First trial of gene therapy for advanced heart failure shows promising results

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Phase I results of the first clinical trial of gene therapy for patients with advanced heart failure show the approach to be promising, with improvements in several measures of the condition's severity.

In Phase I clinical trials, researchers test a new treatment in a small group of people for the first time to evaluate its safety, determine a safe dosage range, and identify side effects.

Patients enrolled in the multicenter CUPID trial (Calcium Up-Regulation by Percutaneous Administration of Gene Therapy in Cardiac Disease) undergo a minimally invasive cardiac catheterization procedure which introduces a specially engineered gene that stimulates production of an enzyme necessary for the heart to pump more efficiently.

NewYork-Presbyterian Hospital/Columbia University Medical Center was the first to offer the therapy in the New York City area. The Hospital is now recruiting patients for the Phase II CUPID trial to further assess safety and effectiveness in patients with advanced heart failure.

Data from the Phase I trial, which was initiated in May of 2007, were presented at the American Heart Association (AHA) Scientific Sessions 2008 in New Orleans yesterday. Seven of nine patients who were given the drug showed improvements over six months in several areas: symptomatic (five patients), functional (four patients), biomarker (two patients) and left ventricular function/remodeling (six patients). Two

patients with pre-existing antibodies to the viral vector delivery system did not show improvements. Importantly, the approach was shown to have an acceptable safety profile, as determined by an independent safety committee and by the study investigators.

"We are encouraged by these initial findings, which indicate that this therapy has the potential to help patients with advanced heart failure," says Dr. Donna Mancini, the study's principal investigator at NewYork-Presbyterian Hospital/Columbia University Medical Center, where she is medical director of cardiac transplantation and is professor of medicine at Columbia University College of Physicians and Surgeons.

The Phase II randomized, double-blind, placebo-controlled clinical trial will compare the therapy at two- or three-dose levels with placebo. CUPID is expected to enroll 46 patients with advanced heart failure at 13 U.S. hospitals.

Gene therapy is a technique for correcting defective genes responsible for disease development by inserting genes into a patient's cells and tissues. In most gene therapy studies, a "normal" gene is inserted into the genome to replace an "abnormal" disease-causing gene. A carrier molecule called a vector must be used to deliver the therapeutic gene to the patient's target cells. Currently, one of the most common vectors is a non-pathogenic virus most people have been exposed to in adolescence that has been genetically altered to carry normal human DNA.

More than 5 million people in the U.S. have heart failure. Patients with severe form of the disease have trouble breathing because the heart muscle is not strong enough to pump fluid out of their lungs. Approximately 70 percent die of the disease within 10 years, and the five-year survival rate is less than 50 percent. Heart failure is the only cardiovascular disease whose incidence has been increasing rather than decreasing in recent years.

Source: New York- Presbyterian Hospital