Update on first transplant recipient in the “Clinical study of autologous induced pluripotent stem cell-derived retinal pigment epithelium (RPE) cell sheets for exudative age-related macular degeneration (AMD)”

The one-year monitoring period of the first recipient of the RPE cell sheet transplant, following the procedure carried out at the Institute of Biomedical Research and Innovation (IBRI) Hospital on September 12, 2014, as part of the above clinical study by the FBRI, RIKEN, and Kobe City Medical Center General Hospital has finished, and the following is a report on the progress of the first subject.

1. Research overview
   This study was launched to examine the safety of transplanting an RPE cell sheet, created from induced pluripotent stem cells (iPSCs) derived from the patient’s own cells, into the subretinal space of the eye, with the aim to develop a new treatment for exudative AMD.

2. Principle investigators
   Yasuo Kurimoto, M.D., Ph.D.
   Senior Director, Division of Ophthalmology
   Foundation for Biomedical Research and Innovation, IBRI Hospital
   Director, Department of Ophthalmology
   Kobe City Medical Center General Hospital

   Masayo Takahashi, M.D., Ph.D.
   Project Leader, Retinal Regeneration R&D Project
   RIKEN Center for Developmental Biology
   Director, Division of Ophthalmology (Retinal Regeneration)
   Foundation for Biomedical Research and Innovation, IBRI Hospital

(A press briefing was held on October 2, 2015 by the principle investigators to give an update described in ‘4. Progress update’ in this document.)
3. Roles of the institutions in the study

Foundation for Biomedical Research and Innovation
- Explanation to patients (informed consent), biopsy of tissue from patient's skin,
- RPE sheet transplantation, tests before and after the surgery

RIKEN
- Management of the clinical study, generation of iPSCs from skin biopsy obtained from patient, generation of RPE sheet from iPSCs

Kobe City Medical Center General Hospital
- Support in the screening process, some of the tests, and provision of emergency medical services during and after surgery

4. Progress update

Examinations including tests of visual acuity, intraocular pressure, ocular fundus and imaging, were carried out daily for the first week following transplantation during which the patient was hospitalized, weekly for the first month after the patient's release from the hospital, and monthly for the remainder of the monitoring period to evaluate safety. The overall results of examinations from the monitoring period are good, with the RPE sheet remaining viable and engrafted in the initial transplanted site without the need for immunosuppression. No signs of tumorigenesis or other major abnormalities were observed as a result of the transplantation. Comprehensive cancer screening (whole-body) conducted one year post-transplantation did not detect signs of tumor formation or abnormalities. Using this treatment protocol (removal of neovascular tissue followed by transplantation of an iPSC -derived RPE cell sheet into affected site), there were no signs of recurring neovascularization and the morphology of the macula showed signs of improvement. The patient's visual acuity, which had been on the decline even with existing treatment before the procedure, remains stable after the surgery, and the QOL scores for visual acuity after the surgery have improved.

The efficacy of the iPSC-derived RPE sheet is difficult to assess at this time. However, in terms of the evaluating the safety of the intervention, which is the primary objective of this clinical study, the progress of the first subject one-year post-transplantation can be described as good.

---

1 QOL: Quality of Life; in this case, assessment was based on subject's answers to a questionnaire on how the changes to subject's vision following the intervention has affected his/her daily life.