*Nature Reviews Cardiology* **12**, 442 (2015); published online 30 June 2015; doi:10.1038/nrcardio.2015.103

GENE THERAPY

## CAN SDF-1 IMPROVE CARDIAC FUNCTION?

Gene therapy to induce transient endocardial overexpression of stromal cell-derived factor 1 (SDF-1) is safe and has the potential to improve cardiac function in patients with ischaemic cardiomyopathy, according to the results of a phase II trial.

SDF-1 is an important regulator in endogenous tissue repair, and can recruit stem cells to sites of ischaemic injury. Local expression for >2 weeks can be achieved by a single injection of JVS-100, a naked DNA plasmid encoding human SDF-1.

In the double-blind STOP-HF trial, 93 patients with ischaemic heart failure were randomly assigned to peri-infarct endomyocardial injections of placebo or JVS-100 (15 mg or 30 mg doses). These injections resulted in no serious adverse events. The primary end point was a composite of improvements in 6-min walking distance and quality of life from baseline to 4 months, but this end point was not met.

The potential of this approach is indicated by the secondary end points of the trial. Previous results in a porcine model suggested the benefits are more pronounced for the treatment of advanced cardiac dysfunction. In the STOP-HF trial, a prespecified analysis demonstrated—in patients in the first tertile for left ventricular ejection fraction (LVEF; values <26%)—a significant difference in the change of LVEF from baseline to 1 year between treatment with 30 mg JVS-100 and placebo (+7% and −4%, respectively; $P=0.01$).

In this trial, nonsignificant trends towards improvement were also seen. From baseline to 1 year, patients treated with JVS-100 had an 18.5 ml decrease in left ventricular end-systolic volume, compared with a 15.0 ml increase for placebo. From baseline to 1 year, patients in the first tertile for LVEF who were treated with 30 mg JVS-100 had a 14 ml increase in stroke volume relative to an 11 ml decrease with placebo. At 1 year, high-dose JVS-100 also reduced levels of N-terminal prohomone of B-type natriuretic peptide relative to placebo, with a difference of 784 pg/ml.

Multiple doses of gene therapy might improve on these promising results and, in the FDA-approved STOP-HF2 trial, responsive patients identified in the STOP-HF trial will be treated with 6-monthly repeat dosing.

***Robert Phillips***

**Original article** Chung, E. S. *et al*. Changes in ventricular remodelling and clinical status during the year following a single administration of stromal cell-derived factor-1 non-viral gene therapy in chronic ischaemic heart failure patients: the STOP-HF randomized phase II trial. *Eur. Heart J.* doi:10.1093/eurheartj/ehv254