Mechanisms of Bone Marrow Derived Cell Therapy in Ischemic Cardiomyopathy with Left Ventricular Assist Device (LVAD) Bridge to Transplant

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Clinical trials report small but significant improvements in cardiac function and myocardial blood flow with direct injection of bone marrow cells (BMC) into the hearts of patients with ischemic cardiomyopathy. Pre-clinical data suggest that these cells improve vascular density. To determine the mechanisms by which BMC improve cardiac function we tested the hypothesis that BMC stem cells (CD34+) will improve histologic measurements of vascularity in human subjects undergoing placement of LVAD as a bridge to cardiac transplantation.

Methods: Eligible subjects with ischemic cardiomyopathy who were scheduled for placement of an LVAD as a bridge to cardiac transplantation underwent collection of bone marrow the day prior to surgery. Bone marrow was processed in a cGMP facility into three different cell fractions (BMC, CD34+, and CD34-). At the time of LVAD placement the fractions and a saline control were injected from the epicardium into predetermined areas of ischemia and each injection site marked via surgical suture. At the time of transplant injected areas were identified, excised and processed for histology. Data are analyzed by paired t-test comparing the effect of cell fractions injected within the each subject.

Results: Six subjects completed the study. There were similar and not statistically significant amounts of bleeding and arrhythmias with the procedure vs nine control subjects. Preliminary histologic analysis of the primary endpoint indicates that myocardium injected with CD34+ stem cells has decreased density of CD31+ endothelial cells in comparison to saline injected myocardium (0.58±0.32 versus 1.1±0.79 percent CD31 positive area ± S.D., P = 0.02 by paired t-test). There were no major differences in fibrosis or inflammation between groups. Analysis of differences in microvascular density and cell proliferation between cell therapies and control injections will be completed for all groups and presented.

Conclusions: Tissue analysis in these patients does not support the hypothesis that bone marrow derived CD34+ cells promote increased vascular tissue in humans with ischemic cardiomyopathy via direct injection. We anticipate that further analysis will uncover novel mechanisms by which cell therapy improves cardiac function.