Highlights of the 66th Annual Scientific Meeting of the American College of Gastroenterology

by Lawrence M. Prescott, PhD

Las Vegas, Nevada was the venue for nearly 3,000 gastroenterologists, research scientists, nurses, and other healthcare professionals attending the 66th Annual Scientific Meeting of the American College of Gastroenterology from October 22 to 24, 2001. Participants met to hear the latest advances in the detection, treatment, and prevention of gastrointestinal (GI) diseases. The most recent studies included new therapeutic approaches and novel agents for the treatment of gastroesophageal reflux disease (GERD), with or without erosive esophagitis, prevention of upper GI bleeding in ICU patients, steroid sparing in autoimmune hepatitis, relief of irritable bowel syndrome (IBS), and the treatment of Crohn’s disease. Below are highlights of these presentations.

Novel Proton Pump Inhibitor for GERD with EE

Speaker: Donald O. Castell, MD, Professor of Medicine, Medical University of South Carolina, Charleston, South Carolina

Esomeprazole (Nexium, AstraZeneca), the S-isomer of omeprazole, when taken in doses of 40 mg daily, is more effective in rapidly achieving sustained resolution of daily and nocturnal heartburn in patients with gastroesophageal reflux disease (GERD) with erosive esophagitis (EE) than lansoprazole (Prevacid, TAP) 30 mg daily.

This conclusion was based on a large-scale, U.S., multicenter, randomized, double-blind trial including 5,241 adult GERD patients with endoscopically confirmed EE to assess the efficacy of esomeprazole compared with lansoprazole for treating daily and nocturnal heartburn in these patients. Patients were randomly assigned to once-daily esomeprazole 40 mg or lansoprazole 30 mg, for up to eight weeks.

Baseline severity of heartburn was balanced between treatment groups. Time to sustained resolution of heartburn, recorded by patient diary data, was achieved significantly faster with esomeprazole (seven days) than with lansoprazole (eight days).

In addition, faster sustained nocturnal heartburn resolution was recorded with esomeprazole (one day) than with lansoprazole (two days). Finally, more patients treated with esomeprazole had complete resolution of investigator-recorded heartburn at the end of week 4 than did those on lansoprazole (62.9% vs. 60.2%). Overall, both esomeprazole and lansoprazole were well-tolerated.

Intravenous PPI for ICU Patients

Speaker: Robert Aris, MD, Associate Professor of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina

Intermittent dosing with intravenous (IV) pantoprazole (Protonix IV, Wyeth-Ayerst) a proton pump inhibitor (PPI), rapidly achieves and maintains pH equal to or greater than 4 in critically ill intensive-care unit (ICU) patients at risk for upper gastrointestinal (UGI) bleeding, resulting in the elimination of UGI bleeding events or related symptoms during a recent study.

The multicenter study randomized 86 ICU patients at risk for UGI bleeding to one of four dosing regimens of IV pantoprazole (P)—P 40 mg once daily, P 40 mg twice daily, P 80 mg twice daily, P 80 mg three times daily—or the standard approved regimen of continuous infusion cimetidine (Tagamet, GlaxoSmithKline), to evaluate the potential ability of an IV PPI to rapidly raise intragastric pH in ICU patients. Patients were treated with the study drug for at least 48 hours and up to seven days. Gastric aspirations were taken every two hours for the determination of gastric pH and the detection of possible bleeding.

Preliminary results suggested that all IV pantoprazole groups could achieve and maintain gastric pH over 4 within 2.9 to 3.2 hours of the initiation of therapy, with a progressive increase in pH by day 2. Cimetidine reached a pH over 4 in approximately the same time frame (2.5 hours) on day 1, but was unable to maintain control of the percentage of time with pH over 4 by day 2, presumably because of tolerance. The percentage of time that pH was greater than 4 on days 1 and 2, respectively, was 45% and 55% for P 40 mg every 24 hours; 55% and 69% for P 40 mg every 12 hrs; 71% and 82% for P 80 mg every 12 hours; 73% and 83% for P 80 mg every eight hours; and 81% and 73% for cimetidine.

Steroid-Sparing Agent for Autoimmune Hepatitis

Speaker: Abdullah Rashdan, MD, Senior Fellow, Division of Gastroenterology and Hepatology, St. Louis University School of Medicine, St. Louis, Missouri

Mycophenolate mofetil (MMF) (Cellcept, Roche Laboratories, Inc.), a drug indicated for the prophylaxis of organ rejection in patients receiving allogenic renal, cardiac, or hepatic transplants, appears to be a safe and effective steroid-sparing alternative to the standard treatment with azathioprine (Imuran, Faro) for the treatment of autoimmune hepatitis (AIH).

Five patients with AIH who were intolerant of or resistant to standard therapy were identified prospectively and treated with MMF. Azathioprine was discontinued in all patients. The initial dose of MMF was 500 mg daily and this was gradually increased in 500-mg daily increments to 2 gm daily or to the
highest tolerated dose. Prednisone was subsequently tapered to 5 mg daily or less.

All patients achieved and maintained a biochemical remission over an average follow-up period of 18 months. Two patients had resolution of potentially serious azathioprine-related complications (cervical dysplasia and skin cancer) when switched to MMF. While on MMF, two patients were able to completely discontinue prednisone; two patients had prednisone doses tapered to 5 mg daily; and one patient had prednisone tapered to 3 mg daily. None of the patients had any adverse effects from MMF. Based on these findings, further larger controlled trials, using histologic endpoint and longer-term follow-up, are strongly suggested to confirm these observations.

**CCK Receptor Antagonist for Constipation-Dominant IBS**  
**Speaker:** Massimo D’Amato, MD, Senior Investigator, Clinical Pharmacology, Rotta Research Laboratories, Monza, Italy

The cholecystokinin (CCK) receptor antagonist dexloxioglu-  
mide (Rotta Research Laboratories/Forest Laboratories) might be a novel therapeutic agent for the treatment of constipation-  

dominant irritable bowel syndrome (C-IBS) in female patients, having demonstrated its effectiveness in relieving IBS symptoms, and because it is well-tolerated.

Because CCK might play a role in the pathogenesis of IBS, as a result of its involvement in the modulation of GI visceral sensory and motor responses, a study was designed to assess the safety and efficacy of the selective CCK receptor antagonist dexloxioglu-  
mide. A total of 405 patients (328 females, 77 males) with IBS were randomized to receive either dexloxioglu  
mide 200 mg three times daily (202 patients) or placebo (203 patients) for 12 weeks, in a randomized, double-blind, parallel-group clinical trial. Prior to randomization, patients were stratified to IBS subgroups according to their bowel habit predominance: alternating–134 patients; diarrhea–113 patients; constipation–126 patients. At the end of the treatment period or at early termination, patients rate their response as much better (improved), no change, or much worse (not improved). Responders, according to a validated Global Improve-  
ment Assessment (GIA), were those patients who judged themselves improved and had a decrease in mean abdominal pain during the last two weeks of treatment compared to baseline.

The proportion of responders with dexloxiogluomide was higher than with placebo in the patient population as a whole (39% vs. 34%). This improvement reached statistical significance in the subgroup of female patients with C-IBS (dexloxiogluomide, 40% vs. placebo, 22%). In addition, actively treated female C-IBS patients reported significantly reduced abdominal pain or discomfort; improved straining, incomplete evacuations, and global well-being; and they had more pain-free and bloating-free days.

**Locally Active Corticosteroid for Crohn’s Disease**  
**Speaker:** Sunanda Kane, MD, Assistant Professor of Medicine, University of Chicago Medical Center, Chicago, Illinois

A systematic review and meta-analysis of selected clinical trials reveals that budesonide modified release capsules (MRC) (Ento-  
cort, EC), a synthetic locally active glucocorticoid, at a 9mg dose, has been shown to be more active than the commonly used 5-acetylsalicylic acid product mesalamine or placebo for inducing remission in patients with mild to moderate active Crohn’s disease and can be used as first-line treatment. Also, while equivalent in  
action with conventional corticosteroids, budesonide MRC is markedly less likely to cause corticosteroid-associated adverse events than conventional steroids like prednisolone.

The meta-analysis was carried out on approximately 1,000 patients with mild to moderate active Crohn’s disease of the ileum and/or ascending colon enrolled in five randomized control trials comparing either the safety and efficacy of mesalamine (one study), placebo (two studies), or prednisolone (two studies). The trials reported on the effectiveness of treatment, defined as decreasing or maintaining Crohn’s Disease Activity Index (CDAI) scores of 150 points or less, and on adverse event data.

The main results showed that budesonide MRC was more likely to induce remission of mild to moderately active Crohn’s disease than placebo (relative risk [RR]=1.82) or mesalamine (RR=1.73), with no significant difference in inducing remission between budesonide MRC and prednisolone. Budesonide, however, was less likely to cause corticosteroid-related adverse events than prednisolone (RR=0.65).

**Monoclonal Antibody for Crohn’s Disease**  
**Speaker:** Gary R. Lichtenstein, MD, Associate Professor of Medicine and Director of the Center for Inflammatory Bowel Disease, Hospital of the University of Pennsylvania and University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

Data from the ACCENT I (A Chronic Clinical Trial Evaluating Infliximab in a New Long-Term Treatment Regimen demonstrat-  
ed that infliximab (Remicade, Centocor) maintenance therapy in corticosteroid-dependent Crohn’s disease (CD) patients makes it possible for these individuals to reduce or discontinue corticos-  
teroid use, while maintaining disease remission.

Although the ACCENT I study was designed to determine whether maintenance dosing with infliximab could prolong dis-  
eease progression, after six weeks in the trial, patients who were on corticosteroids at baseline and had a clinical response at week 2 were allowed to taper their corticosteroid doses by 5 mg per week if their baseline doses were 20 mg daily or more of prednisolone or equivalent, or 2.5 mg per week if their baseline doses were less than 20 mg daily.

Initially, 573 CD patients were enrolled in the trial and 335 per-  
sons were included in the efficacy analysis to be carried out at 30 and 54 weeks. Some 52.2% of week-2 responders were receiving corticosteroids at baseline, with a median dose of 20 mg daily. At week 30, the period of these reported data, the median dose of corticosteroids was 10 mg daily in the placebo maintenance group and 0 mg daily in the two infliximab maintenance groups (5 mg daily and 10 mg daily). In addition, approximately three times as many patients in the infliximab maintenance groups were able to discon-  
tinue corticosteroids while maintaining clinical remission as com-  
pared to those who received a single dose of infliximab 5 mg for induction, followed by placebo maintenance. This included 10.7% of placebo maintenance patients, 31% of 5-mg daily maintenance patients, and 36.8% of 10-mg daily maintenance patients. This bene-  
fit was seen whether patients had been on corticosteroids for less than a year or more than a year before entering the study.