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Tegaserod
A Viewpoint by M. Scott Harris

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Irritable bowel syndrome (IBS) is a disorder characterised by altered bowel habits, abdominal discomfort and absence of identifiable organ pathology. IBS represents one of the most commonly encountered gastrointestinal problems. Excess medical charges for IBS-like symptoms surpass $US8 billion annually.[1] Cost-effective strategies for IBS treatment are certain to become a future focus of managed care organisations.

Diagnosis and treatment of IBS has been hindered by incomplete understanding of disease pathophysiology. IBS is believed to represent dysregulation of visceral and motor function. In patients with IBS there is a tendency for both the large and small intestine to over react to various stimuli, such as drugs, balloon distension and eating.[2] High amplitude colonic contractions are more frequent in patients with IBS.[2] However, these findings lack diagnostic specificity and sensitivity.

Drugs affecting gastrointestinal (GI) motility have been evaluated with the aim of reducing pain or improving bowel function. Methodological problems, which include heterogeneity among patients with IBS (i.e. the possibility of diarrhoea and constipation representing different abnormalities of motor and sensory function), render earlier studies inconclusive.[3]

The prevalence of IBS has made it a target for pharmaceutical development. Drugs which reduce contractile activity (selective muscarinic antagonists, GI-selective calcium antagonists) or visceral perception (5-HT_3 antagonists) offer promise in diarrhoea-predominant IBS. Prokinetic agents may play a role in constipation-predominant individuals. Despite earlier studies,[4,5] cisapride (a 5-HT_4 agonist and 5-HT_3 antagonist) has proved to be of limited usefulness in this latter subclass of patients.[6]

Tegaserod, a new selective partial 5-HT_4 receptor agonist, may offer greater efficacy in the treatment of constipation-predominant IBS.[7,8] How tegaserod and other emerging therapies will fit into the IBS treatment armamentarium is uncertain. Until greater clinical experience is available, symptom-specific treatment, education, reassurance, and dietary and lifestyle modification[9] remain the mainstays of treatment for individuals with IBS. ▲

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Tegaserod
A Viewpoint by Peter J. Whorwell

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The abundance of serotonin (5-hydroxytryptamine; 5-HT) and its associated receptor subtypes in the gastrointestinal (GI) tract has led to the assumption that the serotoninergic system plays a key role in the control of GI physiology. Thus, it has been suggested that modification of this system might be a good therapeutic strategy for the treatment of irritable bowel syndrome (IBS). However, the concept that IBS is a disorder of gut physiology is only an assumption for which there is some, but not an overwhelming amount of, scientific support.

Patients with IBS experience a variety of symp-

toms which vary considerably in their degree of intrusiveness. Therefore, patients have different requirements in terms of symptom relief. Furthermore, it is still not known whether IBS has a single cause or whether it represents a heterogeneous group of disorders. Thus, although the ideal drug for this condition would be one that helps all sufferers, this may be an unachievable goal and we may have to settle for agents that help particular patient subgroups or different symptoms.

A number of drugs with activity at different 5-HT receptor subtypes are currently in development for the treatment of IBS; some even have opposing actions (agonists and antagonists). Tegaserod is one such example which, by virtue of its prokinetic activity, is being targeted at patients with constipation-predominant IBS. Some agents have antidiarrhoeal properties and there is some evidence that there may be gender differences in the activity of others.

One of the problems with the development programmes for all of these drugs is the demanding study entry criteria, with the result that it is difficult to be sure how representative recruited patients are to the real world of patients with IBS. Consequently, it is unlikely that we will know just how effective any of these drugs really are until they are marketed and experience with a broader group of patients is gained. ▲