

Tenofovir Approved for Chronic Hepatitis B

The US Food and Drug Administration (FDA) recently granted marketing approval for tenofovir disoproxil fumarate (Viread, Gilead) for the treatment of chronic hepatitis B in adults, adding a second indication to its earlier one for HIV infection. The recommended dose is 300 mg taken once daily orally, and dose interval adjustment is recommended in patients with renal impairment. FDA approval was based upon data from two ongoing, randomized, double-blind, phase III clinical trials, studies 102 and 103, which analyzed over 48 weeks of treatment of tenofovir versus adefovir dipivoxil (Hepsera, Gilead). Both studies demonstrated that, compared to hepatitis B patients in the adefovir arm, a significantly larger proportion of patients in the tenofovir arm experienced complete response (defined as serum hepatitis B virus [HBV] DNA levels below 400 copies/mL and histologic improvement demonstrated by a reduction in the Knodell necroinflammatory score of at least 2 points, with no concurrent worsening of fibrosis). Patient populations included those naive to HBV therapy (n=375) and those with prior nucleoside treatment (n=51). The manufacturer noted that the small number of patients with nucleoside experience or lamivudine-associated mutations at baseline did not allow them to draw conclusions of efficacy and that patients with decompensated liver disease were not studied in the trials.

The most common adverse reaction was nausea; other reactions reported in more than 5% of patients in the tenofovir arm included abdominal pain, diarrhea, headache, dizziness, fatigue, nasopharyngitis, back pain, and skin rash. Because severe, acute worsening of hepatitis B has been reported in patients who discontinue anti-hepatitis B therapy, including tenofovir, hepatic function should be monitored closely for at least several months if therapy is discontinued. Due to reports of new onset or worsening of renal impairment with tenofovir, it is suggested that creatinine clearance (CrCl) is assessed prior to treatment initiation and that CrCl and serum phosphorus levels are followed in at-risk patients. In addition, avoiding the use of tenofovir with concurrent or recent use of nephrotoxic drugs is also recommended. Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have also been noted with the use of nucleoside analogs alone or in combination with other antiretroviral treatments.

NOTES/NOSCAR Outcomes Registry Created

The Natural Orifice Surgery Consortium for Assessment and Research (NOSCAR) recently established a worldwide outcomes registry for physicians to track human research cases involving Natural Orifice Transluminal Endoscopic Surgery (NOTES) procedures. The NOTES/NOSCAR Outcomes Registry, which began compiling procedures during the recent 3rd International Conference on NOTES, held in San Francisco, California, is modeled on the Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) Outcomes Initiative, which tracks surgical procedures. The goal of the NOTES/NOSCAR Outcomes Registry is to determine trends that will lead to the next phases of research, criteria development, training requirements, and quality and safety issues, as well as guide future guidelines and reimbursement codes. The registry is open to all members of SAGES and the American Society for Gastrointestinal Endoscopy for no cost. Accessible through the website www.noscar.org, the registry includes a general log, where NOTES cases are entered, which enables the tracking of data such as infection rates and length of stay. Detailed reports of submitted data are also available online that can compare the results of a single case with the results of the overall database. Data submission is confidential, as all physician and patient identifiers are removed prior to submission.

Long-term Use of Proton Pump Inhibitors and Risk of Fracture

Researchers at the University of Manitoba in Winnipeg, Canada, conducted a retrospective study to further evaluate the relationship between the duration of proton pump inhibitor exposure and osteoporosis-related fractures. In the study, the results of which were published in the August issue of the *Canadian Medical Association Journal*, administrative claims data were used to identify patients 50 years of age and older with a hip, vertebra, or wrist fracture between April 1996 and March 2004. Each case was then matched with 3 controls based on age, gender, and comorbidities.

The researchers matched 15,792 cases of osteoporosis-related fractures with 47,289 controls. According to their data, a significant association was not evident

between the overall risk of osteoporotic fracture and the use of proton pump inhibitors for durations of 6 years or less. However, exposure to proton pump inhibitors for 7 or more years was found to be associated with a higher risk of osteoporosis-related fracture (adjusted odds ratio [OR], 1.92; 95% confidence interval [CI], 1.16–3.18; $P=.011$). In addition, a higher risk of hip fracture was also found after 5 or more years of exposure to proton pump inhibitors (adjusted OR, 1.62; 95% CI, 1.02–2.58; $P=.04$), with an even higher risk after 7 or more years of exposure (adjusted OR, 4.55; 95% CI, 1.68–12.29; $P=.002$). The authors noted that additional studies are needed to determine the clinical significance of these findings and to evaluate the value of osteoprotective medications for patients with long-term use of proton pump inhibitors.

Telaprevir Trial in Treatment-Failure Hepatitis C Patients Announced

The start of the Re-treatment of Patients with Telaprevir-based Regimen to Optimize Outcomes (REALIZE) trial was recently announced. This phase III clinical trial will evaluate telaprevir, a hepatitis C virus (HCV) protease inhibitor, as part of combination therapy for patients with chronic HCV infection who were unable to achieve sustained viral response (SVR) with prior therapy. The trial will be conducted at more than 100 centers in the United States and European Union and will enroll approximately 650 genotype 1 HCV patients who failed treatment with pegylated interferon (PEG-IFN) and ribavirin (RBV). The patient population will include null responders (defined as patients who achieved less than a 2-log reduction in HCV RNA levels at Week 12 of prior therapy); partial responders (defined as patients who achieved at least a 2-log reduction at Week 12 but failed to achieve undetectable HCV RNA levels by Week 24 of prior therapy); and relapsers (defined as patients who had undetectable HCV RNA levels after completing at least 42 weeks of prior treatment but relapsed during follow-up). Trial enrollment is expected to be completed in the first quarter of 2009.

The trial will consist of three 48-week trial arms: an arm of 750 mg of telaprevir administered every eight hours for 12 weeks in combination with standard doses of PEG-IFN and RBV, followed by 36 weeks of treatment with PEG-IFN and RBV alone; a delayed start arm of 4 weeks of treatment with PEG-IFN and RBV, followed by 750 mg of telaprevir every eight hours for 12 weeks in combination with standard doses of PEG-IFN and RBV, followed by another 32 weeks of PEG-IFN and RBV alone; and a control arm with standard doses

of PEG-IFN and RBV dosed for 48 weeks. Patients in all treatment arms will be followed for 24 weeks after the completion of treatment to assess the primary endpoint of the trial, SVR (defined as undetectable HCV RNA levels or <10 IU/mL).

The Use of Chewing Gum for Bowel Recovery After Colon Surgery

Researchers at the Imperial College London and St. Mary's Hospital in London, United Kingdom, conducted a meta-analysis to compare outcomes with or without the use of chewing gum during the early postoperative period following abdominal surgery. The results of this meta-analysis were published in the August issue of *Archives of Surgery*. The researchers selected randomized controlled trials reporting 1 or more outcomes related to functional postoperative recovery and used a validated scale to assess the quality of each study. Five trials (for a total of 158 patients) published on or before July 2006 met the inclusion criteria, and data on the time to first passage of flatus, time to first bowel movement, and length of postoperative stay were extracted. In each trial, a group of patients chewed sugarless gum 3 times per day following surgery for 5–45 minutes in contrast to the other group of patients who did not chew any gum.

The researchers found that the time (in days) required for the patient to pass flatus (weighted mean difference [WMD], -0.66 ; 95% CI, -1.11 to -0.20 ; $P=.005$) and the time until the first bowel movement (WMD, -1.10 ; 95% CI, -1.79 to -0.42 ; $P=.002$) were significantly decreased in the chewing gum arm compared with the control arm. However, the authors noted that these findings showed significant heterogeneity. The postoperative length of hospital stay was also decreased in the chewing gum arm by more than 1 day (WMD, -1.25 ; 95% CI, -3.27 to 0.77 ; $P=.23$), though this finding was not statistically significant. However, this result was significant when excluding studies that explicitly included patients with stomas formed during surgery (WMD, -2.46 ; 95% CI, -3.14 to -1.79 ; $P<.001$), with no significant heterogeneity. The authors concluded that chewing gum may improve recovery of intestinal function following complete or partial colectomy and reduce the length of hospital stay. They speculated that the gum chewing acts as a type of “sham feeding,” which stimulates nerves in the digestive system, triggers the release of gastrointestinal hormones, and increases the production of saliva and secretions from the pancreas. The authors also recommend conducting larger-scale, blinded, randomized, controlled trials with placebo arms, because of the potential for cost savings.

Body Mass Index and Risk of Colorectal Adenomas

In a retrospective cohort study conducted at the University of Tokyo in Tokyo, Japan, and the Kameda General Hospital in Kamogawa City, Japan, researchers examined the relationship between body weight and the incidence of colorectal adenoma in both cross-sectional and longitudinal analyses. They examined the records of 7,963 Japanese patients who underwent colonoscopy between 1991 and 2003, excluding patients with a family history of colorectal cancer, colorectal polyps, inflammatory bowel disease, or colorectal surgery, as well as those who took nonsteroidal anti-inflammatory drugs (NSAIDs). The results of the study were published in the August issue of the *American Journal of Gastroenterology*.

The researchers classified the patients into 4 groups based upon their body mass index (BMI) and found that 20.7% of patients had at least 1 colorectal adenoma. They also found that as BMI increased, so did the prevalence of colorectal adenomas: 15.4%, 20.6%, 22.7%, and 24.2%, respectively, in the first (BMI <21.350), second (21.350 ≤ BMI <23.199), third (23.199 ≤ BMI <25.156), and fourth (25.156 ≤ BMI) quartiles. The adjusted ORs in reference to Group Q1 were 1.15 (95% CI, 0.97–1.37; *P*=.1) for Group Q2, 1.19 (1.01–1.41; *P*=.04) for Group Q3, and 1.32 (1.12–1.56; *P*=.001) for Group Q4. Colorectal adenoma incidence rates after 1 year also increased in relation to the initial BMI: 12.9% for Group Q1, 15.7% for Group Q2, 18.3% for Group Q3, and 19.0% for Group Q4. The authors concluded that obesity was associated with increased risk for colorectal adenoma, and recommended reduction in body weight to decrease this risk.

In Brief

Researchers of a prospective study found that placing patients in the right lateral position after ingestion of the capsule endoscope and before the capsule enters the pylorus is a simple method to increase the complete examination rate of the small bowel by reducing the gastric transit time of the capsule. (*Endoscopy*. 2008;40:483-487.)

According to a retrospective case-control study utilizing the inflammatory bowel disease center database at an academic referral center, requiring medical hospitalization for the management of disease activity in ulcerative colitis is an independent predictor for the need for colectomy. The authors also stated that future studies will determine whether aggressive medical management may modify the need for colectomy in this cohort. (*Inflamm Bowel Dis*. 2008 Aug 4. [Epub ahead of print].)

In a prospective study, pepsin measurement in the sputum/saliva collected at the time of symptoms was found to provide a sensitive, noninvasive method for diagnosing gastroesophageal reflux disease in patients with clinically suspected atypical gastroesophageal reflux disease symptoms. (*Digestion*. 2008;77:201-206. [Epub ahead of print].)