W. M. Keck Center for Collaborative Neuroscience
Happy New Year!

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What is taking so long? That is the question I keep hearing. So, here is the story.

Three years ago, we started on the path to begin clinical trials of umbilical cord blood (UCB) mononuclear cell therapy for spinal cord injury (SCI) in the United States. At the time, none of us anticipated the amount of work and time that would be required. We knew we had to convince a company to sponsor the trial, doctors to be part of the trial, and the Food and Drug Administration (FDA) to approve the trial. But then we found out we also had to do additional animal studies, develop new technology for shipping the cells, and train volunteers to help the subjects walk.

Now US102D finally is coming together! US102D is the U.S. trial that will test the safety, feasibility, and efficacy of transplanting UCB mononuclear cell transplants (MC001) to treat people with chronic complete spinal cord injury.

Let me briefly summarize the preparation and work it has taken to get us to this point:

December 2015: Requested a pre-IND meeting with the FDA to discuss requirements for a clinical trial in 18 subjects to compare the effects of MC001 transplants with and without lithium, followed by six months of intensive locomotor therapy.

January 2016: Met with the FDA. After a 20-minute meeting, we agreed to do additional animal studies to establish safety and efficacy of the cells, to include a control group with no treatment in the trial (now called the 'pre-training group', to show safety in thoracic spinal cord injury before transplanting into cervical spinal cord injury, and to study only people with 'complete' spinal cord injury.

We immediately formed the Clinical Trial Core Committee consisting of the surgeons, rehabilitation specialists, and representatives of the clinical trial institutions. Since that time, we have been meeting regularly with this group as a committee, as sub-committees, and individually.

January-April 2016: Developed the protocol for transplanting MC001 into immune-deficient rats (RNU), proposed these animal studies to the FDA, and found a clinical research organization (CRO) named MPI in Kalamazoo, Michigan to do the experiments under good laboratory practices (GLP) guidelines.

April-August 2016: Trained and validated MPI to do spinal cord injury studies in RNU rats and initiated the planned randomized studies in 186 rats. Completed in August 2017, the animal studies showed that MC001 is safe, non-toxic, and do not migrate into surrounding tissues or organs.

September 2017: Began writing the full IND for the clinical trial working with the CRO PPD. Progress was slow. In January 2018, Stemcyte changed to the CRO Amarex and writing progressed rapidly.

April 15, 2018: Submitted the completed IND to the FDA. On May 15, FDA approved the protocol but placed a clinical hold on the trial until Stemcyte could validate the hospital facilities that would prepare the final cell injection into the spinal cord.

August 2018: Stemcyte could not find a suitable company or hospital facility that could prepare the final cell injection and decided to change the cell preparation so that the final product could be shipped from Stemcyte directly to the operating room for transplantation into the patients.

October 2018: The new product preparation was completed. Final validation of the product and shipping is now underway. The final IND will be submitted to the FDA by December for approval, hopefully before Christmas.

December 2018: The clinical trial protocol will be submitted to the Western IRB which provides ethical board approval of clinical trials, and clinical trial contracts will be negotiated with the hospitals.

What's Next? Once approved, US102D will be announced on www.clinicaltrials.gov and the three hospitals, Hackensack University Medical Center, Hackensack-Meridian Jersey Shore Hospital, and Mountainside Hospital in Montclair, will start recruiting subjects. Interested candidates will be screened by the hospitals to identify those who fit the trial's inclusion and exclusion criteria. At least 27 subjects will be chosen. (We also will post this information on our website and email an announcement.)

The 27 subjects will be randomized to three treatment groups: Control/Pre-training, Transplant, and Transplant+Lithium. The Control group will receive only intensive locomotor training for 6 months. The Transplant group will receive MC001 transplant and walking training. The Transplant+Lithium group will receive the MC001 transplant, a 6-week course of oral lithium carbonate, and walking training. [At the end of a year, the Control/Pre-training group will be offered the choice to receive the MC001 transplant (and lithium carbonate if the trial results suggest that it is effective) followed by six additional months of intensive walking therapy.]

Much training and validation will need to be done to ensure that the trial runs smoothly. We are testing the shipping and the quality of the cells. All doctors and hospital personnel participating in the trial will be trained to follow the clinical trial protocol. Likewise, walking trainers and therapists supervising the walking are being trained and validated. Rehabilitation protocols have to be finalized and consensus obtained concerning the best approach to walking training.

Compassionate use of MC001 transplant treatment application will be submitted to the FDA as soon as the trial is approved. The three hospitals will negotiate cost with the FDA. Patients in the compassionate use program pay the costs of the therapy and walking therapy but will be able to choose transplant treatment with or without lithium. We also are working with other hospitals to start walking programs, particularly the Veteran Administration (VA) hospitals, so that people can come to New Jersey to get the transplants and return home for walking training.

World-wide Approval in 2021. We then will start Phase III trials to provide market approval in the United States, Europe, India, and China. The goal is to obtain world-wide regulatory approval for the first therapy that restores walking in people with chronic spinal cord injury. Not only will this enable insurance coverage, but it is the only way to dispel the pessimism and skepticism that has dominated the field and achieve consensus that there are safe and effective regenerative therapies to restore meaningful function in people with chronic severe spinal cord injury.

My sincere appreciation to the Rutgers Athletic Department and the Kinesiology Department for their strong support of these trials. Student athletes and kinesiology majors have attended introductory sessions to serve as volunteers in the walking program. My thanks also to the doctors and institutions for their commitment. Most of all, my gratitude to each of you who have worked so hard and have stood with us to bring about this new reality. It is because of you that this long-held dream will become a reality. You mean so much to me.

Merry and Happy!

Wise