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Impact of Rifaximin on Health-Related Quality of Life in Patients With Diarrhea-Predominant Irritable Bowel Syndrome

Brooks D. Cash, MD[1]; Zeev Heimanson, PharmD[2]; Lin Chang, MD[3]
[1]University of South Alabama, Mobile, AL; [2]Salix Pharmaceuticals, Bridgewater, NJ; [3]David Geffen School of Medicine at UCLA, Los Angeles, CA

INTRODUCTION

- Quality of life (QOL), daily activity, and social well-being are aberrantly affected in patients with irritable bowel syndrome (IBS)[1,2]
- Patients with diarrhea-predominant IBS (IBS-D) have quantitative and qualitative alterations in their gut microbiota compared with healthy individuals[3-5]; therefore, IBS treatment options that target the gut microbiota (eg, probiotics, nonsystemic antibiotics) have been considered[6]
- Rifaximin is an oral nonsystemic antibiotic approved in the United States for the treatment of IBS-D in adults
- Rifaximin has been shown in 3 randomized, double-blind, placebo-controlled phase 3 trials to significantly improve global and individual symptoms of IBS-D[7,8]

AIM

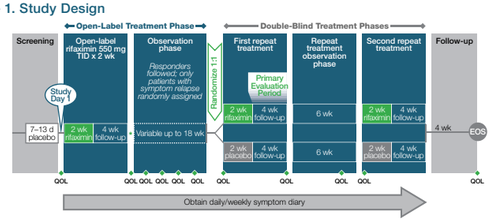
- To examine the effect of repeat (2-week) rifaximin treatment on IBS-related QOL in patients with IBS-D

METHODS

Study Design and Patient Population

- Adults with IBS-D (Rome III criteria) with response to a 2-week course of open-label (OL) rifaximin who experienced relapse during a subsequent 18-week treatment-free observation phase were randomly assigned to receive 2 double-blind (DB) treatments with rifaximin 550 mg or placebo 3 times daily for 2 weeks (**Figure 1**)
  - A responder was defined as a patient simultaneously meeting weekly response criteria for abdominal pain (≥30% improvement from baseline in mean weekly abdominal pain score) and stool consistency (≥50% decrease from baseline in number of days/week with Bristol Stool Scale type 6 or 7 stools) for ≥2 of the first 4 weeks post-treatment
  - DB treatments were separated by 10 weeks

Figure 1. Study Design



*Nonresponders withdrawn and proceeded to EOS.
EOS = end of study; QOL = quality of life; TID = three times daily.
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Quality-of-Life Assessments

- QOL was evaluated using a validated 34-item IBS-QOL questionnaire[9] completed by patients during the OL and DB phases of the study (**Figure 1**)
  - Scoring of each subdomain on the IBS-QOL instrument utilized a 5-point Likert scale (range, 1 = "not at all" to 5 = "extremely" or "a great deal"), with overall and subdomain scores summed (0 to 100; higher score indicative of better QOL)
- Improvement from baseline of ≥14 points in IBS-QOL score at a given time point was considered to be the minimal clinically important difference (MCID)[10]

Statistical Analysis

- Descriptive statistics were used to analyze the change from OL baseline in the IBS-QOL overall and subdomain scores to 4 weeks post-treatment
- Comparisons of IBS-QOL scores between groups (ie, OL responders vs nonresponders, OL responders with relapse vs those without relapse, rifaximin vs placebo) were analyzed using 1-way analysis of variance
- An unstratified Cochran-Mantel-Haenszel general association test for categorical data was used to compare IBS-QOL scores in patients receiving OL treatment who achieved improvement from baseline ≥14 points
- A Cochran-Mantel-Haenszel test stratified by analysis center, time to recurrence, and recurrence type was used to compare IBS-QOL scores in patients receiving DB treatment who achieved improvement from baseline of ≥14 points

RESULTS

Table 1. Demographic and Baseline Characteristics

Characteristic	OL Population	DB Population	
	Rifaximin 550 mg (N=2579)	Rifaximin 550 mg (n=328)	Placebo (n=308)
Age, y, mean (SD)	46.4 (13.7)	47.9 (14.2)	45.6 (13.8)
Sex, female, n (%)	1760 (68.2)	222 (67.7)	219 (71.1)
Race, n (%)			
White	2155 (83.6)	273 (83.2)	262 (85.1)
Black	289 (11.2)	37 (11.3)	31 (10.1)
Other	135 (5.2)	18 (5.5)	15 (4.9)
Duration since first onset of IBS symptoms, y, mean (SD)	10.9 (10.8)	11.4 (11.0)	11.2 (10.9)
Number of daily bowel movements, mean (SD)	3.9 (2.2)	3.8 (2.1)	3.7 (2.1)
Average daily stool consistency score, mean (SD)	5.6 (0.8)	5.6 (0.8)	5.6 (0.8)
Days with BSS stool type 6 or 7 in a week, mean (SD)	4.9 (1.8)	4.9 (1.8)	5.0 (1.7)
Daily abdominal pain score, mean (SD)	5.5 (1.7)	5.7 (1.7)	5.5 (1.6)
IBS-QOL overall score, n (%)			
≥40 (nonsevere)	1228 (63.2)	193 (58.8)	190 (61.7)
≤40 (severe)	698 (35.9)	133 (40.5)	117 (38.0)
Missing	17 (0.9)	2 (0.6)	1 (0.3)
Baseline IBS-QOL domain scores, mean (SD)			
Overall	48.3 (21.2)*	54.7 (23.5)†‡	55.0 (24.2)
Dysphoria	48.7 (25.5)†	57.8 (26.6)	57.8 (27.5)
Interference with activity	39.5 (23.0)‡	46.3 (25.4)	46.8 (26.6)
Body image	47.9 (24.1)†	52.2 (26.3)	51.9 (26.3)
Health worry	55.1 (21.9)§	59.7 (23.3)	60.7 (24.4)
Food avoidance	34.0 (27.0)¶	39.6 (28.5)	40.2 (29.0)
Social reaction	52.6 (26.1)#	58.1 (28.9)††	59.5 (27.5)
Sexual	65.2 (32.0)**	69.7 (31.8)	69.4 (33.5)
Relationships	58.9 (26.5)#	64.0 (27.2)††	64.2 (28.6)

*Data missing for 20 patients. †Data missing for 14 patients. ‡Data missing for 19 patients. §Data missing for 15 patients. ¶Data missing for 13 patients. #Data missing for 17 patients. **Data missing for 12 patients. ††Data missing for 1 patient.
BSS = Bristol Stool Scale; DB = double-blind; IBS = irritable bowel syndrome; IBS-QOL = irritable bowel syndrome-quality of life; OL = open-label; SD = standard deviation.
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RESULTS

Demographic and Baseline Disease Characteristics

- Demographic and baseline disease characteristics were generally comparable between both the OL (N=2579) and DB populations (n=636) and within the DB population (**Table 1**), except that baseline overall and subdomain IBS-QOL scores were higher (ie, improved) for patients who entered the DB phase versus baseline scores of patients who entered the OL phase

Open-Label Phase

- Responders to OL rifaximin (n=1074) had significantly greater improvement from baseline in IBS-QOL overall and subdomain scores compared with nonresponders (n=1364) at 4 weeks post-treatment (*P*<0.001 for all comparisons; **Table 2**)

Table 2. Improvement From OL Baseline in IBS-QOL Scores at 4 Weeks Post-Treatment

Change in IBS-QOL Domain Score, Mean	OL Responders (n=1074)	OL Nonresponders (n=1364)	OL Responders Who Remained Relapse Free* (n=370)	OL Responders Who Relapsed* (n=636)
Overall	21.8†	5.5	24.3‡	20.8
Dysphoria	24.7†	6.9	26.6	24.0
Interference with activity	24.7†	5.9	28.6‡	23.2
Body image	22.2†	5.2	24.8‡	21.3
Health worry	18.7†	5.9	20.4	17.7
Food avoidance	20.8†	2.9	24.5‡	19.4
Social reaction	20.1†	5.7	21.8	19.4
Sexual function	15.6†	3.5	16.6	15.0
Social relationships	17.3†	4.5	18.5	16.5

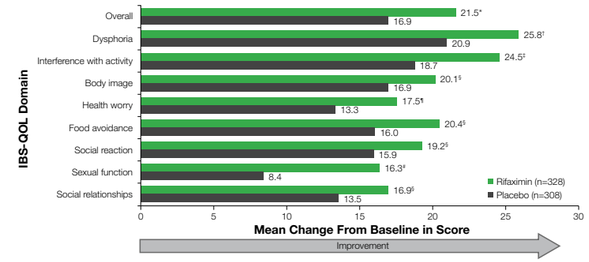
*During OL 18-week observation phase.
†*P*<0.001.
‡*P*<0.05.
IBS-QOL = irritable bowel syndrome-quality of life; OL = open-label.

- The mean change from baseline in IBS-QOL overall score and subdomain scores for interference with activity, body image, and food avoidance was significantly greater in OL responders to rifaximin remaining relapse-free during the OL observation phase (up to 22 weeks post-treatment; n=370) compared with responders who relapsed during the OL observation phase (n=636; *P*<0.05; **Table 2**)
- A significantly greater percentage of responders achieved the MCID in IBS-QOL overall score from OL baseline to 4 weeks post-treatment versus nonresponders (52.2% vs 21.0%, respectively; *P*<0.0001)

Double-Blind Phase

- For patients receiving DB retreatment with rifaximin, the mean change from OL baseline to last visit was significantly greater for IBS-QOL overall score and subdomain scores for dysphoria, interference with activity, health worry, and sexual function compared with placebo (*P*<0.05; **Figure 2**)

Figure 2. Change From OL Baseline in IBS-QOL Overall and Subdomain Scores to Last Visit for Patients Receiving DB Rifaximin or Placebo



*P=0.01; †P=0.02; ‡P=0.006; §P value not significant; ¶P=0.03; #P<0.001.
DB = double-blind; IBS-QOL = irritable bowel syndrome-quality of life; OL = open-label.

- In the DB treatment phase (n=636), a significantly greater percentage of patients in the rifaximin group (38.6%) versus the placebo group (29.6%; *P*=0.009) achieved the MCID for the IBS-QOL overall score from DB baseline to 4 weeks post-treatment

CONCLUSIONS

- **In patients with IBS-D, initial and repeat treatment (2-week courses) with rifaximin resulted in clinically meaningful improvements in QOL**
- **Data support the clinical usefulness of a 2-week course of rifaximin 550 mg 3 times daily as treatment and repeat treatment for the management of IBS-D**

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