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**Standardization of lymphoapheresis in living donor liver transplant patients
for the engineered antigen specific regulatory T cell product for tolerance
induction**

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Introduction: We are developing antigen specific regulatory T cell product that aims to suppress post-transplant rejections in a donor antigen-specific manner and induce immune tolerance and conducting multicenter clinical trial in Japan. Though PBMC collected from patients and donors via apheresis are used as the raw material for this cell product, for the liver pretransplant patients the coagulopathy and severe pancytopenia greatly affect the safety and ensure the collection of enough PBMC by lymphapheresis. We investigated the risk of PBMC collection by apheresis in the liver cirrhosis patients to ensure the patient safety and evaluate the collected PBMC for manufacturing.

Methods: In addition to the patient's disease background and condition, we analyze leukocyte fraction and lymphocyte subpopulation by flow cytometer and estimated the processed inlet volume, time required for lymphapheresis and the implementation conditions. Apheresis data from living donor liver transplant patients participated in the tolerance clinical trial were analyzed from the viewpoint of patient safety. Furthermore, we investigated the quality of collected PBMC as the raw materials for manufacturing process.

Results: In order to ensure patient safety, it was considered necessary to secure puncture of the vascular route and prepare for citric acid poisoning and exacerbating the risk of bleeding due to decreased platelets during apheresis. As for the suitability of the raw materials used for manufacturing, although the cell fractionation profile varies greatly among liver transplant patients, the target number of cells was secured in all patients. The validity of the simulation was confirmed.

Conclusion: Our simulation for lymphapheresis contribute to the safety for liver transplant patients and standardize the apheresis setting to correct enough number and quality of PBMC as the raw material for manufacturing.