STEM CELL CLINICAL TRIAL:
Safety/Feasibility of Autologous Mononuclear Bone Marrow Cells in Stroke Patients

NCT00859014

Sponsor: The University of Texas Health Science Center, Houston
Collaborator: National Institutes of Health (NIH), Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD)

OBJECTIVE:

The objective of this study was to use bone marrow derived autologous mononuclear cells (MNCs) as a cellular therapy for stroke and to determine the safety and feasibility of such a treatment.

THE STUDY:

- The study was conducted from March 2009 to June 2010.
  - Patients aged from 10 to 80 were enrolled.
  - Inclusion criteria required a National Institute of Health Stroke Score between 6 and 15 for the right hemisphere and 6 and 18 for the left hemisphere.

- Patients with significant hepatic or pulmonary disease were excluded.
  - All patients also received an initial CT scan and MRI to serve as a baseline as well as intravenous tissue plasminogen activator treatment. 2ml/kg of bone marrow was aseptically harvested from the posterior iliac crest.

- The MNC fraction was obtained through density gradient separation using Ficoll.
  - Cells were tested for endotoxins, sterility and viability. Acceptance criteria required cells to have a >70% viability to be used.
  - Flow cytometry was also performed to look for cell surface markers.

- For the clinical trial, enrollment, bone marrow harvest, and cell infusion all had to take place within 24-72 hours of stroke symptom onset.

- Cells were administered intravenously via the antecubital vein at a maximum of 10 million cells/kg in saline over a time period of 30 min. At day 7, modified Rankin Scores (mRS) and Barhtel Index (BI) scores were obtained.
  - At 1, 3, and 6 months following discharge, NIHSS, mRS, and BI assessments were performed again.
  - In addition, MRI examinations were again performed at 30, 90, and 180 days following stroke onset with infarct volume and infarct expansion ratio (IER) being calculated.

RESULTS:

At 6 months all surviving participants showed an improvement in their mRS scores with more than half obtaining a score of 0-2. More than half of the participants also received a BI of >90%.

THE DETAILS:

- Overall, the MNCs were successfully infused with no complications in all participants, with no study related adverse effects being reported for all participants up to 6 months post infusion.
- At 6 months all surviving participants showed an improvement in their mRS scores with more than half obtaining a score of 0-2. More than half of the participants also received a BI of >90%.
  - In addition, no participants revealed an increase in infarct expansion in their progressive MRIs.
- This study was the first clinical trial to test the feasibility and safety of a bone marrow harvest in acute stroke patients followed by the autologous IV infusion of MNCs.
  - All results indicate that the study is indeed feasible and safe to perform.
  - With all participants there was no evidence of infusion related toxicity of pulmonary, renal, hematological, or neurological organ systems.
  - There were also no reports of any study related severe adverse effects for any participants 6 months post stroke onset.

MNCs offer an advantageous therapy for acute stroke. They can rapidly be prepared within hours of a bone marrow harvest and the use of autologous cells circumvents issues associated with allogeneic cells.

- Additionally, since MNCs are adult cells, they do not provoke ethically questionable objections that can be associated with the use of other cell types.
- The overall small cell diameter of MNCs of 5-8 um allows them to be easily and non-invasively infused through an IV.
- MNCs like many other cellular therapies, elicit a paracrine effect which may also enhance recovery from acute stroke.
- Improvements of all patients involved in the study with no reported adverse effects support the safety and feasibility of autologous bone marrow MNCs as a cellular therapy for the treatment of ischemic stroke within a 24-72 hour time frame.