POSTER NUMBER

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Characterizing the Effect of Rifaximin on Individual Symptoms of IBS-D: Findings From the Open-Label Phase of TARGET 3

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INTRODUCTION

- Patients with diarrhea-predominant irritable bowel syndrome (IBS-D) often experience multiple gastrointestinal symptoms, including abdominal pain or discomfort, loose stools, bloating, and fecal urgency[1,2]
- Patients with IBS have qualitative and quantitative alterations in the gut microbiota compared with healthy individuals;[3-5] therefore, targeting the gut microbiota may be an effective treatment for IBS-D
- Rifaximin is an oral, nonsystemic antimicrobial agent that modulates the function of the gut microbiota[6]; in two phase 3 studies (TARGET 1 and 2), rifaximin 550 mg 3 times daily (TID) for 2 weeks significantly improve global and individual IBS-D symptoms versus placebo with a safety profile comparable to placebo[7]
- TARGET 3 was designed to evaluate the effects of repeat treatment with rifaximin in patients with IBS-D[8]

OBJECTIVE

- To characterize the profile of symptom improvement in patients with IBS-D who were treated with open-label rifaximin in the TARGET 3 study

METHODS

Patient Population

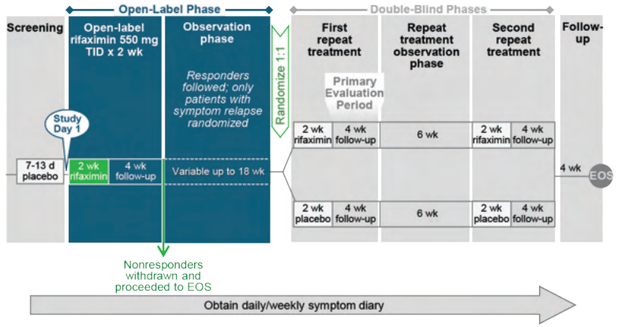
- Diagnosis of IBS-D (based on Rome III criteria) with average symptom severity scores during the screening phase of ≥3 for IBS-related abdominal pain (scale 0–10; 0 = no pain, 10 = worst possible pain you can imagine) and bloating (scale 0–6; 0 = not at all, 6 = a very great deal), and ≥2 days per week of Bristol Stool Scale (BSS) type 6 (loose) or 7 (watery) stool consistency
  - Exclusion criteria included a history of inflammatory bowel disease or having taken antidiarrheals, antispasmodics, narcotics, drugs indicated for IBS (eg, alosetron, lubiprostone), probiotics, or antibiotics within 14 days prior to the study

Study Design and Assessments

- Randomized, double-blind, phase 3, placebo-controlled, multicenter study
- After completion of the screening phase, patients meeting all eligibility criteria entered an open-label treatment (enrichment) phase in which they received rifaximin 550 mg TID for 2 weeks, followed by a 4-week treatment-free follow-up period to assess response (Figure 1)
  - A responder was defined as a patient meeting weekly response criteria (US Food and Drug Administration [FDA] composite endpoint) for *both* 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 stools) for ≥2 of 4 weeks during follow-up
- Responders continued in a treatment-free observation phase lasting up to 18 weeks or until symptom relapse occurred; patients who experienced symptom relapse were eligible to enter the randomized portion of the study
  - Relapse was defined as loss of response for either abdominal pain or stool consistency for ≥3 weeks out of a consecutive, rolling 4-week period during the 18-week observation phase

METHODS

Figure 1. Study Design



EOS = end of study.

Assessments and Statistics

- Analyses, using descriptive statistics, focused on response to open-label rifaximin treatment
- In addition to the FDA composite endpoint, other core IBS-D symptoms were evaluated
  - IBS-related bloating, assessed using a 7-point scale (0 = not at all, 6 = a very great deal), with treatment response defined as ≥1-point decrease from baseline in weekly average score for ≥2 of 4 weeks
  - Fecal urgency, assessed as "yes/no" during the previous 24 hours, with response defined as ≥30% decrease from baseline in the percentage of days with urgency for ≥2 of 4 weeks
  - Global IBS symptoms, assessed by response to the question "How bothersome were your symptoms of IBS in the last 24 hours?" (7-point scale; 0 = not at all, 6 = a very great deal), with response defined as ≥1-point decrease from baseline in weekly average score for ≥2 of 4 weeks

RESULTS

- A total of 2579 patients received open-label rifaximin 550 mg TID (Table); the majority (68.2%) of patients were female; the mean age was 46.4 years; mean duration since initial IBS-D symptom onset was ~11 years
  - Efficacy data were available for 2331 patients

RESULTS

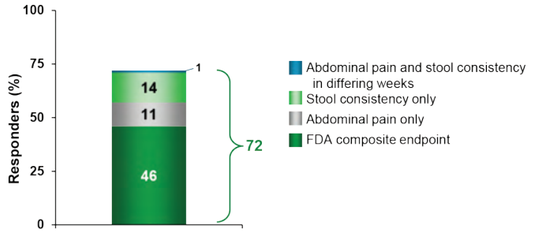
Table. Demographics and Baseline Characteristics

Characteristic	Open-Label Rifaximin 550 mg TID (N = 2579)
Age, y, mean (SD)	46.4 (13.7)
Female, n (%)	1760 (68.2)
Race, n (%)	
White	2155 (83.6)
Black	289 (11.2)
Other	135 (5.2)
Duration since first onset of IBS symptoms, y, mean (SD)	10.9 (10.8)
Daily symptom score, mean (SD)[a]	
Abdominal pain	5.5 (1.7)
Bloating	4.1 (0.9)
Stool consistency	5.6 (0.8)
Global IBS symptoms	4.2 (0.9)
Number of daily bowel movements, mean (SD)	3.9 (2.2)
Days per week with stool type 6 or 7, mean (SD)	4.9 (1.8)
Days per week with fecal urgency, mean (SD)	5.9 (1.7)

[a]Scale score ranges: abdominal pain (scale 0–10), bloating (scale 0–6), stool consistency (scale 1-7), global IBS symptoms (scale 0-6).
SD = standard deviation.

- Overall, 72% of 2331 patients exhibited improvement on at least 1 component of the FDA composite endpoint (Figure 2)
  - 46% met the composite endpoint definition of response
  - 25% were a responder for abdominal pain or stool consistency, but not both
  - 1% of patients were responders for abdominal pain or stool consistency, but improvement occurred on different weeks of the 4-week follow-up period

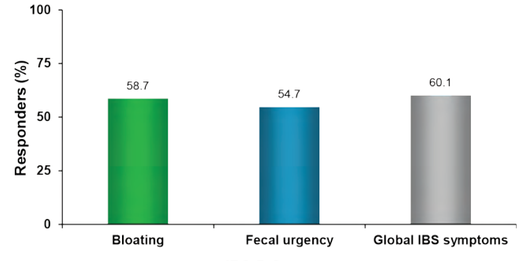
Figure 2. Overall Response to Open-Label Treatment With Rifaximin (n = 2331)



RESULTS

- When IBS-D symptoms were evaluated independently, >50% of patients were responders (Figure 3)

Figure 3. IBS-D Symptom Response to Open-Label Treatment With Rifaximin (n = 2331)



- Of 1074 patients who met the FDA composite endpoint for response, 382 (35.6%) continued to experience symptom relief and did not experience recurrence of abdominal pain or stool consistency symptoms during up to 18 weeks of treatment-free observation

CONCLUSIONS

- **In TARGET 3, >70% of patients with IBS-D who were treated with open-label rifaximin 550 mg TID for 2 weeks showed improvement in at least 1 of 2 IBS symptoms (abdominal pain, stool consistency) that comprised the FDA composite endpoint**
- **Improvements in bloating, fecal urgency, and global IBS symptoms suggest that the potential benefit of rifaximin for patients with IBS-D extends to multiple IBS-related symptoms**

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