

Presentation Number: 2405-3

A double-blind, randomized, placebo controlled clinical trial of allogeneic mesenchymal stem cells for the treatment of patients with acute myocardial infarction

Author Block: Joshua M. Hare, Nabil Dib, Jay H. Traverse, Tim D. Henry, Gary Gerstenblith, Steven P. Schulman, James Hermiller, Moya M. Daniels, Michael P. Archambault.

Background: There are accumulating data that bone marrow contains stem cells capable of ameliorating the damage due to myocardial infarction (MI). To date the majority of clinical trials have utilized autologous whole bone marrow. Mesenchymal stem cells (MSCs) cultured from whole bone marrow are a lead candidate for the active therapeutic cell constituent of bone marrow, and have a number of unique advantages as a cell-based therapy including ease of preparation, ability to serve as an allogeneic graft, and a capacity to home to areas of injury. In animal models, intravenous MSCs home to regions of myocardial infarction, and MSCs administered by a variety of routes, including IV, reduce MI size and improve ejection fraction (EF).

Methods: We performed a double-blind, placebo controlled, randomized, dose-ranging trial to assess the safety of allogeneic MSCs (Provacel, Osiris Therapeutics, Baltimore, MD) infused intravenously to reperfused patients (n=53) within 10-days of an index MI. Three dosing cohorts were studied, 0.5, 1.6, and 5 million cells / kg, each with a 2:1 randomization scheme. The highest dose cohort was repeated following approval from an independent Data Safety and Monitoring Board. The primary endpoint was the incidence of treatment emergent serious adverse events within 6 months (all patients entered an 18 month follow-up study). Whole body CT scanning was performed to determine the incidence of ectopic tissue formation, and echocardiography and cardiac MRI to determine EF and infarct size, exploratory endpoints.

Results: The 6-month safety and efficacy endpoints of this phase I study will be reported for the first time.

Conclusions: This trial is a first in man, phase I trial of allogeneic MSCs for the treatment of acute MI. In addition to the primary endpoint, efficacy was assessed using echocardiographic and MRI indices of global and regional myocardial function. This trial advances the field of cell-based treatment of ischemic cardiac damage by providing pivotal safety and provisional efficacy data for a lead candidate for an allogeneic bone marrow derived stem cell therapeutic strategy.