First US trial of bone-marrow stem cells for heart attack patients proves safe

September 14 2010

The first randomized, placebo-controlled U.S. clinical trial to assess the use of bone marrow-derived mononuclear cells (BMC) in patients after a ST-elevation myocardial infarction (STEMI; severe heart attack) demonstrated a strong safety profile for this cell therapy, based on phase 1 results published in the September issue of the *American Heart Journal*.

"The use of adult stem cells, derived from the patient's own bone marrow, presents a potential new type of therapy to benefit individuals after they suffer a heart attack," says the study's principal investigator Jay H. Traverse, MD, cardiologist at the Minneapolis Heart Institute at Abbott Northwestern Hospital in Minneapolis, Minn. "Also, these types of stem cells do not possess any of the ethical concerns of embryonic stem cell research."

"While the objective of phase 1 clinical trials is to assess safety, researchers also look for hints of efficacy that have been revealed in previous studies," says Traverse. "Based on indications of some improvements in various European studies, we sought to examine whether this therapy could improve ejection fraction at six months, and whether it had an effect on attenuating adverse left ventricular remodeling as measured by cardiac MRI."

In this single-center trial, the researchers enrolled 40 patients with STEMI, randomizing them in a 3:1 ratio to 100 million autologous BMCs versus placebo, administered three to ten days following

successful primary angioplasty and stenting of the left anterior descending coronary artery. Importantly, the researchers elected to deliver cells by an intracoronary infusion as opposed to the stop-flow technique that had been used in all preceding trials and all patients received an identical number of cells.

Administration of BMC was safely performed in all patients with minimal major adverse clinical event rates, and all patients remain alive to date, Traverse and colleagues reported.

While the BMC cell therapy was associated with a significant improvement in left ventricular ejection fraction at six months (49% to 55.2%), the study failed to demonstrate that the cell therapy was superior to placebo because of the similar improvement in the small placebo group (48.6% to 57%). However, the BMC group experienced a significant improvement in left-ventricular volumes at six months compared with the placebo group.

"A review of the available clinical literature reveals a split in the benefit of left ventricular ejection fraction—some studies show no benefit and others show a small improvement," Traverse explains. "Any number of factors can influence this outcome: the way the ejection fraction is measured, the timing of BMC administration, how many cells are delivered, the type of STEMI patient population. There are a lot of variables, leading some to question whether ejection fraction is the most appropriate endpoint for cell therapy trials."

"To this point, no study has been properly powered to assess the appropriate timing of BMC administration after a heart attack," says Traverse.

However, Traverse and his colleagues at the Minneapolis Heart Institute® are involved with the TIME trial, sponsored by the National

Heart, Lung and Blood Institute's Cardiovascular Cell Therapy Research Network (CCTRN), which is randomizing patients to BMCs at three or seven days post-STEMI to determine the most appropriate timing to administer the stem cells following a heart attack.

Provided by Minneapolis Heart Institute Foundation