POSTER NUMBER

P0789

Efficacy of Rifaximin on Bloating in Patients With Diarrhea-Predominant Irritable Bowel Syndrome (IBS-D): A Pooled Analysis of Three Phase 3, Randomized, Placebo-Controlled Trials

Brian E. Lacy, MD, PhD[1]; Mark Pimentel, MD[2]; Christopher Chang, MD, PhD[3,4]; Zeev Heimanson, PharmD[5]; Anthony Lembo, MD[6]

[1]Mayo Clinic, Jacksonville, FL, USA; [2]Cedars-Sinai Medical Center, Los Angeles, CA, USA; [3]New Mexico VA Health Care System, Albuquerque, NM, USA; [4]University of New Mexico School of Medicine, Albuquerque, NM, USA; [5]Salix Pharmaceuticals, Bridgewater, NJ, USA; [6]Beth Israel Deaconess Medical Center, Boston, MA, USA

UNITED EUROPEAN GASTROENTEROLOGY ueg week VIRTUAL 2020

INTRODUCTION

- Bloating is common in patients with irritable bowel syndrome (IBS)[1]; data suggest that up to ~60% of patients with nonconstipation forms of IBS (eg, diarrhea-predominant IBS [IBS-D] or IBS with mixed bowel habits) have bloating[2,3]
  - However, bloating is generally considered subjective in nature in patients with IBS and can be difficult to effectively treat[4]
- The nonsystemic agent rifaximin is indicated for the treatment of IBS with diarrhea in adults; 2-week course(s) have been shown to significantly improve multiple symptoms of IBS-D versus placebo[5,6]
- Given the frequency of bloating in patients with IBS, it is important to further assess the efficacy of rifaximin in treating this symptom in patients with IBS-D

AIM

- To further examine the efficacy of rifaximin in improving bloating in adults with IBS-D

METHODS

- Post hoc analysis of three phase 3 trials (**Table 1**)
  - Adults with IBS-D were randomly assigned to receive double-blind rifaximin 550 mg three times daily (TID) or placebo for 2 weeks, followed by a 4-week treatment-free follow-up period to evaluate response

Table 1. Phase 3, Randomized, Placebo-Controlled Clinical Studies

Study	Baseline Entry Criteria	Treatment
Study 1 (TARGET 1)[2]	• Age ≥18 years meeting Rome II criteria for IBS • Mean daily bloating score, 2 to 4.5* • Mean daily abdominal pain score, 2 to 4.5* • Mean daily stool consistency ≥3.5†	Rifaximin 550 mg or placebo TID for 2 weeks
Study 2 (TARGET 2)[2]	• Age ≥18 years meeting Rome II criteria for IBS • Mean daily bloating score, 2 to 4.5* • Mean daily abdominal pain score, 2 to 4.5* • Mean daily stool consistency ≥3.5†	Rifaximin 550 mg or placebo TID for 2 weeks
Study 3 (TARGET 3)[3]	• Age ≥18 years meeting Rome III criteria for IBS • During placebo screening phase: - Mean daily abdominal pain score ≥3‡ - ≥2 day/week BSS type 6 or 7 stool	Responders§ to open-label rifaximin 550 mg TID for 2 weeks, who had recurrence within 18 weeks¶, entered a randomized, placebo-controlled phase and received rifaximin 550 mg or placebo TID for 2 weeks

*7-point scale (0 = not at all; 6 = a very great deal).
†5-point scale (1 = very hard; 5 = watery).
‡10-point scale (1 = no pain; 10 = worst possible pain).
§Patient simultaneously meeting weekly response criteria of ≥30% decrease from baseline in mean weekly pain score and ≥50% decrease from baseline in number of days/week with BSS type 6 or 7 stool during ≥2 of first 4 weeks post-treatment.
¶Loss of treatment response: <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 an 18-week observation phase.
BSS = Bristol Stool Scale; IBS = irritable bowel syndrome; TARGET = Targeted, nonsystemic Antibiotic Rifaximin Gut-selective Evaluation of Treatment for IBS-D; TID = three times daily.

- Bloating was assessed using a 7-point Likert scale (**Figure 1**)

Figure 1. Bloating Scale

- In Trials 1 and 2, bloating severity was determined by patient response to a daily question "In regards to your specific IBS symptom of bloating: on a scale of 0-6, how bothersome was your IBS-related bloating today" and patient response to a weekly question, "In regards to your IBS symptom of bloating, compared to the way you felt before you started study medication, have you, in the past 7 days, had adequate relief of your IBS symptom of bloating?"
- In Trial 3, bloating severity was determined by patient response to the question "In regards to your specific IBS symptom of bloating, on a scale of 0-6, how bothersome was your IBS-related bloating in the last 24 hours?"

METHODS

Analyses

- Bloating responders were defined in 2 ways in the current analysis
  - Patients achieving a ≥1-point decrease (improvement) from baseline in weekly average bloating score for ≥2 weeks of the first 4 weeks post-treatment
  - Patients achieving a ≥2-point decrease (improvement) from baseline in weekly average bloating score for ≥2 weeks of the first 4 weeks post-treatment
- Durable response was defined as maintenance of bloating response, as defined above, for each week of an additional 6 weeks of follow-up (through Week 10 post-treatment)
- *P* values were obtained from Cochran-Mantel-Haenszel method with adjustment for analysis center

RESULTS

- 1894 patients with IBS-D were included in the analysis: rifaximin (n=952) and placebo (n=942; **Table 2**)
  - Overall, the majority of the 1894 patients were women (71.3%), with a mean age of 46.2 years

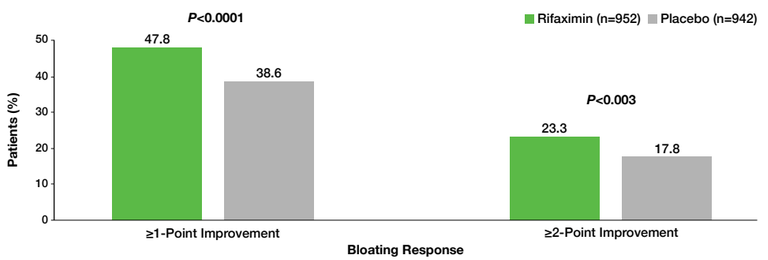
Table 2. Patient Demographic and Baseline Characteristics

Characteristic	Rifaximin 550 mg TID (n=952)	Placebo (n=942)
Age, years, mean (SD)	46.6 (14.4)	45.8 (14.3)
Female, n (%)	684 (71.8)	666 (70.7)
Race, n (%)		
White	836 (87.8)	844 (89.6)
Black	82 (8.6)	75 (8.0)
Other	34 (3.6)	23 (2.4)
Duration since first onset of IBS symptoms, years, mean (SD)	11.3 (10.6)	11.5 (11.1)
Number of daily bowel movements, mean (SD)	3.2 (1.7)	3.2 (1.7)
Average daily bloating score, mean (SD)	3.4 (1.0)	3.4 (1.0)

IBS = irritable bowel syndrome; SD = standard deviation; TID = three times daily.

- A significantly greater percentage of patients receiving rifaximin were bloating responders versus placebo when response was defined as ≥1-point improvement or as ≥2-point improvement in weekly average bloating score for ≥2 weeks of the first 4 weeks post-treatment (**Figure 2**)

Figure 2. Bloating Responders*

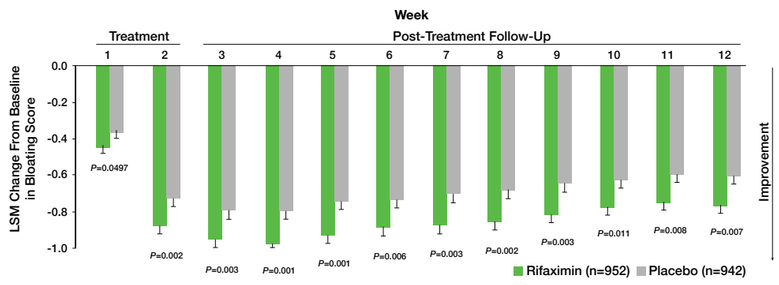


*≥1-point or ≥2-point decrease (improvement) from baseline bloating score during ≥2 of the first 4 weeks post-treatment.

- Least square means change from baseline in bloating scores significantly favored rifaximin versus placebo through 12 weeks, including during 2 weeks of treatment and 10 weeks of post-treatment follow-up ($P \leq 0.05$ vs placebo; **Figure 3**)

RESULTS

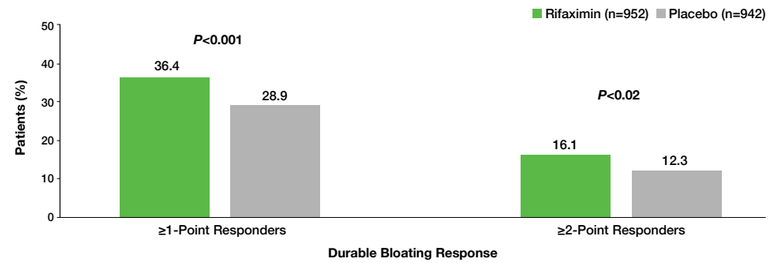
Figure 3. Bloating Responders by Post-Treatment Week*



*Data are least square means (LSM) data and error bars represent standard error.

- In addition, durable bloating response was achieved by a significantly greater percentage of patients receiving rifaximin versus placebo for both ≥1-point and ≥2-point responders (**Figure 4**)

Figure 4. Durable Bloating Response*



*Maintenance of bloating response (≥1-point or ≥2-point improvement from baseline bloating score during ≥2 of the first 4 weeks post-treatment) for each week of an additional 6 weeks of follow-up (through Week 10 post-treatment).

CONCLUSIONS

- **Rifaximin 550 mg TID for 2 weeks provided significant and durable improvement in bloating versus placebo in adults with IBS-D**

REFERENCES: 1. Lacy BE, et al. *Gastroenterology.* 2016;150(6):1393-1407. **2.** Tuteja AK, et al. *Am J Gastroenterol.* 2008;103(5):1241-1248. **3.** Chang L, et al. *Am J Gastroenterol.* 2001;96(12):3341-3347. **4.** Schmulson M, et al. *Aliment Pharmacol Ther.* 2011;33(10):1071-1086. **5.** Lembo A, et al. *Gastroenterology.* 2016;151(6):1113-1121. **6.** Pimentel M, et al. *N Engl J Med.* 2011;364(1):22-32.

ACKNOWLEDGMENTS: The 3 trials and post hoc analyses were supported by Salix Pharmaceuticals. Technical editorial and medical writing assistance was provided under the direction of the authors by Mary Beth Moncrief, PhD, Synchrony Medical Communications, LLC, West Chester, PA. Funding for this assistance was provided by Salix Pharmaceuticals.

DISCLOSURES: BL reports serving as an advisory board member for Forest Laboratories, a subsidiary of Allergan plc, Ironwood Pharmaceuticals, Inc., and Salix Pharmaceuticals. MP reports being a consultant for and has received research grants from Salix Pharmaceuticals. Additionally, Cedars-Sinai Medical Center has a licensing agreement with Salix Pharmaceuticals. CC reports serving as an advisory board member for Salix Pharmaceuticals. ZH is an employee of Salix Pharmaceuticals. AL reports serving as a consultant for Salix Pharmaceuticals.

Research funded by: Salix Pharmaceuticals