GASTRO-HEP News

By Samantha Alleman

US Food and Drug Administration Approves 8-Week Treatment for Pangenotypic Hepatitis C Virus Infection

On August 3, 2017, the US Food and Drug Administration (FDA) approved the combination glecaprevir/pibrentasvir (Mavyret, AbbVie) for the treatment of pangenotypic chronic hepatitis C virus (HCV) infection in adult patients with mild or no cirrhosis, including patients who have moderate to severe kidney disease and patients who are on dialysis, according to a press release published online. The drug also received approval to treat HCV genotype 1 infection in adults who were previously treated with a nonstructural (NS) 5A inhibitor– or NS3/4A protease inhibitor–containing regimen.

Glecaprevir/pibrentasvir is indicated for an 8-week treatment period, reducing the standard treatment length by at least 4 weeks. Clinical trials involving approximately 2300 adults with HCV genotypes 1 through 6 infection with no or mild cirrhosis were conducted to assess the safety and efficacy of the drug. Trial results showed that 92% to 100% of patients receiving glecaprevir/pibrentasvir had no detectable virus in their blood 12 weeks following treatment, regardless of whether treatment lasted 8, 12, or 16 weeks. Treatment duration was dependent upon patients' HCV genotype, cirrhosis status, and prior treatment.

Adverse events included fatigue, headache, and nausea. Glecaprevir/pibrentasvir is not recommended for patients with moderate cirrhosis and is contraindicated in patients with severe cirrhosis and in patients taking rifampin and atazanavir. The FDA recommends screening in all patients for evidence of current or prior infection with hepatitis B virus (HBV) before beginning treatment with glecaprevir/pibrentasvir to avoid possible reactivation of HBV infection.

Less Invasive Pancreatic Necrosectomy for Necrotizing Pancreatitis Associated With Reduced Death Rates Compared With Open Necrosectomy in Patients at High Risk

Endoscopic and minimally invasive surgical pancreatic necrosectomy are linked to lower death rates compared with open necrosectomy in patients at high risk for necrotizing pancreatitis, according to data from 51 hospitals across 8 countries. Study results were published online on August 3, 2017 ahead of print publication in *Gut*.

In a head-to-head comparison of 15 published and unpublished patient cohorts, Dr Sandra van Brunschot and colleagues analyzed death rates in 1980 patients with necrotizing pancreatitis who underwent endoscopic necrosectomy (n=346) or minimally invasive surgical necrosectomy (n=467) vs open necrosectomy (n=1167). The researchers performed 2 methods of analysis: logistic multivariable regression and propensity score matching, in which patients were stratified according to their predicted risk of death at baseline (low, intermediate, high, and very high).

Overall, 325 patients (16%) died during the index admission. Minimally invasive surgical necrosectomy and endoscopic necrosectomy were associated with a reduced risk of death (odds ratio [OR], 0.53; 95% CI, 0.34-0.84; *P*=.006 vs OR, 0.20; 95% CI, 0.06-0.63; *P*=.006, respectively). In patients considered high risk (baseline risk of ≥15% to <35%) and very high risk (baseline risk of ≥35%), endoscopic necrosectomy had a lower mortality risk than open necrosectomy (high risk: risk ratio [RR], 0.27; 95% CI, 0.08-0.88; *P*=.03; very high risk: RR, 0.43; 95% CI, 0.24-0.77; *P*=.005). Among patients in the very high–risk group, minimally invasive surgical necrosectomy was also linked with a lower mortality risk than open necrosectomy (RR, 0.70; 95% CI, 0.52-0.95; *P*=.02).

The researchers conclude that more evidence from large comparative studies is needed.

Fecal Calprotectin Beneficial in Diagnosing Pediatric Inflammatory Bowel Disease

Fecal calprotectin provides significant value in diagnosing pediatric inflammatory bowel disease (IBD) compared with blood markers and should be included in the diagnostic workup, according to findings from a meta-analysis published online on August 14, 2017 ahead of print publication in *JAMA Pediatrics*.

Dr Gea A. Holtman and colleagues analyzed data of 1120 patients from 8 studies and found that the addition of fecal calprotectin, as opposed to blood markers (ie, albumin, C-reactive protein, erythrocyte sedimentation rate, hemoglobin, and platelets), to the diagnostic workup of pediatric patients with symptoms suggestive of IBD led to a decrease in the number of patients considered to be at intermediate risk of IBD.

When combined with symptom evaluation, all blood markers, and fecal calprotectin alone, improved the discrimination between pediatric patients with and without IBD. Fecal calprotectin improved the area under the curve of symptoms by 0.26 (95% CI, 0.21-0.31), followed by

erythrocyte sedimentation rate, which improved the area under the curve of symptoms by 0.16 (95% CI, 0.11-0.21). Adding fecal calprotectin to the model increased the proportion of patients without IBD classified as having low risk of IBD from 33% to 91%. Additionally, the proportion of patients with IBD incorrectly classified as having low risk decreased from 16% to 9%, and the proportion of all patients classified as having intermediate risk fell from 55% to 6%.

A potential limitation to the use of fecal calprotectin is the challenge in obtaining stool samples from pediatric patients.

Immunomodulators Plus Anti–Tumor Necrosis Factor-α Effective Following Intestinal Resection for Crohn's Disease

Combination therapy with immunomodulators and anti–tumor necrosis factor (TNF)-α was efficacious and well tolerated vs monotherapy with either thiopurines or anti–TNF-α medication in patients undergoing intestinal resection for Crohn's disease (CD). Efficacy with combination therapy was also noted in patients with postoperative CD.

For the retrospective analysis, the results of which were published in the August 2017 issue of *Frontline Gastroenterology*, Dr Anthony O'Connor and colleagues analyzed 149 patients who underwent intestinal resection for CD between 2009 and 2013. The study endpoint was treatment success, defined as glucocorticosteroid-free, resection-free survival, without the need for therapy change or escalation, at the last point of follow-up. Patients were observed from the day of surgery to the final follow-up, or January 31, 2015 (median duration of follow-up, 32 months; range, 1-69 months). Prescribing databases, radiology and endoscopy reports, and chart reviews provided relevant clinical information.

In total, 101/149 patients received prophylactic therapy following surgery. Thiopurines were used as first-line therapy in 77 patients (51.7%), with 32 (41.6%) achieving treatment success. Anti–TNF-α alone was used in 11 patients (7.4%), 5 (45.5%) of whom achieved treatment success. Combination therapy was provided as first-line treatment to 13 patients (8.7%), 11 (84.6%) of whom achieved treatment success.

Combination therapy may be superior in carefully selected postoperative patients whose care has been individualized through a multidisciplinary format. The researchers conclude that prospective, controlled studies are needed to further assess the efficacy and safety of combination therapy for postoperative prophylaxis in CD.

Endoscopic Dilation Safe and Effective in Patients With Eosinophilic Esophagitis

Endoscopic dilation is effective and safe in pediatric and adult patients with eosinophilic esophagitis (EoE), according to results of a meta-analysis published in the July 2017 issue of *Alimentary Pharmacology & Therapeutics*. Earlier studies reported an increased risk of complications associated with esophageal dilation as an adjunct therapy for relief of symptoms arising from EoE-related fibrostenotic remodeling.

For the study, Dr Fouad J. Moawad and colleagues analyzed 27 studies comprising 845 patients (758 adults and 87 pediatric patients) with EoE. A total of 1820 esophageal dilations were performed (median, 3; range, 1-35). Ninety-five percent of patients experienced clinical improvement (95% CI, 90%-98%; I^2, 10%) following dilation. Clinical response was similar between children and adults (95% CI, 83%-100%; I^2, 8.6% vs 95% CI, 89%-99%; I^2, 15%, respectively). Major complications had rates of less than 1%; hemorrhage occurred in .05% of patients (95% CI, 0%-0.3%; I^2, 0%), perforation in .38% (95% CI, 0.18%-0.85%; I^2, 0%), and hospitalization in .67% (95% CI, 0.3%-1.1%; I^2, 44%). No deaths occurred (95% CI, 0%-0.2%; I^2, 0%).

In Brief

Researchers conducting a 12-week, randomized, placebo-controlled, phase 2B study of 393 diabetic patients with moderate to severe gastroparesis symptoms found that relamorelin (RM-131), a selective, prokinetic agonist of ghrelin, significantly reduced abdominal pain, bloating, nausea, and postprandial fullness; accelerated gastric emptying; and was safe and well tolerated compared to placebo. Frequency in vomiting was not significant compared to placebo, and some patients receiving relamorelin required insulin or other diabetes drug dosage adjustments. *Gastroenterology*. 2017 Jul 28. Epub ahead of print. doi:10.1053/j.gastro.2017.07.035.