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Summary Results of a Clinical Trial with Muse Cell-based Product CL2020 in Patients with Cerebral Infarction

Life Science Institute, Inc.

Life Science Institute, Inc. (LSII; Headquarters: Chiyoda-ku, Tokyo; President: Seiichi Kiso) is pleased to announce the results of a clinical trial in patients with cerebral infarction.

LSII, in collaboration with the Department of Neurosurgery at Tohoku University (Principal Investigator: Kuniyasu Niizuma, Professor, MD, PhD, Department of Neurosurgical Engineering and Translational Neuroscience, Graduate School of Biomedical Engineering, Tohoku University; Medical Expert: Teiji Tominaga, Professor, MD, PhD, Department of Neurosurgery, Graduate School of Medicine, Tohoku University), began a clinical trial of the Muse cell-based product CL2020 for patients with cerebral infarction in September 2018. In April 2020, the interim results were announced. More recently, preliminary results of the clinical trial of CL2020 for 52 weeks after intravenous administration in patients with cerebral infarction compared to placebo were presented at the 41st Annual Meeting of the Japan Neurological Surgery Congress (May 13-16, 2021, Yokohama). This press release provides a summary of these preliminary results.

The study was a randomized, double-blind, placebo-controlled clinical trial evaluating the safety and efficacy of a single intravenous infusion of CL2020 within 14 to 28 days after the onset of cerebral infarction in patients who continued to exhibit physical dysfunction after standard acute treatment. The highlights of the conference presentation are outlined below.

The primary endpoint of the clinical trial was patient safety for up to 52 weeks after administration of CL2020. No adverse events that would prevent advancement of the clinical study were observed throughout the clinical study period, and CL2020 was confirmed to be well tolerated.

The secondary endpoints included the following:

- Prior to administration of placebo or CL2020, most patients had a modified Rankin Scale (mRS[1)]) score of 4 (moderately severe disability: unable to walk and attend to bodily functions without assistance) or 5 (severe disability: bedridden, incontinent, and requires continuous care and attention).
- At 12 weeks after administration, the average mRS score was a 2 (slight disability: able to look after own affairs, such as using public transportation, etc., without assistance) or lower, and the lower limit of the 95% confidence interval (21.1%-61.3%) of subjects (responder ratio) exceeded the preset threshold responder ratio (8.7%), confirming the therapeutic effect of CL2020. The proportion of responders in the CL2020 group at 12 weeks after administration was 40% (10/25 cases), and 30% higher than that in the placebo group (10%; 1/10 cases; $p = 0.08$). At 52 weeks after administration, the proportion of responders in the CL2020 group was 68.2% (15/22 cases), and the difference between the CL2020 group and the placebo group (37.5%, 3/8 cases) was maintained at more than 30%.
- Evaluation of the efficacy at 52 weeks after administration revealed that 7 of 22 (31.8%) subjects in the CL2020 group achieved an mRS score of 1 (no significant disability despite symptoms: able to carry out all pre-stroke activities without assistance, such as return to work). No one in the placebo group achieved an mRS score of 1 within 52 weeks.
- The National Institute of Health Stroke Scale (NIHSS), a measure of the severity of neurological disorders[2)] evaluates 15 items, including consciousness, visual field, eye movements, facial paralysis, limb muscle strength, ataxia, sensation, and language. A higher NIHSS indicates greater impairment. Subjects who had an NIHSS of 6 or higher prior to placebo or CL2020 administration were enrolled in the study, and no subject had an NIHSS of 1 (nearly normal) or lower. At 52 weeks, however, 5 of 21 (23.8%) subjects in the CL2020 group had an NIHSS of 1 compared with none in the placebo group.
- We compared the average amount of change in the motor function of the upper and lower extremities from baseline using the Fugl-Meyer Motor Scale (FMMS[3)]). In the CL2020 group, motor function significantly improved in the upper extremities from week 4 to week 52 ($p < 0.01$) compared with that in the placebo group. Both groups showed improved motor function in the lower extremities at 52 weeks.

Details of the study results will be reported at academic conferences and in conference proceedings, as well as in medical journals.

LSII is encouraged by the results indicating that CL2020 administered within 14 to 28 days after the onset of cerebral infarction can be expected to effectively ameliorate the physical dysfunction associated with cerebral infarction remaining after standard acute treatment. We believe that CL2020 may provide a new treatment option for certain patients with cerebral infarction. On the basis of the results of this study, LSII will further promote the development of CL2020 in consultation with regulatory authorities.

LSII will continue to contribute to the future health and medical care of people around the world by developing healthcare businesses and products, including Muse cell-based products, with the aim of realizing a healthy and secure society, KAITEKI, for the next generation.

Muse cells

Muse cells (Multilineage-differentiating Stress Enduring cells) are endogenous pluripotent repair stem cells discovered in 2010 by a group of scientists led by Professor Mari Dezawa of Tohoku University. Muse cells are naturally present in the bone marrow, peripheral blood, and connective tissues of all body organs. They normally accumulate in injured organs where they replace and replenish injured cells by differentiating into the damaged cell type, and exert pleiotropic effects including anti-inflammatory actions and vascular protection over an extended period of time, without the need for HLA-matching test or long-term immunosuppressive drug administration for the use of donor Muse cells. Donor Muse cells, administered by simple intravenous drip, accumulate in the injured tissue to exert their tissue repair effects by spontaneously differentiating into healthy cells corresponding to the damaged tissue. Because the donor Muse cells that engraft into the injured tissue are maintained as living, functional cells over an extended period of time, the anti-inflammatory, vascular-protective, tissue protective, and anti-cell-death effects continue to be exerted for a long time. Administration of Muse cells is significantly more effective than administration of another type of stem cell, human mesenchymal stem cells, for the repair of damaged tissue. Owing to these properties, Muse cells are expected to enable regenerative medicine by a simple infusion of donor-derived cells.

1) modified Rankin Scale (mRS)
(a) Banks JL, Marotta CA. Outcomes validity and reliability of the modified Rankin scale: Implications for stroke clinical trials. Stroke 2007;38(3):1091-1096.
(b) Shinohara Y, Minematsu K, Amano T, Ohashi Y. Modified Rankin Scale with expanded guidance scheme and interview questionnaire: Interrater agreement and reproducibility of assessment. Cerebrovasc Dis 2006;21:271-278.

2) The National Institute of Health Stroke Scale (NIHSS)
Lyden PD, Lu M, Levine SR, Brott TG, Broderick J. NINDS rtPA Stroke Study Group. A modified National Institutes of Health Stroke Scale for use in stroke clinical trials: preliminary reliability and validity. Stroke 2001;32:1310-1317.

3) Fugl-Meyer Motor Scale (FMMS)
Fugl-Meyer AR, Jääskö L, Leyman I, Olsson S, Steglind S. The post-stroke hemiplegic patient. 1. a method for evaluation of physical performance. Scand J Rehabil Med. 1975;7:13-31.