

Esomeprazole Approved for Gastroesophageal Reflux Disease (GERD) in Young Children

The US Food and Drug Administration (FDA) recently approved esomeprazole magnesium (Nexium, AstraZeneca) in both delayed-release capsule and liquid formulations for short-term use in children 1–11 years of age with GERD. The approved doses for this age group are 10 mg or 20 mg daily, even though esomeprazole was previously approved in doses of 20 mg or 40 mg for children 12–17 years of age. FDA approval for the use of esomeprazole in children aged 1–11 was based upon extrapolation of data from previous study results in adults to pediatric patients, as well as safety and pharmacokinetic studies conducted in children. In one study, 109 patients aged 1–11 years who were diagnosed with GERD were treated with esomeprazole once daily for up to 8 weeks to evaluate the safety and tolerability of the drug. Most of these patients demonstrated healing of esophageal erosions after 8 weeks of treatment. The most common adverse reactions in the children included headache, diarrhea, abdominal pain, nausea, gas, constipation, dry mouth, and sleepiness. The safety and efficacy of esomeprazole has not been established in children younger than 1 year of age.

Combined Immunosuppression Therapy Versus Conventional Therapy for Crohn's Disease

According to a recent issue of *Lancet*, researchers led by Geert D'Haens, MD, of the Imelda Gastrointestinal Clinical Research Centre in Belgium, conducted a study comparing efficacy of the early use of combined immunosuppression with conventional therapy in patients with active Crohn's disease who did not previously receive glucocorticoids, antimetabolites, or infliximab (Remicade, Centocor). This 2-year, open-label, randomized trial was conducted in 18 centers in Belgium, The Netherlands, and Germany between May 2001 and January 2004. Of the total 133 study participants, 67 were assigned to early combined immunosuppression, which consisted of 3 infliximab infusions (5 mg/kg) at Weeks 0, 2, and 6, with azathioprine. Additional infliximab and, if necessary, corticosteroids were also administered to control disease activity. The remaining 66 patients were assigned to conventional treatment, which consisted of corticosteroids, followed by azathioprine and then infliximab. The primary outcome measures were defined as remission without corticosteroids and without bowel resection at Weeks 26 and 52. The researchers analyzed the results by performing modified intention-to-treat analysis (ITT).

Four patients (2 in each group) did not receive treatment according to protocol. At Week 26, 39 (60.0%) of the 65 patients in the combined immunosuppression group were in remission without corticosteroids and without surgical bowel resection compared with 23 (35.9%) of the 64 control patients, signifying an absolute difference of 24.1% (95% confidence interval [CI], 7.3–40.8; $P=.0062$). At Week 52, 40 (61.5%) of the 65 patients in the combined immunosuppression group and 27 (42.2%) of the 64 patients in the control group were in remission, for an absolute difference of 19.3% (95% CI, 2.4–36.3; $P=.0278$). In the early combined immunosuppression group, 20 (30.8%) of the 65 patients experienced serious adverse events compared with 19 (25.3%) of the 64 control patients ($P=1.0$). The authors concluded that combined immunosuppression was more effective than conventional treatment for induction of remission and reduction of corticosteroid usage in patients recently diagnosed with Crohn's disease and that more intensive treatment early on in the disease course could produce better outcomes.

Interferon Plus Ribavirin in Patients With HIV/Hepatitis C

At the recent 2008 Conference on Retroviruses and Opportunistic Infections held in Boston, Massachusetts, Juan Berenguer, MD, of the Hospital Gregorio Marañón in Madrid, Spain, and colleagues presented an analysis of the Grupo de Estudio del SIDA (GESIDA) 3603 Study Cohort. This cohort was established to follow HIV/hepatitis C virus (HCV) patients who started interferon plus ribavirin therapy between January 2000 and December 2005. Overall, 711 co-infected patients were analyzed. Most participants had been treated with ribavirin-boosted pegylated interferon (44% with pegylated interferon alfa-2a; 38% with pegylated interferon alfa-2b), and 18% had received conventional (nonpegylated) interferon plus ribavirin. All study participants were followed every 6 months after treatment completion, for a median of 20 months. Cox regression analysis was adjusted for Center for Disease Control clinical category, HCV genotype, and stage of liver fibrosis.

According to the authors, patients who achieved sustained virologic response with interferon plus ribavirin had a decreased risk of developing a liver-related event (liver-related mortality, liver decompensation, hepatocellular carcinoma, liver transplantation) compared with those who did not achieve sustained virologic response. Specifically, the rate of liver-related mortality was 0.23 per 100 person-years in patients who achieved sustained virologic

response versus 1.65 per 100 person-years in patients who did not achieve sustained virologic response; the rate of liver decompensation was 0.23 versus 4.33, respectively; the rate of hepatocellular carcinoma was 0 versus 0.83, respectively; the rate of liver transplantation was 0 versus 1.02, respectively; and the rate of overall mortality was 0.46 per 100 person-years versus 3.12 per 100 person-years, respectively. HIV-positive patients with chronic HCV experienced a more rapid progression of liver disease in general than did patients with HCV alone. The authors concluded that achievement of sustained virologic response after interferon plus ribavirin therapy in HIV/HCV co-infected patients reduces liver-related complications and mortality.

Preoperative Versus Postoperative *Helicobacter pylori* Eradication Therapy in Gastric Cancer Patients

Researchers at the Research Institute and Hospital in Goyang, Korea, conducted a study examining a total of 138 distal gastric cancer patients with *H. pylori* infection who were randomized to receive either preoperative (n=68) or postoperative (n=70) proton pump inhibitor-based triple therapy for *H. pylori* eradication. The treatment regimen consisted of 10 mg of rabeprazole, 500 mg of clarithromycin, and 1,000 mg of amoxicillin, all twice daily for 7 days. Eradication was evaluated by rapid urease examination and histologic evidence 12 weeks after surgery. The results of this study were published in a recent issue of the *American Journal of Gastroenterology*.

According to ITT analysis, *H. pylori* eradication rates were 84.6% (95% CI, 73.5–92.4) in the preoperative arm and 83.1% (95% CI, 71.7–91.2) in the postoperative arm ($P=.99$). Per-protocol analysis found the rates to be 87.3% (95% CI, 76.5–94.4) in the preoperative arm and 86.9% (95% CI, 75.8–94.2) in the postoperative group ($P=.99$). In the postoperative arm, the eradication rates did not differ with the reconstruction method (Billroth I vs II, 80.4% [95% CI, 66.1–90.6] vs 89.5% [95% CI, 66.9–98.7], according to ITT analysis [$P=.49$] and 85.7% [95% CI, 71.5–94.6] vs 89.5% [95% CI, 66.9–98.7], according to per-protocol analysis, [$P=.99$]). The authors concluded that in distal gastric cancer patients, the effect of proton pump inhibitor-based triple therapy for *H. pylori* eradication did not differ when administered postoperatively or preoperatively.

Wireless Capsule Endoscopy in Celiac Disease

Joseph Murray, MD, of the Mayo Clinic in Rochester, Minnesota, and colleagues examined the use of wireless capsule endoscopy in celiac disease by evaluating the distribution of atrophy in untreated celiac disease; the correlation between the extent of changes and the clinical manifestations; the accuracy and interobserver agreement of wireless capsule endoscopy assessment; and

the effect of gluten withdrawal. This study, the results of which were recently published in *Clinical Gastroenterology & Hepatology*, examined 38 consecutive patients with untreated biopsy-confirmed celiac disease who underwent wireless capsule endoscopy. Each study participant was invited to undergo repeat testing after 6 months or more of gluten withdrawal. Two investigators independently reviewed the video images of each patient.

The authors found that capsule endoscopy detected visible atrophy in 35 (92%) of the patients. Extensive enteropathy was found in 22 (59%) of the patients, enteropathy limited to the duodenum in 12 (32%) of the patients, and jejunal enteropathy in only 1 of the patients. No association was demonstrated between the extent of the lesion and the clinical manifestations. Capsule endoscopy had a better overall sensitivity for detecting atrophy compared with upper endoscopy (92% vs 55%; $P=.0005$), with a specificity of 100%. The overall interobserver agreement for the 2 independent reviewers was relatively high (total agreement, 86.5%). The extent and pattern of visually detected villous atrophy was shown to have a clinically significant improvement both qualitatively and quantitatively after gluten withdrawal. The authors concluded that celiac disease affects a highly variable portion of the small intestine starting at the duodenum and that the extent of visible enteropathy does not explain differences in clinical presentation.

In Brief

Researchers conducting a prospective study found that surface-enhanced laser desorption/ionization time-of-flight mass spectrometry accurately distinguished patients with hepatocellular cancer from those with HCV cirrhosis, was more accurate than traditional biomarkers in identifying small tumors, and should be further evaluated. (*Clin Cancer Res.* 2008;14:470-477.)

In a retrospective study, researchers found that the standard dose of 6-mercaptopurine/azathioprine may not be adequate for inflammatory bowel disease patients 6 years of age and younger. Closely monitored dose escalation beyond the standard dosing range was effective and well tolerated. (*Inflamm Bowel Dis.* 2008 Feb 11 [Epub ahead of print].)

According to a prospective study, irritable bowel syndrome and psychological distress affected GERD symptoms and quality of life before and after proton pump inhibitor therapy. Symptoms and quality of life before and after proton pump inhibitor therapy were similar in nonerosive reflux disease and erosive esophagitis patients. (*Aliment Pharmacol Ther.* 2008;27:473-482.)