Experimental drug suppresses rebound of hepatitis C virus in liver transplant patients

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A human monoclonal antibody developed by MassBiologics of the University of Massachusetts Medical School (UMMS) given to patients with chronic hepatitis C virus (HCV) infection undergoing liver transplantation significantly suppressed the virus for at least a week after transplant and delayed the time to viral rebound. Results from a randomized, double-blind, placebo-controlled, phase 2 study were presented this week at The Liver Meeting, the annual meeting of the American Association for the Study of Liver Diseases, in San Francisco.

"The challenge for patients with end-stage liver disease from HCV is that a transplant is not a cure. Because the virus remains in the blood stream, the new liver eventually becomes infected with the hepatitis C virus," said Deborah C. Molrine, MD, deputy director of clinical and regulatory affairs at MassBiologics. "These results show that a human monoclonal antibody targeting the hepatitis C virus can significantly reduce viral loads in infected patients who receive donor livers and moves us one step closer to clearing the virus so the new liver doesn't become chronically infected."

Five hospitals enrolled patients in the trial —Massachusetts General Hospital, Beth Israel Deaconess Medical Center, both in Boston, Lahey Clinic in Burlington, Massachusetts, Yale-New Haven Hospital in Connecticut and Mount Sinai Hospital in New York City. Patients enrolled in the study were treated with a total of 11 intravenous infusions of either the human monoclonal antibody, designated MBL-HCV1, prior to, during, and after surgery or a placebo (salt solution). The first three

infusions were administered on the day of transplantation followed by a daily infusion in the first week following surgery and a final infusion 14 days after transplant. Of the 11 patients enrolled in the first part of the trial, six received the MBL-HCV1 antibody. "The commitment of the transplant team at each site working with study investigators ensured the delivery of the multiple infusions according to schedule and all infusions were well tolerated by the patients. The infusions did not add to any patient's length of stay in the hospital." said Fredric Gordon, MD, medical director of liver transplantation at Lahey Clinic Medical Center.

The group of patients who received the monoclonal antibody had a significantly greater reduction in viral load from pre-transplant levels at days three through six post-transplant compared to patients who received the placebo. One patient's viral load dropped below the detection limit starting at day two after transplant and didn't have a viral rebound until day 35.

"Because the HCV virus is prone to mutations, patients develop variants of the virus that can escape from the effect of a single type of treatment," said Molrine. "In the next phase of the study, we plan to combine the monoclonal antibody with another HCV antiviral agent to see if the activity of two drugs against the virus results in further suppression, if not clearance, of the virus."

HCV damages the liver and is the leading indication for liver transplantation, diagnosed in about half of the 6,000 patients who receive liver transplants each year in the United States. According to the US Centers for Disease Control and Prevention, 3.2 million Americans are chronically infected with HCV and approximately 10,000 die annually of the disease. Globally, as many as 170 million people are estimated to suffer from HCV infection.

For patients with end-stage liver disease from HCV infection, liver

transplantation is the only option. While it can be a life-saving treatment, transplantation does not cure the disease. In nearly all cases, the patient's new liver is eventually infected by HCV because the virus remains in the patient's bloodstream during surgery. The course of recurrent HCV disease is accelerated after transplantation and up to 20 percent of transplant patients develop cirrhosis within five years. Unfortunately, the standard antiviral drugs currently used to treat HCV prior to the onset of end-stage liver disease are poorly tolerated after liver transplantation, leaving these patients with few options.

"The ability to prevent allograft infection using strategies such as immunoprophylaxis would have an enormous impact on outcomes of liver transplantation for HCV," said Raymond T. Chung, MD, director of hepatology at Massachusetts General Hospital.

Provided by University of Massachusetts Medical School