

March 2, 2009

Discussion of procedure involving the withdrawal of peripheral blood* from ALS patients to procure and refine C133 stem cells, injecting cells into the frontal motor cortex of the brain toward the purpose of delaying further progression of ALS, extending life and improving the quality of life. Procedure performed by a neurological team in Monterrey, Mexico and previously subjected to clinical test study.

*Peripheral blood stem cells (PBSC's) are one source of cells for hematopoietic cell transplant recipients. PBSCs circulate in the bloodstream, and they are collected from the donor using a process called apheresis. It involves passing whole blood through a large bore blood catheter inserted into the patient and into a machine that separates out nucleated cells (stem cells have nuclei) and returns the other blood components back to the donor. Donors receive an injectable marrow stimulate called G-CSF (Neupogen) to increase the numbers of stem cells in the blood. Once collected, the PBSC can then be given immediately to the recipient or frozen for later use.

Many ALS families who have requested information about this promising stem cell procedure developed specifically for ALS and already showing notable promise. Further, the procedure would have little or no detectable risk due to location, hospital conditions, quality of surgeon, surgical procedure, post-operative peril, etc. These are among the primary concerns of ALS WORLDWIDE and we feel there are no such issues with the superb neurology team and hospital facility in Monterrey, Mexico.

Attached is the Clinical Test Study in its entirety, which should be thoroughly read, and digested, prior to making even a tentative decision regarding the advisability of undergoing this procedure. This study should be among the main criteria by which its potential, efficacy and safety is judged.

Since the initial test study, an additional 15 patients have also had the procedure under the clinical study conditions and are being reviewed for analysis of long-term benefit maintenance, possible side effects, and general responsiveness to the procedure. Recent questions have been answered as follows by the surgical team:

- 1. Is primary physician referral required? Not necessarily, but we need to obtain information from the physician in charge of the patient for additional data and to be in contact during follow-up. We also require a prior summary of clinical data as well as neurophysiologic studies and Cervical & Cranial Magnetic Resonance Imaging. After admission to the protocol the patient will be submitted to a tractography (MRI reconstruction of neural connections).**
- 2. What specific medical records are needed for patient review? The patient will have a cardiological evaluation including thoracic X-ray, spirometry test, blood tests, coagulation profile and physician has to assure that patient does not have malignant systemic diseases (cancer or leukemia).**
- 3. Cost to patient for entire procedure including hospitalization? The total cost is about \$ 18,000 USD**
- 4. Time allowance for patient to remain in Monterrey including pre- and post-procedure examinations? One week. Usual patient arrival is Monday, hospitalization is Wednesday, procedure is on Thursday and discharge is on Friday. The patient returns to own residence or local hotel Friday or Saturday.**
- 5. Frequency and duration of follow-up visits? Clinical evaluation each month during the first three months and then at 6 and 12 months with MRI tractography during the sixth month after procedure for Mexico patients. We propose, for patients from**

other countries, evaluation at the third and sixth months after procedure (tractography at sixth month).

Please note: ALS WORLDWIDE is not advocating for, promoting, or even suggesting this procedure for you and others receiving this email. Rather, we are bringing to your attention one of several protocols for the possible minimization of symptoms of ALS that has been the object of our continuing effort---to find potentially efficacious protocols for this purpose. You and your family and physician(s) should consult together to determine whether or not this is something you wish to pursue. If so, we will then be happy to assist in the coordination of obtaining and sending your medical records to the hospital and assisting in the schedule of your medical visit. Alternatively, you may choose to do so yourself. There is no charge or fee from ALS WORLDWIDE in providing these services to you and others. It is simply the fulfillment of our stated goal to support to ALS families internationally through scientific research interpretation, individual patient advocacy and community activism.

Link to Hospital San Jose TEC de Monterrey, at which the surgery is performed and where the physicians are located:

<http://portal.hsj.com.mx/lwp/wcm/connect/HSJ/AREAS+GENERALES/ENGLISH/>

Link to a complete PDF file about the hospital, which works in close collaboration with Methodist Hospital and Baylor College of Medicine, both of Houston:

<http://www2.hsj.com.mx/English/HSJenglish.pdf>

Link to University Hospital UANL College of Medicine, with which the neurology team at San Jose TEC de Monterrey are also associated:

http://en.wikipedia.org/wiki/Universidad_Aut%C3%B3noma_de_Nuevo_Le%C3%B3n

Link about Monterrey, Mexico: <http://en.wikipedia.org/wiki/Monterrey>

Link to 2007 article about the proliferation of very high quality, relatively inexpensive hospitals in Monterrey:

<http://www.dallasnews.com/sharedcontent/dws/news/nationworld/stories/072807dninthospitals.36608c1.html>

Link to OSAC (Overseas Security Advisory Council) about the high level of safety in Monterrey and how to avoid being a crime victim: <https://www.osac.gov/Reports/report.cfm?contentID=79049>

Link to the abstract immediately below:

<http://www.ncbi.nlm.nih.gov/pubmed/19191058?dopt=Abstract>

Related Articles, Links

Stem-cell transplantation into the frontal motor cortex in amyotrophic lateral sclerosis patients.

[Martinez HR](#), [Gonzalez-Garza MT](#), [Moreno-Cuevas JE](#), [Caro E](#), [Gutierrez-Jimenez E](#), [Segura JJ](#).

Servicio de Neurología, Hospital Universitario UANL.

Background aims Amyotrophic lateral sclerosis (ALS) is characterized by the selective death of motor neurons. CD133(+) stem cells are known to have the capacity to differentiate into neural lineages. Stem cells may provide an alternative treatment for ALS and other neurodegenerative diseases. Methods Five men and five women (aged 38-62 years) with confirmed ALS were included in this study. Our institutional ethics and research committees approved the protocol. After informed

consent was obtained, patients underwent Hydrogen-Magnetic Resonance Imaging (H-MRI) spectroscopy and were given scores according to an ALS functional rating scale, Medical Research Council power muscle scale and daily living activities. Bone marrow was stimulated with 300 microg filgrastim subcutaneously daily for 3 days. Peripheral blood mononuclear cells were obtained after admission by leukapheresis. The cell suspension was conjugated with anti-human CD133 superparamagnetic microbeads, and linked cells were isolated in a magnetic field. The isolated cells ($2.5-7.5 \times 10^5$) were resuspended in 300 microL of the patient's cerebrospinal fluid, and implanted in motor cortexes using a Hamilton syringe. Ten patients with confirmed ALS without transplantation were used as a control group. Patients were followed up for a period of 1 year. Results The autologous transplantation of CD133(+) stem cells into the frontal motor cortex is a safe and well-tolerated procedure in ALS patients. The survival of treated patients was statistically higher ($P=0.01$) than untreated control patients. Conclusions: Stem-cell transplantation in the motor cortex delays ALS progression and improves quality of life.

PMID: 19191058 [PubMed - as supplied by publisher]

Link to scientific articles regarding the relevance and importance of CD133 stem cells in muscle repair, their capacity to multiply, and usefulness in both ALS and Duchenne muscular dystrophy: <http://www.connotea.org/user/SByer> We urge those who consider this innovative therapy to learn everything you possibly can prior to making any decision and also prior to any emotional commitment to this or any stem cell therapy, which is a category of treatment that is promising but still largely unproven for those with ALS.