

Rabeprazole Approved for Short-term Reflux Treatment in Adolescents

Rabeprazole sodium (Aciphex, Eisai) was recently approved by the US Food and Drug Administration (FDA) for short-term treatment (up to 8 weeks) of gastroesophageal reflux disease (GERD) in patients 12 years of age and older. FDA approval was based upon a 12-week, multicenter, open-label, randomized, parallel-group study of 111 adolescent patients who had GERD. Rabeprazole was well tolerated in this patient population and had a safety profile similar to that of adults. Adverse events experienced in more than 2% of patients included headache (9.9%), diarrhea (4.5%), nausea (4.5%), vomiting (3.6%), and abdominal pain (3.6%). The researchers concluded that once-daily, 8-week treatment with rabeprazole 20 mg reduced the severity and frequency of GERD symptoms.

R1626 Plus Standard Hepatitis C Virus Treatment

In the August issue of *Hepatology*, two recent studies evaluated the use of R1626, a nucleoside polymerase inhibitor, in combination with standard hepatitis C virus (HCV) therapy. In a phase IIa study conducted by Paul J. Pockros, MD, of Scripps Clinic in La Jolla, California, and associates at various institutions, 104 HCV treatment-naïve patients with genotype 1 were randomized to receive either 1,500 mg of R1626 BID plus peginterferon alfa-2a (n=21); 3,000 mg of R1626 BID plus peginterferon alfa-2a (n=32); 1,500 mg of R1626 BID plus peginterferon alfa-2a and ribavirin (n=31); or the standard treatment of peginterferon alfa-2a and ribavirin (n=20). HCV RNA levels were undetectable (<15 IU/mL) after 4 weeks of treatment in 29%, 69%, and 74% of patients in the R1626 arms, respectively, in comparison to 5% of patients receiving HCV standard therapy. The authors noted synergy between R1626 and peginterferon alfa-2a as well as between R1626 and ribavirin. In addition, there was a lack of viral resistance and the reported adverse events were mainly mild or moderate. The authors concluded that due to the strong synergistic antiviral effect among R1626, peginterferon alfa-2a, and ribavirin, dosage of one or both agents could be reduced to increase tolerability without compromising efficacy.

In another study, Stuart K. Roberts, MD, of the Alfred Hospital in Melbourne, Australia, and colleagues at various institutions conducted a multicenter, observer-blinded, randomized, placebo-controlled, multiple ascending dose, phase Ib study to assess safety, pharmacokinetics, and antiviral activity and identify the maximum tolerated dose of R1626 in patients with chronic HCV. In the study, 47 treatment-naïve patients with chronic HCV genotype 1 received R1626 doses of 500 mg BID; 1,500 mg BID; 3,000 mg BID; 4,500 mg BID; or placebo BID. Mean decreases (median; range) in HCV viral load after 14 days of treatment with doses of 500 mg, 1,500 mg, 3,000 mg, and 4,500 mg were 0.32 (0.22; 0.01–0.71), 1.2 (0.8; 0.49–2.46), 2.6 (2.7; 1.27–3.93), and 3.7 (4.1; 2.15–4.39) \log_{10} , respectively. The authors noted that the reductions in HCV RNA levels from baseline due to the use of R1626 signified potent antiviral activity and the lack of HCV RNA viral load rebound in most patients after 14 days. In addition, R1626 was well tolerated in doses of up to 3,000 mg and viral resistance was not seen, which may have reflected the antiviral potency of R1626. The authors concluded that additional studies are needed to further examine R1626 in combination with peginterferon alfa-2a and ribavirin in the treatment of patients with chronic HCV infection.

Incisionless Appendectomy With Gastrostomy Closure Performed

At the recent Natural Orifice Surgery Consortium for Assessment and Research's 3rd International Conference on Natural Orifice Transluminal Endoscopic Surgery (NOTES), held in San Francisco, California, Santiago Horgan, MD, of the University of California San Diego Center for the Future of Surgery, performed the first appendectomy, including a gastrostomy closure, from inside the stomach, without making any abdominal incisions. This ability to close the gastrostomy from inside the stomach is considered an important step in the widespread adoption of incisionless NOTES surgery. NOTES, the emerging surgical field that involves passing surgical instruments through the body's natural orifices (eg, the mouth) for removal of organs such as the appendix or gallbladder, may have the potential to reduce pain, length of hospital stays, and healthcare costs as well as eliminate external incisions and scars in comparison to traditional and laparoscopic surgery. Other incision-

less surgical procedures that have been performed thus far include removal of the appendix through the mouth and closure of the gastrostomy through the mouth after a NOTES appendectomy.

Guidelines for Endoscopy in Bariatric Surgery Patients

The American Society for Gastrointestinal Endoscopy recently published guidelines clarifying the role of endoscopy in preoperative and postoperative bariatric surgery patients in the July issue of *Gastrointestinal Endoscopy*. The following recommendations were included among the guidelines:

- All patients with upper gastrointestinal tract symptoms who are planning to undergo bariatric surgery should first undergo upper endoscopy.
- Upper endoscopy should also be considered in all patients planning to undergo Roux-en-Y gastrojejunobypass (RYGB), whether or not they are symptomatic.
- In asymptomatic patients who are not planning to undergo endoscopy, it is recommended to perform non-invasive *Helicobacter pylori* testing followed by treatment, if positive.
- In asymptomatic patients who are undergoing gastric banding, the exclusion of large hernias that may affect the surgical approach should be considered.
- Endoscopic assessment can aid in the diagnosis and treatment of postoperative bariatric surgical symptoms and complications.
- Patients should undergo magnetic resonance cholangiopancreatography when other noninvasive imaging studies are inconclusive.
- The use of endoscopic retrograde cholangiopancreatography in RYGB patients should be selective.

Elderly Liver Transplant Donors for Hepatitis C Virus Patients

According to a study in the July issue of *Archives of Surgery*, M.B. Majella Doyle, MD, of the Washington University School of Medicine in St. Louis, Missouri, and colleagues evaluated the effect of utilizing older liver donor grafts on short- and medium-term survival. The researchers analyzed data from 489 adult liver transplantations performed at the school between 1997 and 2006. Of these patients, 187 (38.2%) were HCV patients whereas the other 302 (61.8%) patients had other indications for liver transplantation. Of the HCV patients, 88.1% survived 1 year, 78.3% survived 3 years, and 69.2% survived 5 years. In HCV patients, donor livers were still effective in 85.6% of patients after 1 year, 75.6% of patients

after 3 years, and 65.6% of patients after 5 years. No differences in patient survival and graft survival rates were noted between patients with or without HCV at 1, 3, or 5 years. Nevertheless, a negative effect, similar to that seen at other long-term liver transplant centers, was noted from recurrent HCV infection, trending toward worsened long-term survival from years 5 to 10.

As for the effect of the age of the donor, 72 patients in the study received livers from donors 60 years of age or older. Of these patients, 24 (12.8%) were HCV patients whereas 48 (15.9%) were not. No differences were noted in 1-, 3-, or 5-year patient or graft survival rates when these patients, or those patients whose donors were 65 years of age or older, were compared with patients whose donors were younger. However, long-term comparisons of this nature have not been analyzed, as elderly donors have been utilized mainly within the past 5 years. Nevertheless, based upon these early results, the authors concluded that the use of elderly liver donors is safe.

Helicobacter pylori Eradication and Redevelopment of Gastric Cancer

Mototsugu Kato, MD, and Masahiro Asaka, MD, of the Hokkaido University Graduate School of Medicine in Sapporo, Japan, and colleagues designed a randomized, controlled trial of 544 patients to evaluate the prophylactic effect of *H. pylori* eradication therapy on the development of metachronous stomach cancer following surgery for removal of early gastric cancer. The results of this study were published in an August issue of *The Lancet*. The patients were newly diagnosed with stomach cancer and were either scheduled to undergo endoscopic treatment or were in postresection follow-up following endoscopic treatment. These patients were randomized to receive either *H. pylori* eradication therapy (lansoprazole 30 mg BID, amoxicillin 750 mg BID, and clarithromycin 200 mg BID for 1 week; n=272 patients) or no treatment (standard care but no additional treatment for eradication of *H. pylori*; n=272). Endoscopic follow-up was noted at 6, 12, 24, and 36 months to detect any development of new cancer at a different site in the stomach.

By the 3-year follow-up, metachronous gastric cancer had been detected in only 9 patients in the *H. pylori* eradication therapy arm compared to 24 patients in the control arm. Overall, the risk of developing gastric cancer decreased by approximately two thirds in the *H. pylori* eradication therapy arm in comparison to the control arm. In the eradication arm, 19 (7%) patients experienced diarrhea and 32 (12%) experienced soft stools. The authors concluded that *H. pylori* treatment decreased the risk of redeveloping gastric carcinoma.

Survival Rates With the Use of Sorafenib in Hepatocellular Carcinoma

Led by Josep Llovet, MD, of Mount Sinai School of Medicine in New York and the Barcelona Clinic Liver Cancer Group in Barcelona, Spain, researchers recently conducted a multicenter, phase III, double-blind, placebo-controlled trial that randomly assigned 602 treatment-naïve patients with advanced hepatocellular carcinoma to receive either sorafenib (Nexavar, Bayer/Onyx) 400 mg BID daily (n=299) or placebo (n=303). The findings of the study were published in a July issue of the *New England Journal of Medicine*.

At the second planned interim analysis, 321 deaths had occurred, and the study was stopped due to the positive findings of the sorafenib arm. Patients in the sorafenib arm lived significantly longer: a median of 10.7 months compared to 7.9 months for patients in the placebo arm (hazard ratio in the sorafenib arm, 0.69; 95% confidence interval, 0.55–0.87; $P < .001$). No significant difference was noted between the two arms in the median time to symptomatic progression (4.1 months vs 4.9 months; $P = .77$). The median time to radiologic progression, however, was significantly different: 5.5 months in the sorafenib arm in comparison to 2.8 months in the placebo arm ($P < .001$). The incidence of adverse side effects was similar in both arms: 52% in the sorafenib arm and 54% for the placebo arm. Moderate-to-serious side effects in the sorafenib arm compared to the placebo arm included diarrhea (11% vs 2%), hand and feet skin reactions (8% vs 1%), fatigue (10% vs 15%) and bleeding (6% vs 9%).

In Brief

In a retrospective chart review, adalimumab was well tolerated in pediatric patients with Crohn's disease, with complete or partial response observed in 64% of patients and no serious adverse events.

Nevertheless, the researchers stated that additional studies are needed to evaluate the efficacy and determine the optimal dosing of adalimumab in the pediatric population with Crohn's disease. (*J Pediatr Gastroenterol Nutr.* 2008;47:19-25.)

According to a meta-analysis, high-dose proton pump inhibitors appear to be more effective than standard-dose therapy for curing *H. pylori* infection in 7-day triple therapy. (*Aliment Pharmacol Ther.* 2008 Jul 17; [Epub ahead of print])

An oral administration of 50 mg of sildenafil significantly decreased the mean pulmonary arterial pressure and hepatic sinusoid resistance with a significant increase in hepatic nitric oxide and cyclic guanosine monophosphate production and did not worsen portal hypertension in cirrhotic patients. (*Hepatol Res.* 2008 Jul 4; [Epub ahead of print])