Posttransplant HCV Prophylaxis Shows Promise

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BOSTON — Prophylaxis with pegylated interferon plus ribavirin is relatively safe and well tolerated following liver transplantation for hepatitis C, a study has shown.

Preliminary findings from the first randomized control trial of antiviral prophylaxis for the prevention of recurrent hepatitis C infection in orthotopic liver-transplant (OLT) patients suggest that although adverse events are common during prophylactic treatment with peginterferon α-2a (Pegasys) plus ribavirin (Copegus), only a small percentage of those adverse events necessitate treatment withdrawal, Dr. Natalie H. Bzowej said at the annual meeting of the American Association for the Study of Liver Diseases.

Because recurrent infection with the hepatitis C virus (HCV) can cause graft failure and death following liver transplantation, preemptive antiviral therapy has been suggested as a way to enhance viral clearance. However, safety concerns—particularly regarding anemia, neutropenia, and acute cellular rejection—have limited its use, said Dr. Bzowej of California Pacific Medical Center in San Francisco.

To assess the safety and efficacy of preemptive antiviral therapy following liver transplant and to compare the outcomes of patients undergoing prophylactic treatment to those of patients who don't receive treatment until recurrent hepatitis has become established in the graft, Dr. Bzowej and her colleagues in the ongoing Phoenix study out of the Mayo Clinic to date have randomized 115 post–liver transplant patients to either a prophylaxis or an observation arm. Dr. Bzowej presented data on the first 60 randomized patients.

Of the 60 patients, 33 were randomized to prophylaxis with 135 mcg peginterferon α-2a per week for 4 weeks, followed by 180 mcg/week for 44 weeks, plus ribavirin, at an initial dosage of 400 mg/day, escalating to 1,000 mg or 1,200 mg/day over the first 12 weeks, for 48 weeks. The 27 patients randomized to observation received no treatment until histologic recurrence of HCV, Dr. Bzowej reported.

All of the patients in the study were randomized 10-26 weeks post transplant. Previous investigations into preemptive therapy have begun prophylaxis as early as 4 weeks post transplant, "but doing so excludes a number of potential candidates who are still recovering from surgery," Dr. Bzowej said.

After randomization and before treatment initiation, one patient in the prophylaxis arm and three patients in the observation arm withdrew consent for the study. Of the 32 patients who began treatment in the prophylaxis arm, 7 withdrew. Four of the patients in the observation arm crossed over to treatment because of HCV recurrence.

During the first 12 study weeks, 94% of the prophylaxis arm and 82% of the observation arm experienced one or more adverse events, with a total of 278 and 107 adverse events, respectively. Additionally, 19% of patients in the prophylaxis arm and 15% in the observation arm experienced one or more serious adverse events, with a total of seven and six serious adverse events, respectively.

"The most common treatment-related adverse events were fatigue, anemia, headache, and nausea," Dr. Bzowej said.

With respect to treatment modifications or interruptions, of the 32 patients assigned to the prophylaxis arm, 6 (19%) withdrew from therapy because of adverse events. Five of the six withdrew from both pegylated interferon α-2a and ribavirin—one for rash and anemia, one for thrombocytopenia, one for increased bilirubin, one for dehydration, and one for neutropenia. The sixth patient withdrew from the ribavirin only because of anemia. None of the four crossover patients in the observation arm withdrew from treatment.

Importantly, "no clinically apparent episodes of acute cellular rejection occurred through week 12," Dr. Bzowej said. And although adverse events occurred in 94% of the prophylactically treated patients, "only 19% experienced events necessitating therapeutic withdrawal—a figure that compares favorably with other studies, suggesting the regimen is reasonably well tolerated," she said.

Dr. Bzowej disclosed that she has been a speaker for Schering and Glaxo and that she has served as a consultant for Intarcia. She has also been an investigator on clinical trials supported by numerous companies, including Roche Laboratories, which manufactures Pegasys. ■