

GI Profile Not Affected By COX Inhibitor Selectivity

BY MARY ANN MOON
Contributing Writer

Cyclo-oxygenase-2 inhibitors were found to be no safer than nonselective NSAIDs in averting adverse gastrointestinal events in a large observational study in the United Kingdom.

The finding is important "given that enhanced gastrointestinal safety has been one of the main justifications for these drugs," wrote Dr. Julia Hippisley-Cox and her associates at the University of Nottingham (England).

They also found that the concomitant use of ulcer-healing drugs reduces the GI risks of COX-2 inhibitors, which suggests "there is some risk to protect against." Taken together, these results indicate that COX-2 inhibitors "may not be as safe as originally thought," the authors said (BMJ 2005;331:1310-6).

The COX-2 inhibitors were developed to relieve pain without inducing the GI side effects common with NSAIDs, but data on their long-term safety are lacking. The University of Nottingham re-

searchers calculated the comparative risks of GI events in patients who took these prescription pain relievers between 2000 and 2004.

After reviewing the medical records in a database of more than 7 million patients treated at general practices throughout England, Scotland, and Wales, the investigators identified 9,407 who had an adverse GI event and matched them with more than 88,000 controls who had no such events. Patients with GI events were more likely to have taken either prescription NSAIDs (odds ratio 1.69) or prescription COX-2 inhibitors (OR 1.89) than were control subjects.

Celecoxib was the only agent out of 27 pain relievers used by the study subjects to show no link with adverse GI events. However, the number of celecoxib users was small, so this finding remains "difficult to interpret," they noted.

Use of ulcer-healing drugs such as proton pump inhibitors cut the risk for GI events in users of both COX-2 inhibitors and NSAIDs, again suggesting that the GI risks of the two types of pain relievers are similar, the authors wrote. ■

More Time May Be Needed for PPI Effects to Become Evident

BY MITCHEL L. ZOLER
Philadelphia Bureau

COPENHAGEN — Some patients with dyspepsia not caused by reflux or a peptic ulcer who do not respond to a proton-pump inhibitor during the first week of treatment will respond after a few more weeks of ongoing treatment, according to results from two studies.

The first week on a proton-pump inhibitor (PPI) "is only moderately useful for predicting responses after 4 and 8 weeks of treatment," Dr. Sander Veldhuyzen van Zanten said at the 13th United European Gastroenterology Week.

"It therefore makes sense to treat for 4-8 weeks" to see if the patient will eventually respond, said Dr. van Zanten, a gastroenterologist and professor of medicine at Dalhousie University in Halifax, N.S.

The results also showed that a double dose of a PPI was no more effective than the standard dose when starting treatment.

One of the studies enrolled 1,250 patients, aged 18-50 years, who had epigastric pain or burning for at least 3 months, were negative for *Helicobacter pylori*, and had not been investigated by endoscopy. The study excluded patients whose predominant symptom was heartburn or acid regurgitation and those with more than one episode of heartburn or acid regurgitation per week. The severity of epigastric pain or burning was rated by patients on a 4-point scale on which

0 indicated no symptoms and 3 indicated severe symptoms. The average severity score at enrollment was 1.3.

Patients were randomized to start treatment with 40 mg of esomeprazole either once or twice daily for 1 week. About 44% of patients responded to both regimens, with no difference between the two groups. Patients were considered responders if they had a score of 0 or 1 during the last 3 days of treatment.

After this initial week, the patients were rerandomized either to continue on 40 mg of esomeprazole once daily or to placebo for 7 more weeks. The full 8 weeks of the study were completed by 1,084 patients.

Of the 716 patients who were on esomeprazole for 8 weeks, 339 patients (47%) responded. In this phase, responders were defined as patients with a symptom score of 0 or 1 on each of the final 7 days of treatment. Of the 339 responders, 198 also had responded after 1 week but 141 patients (42% of all responders) had not shown any response during the first week of treatment.

Similar results were seen in a second study of 1,589 patients. The design of that study was similar to the first, and 743 patients received esomeprazole treatment for 8 weeks. The 295 patients who responded after 8 weeks included 158 patients (54% of all responders) who had not responded during the first week of treatment.

AstraZeneca, which markets esomeprazole (Nexium), funded both studies. ■

Pediatric GERD Safely Relieved by Half Adult Dose of Pantoprazole

BY KATE JOHNSON
Montreal Bureau

MONTREAL — Pantoprazole safely reduces gastroesophageal reflux symptoms in children and adolescents at roughly half the adult dosage, according to two studies funded by Wyeth Pharmaceuticals, which manufactures the proton pump inhibitor.

The company does not yet have pediatric approval for the drug (Protonix), but the study fills "an unmet need for appropriate dosing information across the spectrum of pediatric patients," said Elaine Soffer, director of clinical research and development for the company, which is based in Collegeville, Pa.

The studies, presented as posters at the 13th World Congress of Gastroenterology, compared once-daily treatment at 10, 20, or 40 mg in 53 children aged 5-11 years, and once-daily treatment at 20 or 40 mg in 136 adolescents aged 12-16 years.

The younger age group had endoscopically proven gastroesophageal reflux disease (GERD), while the older age group had a clinical diagnosis of GERD. All patients were ran-

domized into one of the treatment groups for 8 weeks.

The GERD Assessment of Symptoms in Pediatrics Questionnaire (GASP-Q) was used at baseline and then weekly to measure the frequency and severity of abdominal pain, chest pain or heartburn, difficulty swallowing, nausea, vomiting or regurgitation, choking when eating, belching, and pain after eating.

After 1 week of treatment, there was a significant improvement in the mean symptom score for children in the 20-mg and 40-mg treatment groups, but this change was not seen until week 3 in the 10-mg treatment group. The difference between the 10-mg and 40-mg groups after 1 week was statistically significant (25 vs. 87 mean change in score from baseline); but scores improved significantly from baseline in all groups by week 8.

In the adolescents, the 40-mg dose was significantly more effective at week 1 and week 6 than was the 20-mg dose, but by week 8, a significant improvement in symptoms was evident in both groups, as measured by the Physicians Global Assessment and the GASP-Q scores.

Teens in the 40-mg group, but not the 20-mg group, significantly decreased their antacid use in the last week of the study, compared with the first week (1.3 tablets vs. 3.2 tablets per week).

Safety was comparable in both teen treatment groups, although there were more early exits and significantly more diarrhea in the high-dose group.

Among the children, one withdrew in the low-dose group because of lack of efficacy. No significant adverse events occurred in any of the treatment groups, and no patients dropped out because of adverse events.

"What these studies demonstrate is that at 8 weeks, there is a significant reduction in symptoms at all doses, and that even at 1 week, you can see a dose effect at the higher dose," Ms. Soffer said in an interview. Treatment also resulted in healing of erosive esophagitis in all four patients with this diagnosis, she added.

"In children, one might want to be conservative and select the middle dose because it shows an effect at 1 week. ... Then if the child doesn't respond fast enough, the higher dose is available," Ms. Soffer said. ■

Data Reassuring on Gastro Complaints in Schoolchildren

SALT LAKE CITY — Abdominal pain and other gastroenterologic symptoms commonly occurred in 48 schoolchildren but improved with time and did not keep the students out of school, according to results of a prospective study.

In the first systematic, community-based study of GI symptoms in North American school-

the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition.

The prevalence of abdominal pain decreased significantly, from 64% of children-weeks in the first month of the study to 33% in the last month. All other symptoms decreased in prevalence over time, although not significantly.

"The natural improvement of every GI symptom can justify delaying invasive testing" and may help to reassure physicians and parents about the short-term progression of these symptoms, said Dr. Saps of Children's Memorial Hospital in Chicago and Dr. Di

Lorenzo of Columbus (Ohio) Children's Hospital. The study was conducted while both physicians were at Children's Hospital of Pittsburgh.

The decline in symptoms suggests a decrease in stress as school progressed or, alternatively, seasonal variation in symptoms between the start of the study in February and the end of it in June, the doctors suggested.

—Sherry Boschert



'The natural improvement of every GI symptom can justify delaying invasive testing.'

DR. DI LORENZO

children, 48 white fourth and fifth graders in an urban private school were asked to fill out weekly confidential, eight-item symptom surveys for 16 weeks, generating 690 out of 768 possible survey responses (or children-weeks).

Students reported at least one GI symptom in 60% of children-weeks and reported headaches in 70% of children-weeks, said Dr. Miguel Saps and Dr. Carlo Di Lorenzo in a poster presentation at the annual meeting of