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Improvements Over Time in Individual Diarrhea-Predominant Irritable Bowel Syndrome Symptoms (IBS-D) With Rifaximin Repeat Treatment

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BACKGROUND

- Irritable bowel syndrome (IBS) is a condition of recurrent abdominal pain associated with defecation or a change in bowel habits[1]; although not part of the diagnosis, patients with diarrhea-predominant IBS (IBS-D) may frequently have additional symptoms, such as bloating and fecal urgency[1]
- Rifaximin is a nonsystemic antibiotic that was approved in 2015 for the treatment of IBS-D in adults
- In two phase 3 trials (TARGET 1 and 2), rifaximin 550 mg 3 times daily (TID) for 2 weeks was significantly more efficacious than placebo in adequately relieving multiple symptoms of IBS, including global and individual IBS symptoms (eg, bloating) during at least 2 of the first 4 weeks post-treatment[2]
- It was unclear how repeat courses of rifaximin might impact individual IBS-D symptoms in patients who have symptom recurrence after initial response to rifaximin therapy

AIM

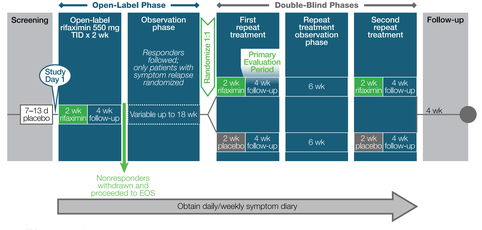
- To evaluate the effect of up to two 2-week repeat rifaximin courses on IBS-D symptoms

METHODS

Study Design and Patient Population

- Eligible patients were ≥18 years of age diagnosed with IBS-D (based on Rome III criteria) with average symptom severity scores during a placebo-screening phase of ≥3 for IBS-related abdominal pain and ≥3 for bloating, and had ≥2 days per week with Bristol Stool Scale (BSS) type 6 (loose) or 7 (watery) stool
- Patients had also responded to a 2-week course of open-label rifaximin 550 mg TID and relapsed (<30% decrease in abdominal pain scores from baseline or a <50% decrease in the number of days with BSS type 6 or 7 stools for ≥3 weeks of a consecutive, rolling, 4-week period) during a treatment-free 18-week observation phase (Figure 1)
- Patients randomly assigned to receive two 2-week repeat treatment courses of rifaximin 550 mg or placebo TID (Figure 1)
  - Two courses were separated by 10 weeks, and all patients received the second course irrespective of response or relapse status after the first course

Figure 1. Study Design



EOS = end of study; TID = 3 times daily.
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Assessments

- A voice or web system was used to collect responses to predefined daily symptom questions
- Abdominal pain was rated on a scale of 0 to 10 (0 = no pain; 10 = worst possible pain) and bloating and global IBS symptoms were rated on a scale of 0 to 6 (0 = not at all; 6 = a very great deal)
- Stool consistency was assessed using the BSS and urgency was assessed as a response of yes/no to "Have you felt or experienced a sense of urgency in the last 24 hours with any of your bowel movements?"
- Data are reported from double-blind baseline, obtained during the week before double-blind randomization; all analyses were conducted by fitting fixed effects linear models to last observation carried forward data

RESULTS

- A total of 636 patients were randomized to double-blind treatment (Table)

Table. Demographics and Baseline Characteristics

Parameter	Rifaximin 550 mg TID (n=328)	Placebo (n=308)
Age, mean (SD), y	47.9 (14.2)	45.6 (13.8)
Sex, female, n (%)	222 (67.7)	219 (71.1)
Race, n (%)		
White	273 (83.2)	262 (85.1)
Black	37 (11.3)	31 (10.1)
Other	18 (5.5)	15 (4.9)
Time since first onset of IBS symptoms, mean (SD), y	11.4 (11.0)	11.2 (10.9)
Average daily symptom score, mean (SD)		
Abdominal pain	5.7 (1.7)	5.5 (1.6)
Stool consistency	5.6 (0.8)	5.6 (0.8)
Bloating	4.2 (0.9)	4.1 (0.9)
IBS symptoms	4.2 (0.9)	4.1 (0.9)
Number of daily bowel movements, mean (SD), d	3.8 (2.1)	3.7 (2.1)
BSS type 6 or 7 stool in a week, mean (SD), d	4.9 (1.8)	5.0 (1.7)
Bowel movement urgency in a week, mean (SD), d	5.9 (1.7)	5.8 (1.7)

BSS = Bristol Stool Scale; IBS = irritable bowel syndrome; SD = standard deviation; TID = 3 times daily.
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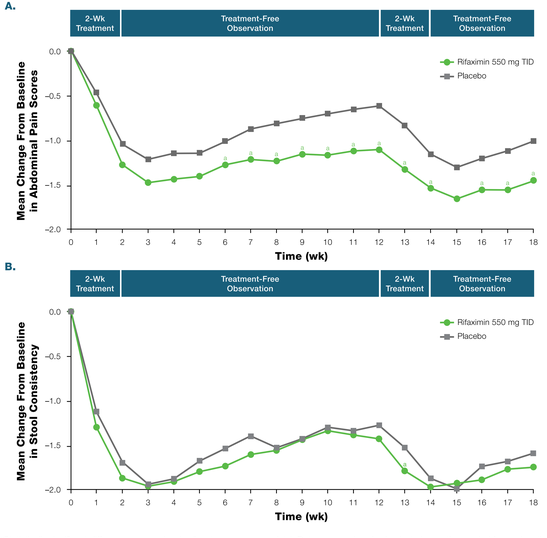
RESULTS

- Mean changes over time for abdominal pain and stool consistency improved following first rifaximin repeat treatment and improved again following the second rifaximin repeat treatment (Figure 2A and 2B)

Figure 2. Change From Baseline in Mean Daily Abdominal Pain Scores (A) and Weekly Stool Consistency (Days Per Week With BSS Type 6 or 7 Stools) (B)



[a]Statistically significant difference versus placebo (least squares mean data). Data were analyzed using last observation carried forward methodology.
BSS = Bristol Stool Scale; TID = 3 times daily.
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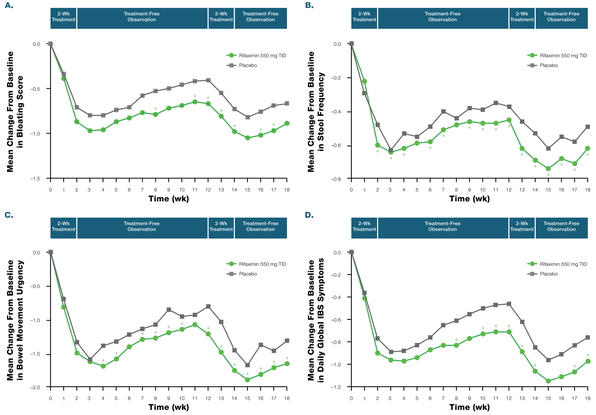
- Improvements over time were also noted for bloating, stool frequency, bowel movement urgency, and global IBS symptom score (Figure 3A-D)
- In general, symptoms continued to show incremental improvement versus baseline through 4 weeks after the second rifaximin repeat retreatment course (Figures 2A-B and 3A-D)
  - Significantly larger improvements from baseline in abdominal pain (P<0.0001), daily IBS symptoms (P=0.01), fecal urgency (P=0.005), and bowel movement frequency (P=0.01) were observed with rifaximin versus placebo 4 weeks after completion of the second retreatment course

Figure 3. Change From Baseline in Mean Daily Bloating Score (A), Stool Frequency (B), Days Per Week With Bowel Movement Urgency (C), and Global IBS Symptom Score (D)



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CONCLUSION

- **In patients with IBS-D who experienced recurrent symptoms, additional courses (up to 2 repeat treatments) of rifaximin continued to improve individual IBS symptoms over time**

REFERENCES: 1. Lacy BE, et al. *Gastroenterology*. 2016;150:1393-1407. **2.** Pimentel M, et al. *N Engl J Med*. 2011;364(1):22-32. **3.** Lembo A, et al. *Gastroenterology*. In press.

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