

Stem cells continue to show promise in MI patients

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Washington, DC – Incremental updates from studies looking for new ways to take advantage of the body's own cellular-regeneration processes hint that different cell-based approaches may one day help to improve angina symptoms and restore myocardial function [1].

At **CRT 2011**, the **Cardiovascular Research Technologies** conference, director of research at the Minnesota Heart Institute (MHI), **Dr Tim Henry**, presented the latest data from a variety of ongoing efforts to use adult stem cells to grow new blood vessels or new myocardium. MHI is part of the **Cardiovascular Cell Therapy Research Network** funded by the **National Heart, Lung, and Blood Institute** (NHLBI).

"This is the body's way of regenerating itself, and our goal in this therapy is to take advantage of the natural process of what the body does itself," he said. "Cells work as a factory, [and] they signal other cells to become what they are and start the whole process of regeneration."



Dr. Tim Henry

One of the most important ongoing studies of stem cells to grow myocardial blood vessels, according to Henry, is the **ACT-34 CMI** study, which compared two doses of granulocyte colony-stimulating factor mobilized autologous CD34+ cells derived by blood apheresis with placebo in 167 patients with chronic refractory myocardial ischemia. All of the patients had class 3 or 4 angina with ischemia confirmed by single photon-emission computed tomography (SPECT) and did not resolve with best medical therapy. They were not considered candidates for percutaneous or surgical revascularization.

Although the trial was too small to show statistical significant differences in adverse events, all of the event rates trended in the right direction, showing changes in baseline beyond that of the placebo. Importantly, after six months, the placebo group showed a reduction in angina episodes of 8.6 per week, while the low-dose group had 14.2 fewer weekly episodes and the high-dose group had 13.7 fewer weekly episodes ($p=0.04$). Also, the stem-cell treatment improved patients' exercise tolerance by a full minute vs placebo ($p=0.013$). Henry said this is the first therapy for refractory angina to show this kind of improvement in exercise tolerance.

Cellular regeneration in the acute setting

Henry also highlighted several studies intended to regenerate infarcted myocardium, including **PRECISE**, a randomized study comparing stem-cells derived from adipose fat with placebo for the treatment of nonrevascularizable ischemic myocardium. Results from 27 patients showed significant improvements in peak oxygen consumption with the cell therapy vs placebo at both six months and 18-month follow-up.

Another pilot trial, **FOCUS**, is comparing injections of bone-marrow mononuclear cells with placebo in the treatment of left ventricular dysfunction and angina. The phase 1 trial enrolled only 30 patients, but a phase 2 trial is ongoing. A key lesson from the pilot study was that some patients' autologous cells proliferated much faster than others, such that the therapy was not more effective than placebo in patients over 60 but showed promise in patients under 60, Henry said.

Other stem-cell studies are testing the value of different cell lines delivered swiftly after myocardial damage has taken place.

As previously reported by **heartwire**, for example, **REPAIR AMI** showed significant improvements over placebo in death plus MI (10 vs 2, $p=0.02$) and death, MI, and revascularization (43 vs 23, $p=0.01$) in 204 patients with reperfused AMI treated with bone-marrow-derived mononuclear cells. Henry also added that a meta-analysis of 10 similar studies with a total of 698 patients showed a trend toward reduction in death and a significant reduction in recurrent MI.

Because some patients' stem cells, especially those of older patients, do not proliferate effectively, stem-cell researchers are also looking into therapies based on allogenic cells taken from healthy donors. For example, a 53-patient study also reported by **heartwire**, the **Safety Study of Adult Mesenchymal Stem Cells (MSC) to Treat Acute Myocardial Infarction**, by **Dr Joshua Hare** (University of Miami, FL) et al, showed that intravenous allogeneic human mesenchymal stem cells (hMSCs) improved ejection fraction in anterior MI patients vs placebo.

Progress is slow

Henry said that despite the encouraging results, funding for larger trials of stem cells is still slow. A major impediment appears to be the ethical controversies that surround research on embryonic stem cells, even though all of these studies use adult stem cells. He said this controversy is a hang-up for groups identified on both the political right and the political left. The right-wing groups do not want to support or fund anything that could be associated with destroying human embryos, but some left-leaning groups are so committed to pursuing embryonic research that they do not want to fund research with adult stem cells, Henry told **heartwire**.

"There's way too much hype [about stem cells]," he said. "We should think about it [in the same way we do] with any other therapy. What are the relative risks and benefits?"

1. Source

Timothy Henry. Cell therapy for myocardial regeneration in 2011. Refractory ischemia, AMI and end-stage ischemic CHF. CRT2011; February 27, 2011; Washington, DC.