Experimental Drug Shown to Help Prevent Ileus

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PHILADELPHIA — Treatment with the first drug from a new class of opioid-receptor antagonists led to significant reductions in ileus and other postoperative morbidity following open laparotomy, Conor Delaney, M.D., said at the annual meeting of the American Society of Colon and Rectal Surgeons.

An analysis combining the results from three phase III studies with a total of more than 1,600 patients increased the power of the three individual studies to show a significant effect of the new drug, alvimopan, compared with placebo. The results from some of the individual studies, which had all been previously reported, failed in some cases to show a statistically significant effect from alvimopan compared with placebo, added Dr. Delaney, a colorectal surgeon at the Cleveland Clinic Foundation.

Adolor, the company that makes alvimopan (Entereg), sponsored these studies and submitted an application to the Food and Drug Administration last year to approve the drug for managing postoperative ileus. At press time, the application was still pending.

The novel μ-opioid receptor antagonist is believed to stop opioids from slowing the recovery of bowel function after surgery.

Alvimopan is a novel, μ-opioid receptor antagonist. The drug is believed to stop opioids from slowing the recovery of bowel function after open laparotomy without compromising analgesic effects.

The three studies enrolled a total of 1,627 patients who underwent either bowel resection or hysterectomy. Patients were randomized to treatment with alvimopan doses of either 6 mg or 12 mg, or with placebo, in addition to standard postoperative care. Treatments began at least 2 hours before surgery, and continued after surgery on a b.i.d. basis until either hospital discharge or a maximum treatment duration of 7 days.

During postoperative hospitalization, the incidence of serious ileus was 1.9% in the 6-mg group and 1.5% in the 12-mg group, compared with a 5.4% rate in patients on placebo, a statistically significant difference.

The rates of nasogastric tube insertion were 5.5% and 5.6%, respectively, in the 6-mg and 12-mg alvimopan groups, and 9.6% among patients treated with placebo, also a statistically significant difference.

Other measures of bowel dysfunction, such as small-bowel obstruction and anastomotic leak, were not significantly different between the drug-treated and placebo groups. But the fraction of patients who were discharged 7 or more days after surgery was significantly affected. Hospital discharge after 7 or more days occurred in 18.8% and 15.7% of patients treated with 6 mg and 12 mg alvimopan, respectively, compared with a 29.3% rate among patients treated with placebo.

Results from the three studies also showed that no patients developed adverse effects that appeared related to alvimopan, Dr. Delaney said.

The clinical incidence and effect of postoperative ileus were quantified in a second report at the meeting. (See chart.) Data from the Premier Inc. database included 193,407 patients who underwent open laparotomy in the United States during January-December, 2002. The database was limited to patients who spent fewer than 12 hours in the operating room and fewer than 30 days in the hospital, and whose hospitalization costs were at least $500. In this group, 17,417 patients were coded in their medical records as having postoperative ileus, an incidence rate of 9.9%, reported Anthony Senagore, M.D., head of research in the department of colorectal surgery at the Cleveland Clinic Foundation.

A multivariate analysis was done to identify risk factors that were associated with ileus. The only clinical or demographic factor significantly associated with development of ileus was treatment with an opioid, Dr. Senagore said.

Dr. Delaney disclosed that he received research grants from Adolor and is also a speaker for and consultant to the company. Adolor is collaborating with GlaxoSmithKline to develop alvimopan for other applications, including opioid-induced bowel dysfunction, idiopathic constipation, and irritable bowel syndrome. ■