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# Rifaximin Improves Both Abdominal Pain and Bloating in Patients With Irritable Bowel Syndrome With Diarrhea: a Composite Endpoint Analysis of Two Phase 3, Randomized, Placebo-Controlled Trials

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## BACKGROUND

- Abdominal pain and bloating are 2 of the most common and bothersome symptoms experienced by patients with irritable bowel syndrome with diarrhea (IBS-D)[1-3]
- Thresholds for clinically meaningful outcomes for bloating (both independently and in combination with other abdominal symptoms [ie, pain]) have not been clearly delineated
- The nonsystemic antibiotic rifaximin is indicated in the United States for the treatment of adults with IBS-D[4] and has been shown to improve IBS-D symptoms, including abdominal pain and stool consistency[5,6]
- Additional data on the efficacy of rifaximin for simultaneously improving abdominal pain and bloating, 2 of the most bothersome IBS symptoms, are desirable

## AIM

- To evaluate the efficacy of rifaximin in improving abdominal pain and bloating in patients with IBS-D using various thresholds to define response

## METHODS

- Pooled post hoc analysis of two phase 3, identically designed, randomized, double-blind placebo-controlled trials (ClinicalTrials.gov identifiers: NCT00731679; NCT00724126)[6]
- **Patient population:** adults with IBS-D with mean daily abdominal pain and bloating scores of 2 to 4.5 (7-point scale)
- Patients rated daily abdominal pain and bloating separately, using a scale of 0 ("not at all") to 6 ("a very great deal")
- Patients received rifaximin 550 mg three times daily (TID) or placebo for 2 weeks, followed by a 4-week, treatment-free period to evaluate treatment response
- Individual response and composite response for both abdominal pain (mean weekly improvements from baseline of ≥30%, ≥40%, and ≥50%) and bloating (mean weekly improvements from baseline of ≥1, ≥2, or ≥3 points; or ≥30%, ≥40%, or ≥50%) for ≥2 of the first 4 weeks post-treatment were evaluated
- *P* values were determined using the Cochran-Mantel-Haenszel method, adjusting for analysis center

## RESULTS

- The pooled analysis included 1258 patients (rifaximin [n=624], placebo [n=634]); mean age was 45.9 years, and 72.3% were female (**Table**)
- Similar baseline scores for rifaximin and placebo groups were observed for mean daily abdominal pain (3.2–3.3) and mean daily bloating (3.2–3.3)

**Table. Demographic and Baseline Characteristics**

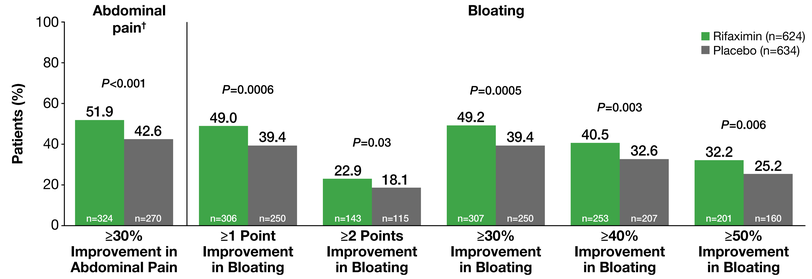
| Parameter | Rifaximin (n=624) | Placebo (n=634) |
|---|---|---|
| **Age, y** | | |
| Mean (SD) | 46.0 (14.4) | 45.9 (14.6) |
| Range | 18–88 | 18–82 |
| **Female, n (%)** | 462 (74.0) | 447 (70.5) |
| **Race, n (%)** | | |
| White | 563 (90.2) | 582 (91.8) |
| Black | 45 (7.2) | 44 (6.9) |
| Other | 16 (2.6) | 8 (1.3) |

SD = standard deviation.

- Findings for the individual components of response were:
  - A significantly higher percentage of patients treated with rifaximin had a ≥30% improvement from baseline in abdominal pain versus placebo (**Figure 1**)[6]
  - For each bloating response definition, a significantly greater percentage of patients receiving rifaximin responded to treatment versus those receiving placebo (**Figure 1**)

## RESULTS

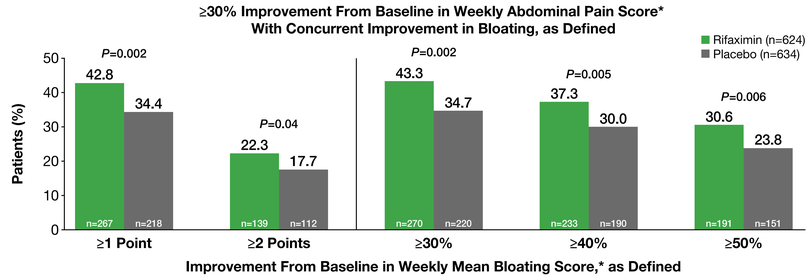
**Figure 1. Individual Component Abdominal Pain and Bloating Responses* in Patients With IBS-D**




*For ≥2 of the first 4 weeks post-treatment.
†Data from Pimentel M, et al.[6]

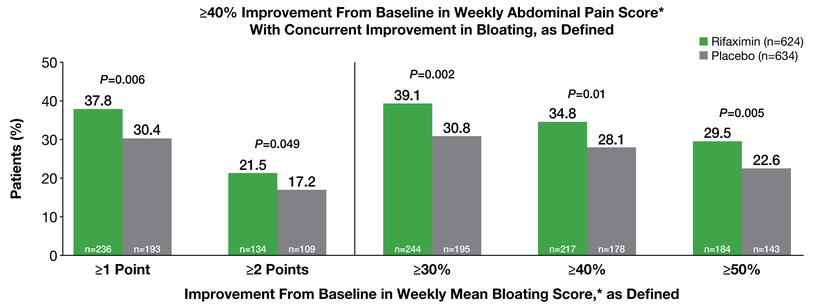
- For the composite endpoint analysis, using varied definitions of response, a significantly greater percentage of patients treated with rifaximin were responders for abdominal pain and bloating versus placebo for ≥2 of the first 4 weeks post-treatment (**Figures 2-4**)

**Figure 2. Composite Abdominal Pain Response (≥30% Improvement) and Bloating Response (Varied Definitions) in Patients With IBS-D**



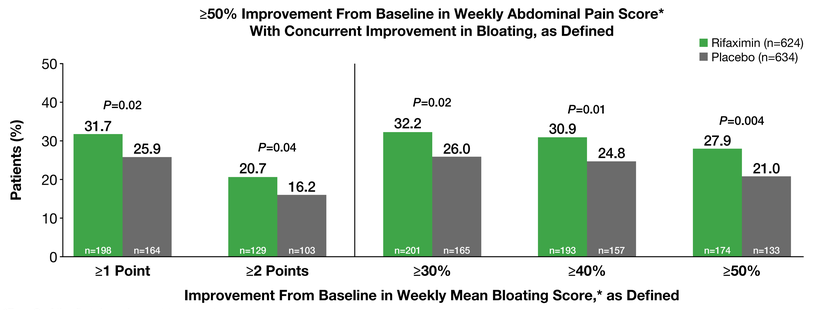

*For ≥2 of the first 4 weeks post-treatment.

**Figure 3. Composite Abdominal Pain Response (≥40% Improvement) and Bloating Response (Varied Definitions) in Patients With IBS-D**




*For ≥2 of the first 4 weeks post-treatment.

**Figure 4. Composite Abdominal Pain Response (≥50% Improvement) and Bloating Response (Varied Definitions) in Patients With IBS-D**




*For ≥2 of the first 4 weeks post-treatment.

## CONCLUSIONS

- **A 2-week course of rifaximin led to significant improvements in both abdominal pain and bloating in adults with IBS-D**
- **This finding was consistent across multiple thresholds used to define response, including more rigorous abdominal pain thresholds that exceed the current guidance standard (≥30% improvement from baseline) of the US Food and Drug Administration[7]**

**REFERENCES:** **1.** Lacy BE, et al. *Gastroenterology.* 2016;150(6):1393-1407. **2.** Törnblom H, et al. *United European Gastroenterol J.* 2018;6(9):1417-1427. **3.** Su AM, et al. *Neurogastroenterol Motil.* 2014;26(1):36-45. **4.** Xifaxan® (rifaximin) tablets, for oral use [package insert]. Bridgewater, NJ: Salix Pharmaceuticals; 2020. **5.** Lembo A, et al. *Gastroenterology.* 2016;151(6):1113-1121. **6.** Pimentel M, et al. *N Engl J Med.* 2011;364(1):22-32. **7.** US Department of Health and Human Services, Food and Drug Administration, Center for Drug Evaluation and Research. 2012. Available at: https://www.fda.gov/media/78622/download.

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