Abstracts

Mesenchymal Stem Cell-Derived Neural Progenitors in Progressive MS: Two-Year Follow-Up of a Phase I Study

Objective To determine the long-term safety and efficacy of repeated intrathecal (IT) administration of autologous mesenchymal stem cell-derived neural progenitors (MSC-NPs) in patients with progressive MS by evaluating subjects 2 years after treatment.

Methods Twenty subjects were enrolled as part of a phase I, open-label single-arm study of 3 IT injections of MSC-NPs spaced 3 months apart. Subjects were evaluated for adverse events and disability outcomes including the Expanded Disability Status Scale (EDSS) and the timed 25-foot walk (T25FW). Long-term evaluation was conducted 2 years after the third treatment. CSF was collected before and 3 months after treatment.

Results Eighteen of the 20 study participants completed the full 2-year follow-up protocol. There were no long-term adverse events associated with repeated IT-MSC-NP treatment. Seven subjects showed sustained improvement in EDSS after 2 years, although the degree of improvement was not maintained in 5 of the subjects. Three of the 10 ambulatory subjects showed sustained improvement in the T25FW after 2 years. CSF biomarker analysis revealed a decrease in C-C motif chemokine ligand 2 and an increase in interleukin 8, hepatocyte growth factor, and C-X-C motif chemokine ligand 12 after treatment.

Conclusions Safety and efficacy of repeated IT-MSC-NP treatment was sustained for 2 years; however, the degree of disability reversal was not sustained in a subset of patients. CSF biomarkers altered in response to IT-MSC-NP treatment may reflect specific immunoregulatory and trophic mechanisms of therapeutic response in MS.

Classification of Evidence This study provides Class IV evidence that for patients with progressive MS, IT administration of MSC-NPs is safe and effective. The study is rated Class IV because of the absence of a non–IT-MSC-NP-treated control group.

Clinicaltrials.gov Identifier NCT01933802.

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Presentations and Mechanisms of CNS Disorders Related to COVID-19

Severe acute respiratory syndrome coronavirus 2 is the cause of the coronavirus disease 2019 (COVID-19) pandemic. In addition to severe respiratory symptoms, there are a growing number of reports showing a wide range of CNS complications in patients with COVID-19. Here, we review the literature on these complications, ranging from nonspecific symptoms to necrotizing encephalopathies, encephalitis, myelitis, encephalomyelitis, and stroke. We postulate that there are several different mechanisms involved in COVID-19–associated CNS dysfunction, particularly activation of inflammatory and thrombotic pathways and, in a few patients, a direct viral effect on the endothelium and the parenchyma. Last, critically ill patients frequently present with protracted cognitive dysfunction in the setting of septic encephalopathy likely due to multifactorial mechanisms. Further studies are needed to clarify the relative contribution of each of these mechanisms, but available data suggest that CNS complications in COVID-19 are rare and probably not directly caused by the virus.

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