

News from DDW

By Christina Lesica

The following studies were presented at the Digestive Disease Week (DDW) 2007 meeting, held in Washington, DC, May 19–24, 2007. Look for commentary by editorial board members on selected DDW presentations in an upcoming issue of *Gastroenterology & Hepatology*.

HCV-positive Livers May Benefit HCV-positive Transplant Patients

New research from a case-control study showed that patients with hepatitis C virus (HCV) who received liver transplants from genotype 1 HCV-infected donors had a slower rate of fibrosis progression at 1 year than patients transplanted with HCV-negative livers.

Led by presenter and lead investigator Paul Kwo, MD, Associate Professor of Medicine and Medical Director of Liver Transplantation, Indiana University School of Medicine, the researchers compared transplant outcomes for liver recipients from HCV-infected donors with outcomes of recipients of standard, nonextended criteria donors (ECDs). Data were analyzed from 38 liver recipients and 76 ECDs. Thirty percent of the donors were standard donors (non-ECD) and were included as potential matches. The researchers matched each HCV-positive liver donor recipient to 2 standard donor recipients and then analyzed recipient data for graft survival and patient survival at 3 months, 1 year, and 2 years. They also noted perioperative death, HCV recurrence, and fibrosis at 4 months and 1 year.

The study reported no difference in the survival rates of patients transplanted with HCV-positive livers compared with those transplanted with HCV-negative livers. In addition, researchers found that the rate of fibrosis appeared to be slower in recipients of HCV-positive livers, who have been followed for approximately 1 year thus far.

The slower rate of fibrosis development may be due to the physiologic response of “peaceful coexistence” that occurs when an HCV-positive liver is transplanted into an HCV-positive patient, explained Dr. Kwo.

Quality Indicators for Colonoscopy

Data analysis from colonoscopy procedures in more than 145,000 outpatients indicates that proper sedation and preprocedure bowel preparation are important quality indicators, which significantly lower the risk of having an incomplete colonoscopy, according to Berndt Birkner, MD, Felix Burda Foundation, Munich, Germany.

Dr. Birkner and colleagues analyzed a database with records of 145,401 colonoscopies performed from January through September of 2006 by the Compulsory Health Insurance Physicians in Bavaria, Germany. The database included demographic characteristics, colonoscopy indications, process quality indicators,

macroscopic and histologic findings, diagnosis, acute complications, and further diagnostic and therapeutic recommendations.

The researchers found that colon preparation achieved a clean bowel in 76.1% of the 145,401 patients, with liquid residues remaining in 22.3% and a dirty bowel in 1.6% of cases. Sedation or analgesia was used in 92.6% of examinations.

The investigators reported that 97.3% of colonoscopies reached the cecum or ileum, 2.7% of examinations were incomplete, and photo documentation was available in 99.0% of the procedures. Reasons given for incomplete examinations included adhesions (12.9% of incomplete colonoscopies), impassable stenosis (12.7%), long and curved colon (7.1%), complications (1.3%), and “no reason specified” in 34.2% of cases.

Statistical analysis revealed a higher risk for incomplete colonoscopies in older patients, patients with insufficient bowel preparation or liquid residues, and in curative colonoscopies. Researchers also found that male and sedated patients were more likely to have a complete colonoscopy.

The authors concluded, “For the first time, we report findings for a large range of process quality indicators for outpatient colonoscopies. They may serve as a benchmark for comparisons with other programs. Sedation and thorough bowel cleansing are modifiable factors conducive to the completeness of colonoscopies.”

Extension Trials on Infliximab Treatment in Ulcerative Colitis

Long-term extension trials of infliximab (Remicade, Centocor) therapy in ulcerative colitis patients with moderate-to-severe disease showed that infliximab responders maintained treatment response for up to 2 years. The investigators, led by Walter Reinisch, MD, University Hospital of the University of Vienna, Austria, and William Sandborn, MD, Mayo Clinic, gathered and analyzed data from long-term extensions of the ACT trials (Active Ulcerative Colitis 1 & 2) conducted in Europe and the United States.

At the start of the extensions, 76% of 229 responders to active treatment in ACT 1 & 2 had achieved mild or no disease activity (Physician’s Global Assessment score of 0 or 1) and 41% of those patients showed no disease. At 56 weeks of the extension trials, 92% of remaining

subjects had mild or no disease and 61% of those patients had no disease. At 104 weeks, 97% of the 97 remaining subjects in the extensions had mild or no disease and 75% of those patients had no disease.

Corticosteroids were used less throughout the extensions, with 80%, 88%, and 98% of subjects becoming corticosteroid-free at 8, 56, and 104 weeks, respectively. In addition, infliximab therapy was generally well tolerated, with less than 5% of patients in the extension trials discontinuing therapy due to an adverse event.

Lubiprostone and Irritable Bowel Syndrome Symptom Relief Rates

Findings were announced from two phase III, multicenter, double-blind, randomized, placebo-controlled trials examining the effects of lubiprostone (Amitiza, Sucampo) 8 µg twice daily in adults with irritable bowel syndrome with constipation (IBS-C). Led by Douglas A. Drossman, MD, primary investigator, University of North Carolina Center for Functional GI and Motility Disorders, and the Chair of the Rome Committee, the trials included 1,171 adults, 91.6% of whom were women, diagnosed with IBS-C (Rome II criteria) who received either lubiprostone 8 µg taken twice daily (n=783) or placebo (n=388) over a 12-week period. The usual dosage prescribed for lubiprostone is 24 µg daily.

Primary efficacy was determined by the question: "How would you rate your relief of IBS symptoms over the past week compared to how you felt before you entered the study?" Patients qualified as monthly responders if they reported at least moderate relief 4 of 4 weeks or significant relief 2 of 4 weeks. To be considered an overall responder (the primary endpoint), patients had to be a monthly responder for at least 2 of 3 months. During the evaluation period, patients who discontinued or reported increased use of rescue medication, lack of efficacy, or moderately or significantly less relief were considered nonresponders. Moderate or better relief of IBS symptoms for at least 2 of 3 months of treatment was considered a complete response.

According to the findings, patients who received lubiprostone 8 µg twice daily were nearly twice as likely to achieve overall response compared with those receiving placebo (17.9% vs 10.1%, $P=.001$). There was a similar incidence of serious adverse events (1% in each group) and related adverse events (22% vs 21%) compared to placebo. The most common treatment-related adverse events (>5% of patients) were nausea (8% vs 4%), diarrhea (6% vs 4%), and abdominal pain (4% vs 5% respectively).

Long-term Safety Study of MMX Mesalamine in Ulcerative Colitis

A post-hoc analysis of a long-term phase III, open-label extension study on MMX mesalamine (Lialda, Shire)

in mild-to-moderate ulcerative colitis patients evaluated maintenance of remission and relapse rates over 12 months. Remission was defined using a modified Ulcerative Colitis Disease Activity Index (UCDAI) score of no more than 1 (with scores of 0 for rectal bleeding and stool frequency), a combined Physician's Global Assessment and sigmoidoscopy score of no more than 1 (with a sigmoidoscopy score reduction of 1 or more points from baseline), and no mucosal friability. Relapse was defined as withdrawing from the study to seek alternative therapy.

Overall, a total of 459 patients entered the maintenance phase of the study. Of these patients, 362 met the above remission criteria at baseline (in 8-week, phase III, placebo-controlled parent studies) and received MMX mesalamine once daily (2.4 g/day, n=171) or twice daily (2.4 g/day, n=191) for 12 months.

At the end of 12 months, 67.8% of the 171 patients on once-daily MMX mesalamine remained in remission and 88.7% of these patients remained relapse-free.

New Agent for Colonoscopy Sedation

The investigative agent fospropofol (Aquavan, MGI Pharma) appears to be safe and effective for providing minimal-to-moderate sedation to patients undergoing colonoscopy, according to a phase III clinical trial led by Lawrence Cohen, MD, Associate Clinical Professor of Medicine, Mount Sinai Hospital and School of Medicine, New York, NY, and Douglas Rex, MD, Professor of Medicine, Indiana University Medical Center, Indianapolis, Ind.

In the study, 312 adults scheduled for colonoscopies were randomized to a 2:3:1 allocation ratio to receive an initial dose of fospropofol 2.0 mg/kg, fospropofol 6.5 mg/kg, or midazolam 0.02 mg/kg after pretreatment with fentanyl citrate (50 µg). The researchers allowed subjects to receive supplemental doses of their sedative per protocol. The primary endpoint was sedation success, which was defined as three consecutive scores of 4 or less on the Modified Observer's Assessment of Alertness/Sedation (MOAA/S) after sedation was given and the procedure was completed without needing an alternative sedative medication or manual or mechanical ventilation.

The investigators reported that 87% of patients who received an initial intravenous bolus of fospropofol 6.5 mg/kg achieved sedation success compared with 26% of patients in the fospropofol 2.0 mg/kg arm and 69% of the midazolam 0.02 mg/kg arm. However, the researchers noted that the study was not powered to show differences between fospropofol and midazolam.

The most common adverse events occurred in the fospropofol groups and included mild burning sensation (22.3%), paresthesia (16.5%), anal discomfort (11.9%), and pruritus (11.9%). There were no drug-related serious adverse events or deaths during the study, and no subjects required manual or mechanical ventilation.