

First Report of Long-Term Safety of Human Embryonic Stem Cells to Treat Human Disease

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NEW YORK -- October 15, 2014 -- New research published in *The Lancet* provides the first evidence of the medium-term to long-term safety and tolerability of transplanting human embryonic stem cells (hESCs) in humans.

hESC transplants used to treat severe vision loss in 18 patients with different forms of macular degeneration appeared safe up to 3 years post-transplant, and the technology restored some sight in more than half of the patients.

"Embryonic stem cells have the potential to become any cell type in the body, but transplantation has been complicated by problems including the risk of teratoma formation and immune rejection," explained lead author Robert Lanza, MD, Advanced Cell Technology, Marlborough, Massachusetts. "As a result, immunoprivileged sites such as the eye have become the first parts of the human body to benefit from this technology."

In the 2 phase 1/2 studies, hESCs were differentiated into retinal pigment epithelium cells and transplanted into 9 patients with Stargardt's macular dystrophy and 9 patients with dry atrophic age-related macular degeneration, the leading causes of juvenile and adult blindness in the developed world, respectively. No effective treatments exist for either

condition, and eventually the photoreceptor cells of the retina degenerate leading to complete blindness.

All participants were injected with 1 of 3 different doses of retinal cells (50,000, 100,000, or 150,000 cells) into the subretinal space of the eye with the worse vision.

The hESC-derived cells were well tolerated for up to 37 months after transplantation. No safety concerns (ie, hyperproliferation or rejection) in the treated eyes were detected during a median follow-up of 22 months. Adverse events were associated with vitreoretinal surgery and immunosuppression, but none were deemed to be related to the hESC-derived cells.

Follow-up testing showed that 10 out of 18 treated eyes had substantial improvements in how well they could see, with 8 patients reading over 15 additional letters in the first year after transplant. Visual acuity remained the same or improved in 7 patients, but decreased by more than 10 letters in 1 patient. Importantly, untreated eyes did not show similar visual improvements.

“Our results suggest the safety and promise of hESCs to alter progressive vision loss in people with degenerative diseases and mark an exciting step towards using hESC-derived stem cells as a safe source of cells for the treatment of various medical disorders requiring tissue repair or replacement,” said co-author Steven Schwartz, MD, Jules Stein Eye Institute, Los Angeles, California.

In an accompanying commentary, Anthony Atala, MD, Wake Forest Institute for Regenerative Medicine, Wake Forest School of Medicine, Winston-Salem, North Carolina, wrote: “The work by Schwartz and

colleagues is a major accomplishment, but the path to get to this point has not been smooth. Since the discovery of hESC in 1998, much has transpired, including political, ethical, and scientific debates, with an overall push to achieve the promise of human therapies. Now, we have follow-up that extends to longer than 3 years in patients treated with hESC-derived stem cells, showing both safety and apparent efficacy. Much work remains to be done before hESC and induced pluripotent stem cell therapies go beyond regulatory trials, but the path is now set in motion.”

SOURCE: The Lancet