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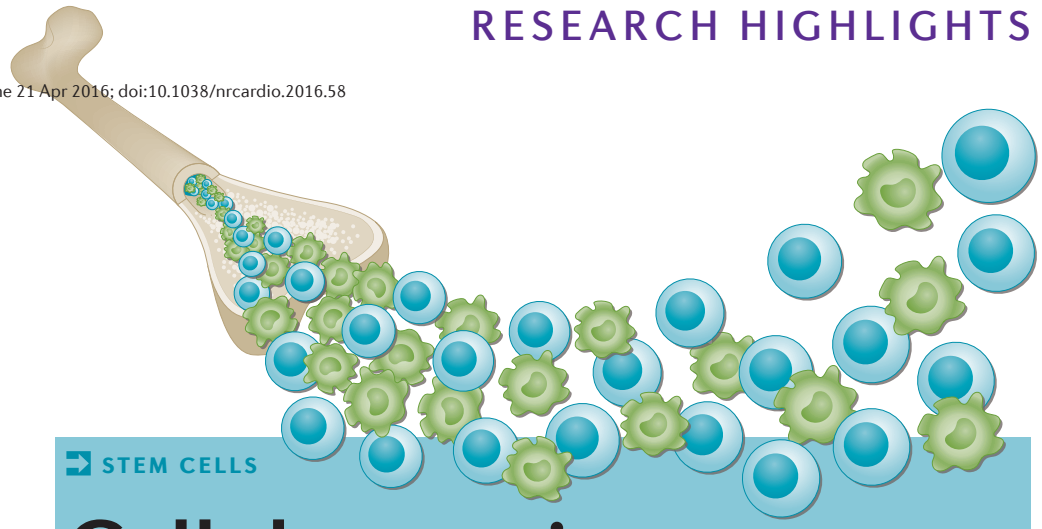

Vicky Summersby/NPG

STEM CELLS

Cell therapy improves outcomes in heart failure

Intramyocardial injection of a multicellular therapy results in an improvement in cardiovascular outcomes in patients with severe and end-stage heart failure, according to a phase IIb clinical trial presented at the ACC.16 Scientific Sessions.

"This is the largest, double-blind, placebo-controlled trial of cell therapy in patients with ischaemic cardiomyopathy," says Timothy Henry, one of the lead investigators of the study. Previous trials of therapies with autologous bone marrow mononuclear cells in patients with heart failure showed a modest improvement in left ventricular function, but no significant effects on cardiovascular events compared with placebo.

"Patients with class III heart failure, despite optimal clinical and device therapy, have limited options beyond cardiac transplantations and left ventricular assist device," says Henry. "This is a large and growing population of patients, and cell therapy appears to be an attractive option for these challenging patients." Ixmyelocel-T, the multicellular therapeutic studied in the ixCELL-DCM trial, is produced from the patient's own bone marrow. This therapeutic contains all the bone marrow mononuclear cells but is expanded in the laboratory for 2 weeks to selectively increase the number of mesenchymal stem cells and M2 macrophages. "Our goal was to affect the inflammatory response related to heart failure," explains the corresponding author of the study Amit Patel. Ixmyelocel-T showed tissue remodelling and immunomodulatory properties in preclinical studies, but the exact mechanisms of action remain unknown.

The trial investigators enrolled 126 patients with NYHA class III or IV symptomatic heart failure caused by ischaemic dilated cardiomyopathy, with left ventricular ejection fraction ≤35%, an automatic implantable cardioverter–defibrillator, and who were ineligible for revascularization procedures. Patients were randomly assigned to receive an injection of either ixmyelocel-T or placebo. The product was injected via catheter to damaged areas of the heart that were identified using 3D electromechanical maps. The primary efficacy end point was a combination of all-cause death, cardiovascular hospitalizations, and clinic visits for decompensated heart failure during the 1-year follow-up.

The analysis of the per-protocol population, which included only patients with ≥50% delivery of the product ($n = 109$), showed a 37% reduction in total clinical events in patients receiving ixmyelocel-T compared with placebo (risk ratio (RR) 0.63, 95% CI 0.42–0.97, $P = 0.03$). This reduction in the prespecified primary end point, which was driven by the reduction in all-cause deaths and cardiovascular hospitalizations, was also significant in the modified intent-to-treat population that included all patients ($n = 114$) who received the injection (RR 0.59, 95% CI 0.40–0.89, $P = 0.01$). No significant changes were found in left ventricular functional parameters, the 6-min walking test, or the NYHA functional class.

The sample size of the ixCELL-DCM trial, however, was not powered for many of the analyses. Henry explains that this trial should lay the groundwork for larger clinical studies, and points out that two large, double-blind, placebo-controlled trials (CHART-1 and DREAM-HF) to evaluate cardiovascular events after cell therapy in patients with heart failure are currently underway.

Irene Fernández-Ruiz

ORIGINAL ARTICLE Patel, A. N. *et al.* Ixmyelocel-T for patients with ischaemic heart failure: a prospective randomised double-blind trial. *Lancet* http://dx.doi.org/10.1016/S0140-6736(16)30137-4 (2016)
FURTHER READING Behfar, A. *et al.* Cell therapy for cardiac repair—lessons from clinical trials. *Nat. Rev. Cardiol.* **11**, 232–246 (2014)