Characterization of Abdominal Pain Response to Rifaximin in Patients With Irritable Bowel Syndrome With Diarrhea, by Baseline Pain Severity

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INTRODUCTION

- Recurrent abdominal pain, a key symptom that must be present to establish the diagnosis of irritable bowel syndrome (IBS), is experienced frequently by patients with IBS and often associated with patients seeking care from a healthcare provider[1,2]
- Alterations in the gut microbiota have been associated with abdominal pain in patients with IBS[3-5]
- Rifaximin 550-mg tablets is a nonsystemic antibiotic, indicated in the United States for the treatment of adults with IBS with diarrhea (IBS-D),[6] and may have beneficial modulatory activities towards the gut microbiota of patients with IBS[7,8]

AIM

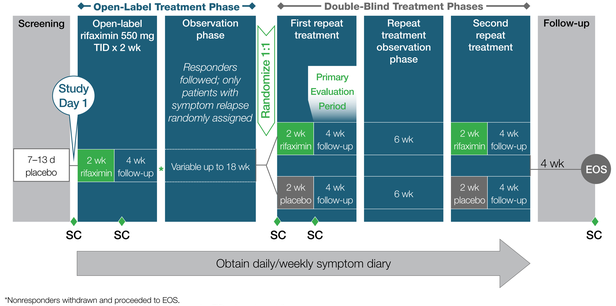
- To evaluate the response to repeat rifaximin treatment in patients with IBS-D subgrouped by baseline abdominal pain severity

METHODS

Study Design and Patient Population

- Adults with IBS with a mean daily abdominal pain score ≥3 (range, 0 = "no pain at all"; 10 = "worst possible pain you can imagine"), mean daily bloating score ≥3 (range, 0 = not at all; 6 = a very great deal), and loose stools for ≥2 days/week with Bristol Stool Scale (BSS) type 6 or 7 (mushy/watery) stool during a placebo-screening phase received a 2-week (initial) course of open-label rifaximin 550 mg three times daily (Figure 1)
  - Abdominal pain was assessed daily by patient response to the question "In regards to your specific IBS symptom of abdominal pain, on a scale of 0-10, what was your worst IBS-related abdominal pain over the last 24 hours?"

Figure 1. Study Design



*Nonresponders withdrawn and proceeded to EOS.
EOS = end of study; SC = stool sample collection time point; TID = three times daily.
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- Patients who responded during the 4-week post-treatment period and then experienced symptom recurrence during an up to 18-week, treatment-free observation period (up to 22 weeks post-treatment) received a second 2-week rifaximin course or placebo (placebo population not included in these analyses)

METHODS

- Response was defined as a ≥30% decrease from baseline in mean weekly abdominal pain score and ≥50% decrease from baseline in days/week with BSS type 6 or 7 (mushy/watery) stool (composite endpoint) for ≥2 of the first 4 weeks post-treatment
- Response to the individual component of abdominal pain was also evaluated (≥30% decrease from baseline in mean weekly abdominal pain score for ≥2 of the first 4 weeks post-treatment)
- For the post hoc subgroup analyses, patients were grouped by baseline abdominal pain scores of <5.0 (group A), ≥5.0 to <8.0 (group B), and ≥8.0 (group C)

Statistical Analyses

- The open-label rifaximin population included all patients enrolled who received ≥1 dose of rifaximin; the repeat rifaximin population included all patients randomly assigned to double-blind treatment who received ≥1 dose of rifaximin
- Last observation carried forward analysis was utilized, in which missing values were replaced with the last previous non-missing post-baseline value

RESULTS

Demographic and Baseline Characteristics

- 2579 patients received open-label treatment with rifaximin; the mean baseline abdominal pain score was 5.5 (median, 5.4; Table 1)

Table 1. Demographics and Baseline Characteristics (Open-Label Population)*

Parameter	Rifaximin (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)
Average daily bowel movements, mean (SD)	3.9 (2.2)
Duration since first onset of IBS symptoms, y, mean (SD)	10.9 (10.8)
Average daily score, mean (SD)	
Abdominal pain	5.5 (1.7)
Bloating	4.1 (0.9)
Stool consistency	5.6 (0.8)
IBS symptoms	4.2 (0.9)
Days with BSS type 6 or 7 stool in a week, mean (SD)	4.9 (1.8)

BSS = Bristol Stool Scale; IBS = irritable bowel syndrome; SD = standard deviation.
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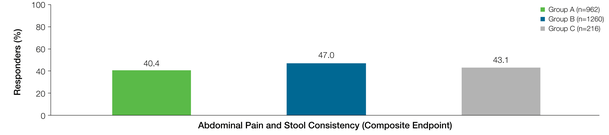
Open-Label (Initial) Treatment With Rifaximin

- Of the 2438 patients in the open-label phase evaluable for efficacy (group A, n=962; group B, n=1260; group C, n=216), a generally similar percentage (40.4%–47.0%) of patients, regardless of baseline abdominal pain severity, were responders to rifaximin (abdominal pain and stool consistency; Figure 2)

RESULTS

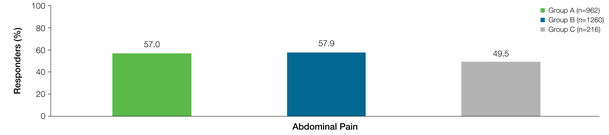
Figure 2. Open-Label (Initial) Rifaximin Abdominal Pain and Stool Consistency Response* by Baseline Abdominal Pain Score†



*Defined as ≥30% decrease from baseline in mean weekly abdominal pain score and ≥50% decrease from baseline in days/week with BSS type 6 or 7 (mushy/watery) stool (composite endpoint) for ≥2 of the first 4 weeks post-treatment.
†Baseline abdominal pain scores: group A, <5; group B, ≥5 and <8; group C, ≥8.

- For the individual component of abdominal pain, 57.0%, 57.9%, and 49.5% of patients in groups A, B, and C, respectively, were responders (Figure 3)

Figure 3. Open-Label (Initial) Rifaximin Abdominal Pain Response* by Baseline Abdominal Pain Score†

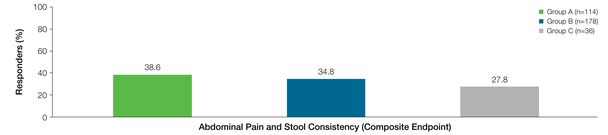


*Defined as ≥30% decrease from baseline in mean weekly abdominal pain score for ≥2 of the first 4 weeks post-treatment.
†Baseline abdominal pain scores: group A, <5; group B, ≥5 and <8; group C, ≥8.

Repeat Treatment With Rifaximin

- Of the 328 patients who received repeat rifaximin treatment, the mean double-blind baseline abdominal pain score was 4.6 (median, 4.4), which was lower than that observed at open-label baseline
  - When subgrouped by double-blind baseline abdominal pain scores, there were 114 patients in group A, 178 in group B, and 36 in group C
- After repeat rifaximin treatment, more than one third of patients with mild or moderate baseline pain severity (groups A and B) were responders for the composite endpoint (abdominal pain and stool consistency; Figure 4)

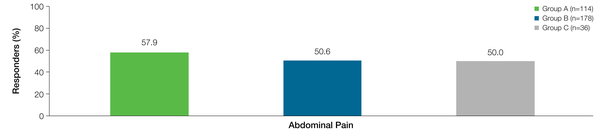
Figure 4. Repeat Rifaximin Abdominal Pain and Stool Consistency Response* by Double-Blind Baseline Abdominal Pain Score†



*Defined as ≥30% decrease from baseline in mean weekly abdominal pain score and ≥50% decrease from baseline in days/week with BSS type 6 or 7 (mushy/watery) stool (composite endpoint) for ≥2 of the first 4 weeks post-treatment.
†Baseline abdominal pain scores: group A, <5; group B, ≥5 and <8; group C, ≥8.

- For the individual component of abdominal pain, 57.9%, 50.6%, and 50.0% of patients in groups A, B, and C, respectively, were responders (Figure 5)
  - Percentage of abdominal pain responders with repeat rifaximin treatment was generally similar by groups to the response observed with initial open-label rifaximin treatment (Figure 3)

Figure 5. Repeat Rifaximin Abdominal Pain Response* by Double-Blind Baseline Abdominal Pain Score†



*Defined as ≥30% decrease from baseline in mean weekly abdominal pain score for ≥2 of the first 4 weeks post-treatment.
†Baseline abdominal pain scores: group A, <5; group B, ≥5 and <8; group C, ≥8.

CONCLUSIONS

- **In adults with IBS-D treated with rifaximin, a high percentage of patients had clinically meaningful improvement in abdominal pain irrespective of baseline abdominal pain severity category and treatment course (initial vs repeat treatment)**
- **These data support the efficacy of rifaximin in improving IBS-related abdominal pain**

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DISCLOSURES: CA and ZH report being employees of Salix Pharmaceuticals. AL reports having served as a consultant and advisory board member for Alkermes, Allergan, Ardelyx, AstraZeneca, Forest, Ironwood, Prometheus, Salix Pharmaceuticals, and Valeant. BDC reports having served as a speaker, consultant, or advisory board member for Allergan, AstraZeneca, IM HealthScience, Ironwood, Salix Pharmaceuticals, Takeda, and Valeant.

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