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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

Brian E. Lacy, MD, PhD[1]; Lin Chang, MD[2]; Satish S. C. Rao, MD, PhD[3]; Zeev Heimanson, PharmD[4]; Gregory S. Sayuk, MD, MPH[5]

[1]Mayo Clinic, Jacksonville, FL; [2]David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, CA; [3]Augusta University, Medical College of Georgia, Augusta, GA; [4]Salix Pharmaceuticals, Bridgewater, NJ; [5]St. Louis Veterans Affairs Medical Center, St. Louis, MO

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)

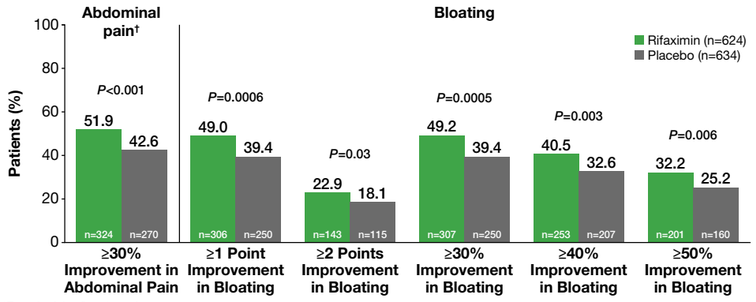
Table. Demographic and Baseline Characteristics

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**)

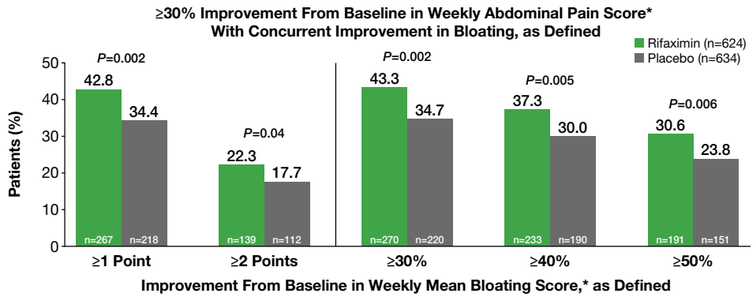
Figure 1. Individual Component Abdominal Pain and Bloating Responses* in Patients With IBS-D



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

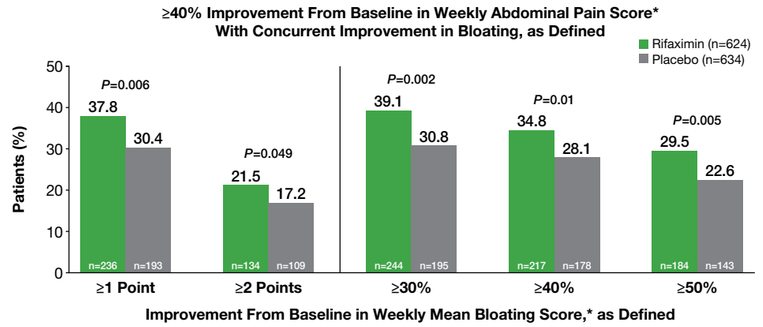
- For the composite endpoint analysis, using varied definitions of response, a significantly greater percentage of patients treated with rifaximin were responders for abdominal pain and bloating versus placebo for ≥2 of the first 4 weeks post-treatment (**Figures 2-4**)

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



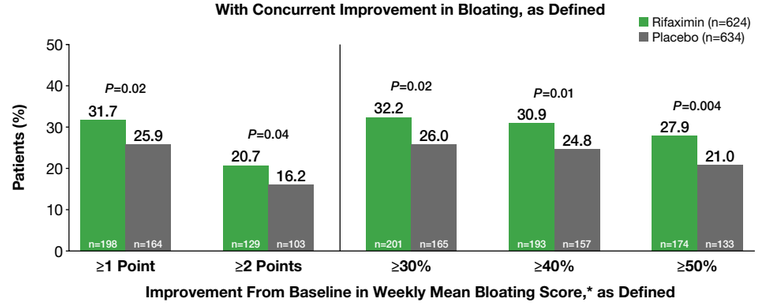
*For ≥2 of the first 4 weeks post-treatment.

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]**

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