Implantation of neural stem cells into the spinal cords of ALS patients appears to be safe, according to results from the Phase I safety trial conducted by NeuralStem. Those results held a surprise for investigators: one patient improved markedly after treatment, a phenomenon not easily explained by any effects from the implanted cells. An alternative explanation is that the immune system suppression used in the trial may have exerted a beneficial effect on ALS disease progression in this patient. Researchers are now planning a trial to test that hypothesis, and to see if they can better understand the mechanism of that improvement. These twin developments were discussed in a webinar given by Jonathan Glass, MD, professor of neurology at Emory University in Atlanta, Georgia, where he is also the Director of the Emory ALS Center, which provides multidisciplinary care for people and families with ALS and related disorders.

Phase I Results and Planning for Phase II

The stem cells used in the trial were of fetal origin, capable of making any cell type in the nervous system. “Our role is to determine whether it is a viable treatment, and if so, what is the right cell, and the right dose?,” Dr. Glass said. “It’s a slow process,” noting that a long preclinical development program was needed to determine how to safely deliver cells to the spinal cord. “The goal for this phase I trial was safety, safety, safety,” he said, evidenced by the design of the trial, which started with patients already significantly affected by ALS. Only after ensuring it was safe in those patients was treatment offered to those earlier in their disease, with a longer expected survival time and more quality of life. “We didn’t want to make people worse,” he said.

In all, 15 patients were treated, with about half a million cells delivered into the injection site. Post-mortem examination indicated the cells survived for long periods of time—“They set up residence in the spinal cord,” Dr. Glass said—and had no harmful effects.

Based on these results, Dr. Glass reported that the next trial, using more cells and in more sites in the spinal cord, has just received FDA approval, and will begin later this year. Patients will primarily be treated at Emory University, but there is also a second site, at the University of Michigan, which will enroll a small number of patients. Both the first trial and the new one have been supported by The ALS Association.

The target for the trial is to inject in enough sites, with enough cells, to affect all the motor neurons that control the diaphragm, the major breathing muscle. Dr. Glass suspects that any benefits of treatment would be from a “nursing” function of the injected cells, which may
release growth and survival factors for existing neurons. It would likely be too much to expect for the injected cells to take the place of dying motor neurons in the patient, he said.

**Immunosuppression Trial Planned**

One patient in the Phase I trial, called “Patient 11,” “got remarkably better,” Dr. Glass reported. Strength, vital capacity, and an electrical measure of nerve function all improved. It could have been due to an effect of the cells, or he may not have actually had ALS, but an alternative explanation is that the immunosuppressants he received may have been responsible. To test that hypothesis, Dr. Glass and others are planning a trial of immunosuppression in early ALS patients. The trial is also supported by The ALS Association and will be conducted at Emory University, Massachusetts General Hospital, and University of Massachusetts Medical Center.

“There is a long history of information on immune involvement in onset and progression in ALS, and a long history of trials,” Dr. Glass said. “None of them worked in changing the course of the disease, but there is a scientific basis for trying again.”

Recent work has suggested there may be a window of opportunity early in the disease, when the body’s immune system may be producing helpful, rather than destructive, immune cells. Boosting those cells, while suppressing others, may be the key. The trial will test combination therapy with four different drugs, each acting in different ways. The drugs are prednisone, tacrolimus, mycophenolate-mofetil, and a monoclonal antibody called basiliximab. Thirty patients will be enrolled, with a goal of seeing improvement, not just slowing of progression, over 6 months.

“This is more like a Phase II trial,” Dr. Glass pointed out, in that the outcome to be measured is not just safety, but efficacy. If an effect is seen, “we will interrogate the data” from fluid samples collected of blood and cerebrospinal fluid, “to design a more conclusive trial to hit immune function.”

To view the entire presentation, visit: [https://alsa.webex.com/alsa/ldr.php?AT=pb&SP=MC&rID=66542607&rKey=3a99b3dbc6d52adf](https://alsa.webex.com/alsa/ldr.php?AT=pb&SP=MC&rID=66542607&rKey=3a99b3dbc6d52adf).