

Rifaximin Use in IBS Symptoms



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Disclosure



The individual reported that no relevant financial relationship exists.

Objective



- Describe the safety and effectiveness of rifaximin in patients with irritable bowel syndrome (IBS) diarrhea symptoms

Irritable Bowel Syndrome



- IBS affects between 25 and 45 million people in the United States
- IBS is unpredictable
 - Symptoms vary
 - Diarrhea can alternate with constipation
- What are options for treatment?

Diagnosis



Rome Diagnostic Criteria for IBS

Rome III criteria (2006)

- At least 3 months, with onset at least 6 months previously of recurrent abdominal pain or discomfort** associated with 2 or more of the following:
 - Improvement with defecation;
and/or
 - Onset associated with a change in frequency of stool;
and/or
 - Onset associated with a change in form (appearance) of stool

****Discomfort means an uncomfortable sensation not described as pain.**

Rome II criteria (1999)

12 weeks or more in the last 12 months of abdominal discomfort or pain with 2 /3 of the following

- Relieved by defecation
- Associated with a change in frequency of stool
- Associated with a change in consistency of stool

The second group of criteria included in Rome I are now considered supportive rather than mandatory in the diagnosis.

Rifaximin



- Recently approved for use in patients with IBS diarrhea symptoms
- Target 1 and Target 2
 - Two identically designed, phase 3, double blind, placebo controlled trials
- Patients were given either rifaximin 550 mg or placebo three times daily
 - 2 weeks of treatment
 - 10 week follow up

Study Endpoints



- The primary endpoint was the proportion of patients that had adequate relief of global IBS symptoms
 - Abdominal pain and discomfort
 - Bloating
 - Diarrhea
 - Gas
 - Altered bowel function
- Secondary endpoints
 - Relief of IBS-related bloating
 - Daily assessment of IBS symptoms

Results

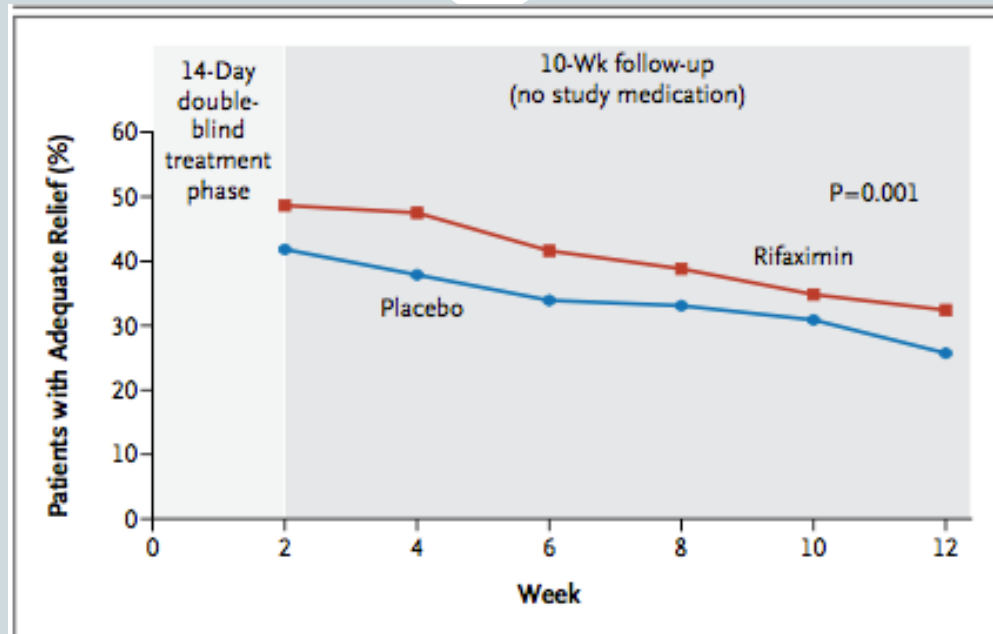


Figure 4. Percentage of Patients with Adequate Relief of Global IBS Symptoms in the TARGET 1 and TARGET 2 Studies Combined.

Adequate relief was defined as self-reported relief from symptoms for at least 1 week of every 2-week period. The P value was calculated on the basis of a longitudinal data analysis with the use of a generalized-estimating-equation model, with fixed effects of treatment, analysis center, and week. Similar figures for the individual TARGET 1 and TARGET 2 trials are shown in the Supplementary Appendix.

Safety



Event	Rifaximin (N=624)	Placebo (N=634)
Headache	38 (6.1)	42 (6.6)
Abdominal Pain	29 (4.6)	35 (5.5)
Nausea	27 (4.3)	24 (3.8)
Diarrhea	27 (4.3)	22 (3.5)
Vomiting	15 (2.4)	9 (1.4)
Flatulence	10 (1.6)	14 (2.2)
Gastroenteritis	6 (1)	3 (0.5)

Other Rifaximin Data



- Randomized, double-blind, placebo-controlled trial of rifaximin in patients with abdominal bloating and flatulence
 - Treatment of rifaximin 400 mg or placebo twice daily
- Used Rome II criteria
- Patients who used rifaximin had an improvement in global symptom relief
 - Mean bloating-specific scores were lower for the rifaximin group
 - H₂-breath excretion also lower for rifaximin group

Where do we go from here?



- Both trials were based on self-reported symptom relief
 - Heavily subjective
 - No actual lab values
- Cost
 - 2 week course of treatment = \$1,295.00
- IBS symptoms vary
 - Treatment is very patient specific

Other Treatment Options for IBS-D



Drug class	Generic name (dose)	Key points
Antidiarrheals	Loperamide (1–8 mg four times daily in divided doses) Diphenoxylate (5 mg up to four times daily)	Useful for the treatment of diarrhea but no global symptom relief shown Titrate dose to desired effect and avoid constipation
5-HT ₃ antagonist	Alosetron (0.5–1.0 mg twice daily)	Efficacious for IBS-D Only available for treatment of severe IBS-D in women under a risk management program Concerns of serious complications of constipation and ischemic colitis
Tricyclic antidepressants	Amitriptyline (10–150 mg at night) Doxepin (10–150 mg at night) Imipramine (10–150 mg at night) Clomipramine (25–100 mg at night) Trimipramine (10–150 mg at night) Desipramine (10–150 mg at night) Nortriptyline (10–150 mg at night)	Post hoc analysis of an IBS trial suggests greater efficacy in IBS-D Initiated at lower dose than usual dose for mood disorders Recommend titrating dose for desired effect and to minimize adverse effects
Antibiotics	Rifaximin (400–550 mg three times daily)	Global efficacy demonstrated in nonconstipating IBS Improvement in bloating also demonstrated

Abbreviation: IBS-D, diarrhea-predominant IBS.

Review



IBS can be predominately:

- a) Constipation
- b) Diarrhea
- c) Both

Review



Rifaximin is FDA approved in IBS with:

- a) Constipation
- b) Diarrhea
- c) Both



Thank you for your attention!

Questions?

References



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