POSTER NUMBER

5

Rifaximin for Abdominal Pain in Irritable Bowel Syndrome With Diarrhea

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INTRODUCTION

- Recurrent abdominal pain is a key symptom of irritable bowel syndrome (IBS)[1] and a common reason, along with symptom frequency, for patients to seek out healthcare services[2]
- Alterations in the gut microbiota may cause IBS and impact pain perception[3]
- The nonsystemic antibiotic rifaximin is approved in the United States for the treatment of adults with IBS with diarrhea (IBS-D) and has demonstrated efficacy in phase 3 trials,[4,5] possibly through its effects in the gastrointestinal tract (eg, gut microbiota)
- Given that abdominal pain is a key symptom in patients with IBS-D, the efficacy of rifaximin in improving abdominal pain was further evaluated

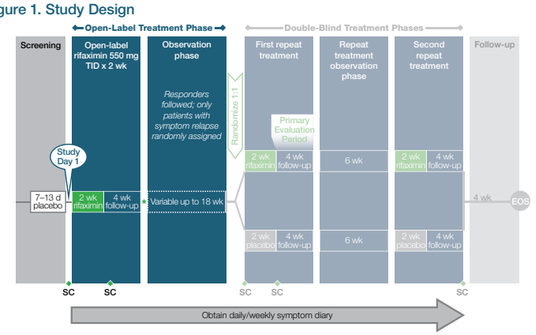
AIM

- To characterize the impact of a 2-week course of open-label rifaximin therapy on abdominal pain in adults with IBS-D

METHODS

- Post hoc analysis of data from the phase 3 Targeted nonsystemic Antibiotic Rifaximin Gut-selective Evaluation of Treatment for IBS-D (TARGET) 3 trial[4]
- Eligible patients were ≥18 years of age, diagnosed with IBS (based on Rome III criteria), with average symptom severity scores during a 2-week, 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 (mushy) or 7 (watery) stool
- Patients received open-label rifaximin 550 mg three times daily for 2 weeks (**Figure 1**)

Figure 1. Study Design



*Nonresponders withdrawn and proceeded to EOS.
EOS = end of study; TID = three times daily; SC = stool collection.
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METHODS

- Responders (patients with ≥30% decrease from baseline in mean weekly pain score *and* ≥50% decrease from baseline in frequency of BSS type 6 or 7 stool during ≥2 of the first 4 weeks post-treatment) were followed for up to an additional 18 weeks or until loss of treatment response (observation phase; **Figure 1**)[4]
  - Loss of treatment response was defined as <30% decrease from baseline in mean weekly pain score *or* <50% decrease from baseline in number of days/week with BSS type 6 or 7 stool for ≥3 weeks of a consecutive, rolling 4-week period during the 18-week observation phase
- Abdominal pain scores were assessed daily by patient response to the question "In regards to your specific IBS symptom of abdominal pain, on a scale of 0 ("no pain at all") to 10 ("worst possible pain"), what was your worst IBS-related abdominal pain over the last 24 hours?"
- Abdominal pain responders were defined as patients with ≥30% improvement from baseline in the weekly mean abdominal pain score during ≥2 of the first 4 weeks post-treatment
- For the current analysis, abdominal pain recurrence was defined as <30% improvement in weekly mean abdominal pain score for ≥3 weeks during a rolling 4-week consecutive period of the 18-week observation phase
- Results were analyzed using observed case methodology (patients were excluded if they had insufficient data to determine efficacy)

RESULTS

- A total of 2579 individuals were treated with rifaximin (**Table 1**)

Table 1. Demographic and Baseline Characteristics

Parameter	Overall Population (N=2579)	Abdominal Pain Responders (n=1384)*	Abdominal Pain Nonresponders (n=1054)*
Age, y, mean (SD)	46.4 (13.7)	47.0 (13.8)	45.7 (13.5)
Female, n (%)	1760 (68.2)	952 (68.8)	709 (67.3)
Race, n (%)			
White	2155 (83.6)	1177 (85.0)	857 (81.3)
Black	289 (11.2)	129 (9.3)	146 (13.9)
Other	135 (5.2)	78 (5.6)	51 (4.8)
Duration since first onset of IBS symptoms, y, mean (SD)	10.9 (10.8)	11.4 (11.1)	10.1 (10.2)
Average daily score, mean (SD)			
Abdominal pain	5.5 (1.7)	5.5 (1.6)	5.6 (1.7)
Stool consistency	5.6 (0.8)	5.6 (0.8)	5.6 (0.9)
Bloating	4.1 (0.9)	4.1 (0.9)	4.1 (1.0)
IBS symptoms	4.2 (0.9)	4.1 (0.9)	4.2 (0.9)

*Unpublished study data; 141 of 2579 individuals were excluded because of insufficient data to determine response (ie, observed case methodology).
IBS = irritable bowel syndrome; SD = standard deviation.
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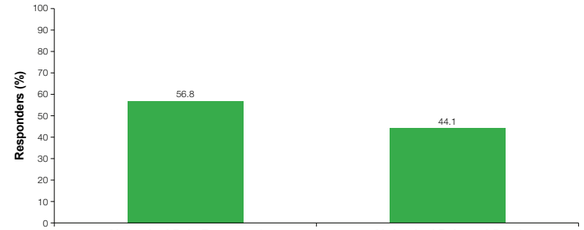
RESULTS

- 56.8% of 2438 evaluable patients were abdominal pain responders (**Table 2; Figure 2**)
  - Baseline demographic and disease characteristics were similar for abdominal pain responders versus nonresponders (**Table 1**)
- 1074 of 1384 abdominal pain responders met the original coprimary endpoint of the study (population of 44.1% of 2438 patients who were abdominal pain *and* stool consistency responders [**Figure 2**])[4] and were included in the up to 18 weeks of additional follow-up (ie, up to 22 weeks post-treatment; **Table 2**)

Figure 2. Response to Open-Label Treatment With Rifaximin



*Patients with ≥30% improvement from baseline in weekly mean abdominal pain score during ≥2 weeks of the first 4 weeks post-treatment.
†Patients with ≥30% decrease from baseline in mean weekly pain score and ≥50% decrease from baseline in frequency of Bristol Stool Scale type 6 or 7 stool during ≥2 of the first 4 weeks post-treatment.
Data from Lembo et al. *Gastroenterology.* 2016;151(6):1113-1121.*

- 382 (35.6%) of 1074 abdominal pain responders did not experience recurrence through 22 weeks post-treatment, and the median time to abdominal pain recurrence was 14.0 weeks (**Table 2**)

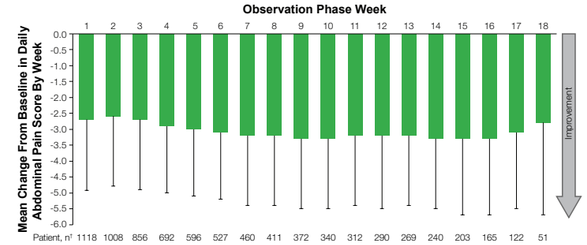
Table 2. Abdominal Pain Response Profile

4 weeks post-treatment	
Abdominal pain responders, n/n (%)*	1384/2438 (56.8)
22 weeks post-treatment	
No recurrence of abdominal pain,† n/n (%)	382/1074‡ (35.6)
Median time to recurrence, wk	14.0

*Patients with ≥30% improvement from baseline in the weekly mean abdominal pain score during ≥2 weeks of the first 4 weeks post-treatment.
†Recurrence was defined as <30% improvement in weekly mean abdominal pain score for ≥3 weeks during a rolling 4-week consecutive period of the 18-week observation phase.
‡Only patients who met response for abdominal pain and stool consistency during ≥2 weeks of the first 4 weeks post-treatment (original analysis)[4] were included in the 18-week observation phase (n=1074).

- For abdominal pain responders evaluated during the additional 18 weeks of follow-up, the decrease (improvement) from baseline in daily pain scores, assessed weekly, ranged from –2.6 to –3.3 (**Figure 3**)

Figure 3. Mean Improvement in Average Daily Abdominal Pain Score By Week in Evaluable Abdominal Pain Responders*



*Patients with ≥30% improvement from baseline in the weekly mean abdominal pain score during ≥2 weeks of the first 4 weeks post-treatment. Error bars represent standard deviation.
†Data may have not been available for multiple reasons, including patient experiencing stool consistency relapse (<50% decrease from baseline in number of days/week with Bristol Stool Scale type 6 or 7 stool for ≥3 weeks of a consecutive, rolling 4-week period) and proceeding into double-blind treatment phase or randomization to double-blind treatment phase closed by sponsor.

CONCLUSIONS

- **A single, 2-week course of rifaximin 550 mg three times daily was efficacious in improving abdominal pain symptoms and provided durable response for a median of 3.5 months post-treatment**
- **Rifaximin is efficacious in relieving abdominal pain in adults with IBS-D**

REFERENCES: **1.** Lacy BE, et al. *Gastroenterology.* 2016;150(6):1393-1407. **2.** Hungin APS, et al. *Aliment Pharmacol Ther.* 2005;21(11):1365-1375. **3.** Mayer EA, et al. *Gastroenterology.* 2014;146(6):1500-1512. **4.** Lembo A, et al. *Gastroenterology.* 2016;151(6):1113-1121. **5.** Pimentel M, et al. *Dig Dis Sci.* 2011;56(7):2067-2072.

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