POSTER NUMBER

Mo1279

Durability of Benefit in IBS-D Patients Responding to a 2-Week Course of Rifaximin: Results of TARGET 3

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INTRODUCTION

- Irritable bowel syndrome (IBS) causes substantial impairment of health-related quality of life and social well-being, loss of work and productivity, and high healthcare costs[1-3]
- Diarrhea-predominant IBS (IBS-D) is characterized by abdominal pain, bloating, and loose stools in the absence of inflammation or structural abnormalities[4]
- Rifaximin is an oral, minimally absorbed antimicrobial agent that is associated with a low risk of clinically relevant bacterial antibiotic resistance[5,6]
- A 2-week course of rifaximin 550 mg 3 times daily (TID) significantly improved global and individual IBS-D symptoms compared with placebo in 2 randomized, placebo-controlled, phase 3 studies (TARGET 1 and 2)[7]
  - In addition, a greater percentage of patients treated with rifaximin reported durable improvement in IBS-D symptoms versus placebo for at least 10 weeks post-treatment
- Clinical experience suggests that the treatment effect may persist beyond the 12 weeks evaluated in the TARGET 1 and 2 studies

OBJECTIVE

- To further characterize the duration of benefit in patients with IBS-D who responded to an initial 2-week course of rifaximin therapy in the TARGET 3 study[8]

METHODS

Patient Population

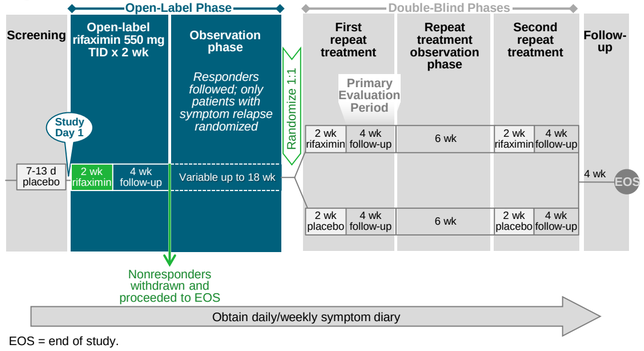
- Adults were eligible who were diagnosed with IBS-D (based on Rome III criteria) with average symptom severity scores during the screening phase of ≥3 for IBS-related abdominal pain (scale 0–10; 0 = no pain, 10 = worst possible pain you can imagine) and bloating (scale 0–6; 0 = not at all, 6 = a very great deal), and ≥2 days per week with 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 of the study

Study Design

- Randomized, double-blind, phase 3, placebo-controlled, multicenter study conducted in the United States, United Kingdom, and Germany
- After completion of the screening phase, patients meeting all eligibility criteria entered a treatment phase of open-label 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 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 stool consistency) for ≥2 of 4 weeks during follow-up
  - Nonresponders to open-label rifaximin were withdrawn from the study
- Responders in the open-label phase entered a treatment-free observation phase and were subsequently followed for up to 18 additional weeks or until they experienced a relapse; patients who relapsed were randomized (1:1) to receive 2 double-blind repeat treatments (first and second repeat treatment phases) with rifaximin 550 mg TID or placebo, separated by 10 weeks
  - Relapse was defined as loss of response for either abdominal pain or stool consistency for ≥3 out of a consecutive, rolling 4-week period during the 18-week observation phase
- Time to relapse was summarized using Kaplan-Meier methods

METHODS

Figure 1. Study Design



EOS = end of study.

RESULTS

- 2579 patients with IBS-D received treatment with open-label rifaximin 550 mg TID (Table)

Table. Demographic and Baseline Characteristics

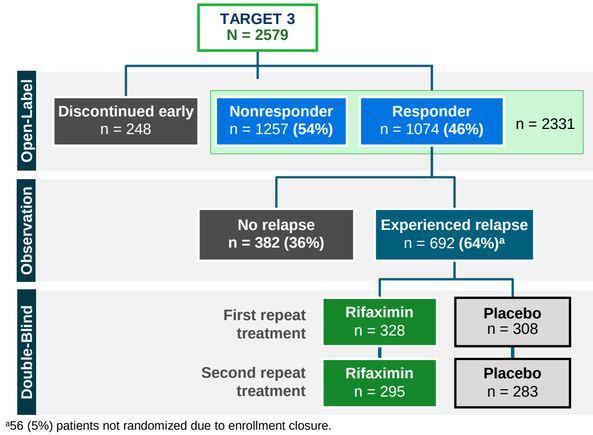
Characteristic		Open-Label Rifaximin 550 mg TID (N = 2579)
Age, y, mean (SD)		46.4 (13.7)
Sex, n (%)	Male	819 (31.8)
	Female	1760 (68.2)
Race, n (%)	White	2155 (83.6)
	Black	289 (11.2)
	Other	135 (5.2)
Duration since first onset of IBS symptoms, y, mean (SD)		10.9 (10.8)
Average daily score, mean (SD)[a]	Global IBS symptoms	4.2 (0.9)
	Bloating	4.1 (0.9)
	Abdominal pain	5.5 (1.7)
	Stool consistency	5.6 (0.8)
Number of daily bowel movements, mean (SD)		3.9 (2.2)
Days per week with stool type 6 or 7[b], mean (SD)		4.9 (1.8)
Days per week with stool 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), and global IBS symptoms (scale 0-6).
[b]Based on Bristol Stool Scale.
SD = standard deviation.

RESULTS

- Of 2579 patients treated in the open-label phase, 2331 were evaluable for efficacy, of which 1074 (46%) were responders based on the composite endpoint of abdominal pain and stool consistency (Figure 2)
  - This initial treatment effect was similar to that observed in the TARGET 1 and TARGET 2 double-blind, placebo-controlled studies that evaluated treatment with a single, 2-week course of rifaximin[7]

Figure 2. Patient Disposition

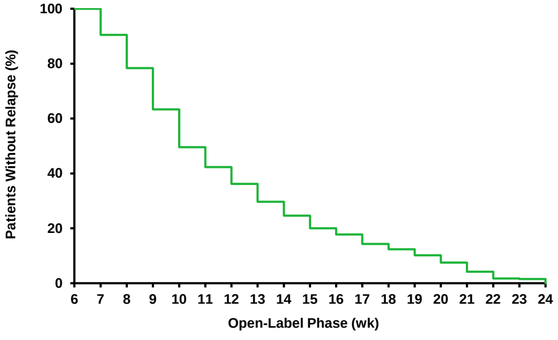


[a]56 (5%) patients not randomized due to enrollment closure.

RESULTS

- Of the 1074 responders, 382 (35.6%) did not experience relapse during the subsequent observation phase (18 weeks total duration)
  - Of the 692 patients who relapsed, 636 were randomized to double-blind repeat treatment with rifaximin or placebo
- Among the 636 patients who relapsed and continued in the study, the mean time (standard deviation) to recurrence of symptoms during the observation phase was 11.9 (4.4) weeks (Figure 3)
- For the majority of patients who did relapse in the observation phase, only a partial recurrence of symptoms, with loss of response for either abdominal pain or stool consistency components, was noted (please see poster Mo1271)

Figure 3. Time to Relapse During the Observation Phase in Patients Randomized to Double-Blind Treatment (n = 636)



CONCLUSIONS

- **36% of patients who responded to a single, 2-week course of rifaximin 550 mg TID continued to experience symptom improvement and did not relapse when followed for up to 18 additional weeks**
- **Patients who did relapse tended to exhibit symptom recurrence for either abdominal pain or stool consistency at a mean of ~3 months after initial treatment with rifaximin**

REFERENCES **1.** Lackner JM, et al. *Am J Gastroenterol.* 2014;109(11):1815-1823. **2.** Nellesen D, et al. *J Manag Care Pharm.* 2013;19(9):755-764. **3.** Wong RK, et al. *Clin Gastroenterol Hepatol.* 2013;11(2):151-155. **4.** Longstreth GF, et al. *Gastroenterology*. 2006;130(5):1480-1491. **5.** Cremonini F, et al. *Expert Opin Pharmacother.* 2012;13(3):433-440. **6.** Jiang ZD, et al. *Chemotherapy* 2005;51(Suppl 1):67-72. **7.** Pimentel M, et al. *N Engl J Med.* 2011;364:22-32. **8.** Lembo A, et al. Presented at: American College of Gastroenterology 2014 Annual Scientific Meeting; Philadelphia, PA; October 17-22, 2014.

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