

# Anatomical and functional improvements in corticospinal tract regeneration in chronic stroke patients after an intracranial implantation of autologous CD34 stem cells — phase II trial

Shinn-Zong (John) Lin MD, PhD; Woei-Cherng Shyu MD, PhD; Demeral Liu Neuropsychiatry Center, China Medical University Hospital, Taichung, Taiwan Department of Neurosurgery, China Medical University Beigan Hospital, Yunlin, Taiwan Graduate Institute of Immunology, China Medical University, Taichung, Taiwan



#### Introduction

Our animal study in chronic stroke rats showed that intracranial implantation of peripheral blood stem cells (PBSC) mobilized by granulocyte colony stimulating factor (GCSF) improved the anatomical regeneration of corticospinal tracts and motor function. Previous phase I trial in 6 old stroke patients by using antologous PBSC also revealed an improvement in functional outcome.

#### Methods

This randomized, controlled phase II trials was conducted in 30 chronic stroke patients who suffered from stroke for 6 months up to 5 years with a stable neurological deficit. CD34+ PBSC about 3-8×10 to the power of six were implanted stereotactically into the damaged corticosipnal tract under local anesthesia in the treatment group. The primary end points were improvement in NIHSS, European Stroke Scare (ESS), ESS motor subscale (EMS) and Modified Rankin Scale (mRS). The secondary end points were fiber numbers asymmetry (FNA) in corticospinal tract (CST) and motor evoked potential (MEP).

## Results

There were no serious adverse events found in all 30 patients in the 12 months follow-up period. Significant improvements (p<0.05) were noted in NISS, ESS, EMS and mRS in treatment group as compared to control. FNAs were increased in every treated patient, but not in the control ones. MEP response reappeared in 9 of the 15 treated patients, but none in the control group.

#### Conclusions

Autologous PBSC intracranial implantation in chronic stroke patients is safe and feasible.

## Learning Objectives

Test safety and efficacy in chronic stroke patients.

#### References

1.Woei-Cherng Shyu, Shinn-Zong Lin, Hui-I Yang, Yi-Shiuan Tzeng, Cheng-Yoong Pang, Poa-Sheng Yen, Humg Li. (2004) Functional Recovery of Stroke Rats Induced by Granulocyte Colony-Stimulating Factor-stimulated Stem Cells. Circulation 110: 1847-1854.

2.Woei-Cherng Shyu, Shinn-Zong Lin, Chau-Chin Lee, Demeral David Liu, Hung Li. (2006) Granulocyte colonystimulating factor for acute ischemic stroke: a randomized controlled trial. Canadian Medical Association Journal; 174(7): 927-33.

3.Shyu WC, Lin SZ, Li H. (2006) Intracerebral peripheral blood stem cell (CD34+) implantation induces neuroplasticity via enhancing ß1integrin-mediated angiogenesis in chronic stroke rats. J. Neurosci; 26: 3444-3453.

4.Woei-Cherng Shyu, Shinn-Zong Lin, Ming-Fu Chiang, Der-Cherng Chen, Ching-Yuan Su, Hsiao-Jung Wang, Ren-Shyan Liu, Chang-Hai Tsai, and Hung Li, (2008) Secretoneurin promotes neuroprotection and neuronal plasticity via the Jak2/Stat3 pathway in murine models of stroke. Journal of Clinical Investigation, Jan 2008; 118(1): 1-16.

5.Shyu WC, Liu DD, Lin SZ, Li WW, Su CY, Chang YC, Wang HJ, Wang HW, Tsai CH, Li H. (2008) Implantation of olfactory ensheathing cells promotes neuroplasticity in murine models of stroke. Journal of Clinical Investigation, July 2008, 118(7):2482-2495.





Transplanted cells retained at the injection sites



Progressive regeneration of the damaged corticospinal tract after transplantation





# 6 months after transplantation

