GASTRO-HEP News

By Samantha Alleman

Daclatasvir/Sofosbuvir/Ribavirin Effective for Patients With Hepatitis C Virus Genotype 3 Infection With Advanced Liver Disease

The all-oral combination of daclatasvir/sofosbuvir/ribavirin for 12 or 16 weeks produced high rates of sustained virologic response at 12 weeks posttreatment (SVR12) in both previously treated and untreated patients with hepatitis C virus (HCV) genotype 3 infection with advanced liver fibrosis or compensated cirrhosis. Results of the phase 3, open-label, randomized study (ALLY-3+) were published in the May issue of *Hepatology*. This is the first randomized study to investigate interferon-free treatment response in this patient population.

For the study, Dr Vincent Leroy and colleagues enrolled 50 patients with chronic HCV genotype 3 infection who were treatment-naive (n=13) or treatment-experienced (n=37). Fourteen patients had advanced fibrosis, and 36 had compensated cirrhosis. The patients were randomly assigned to 12- or 16-week treatments of a once-daily dose of daclatasvir (60 mg) and sofosbuvir (400 mg) with or without food, plus a twice-daily dose of weight-based ribavirin (1000 mg/day for patients <75 kg or 1200 mg/day for patients ≥75 kg). Patients were followed up at 24 weeks.

At 12 weeks after the end of treatment, SVR was achieved by 88% and 92% of patients receiving daclatasvir/sofosbuvir/ribavirin for 12 and 16 weeks, respectively. All 14 patients with advanced fibrosis achieved SVR12. Among patients with compensated cirrhosis, 15 of 18 (83%) in the 12-week group and 16 of 18 (89%) in the 16-week group achieved SVR12.

The most common adverse events included asthenia, diarrhea, dyspnea, fatigue, headache, insomnia, and irritability. Serious adverse events included arteriosclerosis, basal cell carcinoma, dilated cardiomyopathy, pneumonia, and somnolence, none of which were treatment-related. There were no discontinuations due to adverse events. Two patients in each group experienced posttreatment relapse, and 1 patient died from causes unrelated to treatment.

Elafibranor Resolves Nonalcoholic Steatohepatitis Without Fibrosis Worsening

An agonist of the peroxisome proliferator–activated receptor-alpha and -delta known as elafibranor resolves nonalcoholic steatohepatitis (NASH) without fibrosis worsening. The agonist also reduces inflammation, glucose profiles, lipids, and liver enzymes when compared to placebo.

Results of the international, randomized, double-blinded, placebo-controlled trial were published in the May issue of *Gastroenterology*. Dr Vlad Ratziu and colleagues randomly assigned patients with NASH without cirrhosis into 3 arms: 93 patients were given 80 mg of elafibranor, 91 were given 120 mg of elafibranor, and 92 were given placebo daily for 1 year, with laboratory and clinical evaluations performed every 2 months. Data between the 2 elafibranor groups and the placebo group were compared using step-down logistic regression. The primary outcome of the study was NASH resolution without worsening of fibrosis based on protocol and modified definitions.

An intention-to-treat analysis showed that the 3 arms achieved similar primary outcomes. However, a post-hoc analysis showed that 19% of patients receiving 120 mg of elafibranor achieved NASH resolution without fibrosis worsening compared with 12% of patients in the placebo group (odds ratio, 2.31; 95% CI, 1.02-5.24; *P*=.045). Liver fibrosis stage reduction occurred in patients in the 120-mg elafibranor group with NASH resolution vs those without NASH resolution (*P*<.001). Compared to the placebo group, patients given 120 mg of elafibranor showed significant reductions in systemic inflammation marker, glucose profiles, lipids, and liver enzymes.

Elafibranor improved cardiometabolic risk profiles, did not cause weight gain, and was well tolerated. The agonist was shown to produce a slight increase in serum creatinine, which was reversible.

Rectal Indomethacin Administered Pre-ERCP Reduces Postprocedural Pancreatitis

Rectal indomethacin administered prior to endoscopic retrograde cholangiopancreatography (ERCP) reduces the risk of postprocedural pancreatitis compared with administration post-ERCP, according to results of a multicenter, single-blinded, randomized, controlled trial published online on April 28, 2016 in *The Lancet*.

Dr Hui Luo and colleagues randomly assigned 2600 patients with native papilla who were undergoing ERCP to a universal, preprocedural group or a risk-stratified, postprocedural group across 6 centers in China between December 2013 and September 2015. Patients in the universal group received a single 100-mg dose of rectal indomethacin within a half-hour before the procedure. Patients in the risk-stratified group who were identified as high risk received rectal indomethacin immediately following ERCP; patients at average risk did not receive indomethacin. The primary outcome of the study was overall incidence of post-ERCP pancreatitis.

Of the 1297 patients in the universal group, 47 (4%) developed post-ERCP pancreatitis, compared with 100 (8%) of the 1303 patients in the risk-stratified group

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(*P*<.001). Postprocedural pancreatitis also occurred less frequently in the universal group vs the risk-stratified group among high-risk patients (6% vs 12%, respectively; *P*=.0057) and average-risk patients (3% with indomethacin vs 6% without indomethacin, respectively; *P*=.0003). Adverse events in both the universal and risk-stratified groups included post-ERCP pancreatitis, biliary infection (22 patients vs 33 patients, respectively), and gastrointestinal bleeding (13 patients vs 10 patients, respectively).

Golimumab Therapy Effective for Long-Term Maintenance of Ulcerative Colitis

Patients with moderate-to-severe active ulcerative colitis achieve effective long-term maintenance with subcutaneous golimumab (Simponi, Janssen) every 4 weeks, according to results from the PURSUIT-SC (Program of Ulcerative Colitis Research Studies Utilizing an Investigational Treatment-Subcutaneous) extension study published online on April 28, 2016 in *Clinical and Translational Gastroenterology*. Results of the original PURSUIT-Maintenance trial demonstrated clinical response with golimumab therapy through week 54.

For the long-term extension study, Dr Peter R. Gibson and colleagues followed patients who had previously completed the phase 3 PURSUIT-Maintenance study, had moderate-to severe ulcerative colitis (Mayo score 6-12 and endoscopic subscore ≥2), had poor response or were unable to tolerate certain therapies (oral 5-aminosalicylates, oral corticosteroids, azathioprine, or 6-mercaptopurine) or were corticosteroid-dependent, and had not previously undergone treatment with anti–tumor necrosis factor alpha antagonists. Patients received either placebo or golimumab in amounts of 50 or 100 mg. Treatment was provided at week 56 and continued every 4 weeks through week 212, with a safety evaluation at week 228. The published results span weeks 56 through 104. Overall, 86.0% of patients maintained mild or inactive disease activity through week 104, and 88.5% of patients not receiving corticosteroids remained corticosteroid-free at week 104.

Of the 200 patients who received golimumab, 17 (8.5%) stopped use before week 104, with the most common reasons for discontinuation being adverse events and unsatisfactory response; higher rates of discontinuation occurred in the 100-mg group compared with the 50-mg group. Rates of infections of special interest remained low through week 104. Two nonmelanoma skin cancers and 1 metastatic colon cancer were observed between weeks 54 and 104, although these rates were similar to those in the previous trial. Two patients died, one from sepsis and one from various comorbidities.

Helicobacter pylori Infection Treatment Guidelines Updated

The Toronto consensus guidelines for the treatment of *Helicobacter pylori* infection in adult patients have been updated to recommend an extended treatment period of 14 days compared to 10 days and to encourage the use of quadruple therapy (bismuth or concomitant nonbismuth) as first-line treatment. The updated guidelines were published online on April 18, 2016 in *Gastroenterology*.

Dr Carlo A. Fallone and colleagues conducted a systematic literature review of studies on *H pylori* treatment and developed recommendations through an online consensus format. The consensus group was chosen by the Canadian Association of Gastroenterology.

All *H pylori* eradication regimens should be extended to 14 days, replacing the former recommendation of 10 days, due to the difficulty of treating the infection. The consensus group recommends the combination of a proton pump inhibitor (PPI)/bismuth/metronidazole/tetracycline (bismuth quadruple therapy) or PPI/amoxicillin/metronidazole/clarithromycin (concomitant nonbismuth quadruple therapy) for most patients. In areas with low resistance to clarithromycin, PPI triple therapy (PPI/clarithromycin/amoxicillin or metronidazole) should be considered. The consensus group recommends against sequential nonbismuth quadruple therapy and levofloxacin triple therapy as first-line therapies and the use of regimens consisting of levofloxacin or clarithromycin as subsequent therapy in patients who have previously failed eradication therapy containing those drugs. The guidelines also note that evidence supporting the use of probiotics to increase eradication rates or decrease adverse events is low and advise against the use of such drugs in combination with quadruple therapy.

In Brief

A small, single-center study of 12 patients with severe reflux esophagitis suggested that the cause of reflux esophagitis may be related to an immune reaction rather than to stomach acids leading to a chemical injury. Two weeks after stopping successful PPI therapy, all 12 patients showed evidence of esophagitis, an increase in esophageal acid exposure, and a decrease in mucosal impedance. The researchers note that further studies are needed to confirm these results. *JAMA*. 2016;315(19):2104-2112.