GASTRO-HEP News

By Samantha Alleman

US Food and Drug Administration Approves Treatment for Chronic Hepatitis C Virus Genotypes 1 Through 6

On July 18, 2017, the US Food and Drug Administration (FDA) approved the pangenotypic treatment sofosbuvir/velpatasvir/voxilaprevir (Vosevi, Gilead Sciences) to treat adult patients with chronic hepatitis C virus (HCV) infection with no or mild cirrhosis, according to a press release published online. The FDA also granted the drug priority review and breakthrough therapy designations.

The once-daily single tablet, which contains 400 mg of sofosbuvir, 100 mg of velpatasvir, and 100 mg of voxilaprevir, is the first FDA-approved medication for patients previously treated with sofosbuvir or other nonstructural 5A–inhibiting medications.

Two phase 3 clinical trials evaluated the safety and efficacy of sofosbuvir/velpatasvir/voxilaprevir. Study results showed that a sustained virologic response at 12 weeks occurred in 96% to 97% of patients receiving the drug. Overall, 0.2% of patients receiving the drug for 12 weeks discontinued treatment owing to adverse events, which included diarrhea, fatigue, headache, and nausea. Patients taking rifampin should avoid treatment with sofosbuvir/velpatasvir/voxilaprevir.

The FDA warns that patients with a previous or current infection of hepatitis B virus (HBV) may experience disease reactivation, sometimes fatal, when taking direct-acting antiviral medication for HCV infection. Clinicians are advised to screen patients for HBV infection before prescribing HCV treatment.

Repeat Esophagogastroduodenoscopies Are Overused in the Veterans Health Administration

Nearly half of all repeat esophagogastroduodenoscopies (EGDs) performed within the Veterans Health Administration (VHA) are unnecessary, according to study results published online on July 11, 2017 ahead of print publication in the *American Journal of Gastroenterology*.

Between January 1, 2003 and June 30, 2007, Dr Joel H. Rubenstein and colleagues conducted retrospective analyses of 235,855 veterans undergoing index EGDs across 159 VHA facilities. Patients were excluded if they did not regularly receive health care at a VHA facility or if they were not followed up for 5 years. Repeat EGDs were divided into 3 levels of appropriateness (likely appropriate, possible overuse, probable overuse) based on diagnostic and procedure codes. The impact of site- and patient-level factors on the odds of repeat EGD was estimated using multilevel logistic regression.

A repeat EGD was performed within 5 years in 36.3% (n=85,690) of all patients studied. Of the repeat procedures, 49.5% (n=42,412) were categorized as likely appropriate, 41.4% (n=35,503) were labeled as possible overuse, and 9.1% (n=7756) represented probable overuse, with women more likely to receive a repeat procedure considered probable overuse. Patients were more likely to undergo repeat EGD, both appropriate and overuse, if they regularly visited their primary care physician and had access to facilities offering EGD and other services. Financial incentives did not play a role in EGD overuse.

The authors recommend further research into the reasons for overuse and the barriers to and promotion of appropriate use of repeat EGD.

Proton Pump Inhibitor Use Associated With Increased Risk of Death

Proton pump inhibitor (PPI) use is associated with an increased risk of death compared with histamine H2 receptor antagonist (H2 blocker) use and nonuse of either class of medication, especially with prolonged use and in patients without gastrointestinal conditions.

For the longitudinal, observational, cohort study, the results of which were published online on July 3, 2017 in *BMJ Open*, Dr Yan Xie and colleagues compared data from more than 6 million patients within the US Veterans Affairs system for nearly 6 years (until 2013) or until death. Study participants were divided into 3 cohorts: new PPI users vs new H2-blocker users (n=349,312), PPI users vs non-PPI users (n=3,288,092), and PPI users vs non-PPI and non–H2 blocker users (n=2,887,030). The overall median age at baseline was 61 years (PPI users, 61.67 years; H2-blocker users, 58.48 years; $P<.001$). Treatment duration was longer among PPI users vs H2-blocker users (450 days vs 120 days; $P<.001$). The main outcome measure was risk of death.

The risk of death among PPI users was higher compared with H2-blocker users (hazard ratio [HR], 1.25; CI, 1.23-1.28), even when analyses were adjusted for 2-stage residual inclusion estimation (HR, 1.21; CI, 1.16-1.26), high-dimensional propensity score (HR, 1.16; CI, 1.13-1.18), and 1:1 time-dependent propensity score-matched cohort (HR, 1.34; CI, 1.29-1.39). The

risk of death was also higher among PPI users vs non-PPI users (HR, 1.15; CI, 1.14-1.15) and vs non-PPI and non–H2 blocker users (HR, 1.23; CI, 1.22-1.24). In patients without gastrointestinal conditions, PPI use increased the risk of death. A longer duration of PPI treatment was also associated with an increased risk of death.

The authors suggest limiting the use and duration of PPIs to medically indicated cases.

VSL#3 May Be Effective in Treating Ulcerative Colitis But Not Crohn's Disease

The probiotic VSL#3 may have beneficial effects in inducing remission in active ulcerative colitis (UC) and may be equivalent to 5-aminosalicylates (5-ASAs) in preventing relapse of quiescent UC, but does not appear to have any benefit in inducing remission in active Crohn's disease (CD) or preventing relapse of quiescent CD, according to results of a systematic review and meta-analysis published online on June 27, 2017 ahead of print publication in *Alimentary Pharmacology and Therapeutics*.

Dr Y. Derwa and colleagues performed a literature search on the Cochrane Controlled Trials Register, Embase, and Medline for randomized, controlled trials of adult patients with CD or UC comparing the use of probiotics with the use of 5-ASAs or placebo. Twenty-two studies were included in the final review. A relative risk (RR) of failure to achieve remission in active UC and CD as well as a RR of relapse of quiescent disease, with 95% CI, was pooled from dichotomous symptom data.

The use of probiotics had no benefit in inducing remission in active UC compared to placebo (RR, 0.86; 95% CI, 0.68-1.08), although the use of VSL#3 alone appeared effective (RR, 0.74; 95% CI, 0.63-0.87). Probiotics and 5-ASAs had similar results in preventing relapse of UC (RR, 1.02; 95% CI, 0.85-1.23). The use of probiotics did not have any benefit in inducing remission of active CD or in preventing relapse of quiescent CD or CD following surgically induced remission.

The authors noted that further randomized trials are needed to determine the efficacy of probiotics for the treatment of CD.

Endoscopic Ultrasound Has Good Accuracy Vs Magnetic Resonance Cholangiopancreatography for Detecting Choledocholithiasis

Endoscopic ultrasound (EUS) has better accuracy and sensitivity than magnetic resonance cholangiopancreatography (MRCP) for diagnosing choledocholithiasis, with comparable specificity. Both EUS and MRCP are more accurate in diagnosing suspected choledocholithiasis compared to clinical assessment, according to results of a meta-analysis published online on June 20, 2017 ahead of print publication in *Gastrointestinal Endoscopy*.

Dr Mohammad Yaghoobi and colleagues evaluated sensitivity, diagnostic accuracy, and specificity in a head-to-head comparison of the 2 methods in the setting of choledocholithiasis detection. A total of 5 prospective, cohort studies involving 272 patients were included in the meta-analysis. The QUADAS-2 tool was used to measure study quality; no study had a high risk of bias.

EUS had a higher pooled sensitivity than MRCP (0.97 vs 0.87, respectively; P=.006), leading to a higher overall diagnostic accuracy (162.5 vs 79.0, respectively; P=.008). The specificity was comparable between the 2 methods (EUS, 0.90 vs MRCP, 0.92; P=.4).

Given the safety profile of EUS, the authors recommend that it be included in the diagnostic algorithm for suspected choledocholithiasis, especially in patients undergoing investigational EGD.

In Brief

In a serial diagnostic study, researchers found that the use of a solid test meal compared with 10 single water swallows significantly increased the diagnostic sensitivity of high-resolution manometry for symptomatic esophageal motility disorders. The increase was notable in patients with dysphagia and present in patients with symptoms of reflux. Aside from absent peristalsis, all major motility disorders were more common with a solid test meal than with single water swallows. *Lancet Gastroenterol Hepatol*. 2017 Jul 3. Epub ahead of print. doi:10.1016/S2468-1253(17)30148-6.

Researchers conducting a randomized, controlled trial found that cap-assisted colonoscopy significantly improved independent cecal intubation rates, increased overall Assessment of Competency in Endoscopy tool motor and cognitive scores, and led to learning curves approaching competency when compared with standard colonoscopy in trainees with no previous experience in colonoscopy. Polyp detection rates, polyp miss rates, and adenoma detection rates were comparable between the 2 methods. *Gastrointest Endosc*. 2017 Jun 22. Epub ahead of print. doi:10.1016/j.gie.2017.06.11.