Background

Heart failure is in need of new therapies aimed at preventing or reversing cardiac remodeling and at enhancing cardiovascular regeneration. This past decade has seen the emergence of protein, gene, and cell therapies to enhance cardiovascular regeneration. The clinical safety and efficacy of intramyocardial delivery of autologous bone marrow–derived cells for the treatment of ischemic heart failure and chronic myocardial ischemia have been recently reviewed and the results are overall positive. Significant clinical benefit with a reduction in both mortality and rehospitalization due to heart failure were observed at long-term follow-up in patients with chronic ischemic heart disease and heart failure. Significant improvements in heart failure symptoms measured by New York Heart Association Class (NYHA) and in functional capacity measured by left ventricular ejection fraction (LVEF), left ventricular end systolic volume (LVESV), at short-term and long-term follow-up were observed.

Here, we present the TAC-HFT study, a two placebo controlled studies of distinct autologous cell therapies (bone marrow mononuclear cells - BMC or mesenchymal stem cells - MSC) initiated in the TAC-HFT trials. Outcomes of patients randomized to autologous BMC were analyzed and their respective placebo group.

Secondary Safety Endpoints:
- AE, SAE, MACE (major adverse cardiac event defined as the composite of: death, non-fatal MI, stroke, hospitalization for worsening heart failure, cardiac perforation, pericardial tamponade, or sustained ventricular arrhythmias).

Secondary Efficacy Endpoints:
- Infarct size, regional wall motion at injection sites, global LV size and function measured by cardiac imaging (CT/MRI).
- Exercise peak oxygen consumption
- 6-minute walk test
- NYHA class
- Minnesota Living With Heart Failure Score

Study Design

Phase I/II, multi-center, randomized (2 Treatment: 1 Placebo Control), double-blind, placebo-controlled study of the safety and efficacy of transcatheter injection of autologous bone marrow mononuclear cells (BMC) versus placebo in patients with chronic ischemic left ventricular dysfunction and heart failure secondary to myocardial infarction.

Treatment Group: 19 Subjects treated with 200 million autologous BMC

Placebo Control Group: 10 Subjects treated with placebo (phosphate-buffered saline [PBS] and 1% human serum albumin [HSA])

Study Intervention: Autologous BMC or placebo were injected into 10 left ventricular (LV) sites (0.5 ml per injection site) in the infarcted or peri-infarct region with the Helix™ transcatheter delivery system.

Results

A. Using LOCF and WOCF imputation techniques, mean change for BMC (+14.3 ± 5.4 SEM) versus placebo (-42.0 ± 5.4 SEM) at 12 months was statistically significant (p=0.045). B. Overall, at 12 Months, the percent of patients improving and improving >35m is greater in the BMC group and the percent of patients deteriorating in the placebo group is over twice that in the BMC group.

Change between BMC and Placebo at 12 M

MNHS with Heart Failure Score (MLHF)

Conclusions

200 million BMC injected with the Helix transcatheter delivery system were safe in patients with chronic ischemic LV dysfunction. The magnitude of the benefit in the TAC-HFT-BMC trials, though modest, are promising and are clinically important when patients are expected to deteriorate. These results have contributed to the design of a recently approved 250-patient randomized controlled pivotal trial of autologous bone marrow mononuclear cells in patients with post myocardial infarction heart failure, the CardiAmp Heart Failure Trial (clinicaltrials.gov Identifier: NCT02438306).

References