Press Release

April 2, 2025

To Members of the Press

Keio University School of Medicine
Keio University Hospital
National Hospital Organization Osaka National Hospital
National Hospital Organization Murayama Medical Center

Completion of Follow-Up Observations in Clinical Study on Regenerative Medicine Using iPS Cell-Derived Neural Stem/Progenitor Cells to Treat Subacute Spinal Cord Injuries

Keio University Hospital has completed the scheduled follow-up observations and data collection for all four cases in its clinical study on regenerative medicine using iPS cell-derived neural stem/progenitor cells to treat subacute spinal cord injuries.

Moving forward, we will promptly submit a comprehensive report and summary to the Minister of Health, Labour and Welfare in accordance with the Act on Securing Safety of Regenerative Medicine and related regulations.

1. Research Background

After receiving approval from the Ministry of Health, Labour and Welfare in 2019, Keio University Hospital began a clinical study in December 2020 on regenerative medicine using iPS cell-derived neural stem/progenitor cells to treat subacute spinal cord injuries.

Follow-up observations for all four cases were completed in November 2024. To formally conclude the study, we will promptly carry out all necessary procedures, including the preparation and submission of the final report summary, in accordance with the Act on Securing Safety of Regenerative Medicine. The clinical study's implementation structure and overview are outlined below.

Study Implementation Framework

- **Principal Investigator:**
  Professor Hideyuki Okano, Keio University School of Medicine (from study launch through 2024)
  Professor Masaya Nakamura, Keio University School of Medicine (from 2024)
- **Lead Physician:** Professor Masaya Nakamura, Keio University School of Medicine
- **Cell Differentiation Facility:** National Hospital Organization Osaka National Hospital
- **Medical Institution Providing Regenerative Treatment:** Keio University Hospital
- **Partner Institution:** National Hospital Organization Murayama Medical Center

Study Overview

- **Study Objective:** The primary objective was to evaluate the safety of cell transplantation. Efficacy was also assessed as the secondary objective.
- **Subjects:** Patients with complete spinal cord injury (Grade A on the American Spinal Injury Association [ASIA] Impairment Scale, hereinafter "AIS") at the C3/4–T10 level, 14 to 28 days post-injury (subacute phase).
- **Target Sample Size:** 4 patients
- **Transplanted Cells:** A regenerative medicine-grade iPS cell stock produced by the Center for iPS Cell Research and Application (CiRA), Kyoto University, was differentiated into neural stem/progenitor cells at Osaka National Hospital,

cryopreserved at Keio University Hospital, and cultured for recovery prior to transplantation upon obtaining informed consent from each patient.

- **jRCT Trial ID:** jRCTa031190228

2. Research Significance and Future Development

All four transplants were successfully performed as planned, followed by one year of post-transplant observation. All cases were included in the safety and efficacy evaluations.

Final data analysis is ongoing, but no serious adverse events with a causal link to the regenerative therapy have been observed, and the primary objective indicates a favorable safety profile. Regarding the secondary objective of efficacy, a median improvement of 13 points from baseline was observed in the ISNCSCI total motor score at 52 weeks post-injury. According to AIS grading, one patient improved from Grade A to C, and another from Grade A to D—indicating that two of the four cases improved to Grade C or higher. By database involving patients with comparable baseline severity, median improvement in ISNCSCI total motor score at 52 weeks was approximately 4–7 points*, and only 10–12% of cases improved to AIS Grade C or higher.* These results suggest that the current treatment may have potential efficacy.

Based on the final data analysis, we plan to compile the summary report and begin working toward the practical implementation of this treatment.

*Data based on analysis of the Japan Spinal Injuries Center database (Ideta, Sakai, Maeda, et al.)

3. Notes

This study was supported by the Japan Agency for Medical Research and Development (AMED) through the following programs: the Research Center Network for Realization of Regenerative Medicine ("Regenerative Medicine for Spinal Cord Injury and Stroke Using Neural Precursor Cells of iPS Cell Origin"), and two projects under the Research Project for Practical Applications of Regenerative Medicine ("Development of Rehabilitation Therapies Supporting Spinal Cord Regeneration" and "Clinical Study on Transplantation of iPS Cell-Derived Neural Stem/Progenitor Cells for Subacute Spinal Cord Injury").

Glossary

(1) iPS Cells: Induced pluripotent stem cells are created by introducing a small number of specific factors into human somatic cells—such as those from the skin or blood—and culturing them. These cells can differentiate into various tissue types and organs and also has the ability to self-replicate.
The name "induced pluripotent stem cell" is often abbreviated as "iPS cell."

(2) Neural Stem/Progenitor Cells: Immature cells of the nervous system capable of self-renewal and differentiation into various types of neural cells.

(3) ASIA Impairment Scale (AIS): A standardized scale used to evaluate the severity of spinal cord injuries.
In general, AIS Grade A indicates complete paralysis with no sensory or motor function preserved; AIS Grade B indicates preserved sensation but no motor function; AIS Grade C indicates some motor function preserved below the level of injury, but less than half of the key muscles have a strength grade of 3 or more; and AIS Grade D indicates that at least half of the key muscles below the level of injury have a strength grade of 3 or more.

(4) ISNCSCI Motor Score: A standardized international method for evaluating motor function following spinal cord injury.
Strength is assessed bilaterally in 20 key muscle groups innervated by spinal segments C5–T1 (upper extremities) and L2–S1 (lower extremities), using a six-point scale from 0

to 5.
The maximum score is 50 points for the upper limbs and 50 for the lower limbs, with a total score out of 100.

*Please direct any requests or inquiries to the contacts listed below in advance of any press coverage.

Inquiries regarding this press release:
Professor Masaya Nakamura
Department of Orthopedic Surgery
Keio University School of Medicine
Tel: 03-5363-3812
Fax: 03-3353-6597
Email: masa@keio.jp

Source of this release:
Iizuka / Kishi
Office of General Affairs
Shinanomachi Campus, Keio University
35 Shinanomachi, Shinjuku-ku, Tokyo 160-8582
Tel: 03-5363-3611
Fax: 03-5363-3612
Email: med-koho@adst.keio.ac.jp
https://www.med.keio.ac.jp/en/

National Hospital Organization Osaka National Hospital
2-1-14 Hoenzaka, Chuo-ku, Osaka-shi, Osaka 540-0006
Tel: 06-6942-1331
Fax: 06-6943-6467
Email: 408-kanrika@mail.hosp.go.jp
https://osaka.hosp.go.jp/fip/index.html

Administration Division, National Hospital Organization Murayama Medical Center
2-37-1 Gakuen, Musashimurayama-shi, Tokyo 208-0011
Tel: 042-561-1221
Fax: 042-564-2210
Email: 218-kanrika@mail.hosp.go.jp
https://murayama.hosp.go.jp/ (Japanese)

Inquiries regarding AMED:
Division of Regenerative Medicine, Japan Agency for Medical Research and Development
1-7-1 Otemachi, Chiyoda-ku, Tokyo 100-0004
Tel: 03-6870-2220
Fax: 03-6870-2246
Email: saisei@amed.go.jp
https://www.amed.go.jp/en/index.html