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Assessing the Efficacy of Rifaximin in Diarrhea-Predominant Irritable Bowel Syndrome: A Post Hoc Analysis of Two Phase 3, Randomized, Placebo-Controlled Trials

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INTRODUCTION

- Rifaximin is a nonsystemic antibiotic indicated for the treatment of diarrhea-predominant irritable bowel syndrome (IBS-D) in adults
  - The efficacy of rifaximin in IBS-D has been evaluated in several phase 3 trials[1,2]
- Recurrent abdominal pain is a key symptom of IBS[3] and a common reason patients consult a healthcare provider[4,5]
- In addition, the degree of fecal urgency is an independent predictor of reduced quality of life in patients with IBS-D[6]
  - Survey data from 2015 indicated that 40% of individuals diagnosed with IBS-D report urgency at least 4 days per week[5]
- Because abdominal pain and fecal urgency are burdensome symptoms in patients with IBS-D, the efficacy of rifaximin in improving these 2 symptoms was further evaluated in a pooled post hoc analysis of 2 identically designed, randomized, double-blind, placebo-controlled trials[2]

AIM

- To evaluate rifaximin efficacy for improving abdominal pain and fecal urgency in adults with IBS-D using modified definitions of response for abdominal pain and fecal urgency

METHODS

- Data were pooled from 2 identically designed, phase 3, randomized, placebo-controlled trials[2]
- Adults with IBS with average daily abdominal pain and bloating scores of 2 to 4.5 (range, 0 = not at all; 6 = a very great deal) and a stool consistency score of ≥3.5 (range, 1 = very hard; 5 = watery) for ≥7 days were included in the trials
- Patients were randomly assigned to receive rifaximin 550 mg or placebo 3 times daily for 2 weeks followed by a 4-week treatment-free follow-up period to assess efficacy
- Symptoms were assessed daily using a computerized interactive voice response system
- Abdominal pain was determined based on patient response to the question "In regards to your specific IBS symptom of abdominal pain and discomfort, on a scale of 0-6, how bothersome was your IBS-related abdominal pain and discomfort today?"
- Fecal urgency was determined based on patient response of yes or no to the question "Have you felt or experienced a sense of urgency today?"

METHODS

- Abdominal pain response (≥20%, ≥30%, ≥40%, or ≥50% decrease from baseline in mean weekly abdominal pain during ≥2 of the first 4 weeks post-treatment) and fecal urgency response (≥20%, ≥30%, ≥40%, or ≥50% decrease from baseline in percentage of days with fecal urgency during ≥2 of the first 4 weeks post-treatment) were assessed
- Patients who did not have any assessments during Weeks 3 to 6 (first 4 weeks post-treatment) were excluded from the analysis

RESULTS

- A total of 1258 patients (72.3% female) with IBS-D were randomly assigned to treatment and received ≥1 dose of study drug (Table)

Table. Demographics and Baseline Characteristics

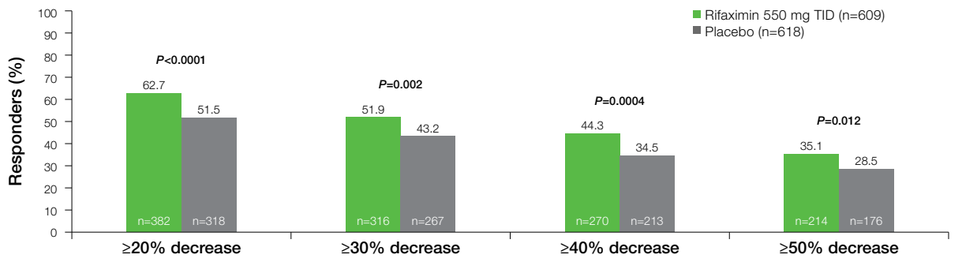
Parameter	Rifaximin 550 mg TID (n=624)	Placebo (n=634)
Age <65 years, n (%)	560 (89.7)	559 (88.2)
Female, n (%)	462 (74.0)	447 (70.5)
Race, n (%)		
White	563 (90.2)	582 (91.8)
Black	45 (7.2)	44 (6.9)
Other	16 (2.6)	8 (1.3)
Duration since first onset of IBS symptoms, y, mean (SD)*	11.3 (10.4)	11.6 (11.1)
Average daily score, mean (SD)		
Abdominal pain†	3.3 (0.7)	3.2 (0.7)
Stool consistency‡	3.9 (0.3)	3.9 (0.3)
Bloating†	3.3 (0.8)	3.3 (0.7)
IBS symptoms†	3.4 (0.7)	3.4 (0.7)
Average number of daily bowel movements, mean (SD)	3.0 (1.5)	3.0 (1.5)
Percentage of time with fecal urgency, mean (SD)	81.6 (22.5)	82.5 (22.4)

*n=624 for rifaximin group and n=633 for placebo group.
†Score range, 0 = not at all; 6 = a very great deal.
‡Score range, 1 = very hard; 5 = watery.
IBS = irritable bowel syndrome; SD = standard deviation; TID = three times daily.

RESULTS

- Overall, 1227 patients (rifaximin, n=609; placebo, n=618) were included in the current analysis
- Regardless of the percentage decrease from baseline in abdominal pain used to define response, rifaximin was significantly more efficacious compared with placebo (Figure 1)

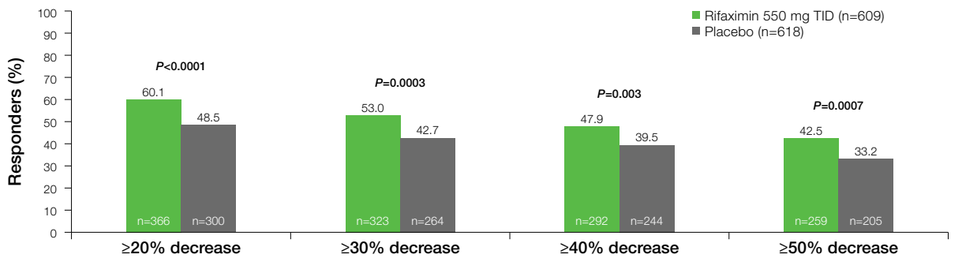
Figure 1. Abdominal Pain Responders*



*Patients with the defined percentage decrease from baseline in mean weekly abdominal pain score during ≥2 of the first 4 weeks post-treatment.
TID = three times daily.

- In addition, regardless of the percentage decrease from baseline in fecal urgency used to define response, rifaximin was significantly more efficacious compared with placebo (Figure 2)

Figure 2. Fecal Urgency Responders*



*Patients with the defined percentage decrease from baseline in percentage of days with urgency during ≥2 of the first 4 weeks post-treatment.
TID = three times daily.

CONCLUSION

- **Rifaximin was significantly more efficacious compared with placebo in adults with IBS-D, regardless of the percentage decrease from baseline in abdominal pain or fecal urgency used to define response**

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