

World Hepatitis Day

World Hepatitis Day will be held on May 19, 2009 to raise global awareness of chronic viral hepatitis and to help bring hepatitis to the forefront of the global healthcare agenda. This year's theme, similar to last year's, is "Am I number 12?," alluding to the fact that 1 in 12 people worldwide are infected with either chronic hepatitis B or C. Organizers have noted that although the incidence rate of hepatitis B or C is higher than that of HIV or of any cancer, there is low awareness of hepatitis in the public and most individuals living with the disease do not know. World Hepatitis Day, a patient-led initiative, is coordinated by the World Hepatitis Alliance, a nongovernmental organization that represents over 200 hepatitis B and C patient groups worldwide. Last year, high-profile campaigns were conducted in over 64 countries, with US activities including a sponsored walk, national poster contest, and poster and logo displays in Times Square and airports across the country, among other events. This year, a US World Hepatitis Day planning committee has been formed to organize a coordinated national campaign to build upon last year's activities. Information regarding this year's global observance will be announced in the coming weeks at www.worldhepatitisday.org, and information on the US campaign will be released at www.nvhr.org, where planning materials, newsletters, postcards, and logos are currently available in several languages.

Peginterferon Alfa-2b/Ribavirin Combination Therapy Approved for Hepatitis C Treatment-Experienced Patients

The US Food and Drug Administration recently approved the use of peginterferon alfa-2b (Pegintron, Schering) and ribavirin (Rebetol, Schering) combination therapy for chronic hepatitis C patients 3 years and older with compensated liver disease. Approval for the new indication of this therapy was granted based upon results from a noncomparative trial evaluating 2,293 adult patients with moderate-to-severe fibrosis or cirrhosis and prior failure of peginterferon alfa-2b/ribavirin combination therapy. The patients in this trial were re-treated with peginterferon alfa-2b 1.5 mcg/kg once weekly plus weight-adjusted ribavirin 800–1,400 mg

daily. The patient population had undergone at least 12 weeks of combination therapy and included patients who had previously relapsed or not responded. Overall, 22% (497/2,293) of the patients responded in the study. More specifically, response rates were 43% (130/300) for relapsers, 35% (113/344) for patients with previous experience with nonpegylated or pegylated alfa interferon/ribavirin, and 18% (158/903) and 6% (30/476) for nonresponders overall. Patients who had relapsed, had hepatitis C virus (HCV) genotype 2 or 3, or were first treated with nonpegylated interferon reached higher rates of sustained virologic response (SVR) overall, compared to patients with prior nonresponse, prior pegylated interferon treatment, significant bridging fibrosis or cirrhosis, or HCV genotype 1 infection. In addition, undetectable HCV RNA levels at Week 12 proved to be a strong predictor of SVR. The adverse reactions reported by the treatment-experienced patients in this trial were similar to those associated with peginterferon alfa-2b/ribavirin combination therapy during treatment-naive clinical trials.

Use of the Water Method for Scheduled Unsedated Colonoscopy

According to the March issue of *Gastrointestinal Endoscopy*, researchers at the Sepulveda Ambulatory Care Center in North Hills, California, conducted an observational study to evaluate the hypothesis that use of the water method improves cecal intubation and increases the willingness of patients to repeat a scheduled colonoscopy without sedation. The patient population consisted of two consecutive groups of veterans. Standard air insufflation (n=62) was used to aid colonoscopy insertion in colonoscopies performed from June 2005 to May 2006, whereas the water method (n=63) was used in colonoscopies performed from June 2006 to October 2007. The main outcome measurements were comprised of cecal intubation and the willingness to repeat an unsedated colonoscopy.

Based upon intention-to-treat (ITT) analysis, cecal intubation using the water method (97% [61/63]) was significantly higher than using the air method (76% [47/62]). More patients expressed willingness to repeat a colonoscopy without sedation using the water method (90% [57/63]) compared to the air method (69%

[43/62]). As the study was limited by being nonrandomized and unblinded as well as involving only one site and a small number of elderly male veterans, the researchers noted the need for a randomized controlled trial.

Pantoprazole Versus Ranitidine for the Prevention of Peptic Ulcer Rebleeding

As there are limited controlled data on the use of pantoprazole for treatment of peptic ulcer bleeding, researchers at the University of Stellenbosch in Cape Town, South Africa, conducted a multicenter, multinational, randomized trial to compare intravenous (IV) pantoprazole with IV ranitidine for treatment of bleeding ulcers. After endoscopic hemostasis, the researchers randomly assigned 1,256 patients to pantoprazole 80 mg+8 mg/h or ranitidine 50 mg+13 mg/h, both for 72 hours. A second-look endoscopy was performed on Day 3 (or earlier, if clinically indicated). The primary endpoint consisted of an overall outcome ordinal score: no rebleeding, rebleeding without/with subsequent hemostasis, surgery, and mortality. The results of the study were published in the March issue of *Alimentary Pharmacology & Therapeutics*.

The authors found no differences between the groups in overall outcome scores (pantoprazole vs ranitidine; S0: 91.2% vs 89.3%, S1: 1.5% vs 2.5%, S2: 5.4% vs 5.7%, S3: 1.7% vs 2.1%, S4: 0.19% vs 0.38%; $P=.083$), 72-hour clinically detected rebleeding (2.9% [95% (confidence interval) CI, 1.7–4.6] vs 3.2% [95% CI, 2.0–4.9]), surgery (1.9% [95% CI, 1.0–3.4] vs 2.1% [95% CI, 1.1–3.5]), or Day 3 mortality (0.2% [95% CI, 0–0.09] vs 0.3% [95% CI, 0–1.1]). In addition, pantoprazole was found to significantly reduce the cumulative frequency of events comprising the ordinal score in spurting lesions (13.9% [95% CI, 6.6–24.7] vs 33.9% [95% CI, 22.1–47.4]; $P=.01$) and gastric ulcers (6.7% [95% CI, 4–10.4] vs 14.3% [95% CI, 10.3–19.2]; $P=.006$).

Albinterferon Alfa-2b Phase III Trial Results in Chronic Hepatitis C Genotype 1

In the randomized, multicenter, active-controlled, noninferiority ACHIEVE 1 phase III trial, 1,331 treatment-naïve patients with chronic hepatitis C genotype 1 were assigned to one of three groups: subcutaneous albinterferon alfa-2b (Albupheron, Human Genome Sciences/Novartis) once every two weeks at 900 mcg or 1,200 mcg or a control group receiving peginterferon alfa-2a (Pegasys, Hoffman-La Roche) once weekly at 180 mcg. All groups also received daily oral ribavirin. In January 2008,

the dose in the 1,200-mcg albinterferon alfa-2b group was modified to 900 mcg, due to an interim analysis that rates of serious pulmonary adverse events appeared to be higher in the 1,200-mcg group. The trial consisted of 48 weeks of treatment, with a primary efficacy endpoint of SVR, defined as undetectable viral levels (HCV RNA <10 IU/mL) at Week 72.

According to ITT analysis of the group assigned to 900-mcg albinterferon alfa-2b, the primary efficacy endpoint of noninferiority was met, with 48.2% (213/442) achieving SVR compared to 51.0% (225/441) taking peginterferon alfa-2a. Adjusted for baseline stratification factors, the primary analysis demonstrated a difference in SVR rates of -1.8% (95% CI, -8.1–4.5%; $P=.0008$ for noninferiority). Rates of serious and/or severe adverse events were similar in patients receiving 900-mcg albinterferon alfa-2b compared to peginterferon alfa-2a (24.0% [106/442] vs 23.1% [102/441], respectively). The rates of serious and/or severe pulmonary infections were also similar, with 1.8% (8/442) for 900-mcg albinterferon alfa-2b compared to 1.1% (5/441) with peginterferon alfa-2a. The rate of serious and/or severe respiratory, thoracic, or mediastinal disorders was 2.5% (11/442) for 900-mcg albinterferon alfa-2b compared to 0.5% (2/441) with peginterferon alfa-2a.

According to ITT analysis of the group originally randomized to 1,200-mcg albinterferon alfa-2b—the results of which did not affect the primary analysis of the 900-mcg group—47.3% (208/440) achieved SVR compared to 51.0% (225/441) with peginterferon alfa-2a, demonstrating statistical noninferiority (95% CI, -9.4–3.2%; $P=.0029$, adjusted for baseline stratification factors). The rate of serious and/or severe adverse events was 28.3% (124/440) in this albinterferon alfa-2b group compared to 23.1% (102/441) receiving peginterferon alfa-2a. Serious and/or severe pulmonary infections were 3.2% (14/440) for 1,200-mcg albinterferon alfa-2b compared to 1.1% (5/441) for peginterferon alfa-2a. Serious and/or severe respiratory, thoracic, or mediastinal disorders were 3.0% (13/440) for 1,200-mcg albinterferon alfa-2b compared to 0.5% (2/441) for peginterferon alfa-2a.

Side Effects Associated With Tricyclic Antidepressants for Functional Bowel Disorders

Researchers at the University of North Carolina in Chapel Hill and the University of Toronto in Canada evaluated female patients in a multicenter National Institutes of Health trial for functional bowel disorders to assess whether symptoms noted before using the tricyclic

antidepressant desipramine increased or worsened after its use for 2 weeks. Baseline factors that predispose patients to report symptoms were also evaluated. The patients completed a 15-item symptom questionnaire at baseline (prior to randomization), 2 weeks following the use of desipramine (n=81) or placebo (n=40), and at the end of the study (12 weeks). The results, which were published in the April issue of *Clinical Gastroenterology and Hepatology*, were based upon 57 patients who took desipramine and answered the questionnaires.

The symptoms that occurred most commonly and worsened at Week 2 in the patients who received desipramine included dizziness, dry mouth/thirstiness, lightheadedness, jittery feelings/tremors, and flushing. The symptoms that improved or did not change in severity at Week 2 in this group of patients included morning tiredness, nausea, blurred vision, headaches, appetite reduction, and trouble sleeping. The reporting of symptoms was found to correlate with psychological distress, but not desipramine blood level. The authors concluded that most of the so-called symptom side effects were not specifically related to desipramine use, as most of these symptoms were present prior to treatment and only a few worsened in severity 2 weeks after the use of desipramine. The authors suggested that these symptoms might instead be related to psychological distress.

In Brief

According to preliminary analysis of a small, prospective, randomized trial, outcomes following endoscopic ultrasound (EUS)-guided common bile duct stone retrieval were equivalent to those following endoscopic retrograde cholangiopancreatography (ERCP). In addition, EUS-related adverse events were similar to those following ERCP, and ERCP- and EUS-guided stone retrieval appeared to be equally effective for therapeutic interventions of the bile duct. However, the authors noted that additional studies are required to valid these preliminary results and determine predictors of success for EUS-guided stone removal. (*Gastrointest Endosc.* 2009;69:238-243.)

Researchers of a prospective study found fecal calprotectin levels to be dramatically elevated in patients with severe ulcerative colitis, raising the possibility that this biomarker can predict response to first- or second-line medical therapy in this setting. (*Am J Gastroenterol.* 2009;104:673-676.)

According to an observational, population-based cohort study of Danish men and women, smoking was independently associated with increased risk of pancreatitis. (*Arch Intern Med.* 2009;169:603-609.)