

The Strong Association Between Bloating, Abdominal Pain, and Global Irritable Bowel Syndrome (IBS) Symptom Scores in IBS With Diarrhea: A Phase 3 Trial Pooled Correlation Analysis of Individual Symptoms

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BACKGROUND

- Although recurrent abdominal pain and altered stool consistency/frequency are diagnostic criteria for irritable bowel syndrome (IBS), other symptoms (eg, bloating) are common and bothersome¹⁻³
- Rifaximin (Xifaxan®, Salix Pharmaceuticals, Bridgewater, NJ) is indicated in the United States for the treatment of adults with IBS with diarrhea (IBS-D)⁴ and has been shown to improve multiple IBS-D symptoms, including abdominal pain, bloating, and stool consistency^{5,6}
- Given the need to address multiple symptoms concurrently in patients with IBS-D, understanding potential relationships between improvement in abdominal pain, bloating, stool consistency, and global IBS symptoms may help guide treatment of these patients

AIM

- To assess potential relationships between improvement in abdominal pain, bloating, stool consistency, and global IBS symptoms in patients with IBS-D

METHODS

- Pooled post hoc analysis of two phase 3, identically designed, randomized, double-blind, placebo-controlled trials⁵
- Patient population included adults with IBS-D with mean daily abdominal pain/discomfort and bloating scores, rated separately, of 2 to 4.5 and a daily mean stool consistency score of ≥ 3.5 (evaluated over a ≥ 7 -day screening period)
 - Daily abdominal pain/discomfort and bloating assessed separately using a 7-point scale: 0 (“not at all”) to 6 (“a very great deal”)
 - Daily stool consistency assessed using a 5-point scale: 1 (“very hard”) to 5 (“watery”)
- Fecal urgency was assessed daily, based on patients’ yes/no responses to “Have you felt or experienced a sense of urgency today?”
- Global IBS symptoms were also assessed daily (“In regards to all your symptoms of IBS; on scale of 0 [“not at all”] to 6 [“a very great deal”], how bothersome were your symptoms of IBS today?”)
- Patients were treated with rifaximin 550 mg three times daily (TID) or placebo for 2 weeks followed by a 10-week treatment-free follow-up period
- Pearson correlation analyses compared change from baseline in abdominal pain/discomfort, bloating, stool consistency, or fecal urgency and global IBS symptoms (overall [12 weeks] or weekly)
 - A coefficient (*r*) value of >0.70 to 1.00 was considered a strong positive correlation (>0.50 - 0.70 [moderate] and ≤ 0.50 [weak-to-negligible])

RESULTS

- The pooled analysis included 1258 patients (rifaximin [n=624], placebo [n=634]; **Table 1**)

Table 1. Demographic and Baseline Characteristics

Parameter	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)
White race, n (%)	563 (90.2)	582 (91.8)
BMI, kg/m ² , mean (SD)	29.2 (6.9)	28.8 (6.7)
Daily abdominal pain/discomfort score, mean (SD)*	3.3 (0.7)	3.3 (0.7)
Daily bloating score, mean (SD)*	3.3 (0.8)	3.3 (0.7)
Daily stool consistency score, mean (SD)†	3.9 (0.3)	3.9 (0.3)
Days with fecal urgency, %, mean (SD)‡	81.6 (22.5)	82.5 (22.4)

*7-point scale (0 = “not at all”; 1 = “hardly”; 2 = “somewhat”; 3 = “moderately”; 4 = “a good deal”; 5 = “a great deal”; 6 = “a very great deal”).

†5-point scale (1 = “very hard”; 2 = “hard”; 3 = “formed”; 4 = “loose”; 5 = “watery”).

‡Calculated using the following formula: $100 \times (\text{number of days with sense of urgency with any bowel movement} \div \text{number of days with bowel movement})$. BMI = body mass index; TID = three times daily.

- A strong positive correlation was observed over time between changes from baseline for bloating and abdominal pain/discomfort scores, for bloating and global IBS symptom scores, and for abdominal pain/discomfort and global IBS symptom scores, whether calculated as an average weekly or daily symptom value ($r \geq 0.78$; **Table 2**)
- There was a moderate correlation between global IBS symptom scores and stool consistency score (calculated as an average weekly or daily symptom score) and between global IBS symptoms scores and the percentage of days with fecal urgency ($r \geq 0.53$ to ≤ 0.60)

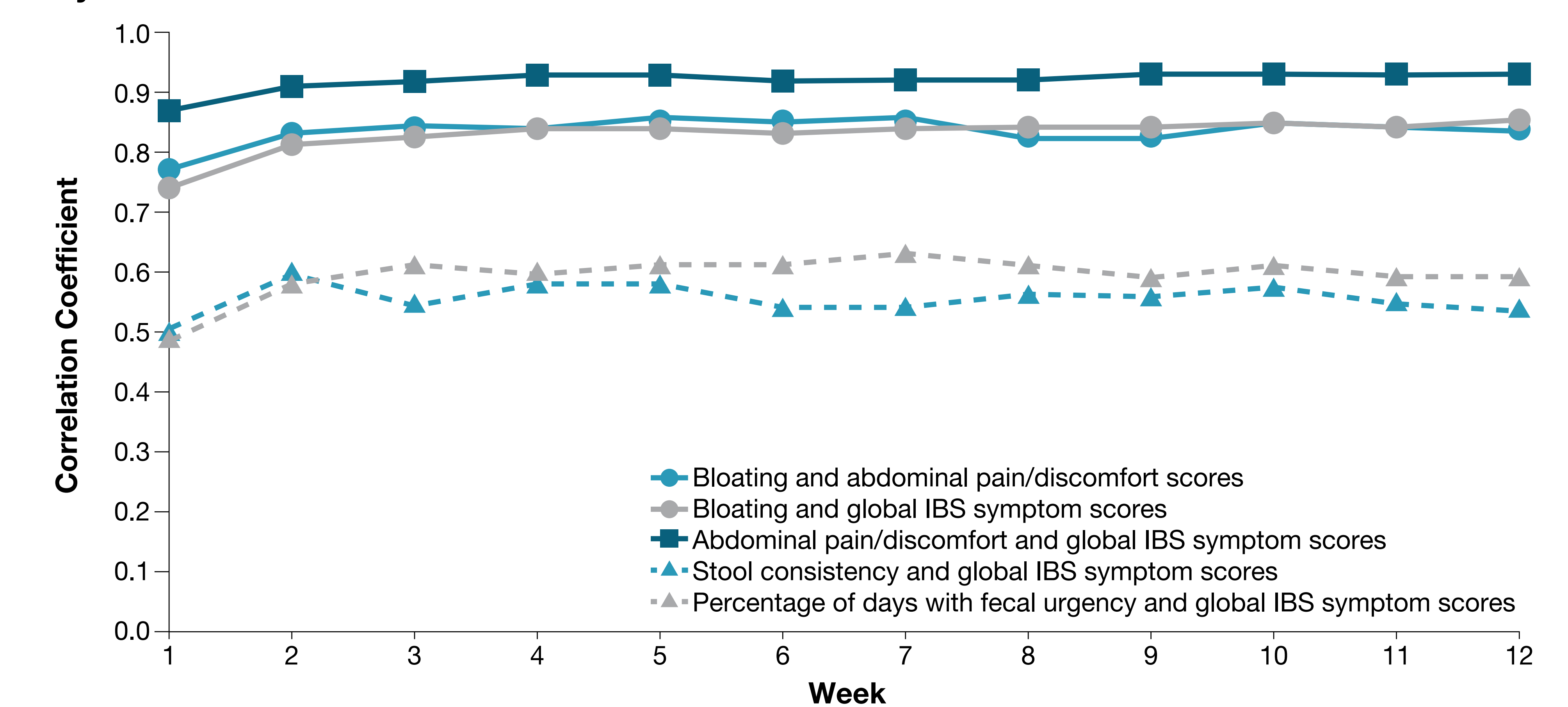
Table 2. Overall Correlations Between Change From Baseline in IBS Symptom Scores

Symptom Comparison	Pearson Correlation Coefficient, <i>r</i>	
	Weekly Average Symptom Scores	Daily Symptom Scores
Bloating and abdominal pain/discomfort scores	0.84	0.78
Bloating and global IBS symptom scores	0.84	0.79
Abdominal pain/discomfort and global IBS symptom scores	0.92	0.88
Stool consistency and global IBS symptom scores	0.56	0.53
Percentage of days with fecal urgency and global IBS symptom scores	0.60	—*

*Due to definition, not assessed daily. IBS = irritable bowel syndrome.

- A weekly comparison of correlations between the various symptoms was consistent for Weeks 2 through 12 (**Figure**)

Figure. Correlation Coefficients for Weekly Average Symptom Score Comparisons, By Week



IBS = irritable bowel syndrome.

CONCLUSIONS

- Bloating and abdominal pain/discomfort are key symptoms in patients with IBS-D
- These 2 symptoms strongly correlated with each other and with global IBS symptom scores in this study
- Bloating and abdominal pain/discomfort may have a greater effect on patient perception of global IBS symptoms than altered stool consistency or fecal urgency
- Therefore, effective therapies for IBS-D should target bloating in addition to abdominal pain/discomfort and diarrhea

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