POSTER NUMBER

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Rifaximin Is Efficacious for the Treatment of Irritable Bowel Syndrome With Diarrhea in Adults Previously Treated With Other IBS Medications

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INTRODUCTION

- A variety of gastrointestinal-targeted therapies, such as antidiarrheals and antispasmodics, are frequently tried to manage symptoms of irritable bowel syndrome with diarrhea (IBS-D) but only target select symptoms[1-4]
- The gastrointestinal microbiota of patients with IBS-D demonstrate compositional and quantitative differences compared with that of healthy individuals[5-6]
- Rifaximin 500 mg (Xifaxan®, Salix Pharmaceuticals, Bridgewater, NJ) is a nonsystemic antibiotic that may target the gastrointestinal dysbiosis potentially associated with symptoms of IBS-D[7]; rifaximin is indicated in the United States and Canada for the treatment of adults with IBS-D[8]
  - Rifaximin 550 mg three times daily (TID) is administered as a short-course (2-week) of therapy, with up to 2 additional 2-week courses to manage symptom recurrence, if needed
- Three phase 3, randomized, double-blind studies have demonstrated the efficacy and safety of rifaximin versus placebo for improving multiple symptoms of IBS-D, including a composite endpoint of abdominal pain plus stool consistency[9,10]
- Data regarding rifaximin efficacy after nonresponse to other IBS-D medications are limited

OBJECTIVE

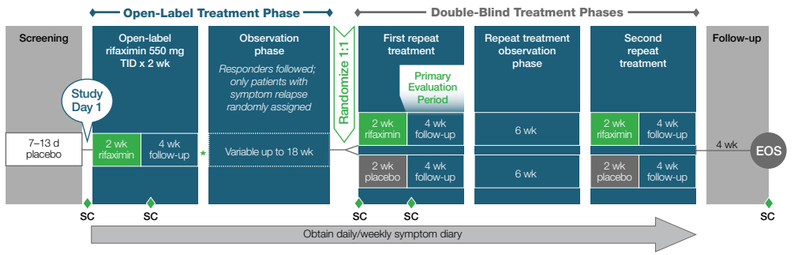
- To assess the efficacy of rifaximin for IBS-D in adults who previously tried other IBS medications

METHODS

Study Design and Patient Population

- Post hoc analysis of data from a phase 3, randomized, double-blind, placebo-controlled, repeat treatment trial (TARGET 3)[9]
- Adults with IBS-D (Rome III criteria) with mean daily abdominal pain score ≥3 (score range, 0-10), bloating score ≥3 (score range, 0-6), and ≥2 days/week with Bristol Stool Scale (BSS) type 6 or 7 (mushy or watery) stool during a placebo-screening phase were eligible (Figure 1)[9]
  - Patients with a medical history of IBS medication use before the study were included in the post hoc analysis

Figure 1. Study Design



EOS = end of study; SC = stool sample collection; TID = three times daily.
Adapted with permission from Lembo A, et al. *Gastroenterology.* 2016;151:1113-1121.[9] © Elsevier. https://creativecommons.org/licenses/by-nc-nd/4.0/.

- Patients who responded to a 2-week course of open-label rifaximin 550 mg TID and who then experienced symptom recurrence during an 18-week treatment-free observation phase were randomly assigned to receive 2 courses of double-blind rifaximin 550 mg TID or placebo for 2 weeks; each double-blind repeat treatment course was separated by 10 weeks and the second course was administered regardless of response status following the first repeat treatment[9]

Assessments

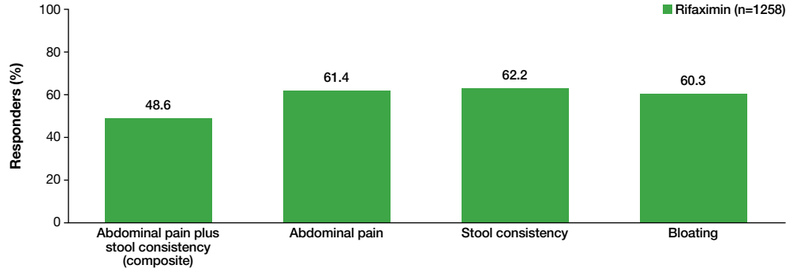
- Composite responders (primary endpoint per protocol[9]; primary evaluation period): defined as percentage of patients simultaneously achieving weekly response for abdominal pain (≥30% decrease from baseline in mean weekly pain score) and stool consistency (≥50% decrease from baseline in number of days/week with BSS type 6 or 7 stool) during ≥2 of the first 4 weeks post-treatment
  - Responders for individual components of the composite endpoint (abdominal pain, stool consistency) were also determined
- Bloating responders: percentage of patients with ≥1-point decrease from baseline in weekly mean score during ≥2 of the first 4 weeks post-treatment
- Sustained responders (double-blind treatment phase): patients who responded to the first treatment (primary evaluation phase) and continued to have a response through the end of the second repeat treatment phase (ie, 12 weeks [6 weeks of observation, 2 weeks of second repeat treatment, 4 weeks of follow-up])
- Last observation carried forward approach was used; treatment differences were determined using Chi-square test (composite; individual abdominal pain and stool consistency) or the Cochran-Mantel-Haenszel method adjusted for center and time to open-label recurrence (bloating)

RESULTS

Open-Label Treatment Phase

- For the open-label population (n=2579), the most commonly reported prior IBS medications were loperamide (22.6%), dicyclomine (10.4%), bismuth subsalicylate (8.1%), and hyoscyamine (6.8%)
- A total of 1258 (48.8%) patients who had taken IBS medications prior to study entry were eligible for the open-label efficacy analysis; ~50% were open-label responders for the composite endpoint and >60% were responders for the individual components of the composite endpoint of abdominal pain and stool consistency (Figure 2)

Figure 2. Response in Patients With History of Prior IBS Medication Use (Open-Label Population)



IBS = irritable bowel syndrome.

Double-Blind Treatment Phase

- 370 patients with a history of prior IBS medication use, who responded to open-label rifaximin and experienced IBS symptom recurrence during an 18-week, treatment-free observation phase, were randomly assigned to receive double-blind treatment with rifaximin (n=185) or placebo (n=185; Table 1)

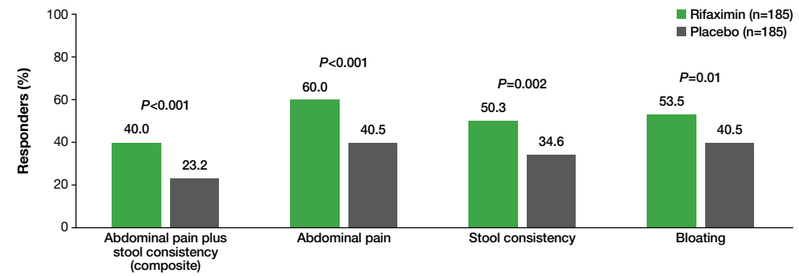
Table 1. Demographics and Baseline Disease Characteristics (Double-Blind Population)

Characteristic	Rifaximin (n=185)	Placebo (n=185)
Age, y, mean (SD)	48.4 (15.0)	45.1 (14.3)
Female, n (%)	134 (72.4)	132 (71.4)
Race, n (%)		
White	159 (85.9)	166 (89.7)
Black	18 (9.7)	13 (7.0)
Other	8 (4.3)	6 (3.2)
Years since first onset of IBS symptoms, mean (SD)	12.6 (11.9)	11.9 (11.5)
Years since diagnosis with IBS, mean (SD)	6.8 (10.5)	5.1 (6.5)
Average daily score, mean (SD)*		
Abdominal pain	5.8 (1.7)	5.6 (1.6)
Bloating	4.2 (1.0)	4.1 (0.9)
IBS symptoms	4.3 (1.0)	4.2 (0.9)
Number of daily bowel movements, mean (SD)	3.8 (2.2)	3.8 (2.2)
Days with BSS type 6/7 stool in a week, mean (SD)	4.9 (1.8)	4.9 (1.6)

*At study entry for patients eventually randomly assigned to double-blind treatment phase.
BSS = Bristol Stool Scale; IBS = irritable bowel syndrome; SD = standard deviation.

- A significantly greater percentage of patients with prior IBS medication use treated with rifaximin versus placebo were abdominal pain plus stool consistency responders (P<0.001), responders to the individual components of the composite endpoint of abdominal pain (P<0.001) and stool consistency (P=0.002), and bloating responders (P=0.01; Figure 3)

Figure 3. Response in Patients With History of Prior IBS Medication Use (Double-Blind Population)



IBS = irritable bowel syndrome.

- In addition, a significantly greater percentage of patients with prior IBS medication use treated with rifaximin were sustained responders relative to placebo-treated patients for the composite endpoint and individual components of the composite endpoint of abdominal pain and stool consistency (Table 2)

Table 2. Sustained Response* in Patients With History of Prior IBS Medication Use (Double-Blind Population)

Endpoint	Sustained Responders, n (%)		
	Rifaximin (n=185)	Placebo (n=185)	*P* value
Abdominal pain plus stool consistency (composite)	31 (16.8)	12 (6.5)	<0.001
Abdominal pain	63 (34.1)	31 (16.8)	<0.0001
Stool consistency	42 (22.7)	26 (14.1)	0.03

*Defined as response to double-blind treatment (primary evaluation phase) without recurrence through the end of the second repeat treatment phase (ie, 12 weeks [6 weeks of observation, 2 weeks of second repeat treatment, 4 weeks of follow-up]).
IBS = irritable bowel syndrome.

CONCLUSIONS

- **Two-week courses of rifaximin were efficacious in improving abdominal pain, stool consistency, and bloating in adults with prior IBS medication use**
- **Rifaximin response for the composite endpoint and individual components of the composite endpoint of abdominal pain and stool consistency was sustained versus placebo in adults with prior IBS medication use**
- **Rifaximin appears to be an effective treatment in patients unresponsive to other IBS-D therapies**

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