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Study shows positive findings in treating patients with advanced hepatitis C

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The hepatitis C therapy peginterferon alfa-2b, when given as low-dose maintenance therapy, can prevent disease progression in certain patients who failed previous interferon-based hepatitis C therapies and have advanced liver disease, according to findings from a large, four-year study presented today at the 43rd annual meeting of the European Association for the Study of the Liver (EASL).

The study, called COPILOT (COlchicine versus Peg-Intron LOng-Term), showed that low-dose peginterferon alfa-2b was superior to colchicine in improving the disease-free survival of patients with cirrhosis and portal hypertension, especially in patients who stayed on treatment. In the study, more than 40 percent of patients had portal hypertension, a condition of high blood pressure in the major vessel going to the liver from the gastrointestinal tract and which often accompanies liver cirrhosis. However, peginterferon alfa-2b maintenance therapy was not superior to colchicine in patients overall.

“These findings make a strong case for considering low-dose peginterferon alfa-2b as a maintenance therapy in patients with cirrhosis and portal hypertension who have failed hepatitis C eradication therapy,” said principal investigator Nezam Afdhal, M.D., Chief of Hepatology at Beth Israel Deaconess Medical Center (BIDMC) and Associate Professor of Medicine at Harvard Medical School. “While other interferon maintenance therapies have been studied in the past few years in previous interferon nonresponders, these findings show, for the first time, a clinical benefit in a specific population with advanced disease,”

he said.

Hepatitis C virus (HCV) infection is transmitted through exposure to infected blood and affects an estimated 4 million individuals in the United States. The current standard treatment, combination therapy with pegylated interferon plus ribavirin for 24 to 48 weeks, can eradicate the virus in about 50 percent of patients. Those who do not respond and have cirrhosis are at far greater risk for developing liver cancer or liver failure, so the development of treatment strategies for these nonresponders is a priority.

Conducted at approximately 40 sites in the United States, the COPILOT study compared weight-based low-dose peginterferon alfa-2b (subcutaneous injection of 0.5 mcg/kg/wk, one-third the dose used in standard HCV combination therapy) versus colchicine (0.6 mg orally, twice daily), an anti-inflammatory and antifibrotic medication, in 555 chronic hepatitis C patients with advanced liver fibrosis who previously failed interferon-based therapies. Patient baseline characteristics were well balanced between the two study arms. Over the four years of the randomized study, investigators monitored the patients to determine how many reached a primary endpoint, defined as death, liver transplant, hepatocellular carcinoma (liver cancer), variceal bleeding, or liver failure (increase in Child-Pugh-Turcotte [CPT] by 2 points with ascites, jaundice or encephalopathy). They analyzed their findings for all 555 patients, who received at least one dose of their assigned drug, in two ways: based on all events that occurred during the entire four years of the study, regardless of whether a patient was still taking their assigned drug or not (the “intent-to-treat” or ITT analysis), and based on only the events that occurred while patients were taking their assigned drug (the “on drug” analysis).

The investigators found a primary endpoint was reached by 17.8% (51/286) of patients in the peginterferon alfa-2b group versus 20.4%

(55/269) in the colchicine group in the ITT analysis, and by 12.2% (35/286) and 16.0% (43/269) patients, respectively, in the on-drug analysis (treatment differences were not statistically significant). Among patients who had portal hypertension (42.3% and 48.0% of patients in the peginterferon alfa-2b and colchicine groups, respectively), peginterferon alfa-2b therapy resulted in significantly improved event-free survival in both the ITT and on-drug analyses (Wilcoxon p = 0.041 and 0.028, respectively). Further, variceal bleeding, a specific complication of portal hypertension, was almost abolished with peginterferon alfa-2b in both the ITT (10 vs. 1 patients) and the on-drug (10 vs. 0 patients) analyses. In the ITT analysis, hepatocellular carcinoma occurred in 7.7% and 5.9% of patients in the peginterferon alfa-2b and colchicine groups, respectively, a non-significant difference.

Overall, 49% of patients discontinued their medication before the end of the four-year study, with 36% due to failure to comply and 13% due to side effects. Peginterferon alfa-2b was generally well tolerated. Among patients who discontinued due to interferon side effects (17.1%, 49/286), the most common reason (45%, 22/49 patients) was general intolerance to interferon (e.g., due to flu-like symptoms, malaise, and other common interferon side effects).

Source: Beth Israel Deaconess Medical Center