

Peginterferon Plus Ribavirin Hepatitis C Treatment for 16 or 24 Weeks

Results of a trial comparing the efficacy of treatment with peginterferon alfa-2a and ribavirin in genotypes 2 or 3 hepatitis C virus (HCV) patients for the standard 24 weeks of therapy or a shortened therapy of 16 weeks were published in a recent issue of the *New England Journal of Medicine*. Led by Mitchell Shiffman, MD, Virginia Commonwealth University, researchers conducted a randomized, multinational, noninferiority trial among 1,469 patients with HCV genotype 2 or 3 who were randomly assigned to receive 180 µg of peginterferon alfa-2a weekly plus 800 mg of ribavirin daily for 16 or 24 weeks. Sustained virologic response in the study was an undetectable serum HCV RNA level (<50 IU/mL) in patients 24 weeks after the end of treatment, and relapse rate was a detectable HCV RNA level during follow-up in patients with an undetectable HCV RNA level at the end of treatment.

Patients treated for 16 weeks experienced significantly lower sustained virologic response rates than patients treated for 24 weeks (62% vs 70%; odds ratio, 0.67; 95% confidence interval, 0.54–0.84; $P<.001$). The relapse rate was significantly greater in patients receiving 16 weeks of treatment than those receiving 24 weeks (31% vs 18%; $P<.001$). However, discontinuation rates were lower in the 16-week arm. Among patients with a pretreatment serum HCV RNA level of 400,000 IU/mL or less, sustained virologic response was similar (82% in the 16-week treatment arm compared with 81% in the 24-week treatment arm). Among patients with rapid virologic response, which was defined as an undetectable HCV RNA level by 4 weeks, sustained virologic response was 79% among patients in the 16-week arm compared with 85% among patients in the 24-week arm ($P=.02$). Researchers concluded that 16-week treatment with peginterferon and ribavirin leads to lower overall sustained virologic response than the standard 24-week treatment. These results contradicted the primary study hypothesis that 16-week treatment would yield sustained virologic response rates similar to those with 24-week treatment.

Capsule Endoscopy Versus Standard Endoscopy for Barrett Esophagus

Researchers from the Virginia Mason Medical Center conducted a prospective, blinded, multicenter study with no adjudication to investigate the accuracy of dual-headed esophageal capsule endoscopy (CE) for the diagnosis of

Barrett esophagus. The results, published in a recent issue of *Gastrointestinal Endoscopy*, were based on 66 screening patients with chronic gastroesophageal reflux and 24 surveillance patients with known Barrett esophagus. The patients underwent CE and then esophagogastroduodenoscopy (EGD) with sedation 1–4 hours later, and the sensitivity, specificity, and positive and negative predictive values of ECE for Barrett esophagus were measured by using results of the EGD. Histologic confirmation served as the criterion standard.

Compared with conventional endoscopy, CE was 67% sensitive and 84% specific for identifying Barrett esophagus, and diagnosed 14 of 21 cases of biopsy-confirmed Barrett esophagus. Positive and negative predictive values, which were measured only for screening patients, were 22% and 98%, respectively. Sensitivity for short- (<3 cm) and long-segment Barrett esophagus was similar. The authors concluded that CE had only moderate sensitivity and specificity for identifying Barrett esophagus and that, currently, CE was not appropriate as a primary screening tool for Barrett esophagus but could be utilized in patients unwilling to undergo EGD. The authors suggested that inadequate visualization of the gastroesophageal junction could be the cause of suboptimal CE accuracy, and could possibly be improved by advances in ingestion protocol and capsule calibration. The study results were in contrast to the favorable results of CE from an earlier pilot study and a validation study, the latter of which used a post-hoc adjudication process that may have biased the results.

Certolizumab Pegol for Treatment in Crohn's Disease

Two studies published in a recent issue of the *New England Journal of Medicine* found certolizumab pegol to be an effective treatment for adults with Crohn's disease, although it has not yet been approved by the United States Food and Drug Administration for this indication.

A double-blind, placebo-controlled trial among 662 adult patients with moderate-to-severe Crohn's disease was led by William J. Sandborn, MD, Mayo Clinic, Rochester, Minn. Patients were randomly assigned to treatment of either 400 mg of certolizumab pegol or placebo subcutaneously at 0, 2, and 4 weeks and then every 4 weeks. Thirty-five percent of patients receiving certolizumab pegol achieved an improvement in symptoms after 6 weeks compared with 27% of patients receiving placebo ($P=.02$). At both 6 and 26 weeks, response rates were 23% and 16%, respectively, ($P=.02$). Remission rates at

6 and 26 weeks did not differ significantly between the arms ($P=.17$). Serious adverse events and serious infections were reported in 10% and 2%, respectively, of the certolizumab pegol arm and 7% and less than 1%, respectively, of the placebo arm. In the certolizumab pegol arm, antibodies to the drug developed in 8%, and antinuclear antibodies developed in 2%. The researchers concluded that in patients with moderate-to-severe Crohn's disease, induction and maintenance therapy with certolizumab pegol was associated with a modest improvement in response rates, but no significant improvement in remission rates.

The second study, led by Stefan Schreiber, MD, Christian Albrechts University, Germany, examined certolizumab pegol as long-term maintenance therapy for Crohn's disease. In a randomized, double-blind, placebo-controlled trial, 668 patients were randomly assigned to receive 400 mg of certolizumab pegol or placebo every 4 weeks for 24 weeks. Among patients who responded to induction therapy at 6 weeks (428 of 668, or 64%), response was maintained through 26 weeks in 63% of the intention-to-treat population receiving certolizumab pegol compared with 36% of the placebo group ($P<.001$). Among patients who responded to induction therapy at 6 weeks, remission, as defined by a Crohn's Disease Activity Index score of no more than 150 at 26 weeks, was achieved in 48% of the certolizumab arm and 29% of the placebo arm ($P<.001$). Infectious serious adverse events (including 1 case of pulmonary tuberculosis) occurred in 3% of the certolizumab pegol arm and in less than 1% of patients receiving placebo. Antinuclear antibodies developed in 8% of the certolizumab group, and antibodies against certolizumab pegol developed in 9% of all patients in the induction phase. The authors concluded that patients with moderate-to-severe Crohn's disease who responded to 400 mg of certolizumab pegol as induction therapy were more likely to maintain response and remission at 26 weeks with continued certolizumab pegol treatment than those who switched to placebo.

Quality-of-Life Assessment Tool for Hepatitis B

The journal *Hepatology* recently reported the development and validation of the first quality-of-life instrument for noncirrhotic chronic hepatitis B virus (HBV) patients to measure the effect of hepatitis B on quality of life beyond physical symptoms and better assess overall well-being and guide treatment.

Led by Brennan M. R. Spiegel, MD, David Geffen School of Medicine at the University of California, Los Angeles, and the Veterans Affairs Greater Los Angeles Healthcare System, the researchers conducted a system-

atic literature review, an expert focus group, and cognitive interviews with HBV patients to create a questionnaire which was given to 138 HBV patients. Factor analysis was used to test hypotheses regarding health-related quality of life domains, and construct validity was measured by comparing scores from the questionnaire across other anchors such as viral response to treatment, SF-36 scores, and global health. Test-retest and internal consistency reliability were also measured. Content validation showed that HBV affected multiple aspects of psychological, social, and physical health, which were summarized with 31 items across 6 subscales: psychological well-being, anticipation anxiety, vitality, disease stigma, vulnerability, and transmissibility. Internal consistency and test-retest reliability were deemed as excellent. The instrument was able to distinguish between viral responders and nonresponders and correlated highly with SF-36 scores and global health.

The researchers concluded that patients with chronic HBV infection attributed a wide range of negative psychological, social, and physical symptoms to their condition, even in the absence of cirrhosis or cancer, and found the questionnaire to be a valid and reliable measure to capture this health-related quality-of-life decrement. The researchers also suggested that the questionnaire be used in clinical trials to help measure outcomes and equip patients with knowledge to help them choose treatment.

"We were shocked to find that for many hepatitis B patients without advanced liver disease, the psychosocial impact of the disease affected their lives more than the physical symptoms," said Dr. Spiegel. "We hope that this quick questionnaire can become a 'vital sign' taken in the doctor's office to help see how the patient is doing."

Probiotic Drinks and Diarrhea Associated With Antibiotics

A randomized, double-blind, placebo-controlled study was conducted to determine the efficacy of a probiotic drink containing *Lactobacillus* in the prevention of diarrhea associated with either antibiotic use or *Clostridium difficile*, according to a study published in a recent issue of *BMJ*. Researchers from Imperial College at Hammersmith Hospital, London, United Kingdom, examined 135 hospital patients (mean age 74) from three London hospitals taking antibiotics. Excluded from the study were patients who had diarrhea on admission, bowel pathology that could result in diarrhea, antibiotic use in the previous 4 weeks, severe illness, immunosuppression, bowel surgery, artificial heart valves, and history of rheumatic heart disease or infective endocarditis.

The patients were randomly given either a 100 g (97 mL) drink containing *Lactobacillus casei*, *L. bulgari-*

cus, and *Streptococcus thermophilus* twice daily during a course of antibiotics and for 1 week afterwards or placebo, within 48 hours of the start of antibiotic therapy. The primary outcome of the study was the occurrence of antibiotic-associated diarrhea, whereas the secondary outcome was the presence of *C. difficile* toxin and diarrhea. In the probiotic arm, 7 of 57 patients (12%) developed diarrhea associated with antibiotic use compared with 19 out of 56 patients (34%) in the placebo group ($P=.007$). Logistic regression to control for other factors formed an odds ratio of 0.25 (95% confidence interval, 0.07–0.85) for the use of the probiotic supplement, with low albumin and sodium also increasing the risk of diarrhea. The absolute risk reduction was 21.6% (6.6–36.6%), and the number needed to treat was 5 (3–15). No patients in the probiotic arm and 9 of 53 (17%) patients in the placebo arm developed diarrhea caused by *C. difficile* ($P=.001$). The absolute risk reduction was 17% (7–27%), and the number needed to treat was 6 (4–14). The researchers concluded that consumption of a probiotic drink containing *L. casei*, *L. bulgaricus*, and *S. thermophilus* could reduce the incidence of antibiotic-associated diarrhea and *C. difficile*-associated diarrhea, and could potentially decrease morbidity, hospital stays and costs, and mortality if used regularly in patients over the age of 50.

Electrode Radiofrequency Ablation for Liver Cancer

The journal *American Journal of Roentgenology* recently published results of a retrospective study conducted by researchers at the University of Wisconsin in Madison to assess the safety and efficacy of percutaneous multiple-electrode radiofrequency ablation for treating hepatic malignancies. The study examined 38 malignant hepatic tumors (mean diameter, 2.7 cm; range, 0.7–10.0 cm) in 23 patients (12 men and 11 women; mean age, 65 years; range, 40–84 years) who were treated in 26 radiofrequency ablation sessions with an impedance-based multiple-electrode system. Contrast-enhanced computed tomography (CT) scans were obtained immediately after ablation, as well as follow-up CT scans at 1, 3, 6, 9, and 12 months

(mean, 4 months) afterwards to assess for tumor progression and new metastases.

Local control was achieved in 37 of 38 tumors, with 34 of these tumors requiring only one session. The total ablation time was reduced by approximately 54% compared to utilizing the single-electrode system (1,014 vs 2,196 minutes). Complications included 1 death from a presumed postprocedure pulmonary embolus, 1 pneumothorax, and 1 asymptomatic perihepatic hemorrhage. The authors concluded that multiple-electrode radiofrequency ablation was safe and efficacious for local control in large or multiple hepatic malignancies at short-term follow-up and that longer term follow-up was necessary to properly assess its impact on patient survival and tumor recurrence rates.

In Brief

Waist circumference, but not body mass index, has some modest independent associations with the risk of Barrett esophagus, according to the results of a case-control study. The findings provide partial support for the hypothesis that abdominal obesity contributes to gastroesophageal reflux disease, which may in turn increase the risk of Barrett esophagus. (*Gastroenterology*. 2007;133:34-41.)

Cholangioscopy-directed lithotripsy is a safe and effective treatment in patients who have failed standard endoscopic retrograde cholangiopancreatography stone removal techniques, according to a prospective study. Stone recurrence was low in patients who had complete stone clearance except in patients with primary sclerosing cholangitis. (*Clin Gastroenterol Hepatol*. 2007 Jul 20; [Epub ahead of print].)

Branched-chain amino acid supplementation improved the oxidized/reduced state of serum albumin, according to a feasibility study. The intervention was effective to maintain the quality of serum albumin in cirrhotic patients. (*Hepatol Res*. 2007;37:765-770.)