# Two-Week Repeat Rifaximin Course in Initial IBS-D Responders

Lembo A, et al. Repeat treatment with rifaximin is safe and effective in patients with diarrhea-predominant irritable bowel syndrome. Gastroenterology. 2016;151(6):1113-1121.

| Inclusion Criteria | Adults with IBS (Rome III criteria) who, during the placebo-screening phase, had mean symptom severity scores of ≥3 for IBS-related abdominal pain* and ≥3 for bloating* and ≥2 days per week with watery/mushy (BSS type 6/7) stool |
|---|---|

## Phase 3 Trial Study Design

7-13 d placebo screening → 2 wk OL rifaximin 550 mg tid; 4-wk period to determine response (6 wk total) → Observation: up to 18 wk *(open-label responders only)* → Patients with recurrence randomized 1:1 → 2-wk DB rifaximin 550 mg tid or placebo (1st repeat treatment) → Observation: 4 wk (1° evaluation period) + 6 wk (10 wk total) → 2-wk DB rifaximin 550 mg tid or placebo (2nd repeat treatment; safety evaluation)† → Observation: 8 wk

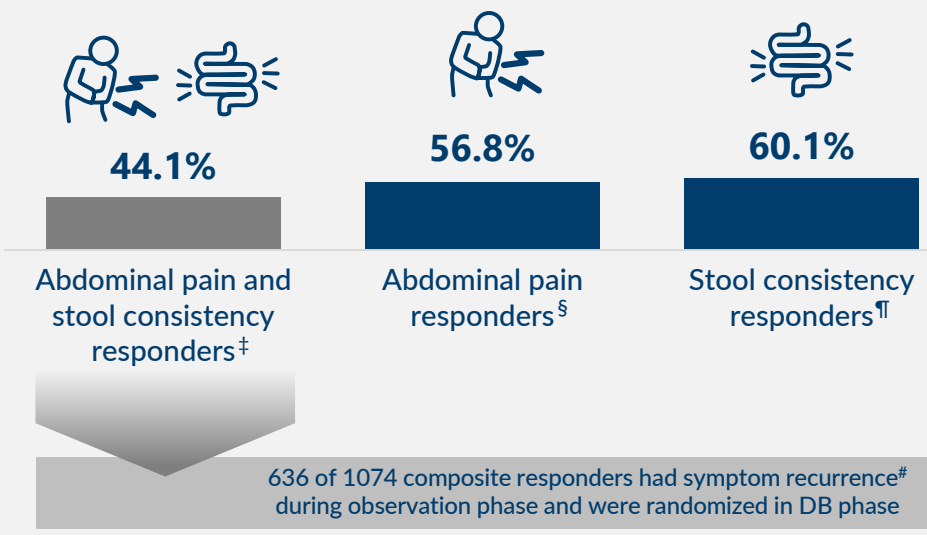
**Open-label (OL) phase (rifaximin 550 mg tid for 2 weeks)**
To identify initial responders who subsequently had IBS-D symptom recurrence

**Double-blind (DB), placebo-controlled phase (rifaximin 550 mg tid for 2 weeks)**
To evaluate if repeat treatment is efficacious and safe in patients who had previously responded to rifaximin

## OL baseline characteristics (N=2579)

| Age | | | | | |
|---|---|---|---|---|---|
| 46.4 (13.7) | 68.2/31.8 | 5.5 (1.7) | 5.6 (0.8) | 4.1 (0.9) | 4.2 (0.9) |
| Mean (SD) age, y | Female/ male, % | Mean (SD) abdominal pain score | Mean (SD) stool consistency score | Mean (SD) bloating score | Mean (SD) IBS symptoms score |

## OL efficacy evaluation (n=2438)

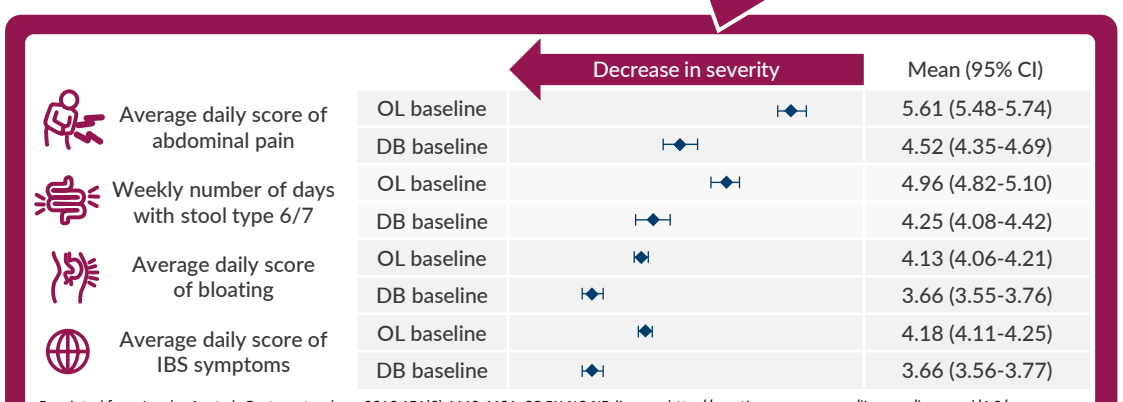



636 of 1074 composite responders had symptom recurrence# during observation phase and were randomized in DB phase

## DB baseline characteristics (n=636)

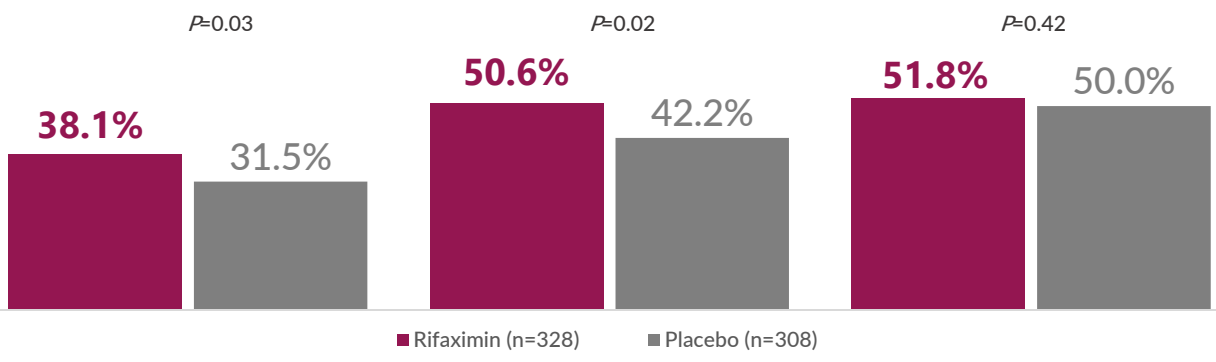
| | Age: Mean (SD) age, y | Female/male, % |
|---|---|---|
| Rifaximin (n=328) | 47.9 | 67.7/32.3 |
| Placebo (n=308) | 45.6 | 71.1/28.9 |

At start of DB treatment (636 patients), baseline symptoms were significantly milder than at the beginning of OL treatment ($P<0.001$), with a 20% reduction in mean abdominal pain severity and 14% reduction in mean weekly number of days with loose stools**






## DB efficacy evaluation of repeat treatment (n=636)




## AE profile (DB phase)

| Patients with an AE, n (%) | Rifaximin (n=328) | Placebo (n=308) |
|---|---|---|
| Any AE | 140 (42.7) | 140 (45.5) |
| Serious AEs | 4 (1.2) | 4 (1.3) |
| | Most common AEs†† | |
| Nausea | 12 (3.7) | 7 (2.3) |
| URTI | 12 (3.7) | 8 (2.6) |
| UTI | 11 (3.4) | 15 (4.9) |
| Nasopharyngitis | 10 (3.0) | 9 (2.9) |

*IBS-related abdominal pain scale of 0-10 (0 = "no pain" to 10 = "worst possible pain"); bloating scale 0-6 (0 = "not at all" to 6 = "a very great deal").
†Primary purpose of second repeat treatment was to gain additional safety and tolerability data with rifaximin retreatment rather than efficacy data.
‡Patient meeting weekly response criteria for both abdominal pain (≥30% decrease from baseline in mean weekly pain score) and stool consistency (≥50% decrease from baseline in number of days/week with BSS type 6/7 stool) for ≥2 of the first 4 weeks post-treatment.
§≥30% decrease from baseline in mean weekly pain score for ≥2 of first 4 weeks post-treatment.
¶≥50% decrease from baseline in number of days/week with BSS type 6/7 stool for ≥2 of first 4 weeks post-treatment.
#Loss of treatment response for either weekly abdominal pain (<30% decrease from baseline in mean weekly pain score) *or* stool consistency (<50% decrease from baseline in number of days/week with BSS type 6/7 stool) for ≥3 weeks of a consecutive, rolling 4-week period during 18-week observation phase.
**BSS type 6/7.
††≥3.0% of patients in either group, regardless of causality.

AE = adverse event; BSS = Bristol Stool Scale; IBS = irritable bowel syndrome; IBS-D = irritable bowel syndrome with diarrhea; tid = 3 times daily; URTI = upper respiratory tract infection; UTI = urinary tract infection.