November 2, 2022

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Results from the TREASURE Study for Ischemic Stroke presented at the 14th World Stroke Conference and the 40th Annual Meeting of Japan Society of Neurological Therapeutics

HEALIOS K.K. ("Healios") conducted the TREASURE study[*1] to investigate the safety and efficacy of HLCM051[*2] (Multistem®) in patients with ischemic stroke. Healios is pleased to announce that Dr. Toshiya Osanai, Hokkaido University, Department of Neurosurgery made a presentation on the results of TREASURE study at a plenary session of the 14th World Stroke Congress held in Singapore on October 26 and at the 40th Annual Meeting of Japan Society of Neurological Therapeutics on November 2, 2022.

The main contents of Dr. Osanai's presentation were as follows:

- Excellent Outcome[*3] (mRS[*4]<=1, NIHSS[*5]<=1 and Barthel Index[*6]>=95)
  After 90-days (primary endpoint), 12 patients (11.5%) in the HLCM051 group and 10 patients (9.8%) in the placebo group with a p-value 0.903. After 365-days (secondary endpoint), 16 patients (15.4%) and 11 patients (10.8%) with a p-value of 0.431. There was no difference between the HCLM051 and placebo groups in Excellent Outcome at 90 or 365 days.

- Global Recovery[*7] (mRS<=2, NIHSS improvement>=75% and Barthel Index>=95)
  After 90-days (secondary endpoint), 20 patients (19.2%) in the HLCM051 group and 16 patients (15.7%) in the placebo group, with a p-value of 0.762. After 365-days, 29 patients (27.9%) in the HLCM051 group and 16 patients (15.7%) in the placebo group, with a p-value of 0.037. There was a statistically significant difference between the HLCM051 group and the placebo group at 365 days.

- Barthel Index >=95
  After 90-day (secondary endpoint), 31patients (29.8%) in the HLCM051 group and 24 patients (23.5%) in the placebo group, with a p-value of 0.437. After 365-days, 37 patients (35.6%) in the HLCM051 group and 23 patients (22.5%) in the placebo group, with a p-value of 0.045. There was a statistically significant difference between the HLCM051 group and the placebo group at 365 days.

- There were no significant differences in safety outcomes, including mortality and adverse events between the treatment and placebo groups.

Dr. Osanai commented as follows: "I concluded that while MultiStem did not show a significant difference in the primary endpoint, the rate of Global Recovery indicated independent life after one

year was possible for 27% of the treatment group versus 15% of the control. The safety of MultiStem therapy has also been confirmed and its use in clinical practice is expected in the future. I also believe that clinical trials evaluating the long-term prognosis for stroke patients treated with Multistem should be conducted."

*[1] TREASURE study
The TREASURE study was conducted to investigate the safety and efficacy of HLCM051 (Multistem®) in patients with ischemic stroke. The study targeted patients with moderate to moderate-severe strokes (baseline NIHSS score 8-20), with administration of a single dose of HLCM051 intravenously within 1836 hours from stroke onset. The trial was conducted at 48 sites in Japan and enrolled 206 patients. HLCM051 is an off-the-shelf, somatic stem cell regenerative medicine product that Healios is developing for both ischemic stroke and acute respiratory distress syndrome in Japan.

*[2] HLCM051
HLCM051 is a somatic stem cell regenerative medicine product. Healios added it to its pipeline by signing an exclusive licensing agreement with the United States based Athersys, Inc. ("Athersys") in January 2016, whereby Healios acquired rights to develop and distribute Athersys' proprietary stem cell product MultiStem® to treat ischemic stroke in Japan. Further, in June 2018 Healios and Athersys expanded their collaboration broadly, and as part of this expansion Healios acquired the development and distribution licenses to use MultiStem to treat ARDS in Japan.

*[3] Excellent Outcome
Functional and neurological deficit and recovery following ischemic stroke are evaluated using three standard methods: the modified Rankin scale (mRS), the NIH stroke scale (NIHSS), and the Barthel Index (BI). "Excellent Outcome" is defined as achieving scores ≤1 on the mRS and on the NIHSS and a score ≥95 on the BI. In this study, Excellent Outcome was set as the primary evaluation item.

*[4] mRS
The mRS measures the degree of disability or dependence in the activities of daily living of people who have had a stroke or have a neurological disability due to other reasons. It is used to categorize the level of functional independence with reference to pre-stroke activities. The scale includes scores from 0 to 6, ranging from perfect health without symptoms of disability (i.e., a score of 0) to death (a score of 6). A lower score indicates a lower degree of disability. In this study, mRS was set as a secondary evaluation item.

*[5] NIHSS
The NIHSS is a systematic assessment tool that provides a quantitative measure of stroke-related neurologic deficit in the following areas: level of consciousness, facial paralysis, visual acuity and function, arm and leg motor function, limb coordination, language and speech, sensory loss, and other parameters. A higher score on the NIHSS indicates a higher degree of neurological impairment in a stroke patient. The score for each function ranges from 0 to 4, with 0 indicating normal function (i.e., no deficit) and 4 indicating complete impairment (Note that some functional assessments use a scale of 0–2, or 0–3). The total NIHSS score of the patient is calculated by adding the score for each element on the scale, based on the individual assessments; 42 is the highest

possible score, which reflects the maximum disability of the patient in each category. In this study, NIHSS was set as a secondary evaluation item.

*[6] Barthel Index
The BI is a 100-point scale that is used to assess the ability of the patient to independently perform activities of daily living and to evaluate a range of different functions. These include the ability of the patient to walk, dress, feed, bathe, climb stairs, use a toilet, self-groom, and certain other metrics. The patient is evaluated for each activity to assess for independence, partial dependence, or complete dependence, and then, a score between 0 and 10 is assigned (10 points = independence, 5 points = partially dependent, and 0 points = completely dependent). The BI score ranges from 0 to 100; a score of 100 indicates no dependence on any activity, and a lower score indicates a greater need for assistance. In this study, BI was set as a secondary evaluation item.

*[7] Global Recovery
Functional and neurological deficit and recovery following ischemic stroke are evaluated using three standard methods: the modified Rankin scale (mRS), the NIH stroke scale (NIHSS), and the Barthel Index (BI). “Global Recovery” is defined as achieving scores ≤2 on the mRS, NIHSS improvement >=75% and a score ≥95 on the BI. A Global Recovery assessment using multivariate, correlation adjustment, was the primary endpoint in Athersys’s Phase 2 MASTERS-1 study run in the United States and Europe, and in this study, Global Recovery was set as a secondary evaluation item.

(Source) Prepared by Healios on the basis of materials provided by The Japan Stroke Society.

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