The NHLBI TIME Trial: One-Year Results

Jay H Traverse1, Timothy D Henry1, Carl J Pepine2, James T Willerson3, David X Zhao4, Stephen G Ellis5, Dejian Lai6, Emerson C Perin3, Marc S Penn7, Antonis K Hatzopoulos8, Jeffrey Chambers9, Kenneth W Baran10, Ganesh Raveendran11, Charles Lambert12, Amir Lerman13, Daniel I Simon14, Adrian P Gee15, John R Forder2, Doris A Taylor3, Christopher R Cogle2, Rachel E Olson1, Sonia I Skarlatos16, Sonia I Skarlatos16, Ray F Ebert16, Lemuel A Moye17, Robert D Simari13; 1Rsch, Minneapolis Heart Institute Foundation at Abbott Northwestern Hosp, Minneapolis, MN, 2Rsch, Univ of Florida College of Medicine, Gainesville, FL, 3Rsch, Texas Heart Institute, St. Luke's Episcopal Hosp, Houston, TX, 4Rsch, Vanderbilt Univ Sch of Medicine, Minneapolis, MN, 5Rsch, The Cleveland Clinic Foundation, Cleveland, OH, 6Rsch, Univ of Texas Sch of Public Health, Houston, TX, 7Rsch, Summa Cardiovascular Institute, Rootstown, OH, 8Rsch, Vanderbilt Univ Sch of Medicine, Nashville, TN, 9Rsch, Metro Cardiology, Mercy Hosp, Coon Rapids, MN, 10Rsch, St. Paul Heart Clinic, United Hosp, St Paul, MN, 11Rsch, Lillehei Heart Institute, Univ of Minnesota, Minneapolis, MN, 12Rsch, Patel Rsch Institute, Pepin Heart Hosp, Tampa, FL, 13Rsch, Mayo Clinic College of Medicine, Rochester, MN, 14Rsch, Univ Hosp Case Med Cntr, Cleveland, OH, 15Rsch, Baylor College of Medicine, Houston, TX, 16Rsch, National Heart, Lung and Blood Institute, Bethesda, MD, 17Biostatistics, Univ of Texas - Sch of Public Health, Houston, TX

Background - The TIME Trial was developed by the NHLBI-sponsored Cardiovascular Cell Therapy Research Network (CCTRN) to determine if the timing of cell therapy administration affects the recovery of LV function following a ST-elevation myocardial infarction (STEMI). TIME was a randomized, placebo-controlled trial of 120 patients with anterior STEMI who were randomized to 150 million autologous bone marrow mononuclear cells (BMCs) or placebo with intracoronary delivery performed on Day 3 or Day 7 following reperfusion with PCI and stenting in patients with at least moderate LV dysfunction (LVEF < 45%). The primary endpoints were changes in global (LVEF) and regional (infarct and border zone) LV function between baseline and 6 months as determined by cardiac MRI. Overall, no benefit of cell therapy was observed at 6 months compared to placebo following cell delivery on Day 3 or Day 7.

Methods and Results - A total of 95 patients had an analyzable sequence of MRI data through one year. Overall, there were significant increases in LVEF and regional LV function, and significant decreases in infarct size and LV mass from Day 3 to 6 months and from Day 3 to one year, that was not enhanced by cell therapy. Each randomized group experienced increases in left-ventricular EDVI and ESVI from Day 3 to one year. No deaths or major adverse events occurred between 6-mo and 1-year in either group confirming the ongoing safety of this therapy in the setting of STEMI with moderate LV dysfunction.

Conclusion - A significant reduction in infarct size and LV mass occurs during the first six months following STEM1 that is not affected by BMC administration. After one year, the initial improvement in LV function remained stable in both groups and is accompanied by a small, ongoing increase in LV volumes. No safety concerns were observed in this high-risk STEMI cohort with moderate LV dysfunction. ClinicalTrials.gov Number, NCT00684021