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CardiAMP Autologous Cell Therapy with Companion Diagnostic for the Treatment of Ischemic Systolic Heart Failure

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Overview

The CardiAMP Phase III Heart Failure Trial is supported by BioCardia's preclinical, Phase I, and Phase II clinical studies, as well as by clinical studies sponsored by others that select specific cells from the marrow for similar indications. The trial will test a novel comprehensive solution for autologous progenitor and stem cell therapy that includes the CardiAMP Potency Assay, CardiAMP Cell Separator (CS) point-of-care processing platform, and the Helix transendocardial delivery system. Each of these below in turn.

- The CardiAMP Potency Assay is a companion biomarker panel used to identify patients with bone marrow progenitor/stem cells above a certain threshold as an inclusion criteria for the CardiAMP cell therapy. The biomarker panel measures the levels of five proprietary biomarkers which are then used to select patients with a minimum threshold scores based on these biomarkers. A score of 3 or greater is required for inclusion in the CardiAMP Phase III trial. While this will likely exclude a number of patients, selecting patients based on the health of their cells minimizes the concern of patient-to-patient variability in cell output and maximizes the potential of a successful trial. It also provides a foundational quality control measure heretofore rare within autologous cell-based clinical trials.

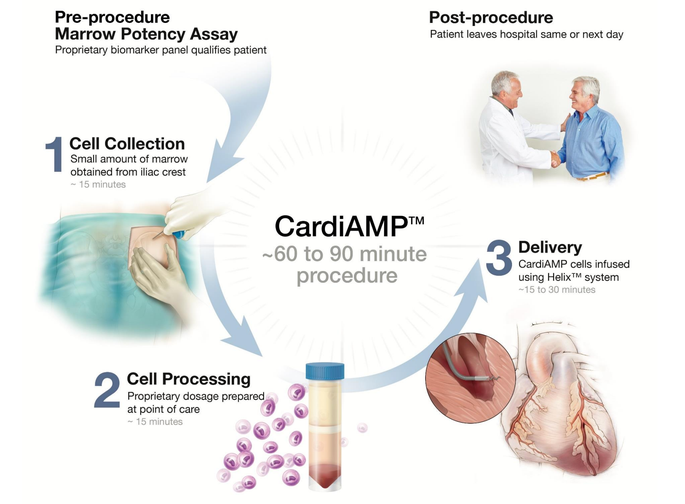
- The CardiAMP CS is a point of care cell processing system that processes the patient's autologous bone marrow aspirate to concentrate the mononuclear cell population of interest, which have been the starting material for many cell therapy programs. This concentrated mononuclear cell population from the bone marrow contains the cells we are most interested in: CD34+ (hematopoietic progenitor cells), CD133+ (multipotent hematopoietic stem and progenitor cells), and CD271+ (mesenchymal stromal cells).

- The Helix transendocardial delivery system to be used in the CardiAMP trial is the most efficient delivery system for the delivery of these cells to the heart muscle due to its unique helical needle that is stable in the beating heart.

CardiAMP cell therapy is the first cardiac cell therapy to enter pivotal trials under an investigational device exemption. It is the first cell therapy trial to receive approval for reimbursement from the Centers for Medicare and Medicaid Services ("CMS") under its IDE. It is the first cardiac cell therapy to utilize a companion diagnostic. It is also expected to be the first cardiac cell therapy to enter a pivotal trial which may be sufficient to support product registration after completing a placebo controlled Phase II trial.

CardiAMP cell therapy

Point of care cell therapy using companion diagnostic potency assay delivered with Helix™ transendocardial delivery catheter



Hypothesis

Demonstrate treatment superiority in subjects treated using the CardiAMP cell therapy (Treatment Group) showing a statistically significant improvement in Six Minute Walk Distance (6MWD) compared to subjects undergoing a sham procedure, after 12M follow-up.

Secondary hierarchical endpoints include overall survival (non-inferiority), freedom from MACE (non-inferiority), Minnesota Living with Heart Failure Questionnaire, time to first MACE, and survival.

Study Design

Prospective, multi-center, randomized (3 Treatment:2 Sham Control), sham-controlled, patient and evaluator-blinded comparing treatment with the CardiAMP cell therapy to a sham treatment in 250 patients with post myocardial infarction heart failure.

Treatment Group: 150 Subjects treated with Autologous Bone Marrow Mononuclear Cells (ABM MNC) using the CardiAMP cell therapy

Sham Control Group: 100 Subjects treated with a Sham Control (no introduction of the Helix transendocardial delivery catheter and no administration of ABM MNC)

Optional Roll-in Phase: Maximum of 10 subjects

Total Number of Patients: Maximum of 260 subjects

Primary Endpoint

Comparison of change in distance walked in 6-minutes between the subjects treated with the CardiAMP cell therapy and subjects undergoing a sham control procedure, at 12-months follow-up

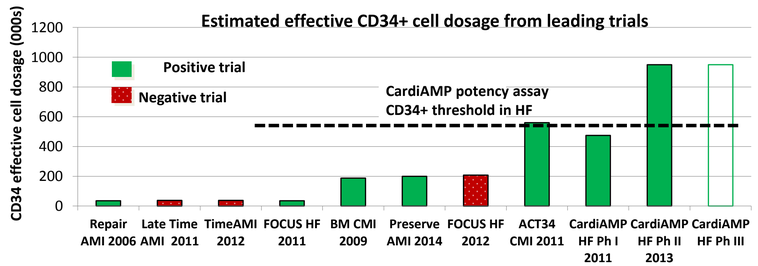
Secondary Hierarchical Endpoints

1. Overall survival at 12-months, as a non-inferiority outcome
2. Freedom from Major Adverse Cardiac Events at 12-months, as a non-inferiority outcome
3. Change in quality of life as measured by Minnesota Living with Heart Failure at 12-months, as a superiority outcome
4. Time to first MACE at 12-months, as a superiority outcome
5. Overall survival at 12-months, as a superiority outcome

Secondary Endpoints at 12M

1. Survival, at 2 years
2. Heart failure death
3. Treatment-emergent Serious Adverse Event, at 30-days
4. Heart failure hospitalization
5. All-cause hospitalization
6. Days alive out of hospital
7. Freedom from Serious Adverse Events
8. NYHA Functional Class
9. 6MWD repeated measure analysis
10. Echocardiographic measures of change in ejection fraction, left ventricular end systolic and end diastolic volumes, left ventricular end systolic and end diastolic dimensions, mitral regurgitation
11. Technical Success defined as successful delivery of ABM MNC, at the time of the procedure

Biomarker panel qualifies patients (CD34+, etc)



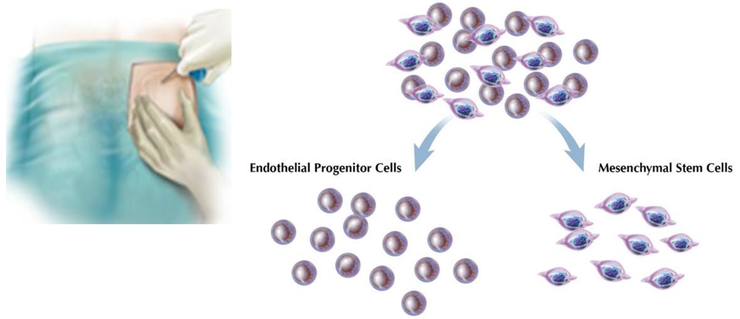
Modified from Wong et al : International Conference on Cell Therapy for Cardiovascular Disease 2014

Clinical and scientific leadership

Carl Pepine, University of Florida, Gainesville, FL,
Amish Raval, University of Wisconsin, Madison, WI
Peter Johnston, Johns Hopkins School of Medicine, Baltimore, MD
Jay Traverse, Minneapolis Heart Institute, Minneapolis, MN
Ian McNiece, MD Anderson Cancer Center, Houston, TX

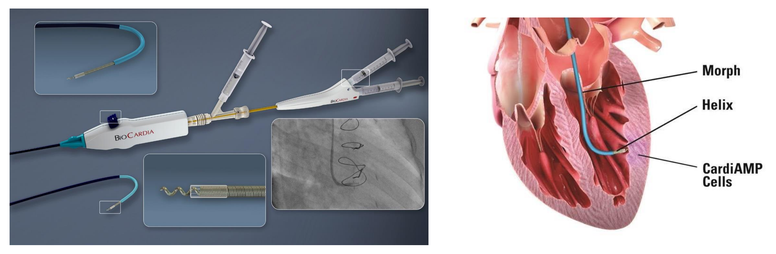
Cell collection of BM cells contain many leading cell types

Potential for broader spectrum paracrine effect



Cell processing in cardiac catheterization laboratory

Cell delivery with Helix system in same procedure



Further Information

www.clinicaltrials.gov (NCT02438306)

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Caution: Investigational device. Limited by United States law to investigational use

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