

Technical Abstract

Protocol Title: MYOHEART-SDF™ (Myogenesis Heart Efficiency and Regeneration Trial), A Phase I, Open-Label, Non-Randomized, Dose Escalation, Multi Center Study to Assess the Safety and Cardiovascular Effects of the Implantation of Autologous Skeletal Myoblasts Modified to Express the SDF-1 Protein (MyoCell™ SDF-1) via Multi-Electrode Percutaneous Transendocardial Catheter (MyoStar™) with Cardiac Navigation Guidance (NOGA™) in Congestive Heart Failure Patients Post Myocardial Infarction(s) With Prior Placement of an Implantable Cardioverter Defibrillator (ICD)

The proposed study is a Phase I Safety study with secondary assessment of indices of regional myocardial effects using MyoCell™ SDF-1 (patient autologous skeletal myoblasts enhanced for expression of SDF-1 via an adenoviral vector which are expanded ex vivo and supplied in buffered suspension medium for injection). The primary objectives of the study are: 1.) To assess the safety and effect on myocardial function of MyoCell™ SDF-1 using a dose escalation methodology following implantation into myocardial scar tissue of subjects with congestive heart failure who have experienced previous myocardial infarction(s) and have had an implantable cardioverter defibrillator (ICD) previously implanted and 2.) To assess the safety and feasibility of using the Multi-Electrode Percutaneous Catheter (MyoStar™) with Cardiac Navigation Guidance (NOGA™) Transendocardial Delivery System for delivering MyoCell™ SDF-1 into the myocardial scar tissue of subjects with congestive heart failure who have experienced previous myocardial infarction(s) and have an implantable cardioverter defibrillator (ICD) previously implanted.

The patient population includes males and/ or females between 30 and 80 years of age with the diagnosis of congestive heart failure secondary to myocardial infarction(s) and coronary artery disease and who have an implantable cardioverter defibrillator (ICD) previously implanted. Subjects must be on optimal medical management and must not be candidates for coronary revascularization. Subjects must have well demarcated nonfunctional left ventricular regions and must be able to undergo surgical skeletal muscle biopsy. Subjects will undergo a screening process and subjects meeting the inclusion criteria and not excluded by the exclusion criteria will be enrolled into the study. Study treatment will be administered, after which subjects will be followed at specified intervals for 12 months.

After a study subject is identified, written consent will be obtained and subject screening undertaken. If study specific screening assessments are satisfied, a biopsy of approximately 5-10 grams of skeletal muscle will be obtained from the subject's quadriceps or gastrocnemius muscle. The biopsy is sent to an offsite culture laboratory for myoblast isolation, expansion and modification to express the angiogenic SDF-1 protein (MyoCell™ SDF-1).

Three to four weeks later, the MyoCell™ SDF-1 will be implanted into myocardial scar in the region of previous infarction, utilizing the Multi-Electrode Percutaneous Catheter

(MyoStar™) with Cardiac Navigation Guidance (NOGA™) Transendocardial delivery system by standard percutaneous techniques.

This will be a dose escalation study with 3 cohort groups consisting of 5 patients each. In the first cohort of this dose escalation study, 4 injections will be performed for the delivery of 200 million cells; for the second cohort, 8 injections will be performed for the delivery of 400 million cells; and for the third cohort, 16 injections will be performed for the delivery of 800 million cells. All injections are to be delivered directly into the akinetic area of the scar resulting from previous myocardial infarct. All 3 dose cohorts will be followed for 12 months.

Regular reports regarding the safety data from each cohort will be provided to an independent Data Safety Monitoring Board (DSMB) for review throughout the study. After all subjects in the first dose cohort complete the 30 day follow-up visit, the medical monitor for the study will conduct a thorough review of adverse events, and if no dose limiting toxicities are observed, enrollment into the next higher dose group can be initiated. This process will be repeated between the second and third dose cohort.

At screening and at subsequent follow-up visits, the following will be assessed:

- Clinical status
- ICD recorded arrhythmias and firing events
- Adverse events monitoring
- 12-lead electrocardiogram
- 48-hour ambulatory Holter
- Routine laboratory tests, including plasma/SDF-1 levels
- NYHA classification
- 6 minute walk
- Echocardiography
- Positron Emission Tomography, (PET) imaging

The Multi-Electrode Percutaneous Transendocardial Catheter (MyoStar™) with Cardiac Navigation Guidance (NOGA™) MyoStar™ delivery system will be monitored and assessed by the following:

- Nature, incidence and rate of MyoStar™ related Adverse Events from implantation to the Day 14 follow-up visit.
- MyoStar™ performance characteristics, including ease of use

The incidence and nature of adverse events will be tabulated and analyzed at baseline, pre, and post procedure as well as 2-week, 1, 3, 6 and 12 months post MyoCell™ SDF-1 mediated MyoStar™ implant procedure. The post-treatment development of clinically significant abnormal laboratory values will be tabulated. Changes from baseline will be summarized for vital signs and laboratory values, including the evaluation of plasma/SDF-1 blood levels. 12-lead ECG and 48-hour ambulatory Holter data will be summarized. Safety will be assessed by monitoring the nature, frequency and rate of adverse events throughout the clinical study. Evidence of acceptable clinical safety for MyoCell™ SDF-1

and the Multi-Electrode Percutaneous Catheter (MyoStar™) with Cardiac Navigation Guidance (NOGA™) Transendocardial Delivery System for further clinical investigation in pivotal trials will be the incidence and nature of any unanticipated Serious Adverse Events which are definitively related to the MyoCell™ SDF-1 and MyoStar™ therapy. In addition, the incidence, nature of, and degree of potential relationship to either MyoCell™ SDF-1 or the MyoStar™ will be used to refine the safety profile for each as guidance for future clinical investigations of these products. The statistical treatment of these measures will be descriptive (i.e., by tabulation) as well as quantitative (i.e., percent of change, amount of change, etc.) for individual patients and with means calculated for the analysis population. Hypothesis testing will not, however, be conducted on this safety study.

The changes from baseline, 6 and 12 month follow up intervals will be tabulated and analyzed for regional left ventricular wall thickness and function in the MyoCell™ SDF-1 implanted myocardial region(s) as well as global function. Particular emphasis will be placed on comparing the area of cellular implantation with pre-procedure studies for any adverse reactions or deleterious changes (i.e. decrease in wall motion, hematoma, etc.).