly greater percentage of patients treated with rifaximin were composite bowel symptom responders for  $\geq 2$  of the first 4 weeks post-treatment compared with placebo (47.9% vs 39.3%, respectively;  $P=0.002$ ; Figure 1)

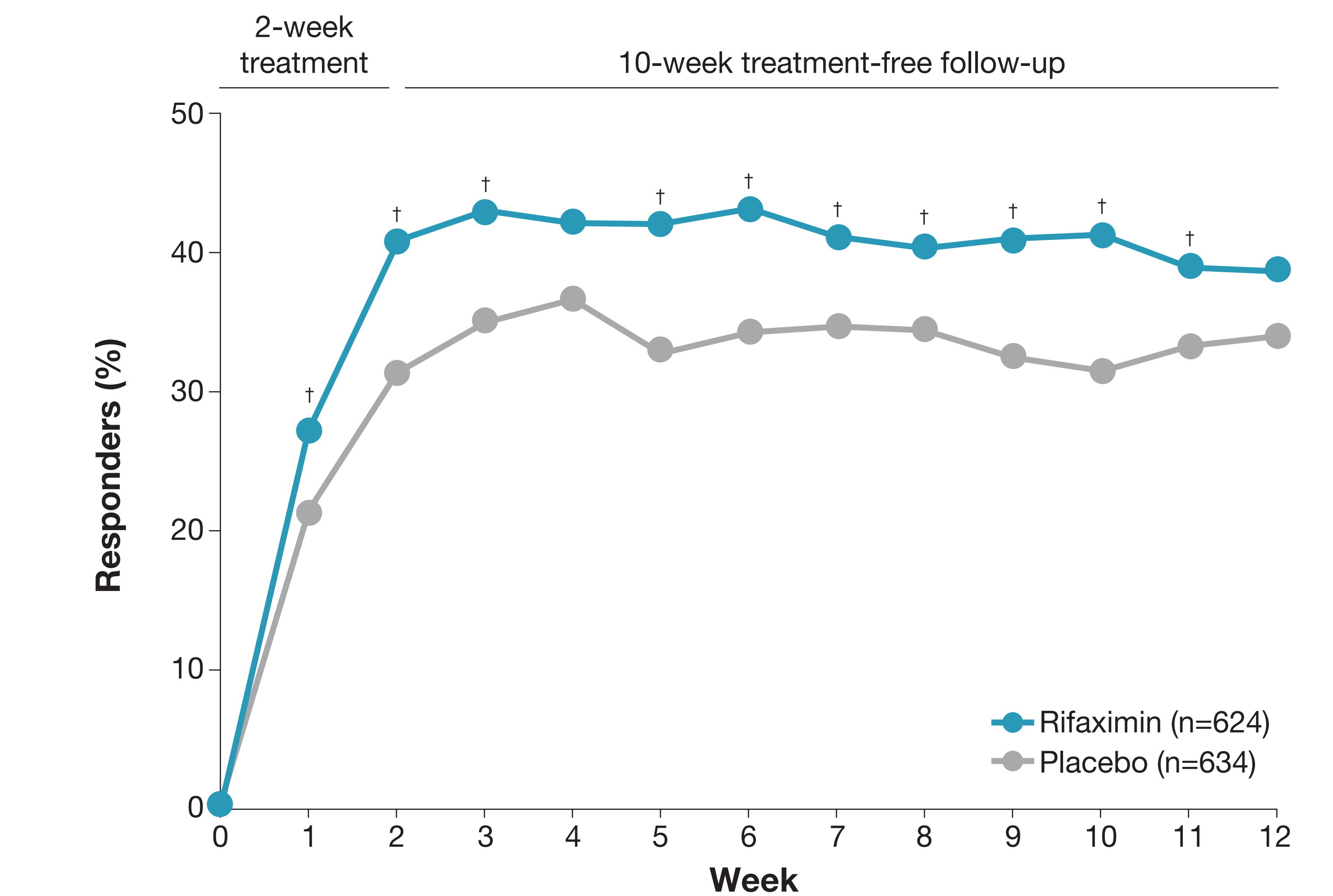
**Figure 1. Composite Bowel Symptom Responders\* and Sustained Composite Bowel Symptom Responders<sup>†</sup>**



\*Patients who simultaneously achieved a  $\geq 30\%$  decrease from baseline in the percentage of days with fecal urgency and a mean weekly average stool consistency score of  $< 4$  for  $\geq 2$  of the first 4 weeks post-treatment.  
<sup>†</sup>Patients who simultaneously achieved a  $\geq 30\%$  decrease from baseline in the percentage of days with fecal urgency and a mean weekly average stool consistency score of  $< 4$  for  $\geq 2$  of the first 4 weeks post-treatment who also maintained both responses for  $\geq 3$  of 6 additional treatment-free weeks (up to 10 weeks post-treatment).

- A significantly greater percentage of patients treated with rifaximin who were composite bowel symptom responders during  $\geq 2$  of the first 4 weeks post-treatment maintained response during  $\geq 3$  of the additional 6 weeks of treatment-free follow-up (up to 10 weeks post-treatment) versus placebo group (44.7% vs 36.1%, respectively;  $P=0.002$ ; Figure 1)
- In addition, a higher percentage of patients receiving rifaximin were composite bowel symptom responders compared with placebo when analyzed weekly (Figure 2)

**Figure 2. Percentage of Composite Bowel Symptom Responders\* by Week**



\*Patients who simultaneously achieved a  $\geq 30\%$  decrease from baseline in percentage of days with fecal urgency and a mean weekly stool consistency score of  $< 4$ .  
<sup>†</sup> $P < 0.05$  vs placebo.

## CONCLUSION

- A 2-week course of daily rifaximin treatment significantly and simultaneously improved fecal urgency and stool consistency compared with placebo in adults with IBS-D

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