Review: Tegaserod prompts global relief of symptoms in the irritable bowel syndrome

Evans BW, Clark WK, Moore DJ, Whorwell PJ. **Tegaserod for the treatment of irritable bowel syndrome.** Cochrane Database Syst Rev 2004;(1):CD003960.

QUESTION

In patients with the irritable bowel syndrome (IBS), does tegaserod reduce symptoms?

METHODS

Data sources: MEDLINE (1966 to 2002), EMBASE/Excerpta Medica (1980 to 2002), Science Citation Index, the Cochrane Central Register of Controlled Trials, the Cochrane Inflammatory Bowel Disease Review Group Specialized Trials register, databases of ongoing trials, the U.S. Food and Drug Administration, and lists of conference abstracts. Bibliographies of relevant articles were scrutinized, and Novartis (the manufacturer of tegaserod) was contacted for unpublished studies.

Study selection and assessment: Randomized controlled trials (RCTs) or quasirandomized controlled trials published in any language that compared tegaserod with placebo, no treatment, or any other intervention, and reported relevant outcomes in patients (≥ 12 y) with objectively documented IBS. Study quality was assessed using 4 criteria (selection, performance, attrition, and detection biases) described in the Cochrane Reviewers' Handbook.

Outcomes: Patient global assessment (PGA) of relief from gastrointestinal (GI) symptoms, including abdominal pain, distention, flatulence, constipation, diarrhea, and stool frequency and consistency. Patients were subsequently classified as responders or nonresponders.

MAIN RESULTS

8 RCTs (5320 patients, about 90% women) met the selection criteria. Types of IBS were constipation-predominant (7 RCTs) or diarrhea-predominant (1 RCT). 2 doses of tegaserod (12 mg [8 RCTs] and 4 mg [6 RCTs]) were compared with placebo. Meta-analyses were done using both fixed-effects (for homogenous data) and random-effects (where significant heterogeneity was detected) models. The rates of response for PGA of relief were greater in the tegaserod groups (at each dose and with both doses combined) than in the corresponding placebo groups (Table). However, a minimal clinically important difference was reported in only 1 RCT comparing tegaserod (12 mg) with placebo. Among individual GI symptoms, only bowel habit was associated with a greater response in the tegaserod (4 mg) group than in the placebo group (relative risk 1.21, 95% CI 1.02 to 1.43). The rate of diarrhea was greater in the tegaserod 12-mg group than in the placebo group (relative risk 2.75, CI 1.90 to 3.97).

CONCLUSION

Tegaserod is more effective than placebo for reducing some symptoms in women with the constipation-predominant irritable bowel syndrome.

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Tegaserod (Teg) (12 or 4 mg) vs placebo for the irritable bowel syndrome at 12 weeks*

Outcome	Number of trials (*n*)	Comparisons	Weighted event rates	RBI (95% CI)	NNT (CI)
Responders with respect to PGA of relief	4 (3194)	Teg, 12 mg vs placebo	43% vs 36%	19% (9 to 29)	15 (10 to 34)
	3 (1685)	Teg, 4 mg vs placebo	39% vs 34%	15% (2 to 31)	20 (10 to 100)
	4 (4040)	Teg, 4 and 12 mg vs placebo	42% vs 36%	17% (8 to 27)	17 (12 to 340)

*PGA = patient global assessment. Other abbreviations defined in Glossary; weighted event rates, RBI, NNT, and CI calculated from data in article using a fixed-effects model.

COMMENTARY

Evans and colleagues assessed the short-term efficacy of tegaserod for the treatment of IBS and concluded that it may be of modest value for treating women with constipation-variant IBS. Most patients had already been treated with fiber or bulking agents, and given the duration of disease (8 to 16 y) in the study populations, it is likely that these patients were particularly refractory to IBS therapy.

Strengths of the review include a comprehensive literature search, contacting drug manufacturers for additional information (although none was provided), and use of Rome I or II inclusion criteria for study selection. However, responder definitions were not comparable across studies and time frames for response variables often differed.

RCT investigators followed several of the methodological recommendations of the Rome II Design of Treatment Trials Committee (1). Thus, the guidelines seem to be effective. Most studies justifiably selected patients based on the anticipated mechanistic action of the drug (i.e., patients with constipation who might benefit from augmenting gut peristalsis). It is important to note that the recommended drug dose (6 mg, twice daily) may not be ideal because no consistent dose response was observed, and the number needed to treat (15 to 20) and number needed to harm (20) were similar, raising the possibility that 8 mg or a titrated dose might be better in clinical practice. However, this observation needs testing.

IBS predominantly affects women, and only 1 small study in the meta-analysis included similar numbers of men and women. Extrapolation of the results to men is therefore inappropriate. The overall benefit of tegaserod from these studies seems to be modest at best (relative benefit increase 15% to 19%), significant only for global relief (with a placebo response of 30% to 40%), and not significant for pain—the primary symptom of IBS—or other symptoms. Evans and colleagues appropriately query whether tegaserod influences visceral sensitivity or psychopathology. The results of this review suggest that tegaserod might be better suited for treating constipation than constipation related to IBS.

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Reference

1. **van Zanten SJ, Talley NJ, Bytzer P, et al.** Design of treatment trials for the functional gastrointestinal disorders. In: Drossman DA, ed. Rome II: The Functional Gastrointestintal Disorders. McLean, VA: Degnon Associates; 2000:577-622.