

Stable Intracerebral Transplantation of Neural Stem Cells for the Treatment of Paralysis due to Ischemic Stroke

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Abstract:

Paralysis due to ischemic stroke is a major cause of prolonged neurological disability world-wide and in particular in China and Asian countries. There are currently no effective therapies to reverse the paralysis. We have investigated the feasibility and safety of transplanting human neural stem cells to reverse the paralysis in stably hemiparetic stroke patients. Neural stem cells are the precursor cells present in the neuroepithelium along the neuraxis during mammalian fetal development. NSI-566, the investigational product used in this study, is a stable cell line consisting of neural stem cells derived from a single human fetal spinal cord tissue, expanded only by epigenetic means with no genetic modification. This cell line is also being tested in clinical trials in the U.S. for treatment of amyotrophic lateral sclerosis (NCT01348451) and spinal cord injury (NCT01772810). In a single-site, Phase I study, 3

cohorts (n=3/cohort) were transplanted with ascending doses of NSI-566, which involved a one-time stereotactic, intracerebral injection of 1.2×10^7 , 2.4×10^7 , or 7.2×10^7 cells.

Immunosuppression therapy with tacrolimus was maintained for 28 days. All subjects had chronic motor stroke, verified by MRI, initiated between 5 and 24 months prior to surgery, with Modified Rankin Score of 2, 3, or 4 and Fugl-Meyer Motor Score of 55 or less. Safety was the primary objective. Changes in Fugl-Meyer Motor Scale, Modified Rankin Scale, and NIH Stroke Scale were measured as secondary outcomes. Changes in FDG-PET, functional MRI, and structural MRI were measured as exploratory outcomes. Twelve-month clinical data of the combined nine participants were analyzed using the Wilcoxon signed rank test. At the 12-Month Visit, compared to Baseline, the mean Fugl-Meyer Motor Score (FMMS, total score of 100) showed 15.6 points of improvement ($p=0.0078$), the mean Modified Ranking Score (MRS) 0.8 points of improvement ($p=0.031$), and the mean NIH Stroke Scale (NIHSS) 3.2 points of improvement ($p=0.016$). The stem cell treatment was well tolerated at all doses. Longitudinal MRI studies showed evidence of graft survival and cavity-filling in all 9 patients. There was no death or any serious adverse event related to the treatment. This result warrants further study with larger cohorts with a randomized control arm.