Stem Cell Therapy for MS Gets Green Light in First U.S. Clinical Trial

Mar. 12, 2015 @ 8:10 a.m.

### No safety issues or signs of MS activation

Mesenchymal stem cell (MSC) therapy for multiple sclerosis (MS) recently cleared its first major clinical development hurdle in a phase 1 study conducted at Cleveland Clinic’s [Mellen Center for Multiple Sclerosis Treatment and Research](http://my.clevelandclinic.org/services/neurological_institute/mellen-center-multiple-sclerosis).

“The goal was to demonstrate safety, feasibility and tolerability, and this was shown,” says lead investigator and Mellen Center Director [Jeffrey Cohen, MD](http://my.clevelandclinic.org/staff_directory/staff_display?doctorid=1061), who presented the study results last year at MS Boston 2014, the joint Americas and European Committees for Treatment and Research in Multiple Sclerosis [(ACTRIMS/ECTRIMS) meeting](http://www.msboston2014.org/images/Program/Scientific_Program_Final-smaller_w_links.pdf).

The study, the first phase 1 investigation of MSCs for MS completed in North America, paves the way for larger human studies that will look more directly at potential benefits from the therapy, which Dr. Cohen says is based on a strategy — repair of damaged tissues in MS — wholly distinct from the mechanisms of MS therapies developed to date.

### No safety issues or signs of disease activation

The phase 1 study involved 24 patients — 14 with secondary progressive MS and 10 with relapsing-remitting MS — who had scores between 3 and 6.5 on the Expanded Disability Status Scale (mean, 5.2), active disease within the prior two years and optic nerve involvement.

Patients underwent treatment with autologous adult MSCs derived from the bone marrow. The cells were expanded in culture, cryopreserved and thawed for administration by IV infusion as a single dose. The mean dosage was 1.9 × 106 cells/kg (range, 1.3 to 2.0).

Cell infusion was well-tolerated, and over six months of serial follow-up, no treatment related severe or serious adverse events were observed. Additionally, no disease activation was observed on MRI assessment for gadolinium-enhancing lesions, which was reassuring since investigational MS therapies can sometimes trigger relapses.

### Phase 2 testing to explore encouraging hints of benefit

The study was not designed to assess efficacy, but patients underwent clinical and MRI monitoring for six months after their infusion. Dr. Cohen says there were no dramatic changes in any patients, but he noted some “encouraging trends” across the results as a whole and “enticing hints of benefits” in individual patients.

Any such benefits will be explored in two studies Dr. Cohen and his team will launch in 2015:

* A larger phase 2 trial to further examine the safety of MSC infusion and more directly evaluate efficacy
* A study to label and track MSCs by MRI following infusion to address unanswered questions about exactly where the cells migrate within the body and how long they survive

“The theory is that MSCs will seek out where they are needed and migrate to damaged tissues,” Dr. Cohen notes.

For these future studies, Dr. Cohen plans to use fresh stem cells, as recent studies have suggested that stem cells may be in shock after thawing. His team will also consider using higher doses of stem cells and/or several doses rather than the single infusion used in this initial study.

### The underlying rationale

Investigation of MSCs (whose characteristic morphology in culture is shown in the image at the top of this post) is one of several avenues being pursued to thwart MS by promoting the activity of oligodendrocytes.

Oligodendrocytes are a class of cells that serve to maintain the myelin sheaths that protect nerve axons. In MS, these cells stop functioning or are killed off. The hope is that if their activity could be restarted, thereby promoting remyelination, disability progression in MS might be prevented or even reversed.

Ongoing research by Dr. Cohen and his collaborators is aimed at producing other types of therapeutic stem cells with the ability to mature into myelin-forming oligodendrocytes, with the goal of spurring repair of the demyelination implicated in MS disability. It represents a wholly different approach from all approved MS therapies, which are aimed at reducing relapses and slowing disease progression. “Stem cells are directed at repair,” he explains. “This is a totally different strategy.”

MSCs of patients with MS are believed not to be affected by the disease, but this premise is being evaluated. “One element of our research is to compare the MSCs from MS patients with those from matched controls,” Dr. Cohen says.  “Although they resemble each other, there may be nuanced differences that aren’t easily detectable.”

### Still a long — albeit promising — road ahead

Dr. Cohen notes that while these encouraging phase 1 findings build on equally promising data from MSC studies in animal models of MS, much work remains before cell therapies’ potential role in MS can be more fully gauged.

“Beyond needing to determine and quantify potential efficacy against the disease, we still need to understand the manipulations the cells undergo before implantation and then optimize cell types, administration routes, numbers of cells to infuse and other factors,” he says. “But this work is off to a strong start.”

The phase 1 study was funded by the U.S. Department of Defense and the National Institutes of Health.[*Dr. Cohen’s*](http://my.clevelandclinic.org/staff_directory/staff_display?doctorid=1061)research team includes co-investigators from the Mellen Center plus colleagues from Case Western Reserve University and University Hospitals Seidman Cancer Center, both in Cleveland.