First liver transplant patients receive experimental drug to prevent hepatitis C infection

18 January 2011

Following a successful Phase 1 study for safety, researchers at MassBiologics of the University of Massachusetts Medical School (UMMS) today announced the beginning of a Phase 2 clinical trial testing the ability of a human monoclonal antibody they developed to prevent hepatitis C virus (HCV) infection of a donor liver in transplant patients.

The first patients were enrolled in the study in December. The primary goal of this randomized, double-blind, placebo-controlled study is to test if the monoclonal antibody, designated MBL-HCV1, prevents re-infection of patients chronically infected with HCV who are undergoing liver transplantation.

MassBiologics plans to enroll 16 patients in the first part of the study. "We are hopeful that positive results from this study will meet an important public health need, and we could not take this important step without the willing and thoughtful participation of these volunteers," said Donna Ambrosino, MD, executive director of MassBiologics and a professor of pediatrics at the Medical School.

There are currently five hospitals participating 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-and others may join in the coming months. The first six patients enrolled have come from three of these sites.

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.

To address this unmet medical need, the team at MassBiologics, working in collaboration with investigators Gyongyi Szabo, MD, PhD, professor of medicine, and Robert Finberg, MD, professor and chair of the Department of Medicine at UMMS, set out to develop a human monoclonal antibody that could clear HCV from a patient's bloodstream and protect the donated liver from infection. In pre-clinical studies, MBL-HCV1 successfully neutralized the virus in cell culture and animal models of infection. A Phase 1 study in 31 healthy volunteers completed in 2009 showed the antibody was well tolerated, with no serious side effects. The Phase 1 study also measured the levels of the antibody in the bloodstream and its ability to bind and inactivate the virus, thereby helping to establish the dosage and protocol for the Phase 2 study now under way.

In the current study, patients will be randomized to receive an infusion of either the antibody or placebo

between one and four hours prior to surgery. Then, during the phase of surgery when the diseased liver is removed, but before the donor liver is implanted, patients will receive a second infusion of either the antibody or placebo. After the surgery is completed, the patients will receive a third infusion, and then daily infusions during the first week of recovery. A final infusion is administered on the 14th day after liver transplantation.

"The liver is the main reservoir for the hepatitis C virus," said Brett Leav, MD, senior director of clinical affairs at MassBiologics. "The virus circulates in the blood, but only resides and replicates in the liver. So the idea here is to clear the virus from the bloodstream before it has an opportunity to re-infect the new liver."

After transplantation, patients' blood will be tested on a regular basis to screen for reemergence of HCV, which is usually detected within the first week after transplantation. The primary goal of the Phase 2 trial is to see if the patients who received the antibody are free of HCV at 42 days after transplantation. An interim analysis is planned after the first 16 patients have been enrolled in the trial, and a Data Safety and Monitoring Board overseeing the study will assess the effectiveness and safety of MBL-HCV1.

Provided by University of Massachusetts Medical School