

Peginterferon Alfa-2a Versus -2b, in Combination With Ribavirin, for Hepatitis C Treatment

The January issue of *Gastroenterology* included two head-to-head studies comparing peginterferon alfa-2a (PEG-IFN-2a) plus ribavirin (RBV) and PEG-IFN-2b plus RBV for hepatitis C virus (HCV) treatment. Although earlier studies have reported the safety and efficacy of both pegylated interferons in combination with RBV, the efficacy of the formulations has been compared in only 2 randomized studies and neither study was sufficiently powered to identify a statistically significant difference in sustained virologic response (SVR).

The first study, led by Massimo Colombo, MD, of the University of Milan in Italy, randomly (1:1) assigned treatment-naïve HCV patients (stratified for genotype) to either 1.5 µg/kg/week PEG-IFN-2b plus RBV 800–1,200 mg/day (n=219) or 180 µg/week PEG-IFN-2a plus RBV 800–1,200 mg/day (n=212) for 24 or 48 weeks, based upon genotype. The study was powered to identify a difference of at least 10% in regimen safety and efficacy. Both arms shared similar baseline characteristics, including cirrhosis (20% vs 18%, respectively). Based upon intention-to-treat analysis, both arms experienced similar rates in terms of treatment-related serious adverse events (1% vs 1%, respectively) and dropout rates for adverse effects (7% vs 6%, respectively). The PEG-IFN-2a arm had a higher SVR than the PEG-IFN-2b arm (66% vs 54%, respectively, $P=.02$). SVR was 48% vs 32% in the 222 HCV-1 and -4 patients ($P=.04$), and 96% vs 82%, respectively, in the 143 HCV-2 patients ($P=.01$). In logistic regression analysis, PEG-IFN-2a independently predicted SVR (odds ratio, 1.88; 95% confidence interval [CI], 1.20–2.96). The researchers concluded that although the formulations demonstrated similar safety profiles, SVR was significantly higher with PEG-IFN-2a than PEG-IFN-2b.

Similar results were found in the second study, led by Antonio Ascione, MD, of Fatebenefratelli Hospital in Naples, Italy, which examined 320 consecutive, treatment-naïve, HCV RNA-positive patients with chronic hepatitis who were randomly assigned to once-weekly PEG-IFN-2a (180 µg) or PEG-IFN-2b (1.5 µg/kg) plus RBV 1,000 mg/day (body weight <75 kg) or 1,200 mg/day (body weight ≥75 kg) for 48 weeks (genotype 1 or 4)

or 24 weeks (genotype 2 or 3). SVR was higher with PEG-IFN-2a than PEG-IFN-2b (110/160 [68.8%] vs 87/160 [54.4%]; $P=.008$). SVR was also higher with PEG-IFN-2a than PEG-IFN-2b among patients with genotype 1/4 (51/93 [54.8%] vs 37/93 [39.8%]; $P=.04$); with genotype 2/3 (59/67 [88.1%] vs 50/67 [74.6%]; $P=.046$); without cirrhosis (96/127 [75.6%] vs 75/134 [55.9%]; $P=.005$); and with baseline levels of HCV RNA greater than 500,000 IU/mL (58/84 [69%] vs 43/93 [46.2%]; $P=.002$). There was no statistical difference in SVR with PEG-IFN-2a as opposed to PEG-IFN-2b among patients with baseline HCV RNA levels of 500,000 IU/mL or less (52/76 [68.4%] vs 44/67 [65.7%]; $P=.727$) or in cirrhotic patients (14/33 [42.4%] vs 12/26 [46.1%]; $P=.774$). The researchers concluded that PEG-IFN-2a and RBV yielded a significantly higher SVR than PEG-IFN-2b and RBV in chronic HCV.

Surveillance Colonoscopy and Colorectal Cancer Risk

According to the January issue of *Gastrointestinal Endoscopy*, researchers at various US institutions assessed the rate of interval colorectal cancer in the Polyp Prevention Trial Continued Follow-up Study (PPT-CFS), which was an observational study of PPT participants that began once the PPT ended. This follow-up study was a prospective, national US community-based trial in which main outcome measurements involved the standardized collection, review, and abstraction of medical records of colorectal cancer patients. The PPT consisted of 2,079 participants; 1,297 (62.4%) of these participants entered the PPT-CFS and were followed for a median of 6.2 years (after having been followed for a mean of 4.3 years in the main PPT). Over a period of 7,626 person-years of observation (PYO), 9 colorectal cancer cases were diagnosed, signifying an incidence rate of 1.2/1,000 PYO. The rate of observed colorectal cancers compared to the rate expected by Surveillance, Epidemiology, and End Results (SEER) database analysis was 0.64 (95% CI, 0.28–1.06). Taking into account all colorectal cancers from the beginning of the PPT (N=22), the ratio of observed colorectal cancers compared to the rate expected by SEER was 0.74 (95% CI, 0.47–1.05). In terms of patients in whom colorectal cancer developed during the PPT-CFS, 78% had a history of advanced adenoma compared to 43% of patients who

remained cancer free ($P=.04$). The majority of the cancers detected were early stage (78% were stage I or II) and, therefore, highly curable. Although the researchers noted that the study was limited by the relatively small number of interval cancers detected, they concluded that there was a persistent ongoing risk of cancer in the years after the trial despite frequent colonoscopy during the PPT. They also noted that patients with a history of advanced adenoma should be followed closely with continued surveillance, as they are at increased risk of subsequent cancer.

St. John's Wort in the Treatment for Irritable Bowel Syndrome

The January issue of the *American Journal of Gastroenterology* included results of a randomized, double-blind, placebo-controlled trial assessing the efficacy of St. John's wort in irritable bowel syndrome (IBS) after 12 weeks. Although antidepressants have been used in the treatment of IBS, no prior study had evaluated the efficacy of St. John's wort in this condition. Researchers at the Mayo Clinic in Rochester, Minnesota and Jacksonville, Florida examined 70 patients diagnosed with IBS (women, 86%; median age, 42 years), who were randomized and assigned to St. John's wort or placebo via concealed allocation. Symptom subtypes were balanced in both treatment arms. The primary endpoint of the trial was defined as the self-reported overall bowel symptom score (BSS) at 12 weeks, whereas secondary endpoints included individual BSS for diarrhea (D-BSS), constipation (C-BSS), pain or discomfort, and bloating; adequate relief (AR) of IBS on at least 50% of the last 4 treatment weeks; and IBS quality-of-life score at 12 weeks. Overall, 29% had C-IBS, 37% had D-IBS, and 31% had mixed IBS.

According to the researchers, both arms experienced reductions in overall BSS from baseline, though the placebo arm experienced significantly lower scores at 12 weeks ($P=.03$) compared to the arm treated with St. John's wort. The placebo arm also did better in terms of secondary endpoints, with significant differences observed at Week 12 for D-BSS ($P=.03$) and percent with AR ($P=.02$). A similar proportion of patients in each treatment arm (St. John's wort: 51% vs placebo: 54%) thought that their study drug decreased IBS life interferences ($P=.79$). The researchers concluded that St. John's wort was less effective than placebo for the treatment of IBS.

Prokinetics Plus Omeprazole in Proton Pump Inhibitor-resistant Nonerosive Reflux Disease

Researchers at the Nippon Medical School in Tokyo, Japan investigated the effects of prokinetics and omeprazole on the clinical symptoms, gastric emptying, and esopha-

geal peristalsis of patients with proton pump inhibitor (PPI)-resistant nonerosive reflux disease (NERD) with or without delayed gastric emptying. The study, the results of which were published online in December ahead of publication in the *Journal of Gastroenterology*, involved 64 consecutive patients who presented with typical PPI-resistant NERD symptoms ($n=44$) as well as 20 healthy volunteers. The treatment arm consisted of the prokinetic agent mosapride citrate (15 mg/day) and omeprazole (20 mg/day) cotherapy for 12 weeks, and clinical symptoms, gastric emptying, and esophageal manometry were evaluated prior to and following treatment.

The researchers found the T_{max} value of PPI-resistant NERD patients to be significantly higher than that of the control arm. Mosapride citrate and omeprazole cotherapy was found to significantly improve reflux symptoms and T_{max} value in $T_{max} > 65$ min NERD patients. In addition, the cotherapy significantly decreased desacylated-ghrelin levels in NERD patients with delayed gastric emptying. The researchers concluded that use of mosapride citrate with omeprazole improved gastroesophageal reflux and gastric emptying in PPI-resistant NERD patients with delayed gastric emptying.

Certolizumab Pegol in an Unselected Crohn's Disease Population

A phase IV study was conducted by researchers at various institutions in Switzerland to examine the use of certolizumab pegol in a multicenter cohort of practice-based patients. The results of the study, also known as the FACTS survey, were published online in December ahead of publication for *Inflammatory Bowel Diseases*. All Swiss gastroenterologists in both hospitals and private practices were administered baseline and Week 6 evaluation questionnaires. The Harvey-Bradshaw Index (HBI) was used to evaluate disease activity, whereas World Health Organization guidelines were used to evaluate adverse events. The study population consisted of 50 patients (31 women), with 56% of patients having complicated disease (ie, stricture or fistula) and 52% having previously undergone Crohn's disease-related surgery. All patients reported prior exposure to systemic steroids (96% to immunomodulators, 78% to infliximab, and 50% to adalimumab). The researchers noted a significant reduction in HBI at Week 6 (vs Week 0) after subcutaneous certolizumab pegol induction therapy (400 mg) at Weeks 0, 2, and 4 (12.6 ± 4.7 at Week 0 vs 6.2 ± 4.4 at Week 6; $P < .001$). Week 6 response and remission rates were 54% and 40%, respectively. The incidence of adverse drug reactions associated with certolizumab pegol was 6%. Beyond Week 6, certolizumab pegol therapy was continued in 80% of patients.

Optical Diagnosis and Small Colorectal Polyps

According to the December issue of *Lancet Oncology*, researchers at St. Mark's Hospital in London, United Kingdom conducted a prospective cohort study to evaluate whether optical diagnosis of small polyps (<10 mm) is feasible and safe in routine clinical practice. The patient population consisted of consecutive patients with a positive fecal occult blood test or previous adenomas who were undergoing surveillance at a single center from June 19, 2008 to June 16, 2009. Polyp histology was predicted by 4 colonoscopists (of varying degrees of expertise) via optical diagnosis with high-definition white light, narrow-band imaging without magnification, and chromoendoscopy. The accuracy of polyp characterization via optical diagnosis compared to the current gold standard of histopathology was defined as the primary outcome. Also evaluated was the accuracy of optical diagnosis to predict the next surveillance interval, which was compared to the surveillance intervals predicted by histopathology (as recommended by current guidelines).

In total, the researchers identified 363 polyps smaller than 10 mm in 130 patients. Of these polyps, 278 were diagnosed by both optical and histopathologic means. Based upon histology, 198 of these polyps were classified as adenomas and 80 as nonneoplastic lesions (with 62 of these as hyperplastic). Optical diagnosis provided an accurate diagnosis of 186 of 198 adenomas (sensitivity, 0.94; 95% CI, 0.90–0.97) and 55 of 62 hyperplastic polyps (0.89; 0.78–0.95). These data signified an overall accuracy of 241 of 260 (0.93, 0.89–0.96) in terms of polyp characterization. Based upon optical diagnosis alone, 82 of 130 patients could be given a surveillance interval immediately following colonoscopy. The same interval was identified via formal histopathology in 80 patients (98%) with British guidelines and in 78 patients

(95%) with US multisociety guidelines. The researchers concluded that in vivo optical diagnosis appeared to be acceptable for the evaluation of polyp histopathology and future surveillance intervals for polyps less than 10 mm in size. They also noted that dispensing with formal histopathology in this patient population might improve efficiency and lead to time and cost savings.

In Brief

According to a prospective, randomized, double-blind, controlled trial of 160 patients with aspirin-related peptic ulcers/erosions, with or without a history of bleeding, high-dose famotidine therapy is inferior to pantoprazole in preventing recurrent dyspeptic or bleeding ulcers/erosions. *Gastroenterology*. 2010;138:82-88.

Researchers of a prospective study found that, despite a modest trend, consumption of caffeine from sources other than coffee or of decaffeinated coffee was not associated with reduced liver fibrosis. A reliable tool for measurement of caffeine consumption demonstrated that caffeine consumption, particularly from regular coffee, above a threshold of approximately 2 coffee-cup equivalents per day, was associated with less severe hepatic fibrosis. *Hepatology*. 2010;51:201-209.

In a prospective study, fecal calprotectin correlated closest with simple endoscopic score–Crohn's disease, followed by C-reactive protein, blood leukocytes, and the Crohn's disease activity index. Furthermore, fecal calprotectin was the only marker that reliably discriminated inactive from mild, moderate, and highly active disease, which underlines its usefulness for activity monitoring. *Am J Gastroenterol*. 2010;105:162-169.