CHART-1: Largest cardiac regenerative therapy trial brings new insights

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A therapy that uses bone-marrow stem cells to promote heart repair did not significantly improve the primary outcome over a sham procedure among patients with congestive heart failure. However, it revealed critical new insights, according to investigators of the CHART-1 trial.

Although findings of CHART-1 (Congestive Heart Failure Cardiopoietic Regenerative Therapy) were neutral in the overall patient population, an exploratory analysis identified a sub-group of patients who may benefit from cardiopoietic cell therapy, according to the principal co-investigator of the study Jozef Bartunek, MD, PhD, from OLV Hospital Aalst, Belgium.

"Within a well-defined patient population, based on baseline heart failure severity, this therapy showed benefit," said Prof Bartunek, who presented the findings at ESC Congress 2016. "Lessons learned from CHART-1 will now provide the foundation for the design of the ensuing CHART-2 trial which will target these patients."

Cardiopoietic cell therapy involves the isolation of mesenchymal stem cells from a patient's own bone marrow. Exposing these cells to a "cardiogenic cocktail" turns them into cardiopoietic cells which are then injected into damaged heart tissue.

The CHART-1 study randomized patients with symptomatic ischemic heart failure from 39 hospital centres in Europe and Israel.

Patients received either a sham procedure (n=151) or cardiopoietic cells (n=120).

At 39 weeks there was no significant difference between groups for the primary efficacy endpoint, which was a composite of all-cause mortality, worsening heart failure events, Minnesota Living with Heart Failure Questionnaire total score, 6-minute walk distance, left ventricular end-systolic volume and ejection fraction.

However, a subgroup analysis of patients with severe heart enlargement at baseline (left ventricular end-diastolic volumes between 200 and 370 mL) suggested a positive effect of the cell treatment over sham.

"Outcomes for all components of the composite endpoint, including mortality and worsening heart failure, were "directionally consistent" said Prof Bartunek, adding that "the effect was also related to clinically meaningful improved quality of life, greater 6-minute walk distance, and reduced left ventricular end-systolic volume for cell treatment versus sham."

In addition, "we observed a modifying effect of treatment intensity with suggestion of a greater benefit at lower number of injections," he added. "Overall safety was demonstrated across the study cohort, with no difference in adverse clinical outcomes observed between the groups."

Ongoing analyses will evaluate 12-month clinical outcomes, said Prof Bartunek. "Insights from the CHART-1 trial have implications for targeting the patient population that should be considered for cardiopoietic cell therapy in future clinical trials or for broader clinical considerations. More generally, indices of heart failure severity and optimized therapeutic intensity should be considered."