INTRACORONARY CARDIOSPHERE-DERIVED CELLS AFTER MYOCARDIAL INFARCTION: MAGNETIC RESONANCE IMAGING ANALYSIS OF REGENERATION AND DETERMINANTS OF EFFICACY IN THE FINAL 1-YEAR RESULTS OF THE CADUCEUS TRIAL

Oral Contributions
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Authors: Konstantinos Malliaras, Ke Cheng, Rachel R. Smith, Edwin Wu, Robert Bonow, Adam Mendizabal, Gary Gerstenblith, Peter V. Johnston, Karl Schuleri, Albert C. Lardo, Linda Marbán, Rajendra Makkar, Eduardo Marbán, Cedars-Sinai Heart Institute, Los Angeles, CA, USA

Background: Cardiosphere-derived cells (CDCs) exert regenerative effects in post-MI patients with LV dysfunction in the CADUCEUS trial. Here we report full 1-year results and correlates of efficacy.

Methods: Autologous CDCs (12.5-25x10^6) grown from endomyocardial biopsies were infused into the infarct-related artery in 17 patients with LV dysfunction 1.5-3 mos post-MI (plus n=1 infused 14 mos post-MI). Eight patients were followed as routine-care controls.

Results: At baseline, mean LVEF (39%) and scar size (24% of LV) did not differ between study groups. In >15 months of follow-up, safety endpoints, including arrhythmia, were equivalent. At 12 mos, MRI revealed relative reduction of scar size by 45% in CDC-treated subjects but not controls (-4.6%, p<0.01). Scar mass decreased in CDC-treated subjects (-11.9±6.8g) but not controls (-1.7±7.8g, p<0.01). Viable heart mass increased in CDC-treated subjects (+22.6±9.4g) but not controls (+1.8±8.7 g, p=0.001). The single subject infused compassionately 14 mos post-MI responded similarly. CDC therapy led to improved regional function of infarcted segments (increased strain, thickening and end-systolic thickness) compared to controls. Analysis of matched delayed enhancement and cine short-axis cardiac slices across timepoints revealed a correlation (r=-0.6, p<0.001) between scar shrinkage and improvement in regional function in CDC-treated segments, consistent with therapeutic regeneration. Covariate analysis revealed that baseline scar size (r=-0.89, p<0.001), and lower % of infused CD90+ cells (r=0.88, p<0.001) were associated with greater scar size reduction in treated patients. Scar reduction did not correlate with history of temporally remote MI, time from MI to infusion, or % of infused c-kit+ cells. The changes in LVEF in CDC-treated subjects (ΔLVEF=5.4±0.6% at 12 mos) were consistent with the known relationship between scar size and EF post-MI.

Conclusions: Final 1-year results reveal that autologous CDCs are safe and effective in regenerating infarcted myocardium. Regenerative efficacy is unrelated to % of infused c-kit+ cells, but correlates with baseline scar size, and inversely correlates with %CD90+ cells in CDCs.