ClinicalTrials.gov: NCT02481440

Unique Protocol ID: hUC-MSC-SCI

Official Title: Repeated Subarachnoid Administrations of Human Umbilical Cord Mesenchymal Stem Cells in Treating Spinal Cord Injury

Document Date: May 1st, 2020

Study protocol

Informed consent forms that had the approval of the institutional review board were obtained from all participants before recruitment. In this clinical study, subarachnoid transplantation of hUC-MSCs was performed a total of four times per subject with the delivery dose of 1×10^6 cells/kg. For the first administration of stem cells, maximum lumbar flexion of subject was maintained, and cerebrospinal fluid (CSF) release with a volume of approximately 10 ml was performed. hUC-MSCs suspension was administered manually at L4/5 level as slowly as possible. This was followed by a two-minute delay before the injection needle was withdrawn. One month later, subject underwent a second subarachnoid engraftment of hUC-MSCs. Following this pattern, subject received the third and fourth stem cell transplantation. During the intervention period of four months, all subjects received the standardized care. After the completion of cytotherapy, subject was regularly followed up in the hospital at four time points, determined at 1, 3, 6, and 12 months following the final administration of hUC-MSCs. At each time point of administration (the first, second, third, and fourth transplantation) and follow-up (the first, second, third, and fourth follow-up), safety and efficacy indicators were collected accordingly. During the intervention and follow-up periods of this trial, any adverse event was identified rapidly and managed properly. The maximum intensity and relationship of any AE with hUC-MSCs administration were identified. Efficacy indicators included ASIA score and the SCI Functional Rating Scale of the International Association of Neurorestoratology (IANR-SCIFRS) for the recovery of spinal cord function; the

International Standards to document remaining Autonomic Function after Spinal Cord Injury (ISAFSCI); Penn and modified Ashworth scales for the evaluation of spasms and spasticity of affected muscles; Geffner scale for the study of bladder function and Neurogenic Bowel Dysfunction (NBD) scale; residual urine volume (RUV). In this trial, ASIA and IANR-SCIFRS total scores at the fourth follow-up were determined as primary outcomes, while these two indicators at the remaining time points and the other efficacy indicators were secondary outcomes.

Statistical analysis

Continuous variables were expressed as means ± standard deviations or median with interquartile range according to their normality, while categorical data were given as frequencies. In terms of efficacy indicators collected at multiple (≥ 3) time points, analysis of variance (ANOVA) for repeated measurement or Friedman test was used to detect overall statistical significance of normal or non-normal continuous data. Following the Bonferroni correction, the paired samples *t*-test and Wilcoxon signed ranks test were applied to analyze normal and non-normal continuous variables, respectively. Subgroup analysis of two primary efficacy indicators (ASIA and IANR-SCIFRS total scores at the fourth follow-up) were performed. Statistical Product and Service Solutions (SPSS v. 22.0) was used to perform all statistical analyses, and $P<0.05$ was considered statistically significant.