Rifaximin is Efficacious for the Treatment of Irritable Bowel Syndrome With Diarrhea in Patients Receiving Concomitant Antidepressants

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INTRODUCTION

- Comorbid psychiatric disorders, including depression, occur more frequently in patients with irritable bowel syndrome (IBS) compared with healthy individuals[1]
  - Data are conflicting on whether treatment of depression provides symptomatic benefit for patients with comorbid IBS[2]
- The nonsystemic antibiotic rifaximin 550 mg (Xifaxan®, Salix Pharmaceuticals, Bridgewater, NJ) is approved in the United States and Canada for the treatment of adults with IBS with diarrhea (IBS-D)[3]
  - Rifaximin 550 mg three times daily (TID) may be administered as a 2-week course of therapy, with up to 2 additional 2-week courses indicated for symptom recurrence[3]
- The efficacy and safety of rifaximin for improving symptoms of IBS-D in adults have been demonstrated in three phase 3, randomized, double-blind, placebo-controlled studies (TARGET 1, 2, and 3)[4,5]
- Data regarding the efficacy of rifaximin in adults with IBS-D receiving concomitant antidepressants are limited

OBJECTIVE

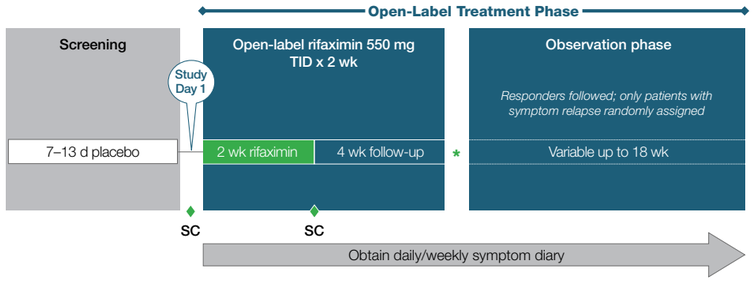
- To assess the efficacy and safety of rifaximin for the treatment of IBS-D in a subgroup of adults receiving concomitant antidepressants

METHODS

Study Design and Patient Population

- Post hoc analysis of data from the open-label treatment phase of TARGET 3 (Figure 1)[5]
- Adults diagnosed with IBS received placebo for 10 ± 3 days and completed a daily symptom diary during a single-blind placebo screening phase

Figure 1. Study Design



*Nonresponders were withdrawn from the study.
SC = stool sample collection; TID = three times daily.
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- During the screening phase, patients who rated their average abdominal pain ≥3 (scale range, 0 [no pain] to 10 [worst possible pain]) and bloating ≥3 (scale range, 0 [not at all] to 6 [a very great deal]), and reported mushy/watery stools (Bristol Stool Scale [BSS] type 6 or 7) for ≥2 days in a week (ie, patients with IBS-D) were eligible to receive open-label rifaximin 550 mg TID for 2 weeks
- In the original protocol, patients could continue taking antidepressants if they were on a stable dose for ≥6 weeks before study entry, including during the screening phase

METHODS

Assessments

- Efficacy assessments
  - Composite response (meeting response criteria for both abdominal pain [defined as ≥30% improvement from baseline in weekly average abdominal pain score] and stool consistency [defined as ≥50% decrease from baseline in number of days/week with BSS type 6 or 7 stool] during ≥2 of the first 4 weeks post-treatment)
    - Response for the individual components of abdominal pain severity and stool consistency
  - Bloating response (≥1-point decrease in weekly average bloating score during ≥2 of the first 4 weeks post-treatment)
  - Bowel movement urgency response (≥30% improvement in percentage of days with urgency during ≥2 of the first 4 weeks post-treatment)
  - Daily global IBS symptoms response (≥1-point decrease in weekly average IBS symptoms score during ≥2 of the first 4 weeks post-treatment)
- Safety assessments included evaluation of adverse events (AEs), laboratory parameters, and vital signs

RESULTS

- 500 (19.4%) of the 2579 patients with IBS-D receiving a 2-week course of open-label rifaximin were taking stable doses of antidepressants (Table)[5]
  - A few differences were observed in the demographic and baseline disease characteristics between the overall group and antidepressant subgroup; for example, a greater percentage of patients receiving antidepressants were female and were white

Table. Demographics and Baseline Disease Characteristics (Safety Population)*

Characteristic	Overall Group[5] (N=2579)	Antidepressant Subgroup (n=500)
Age, mean (SD)	46.4 (13.7)	48.8 (14.0)
Female, n (%)	1760 (68.2)	415 (83.0)
White, n (%)	2155 (83.6)	469 (93.8)
Years since first onset of IBS symptoms, mean (SD)	10.9 (10.8)	15.1 (12.2)
Average daily score, mean (SD)		
Abdominal pain	5.5 (1.7)	5.2 (1.6)
Bloating	4.1 (0.9)	3.9 (0.9)
Bowel movement urgency	5.9 (1.7)	5.8 (1.6)
IBS symptoms	4.2 (0.9)	4.0 (0.8)
Stool consistency	5.6 (0.8)	5.5 (0.9)
Number of daily bowel movements, mean (SD)	3.9 (2.2)	3.5 (1.9)
Days with BSS type 6 or 7 stool in a week, mean (SD)	4.9 (1.8)	4.8 (1.8)

*Received ≥1 dose of study medication.
BSS = Bristol Stool Scale; IBS = irritable bowel syndrome; SD = standard deviation.
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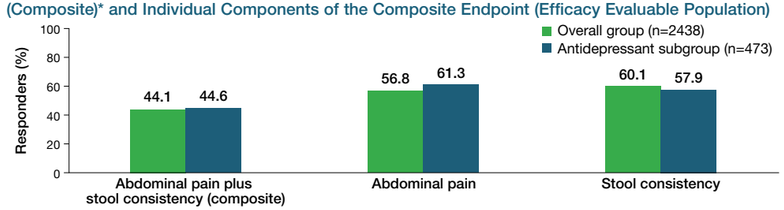
- A total of 2438 patients in the overall group and 473 patients in the concomitant antidepressant subgroup were evaluable for efficacy (efficacy evaluable population)
- A comparable percentage of patients in the overall group and antidepressant subgroup were abdominal pain plus stool consistency (composite) responders, and responders for the individual components of the composite endpoint of abdominal pain and stool consistency (Figure 2)

RESULTS

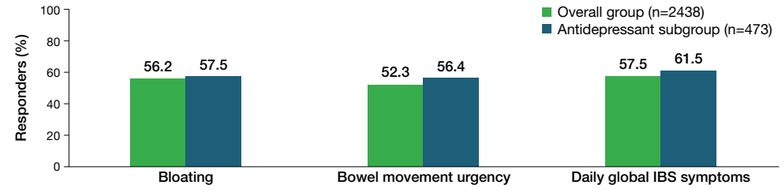
Figure 2. Percentage of Rifaximin Responders for Abdominal Pain Plus Stool Consistency (Composite)* and Individual Components of the Composite Endpoint (Efficacy Evaluable Population)



*≥30% improvement from baseline in weekly average abdominal pain score plus ≥50% decrease from baseline in number of days/week with BSS type 6 or 7 stool during ≥2 of the first 4 weeks post-treatment.

- In addition, the percentage of responders for bloating, bowel movement urgency, and daily IBS symptoms were similar in the overall population and antidepressant subgroup (Figure 3)

Figure 3. Percentage of Rifaximin Responders for Bloating,* Bowel Movement Urgency,† and Daily Global IBS Symptoms‡ (Efficacy Evaluable Population)



*≥1-point decrease in weekly average bloating score during ≥2 of the first 4 weeks post-treatment.
†≥30% improvement in percentage of days with urgency during ≥2 of the first 4 weeks post-treatment.
‡≥1-point decrease in weekly average IBS symptoms score during ≥2 of the first 4 weeks post-treatment.
IBS = irritable bowel syndrome.

- AEs reported in ≥2.0% of patients were sinusitis (2.8% [14/500]) and urinary tract infection (2.0% [10/500]) in the concomitant antidepressant subgroup and nausea (2.0% [52/2579]) in the overall group

CONCLUSIONS

- **A 2-week course of rifaximin 550 mg TID was well tolerated and improved symptoms of IBS in adults taking concomitant antidepressants**

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