

## Executive Summary

### Comparing outcome of unrelated allogeneic transplantation according to donor's nationality

Youngil Koh<sup>1,2</sup>, Sangjin Shin<sup>1</sup>, Jayoun Lee<sup>1</sup>, Minjoo Kang<sup>1</sup>, Minkyung Shin<sup>1</sup>, Junho Moon<sup>3</sup>, Hyewon Lee<sup>4</sup>, Junho Jang<sup>5</sup>, Junwon Jung<sup>6</sup>, Jeonghwan Youk<sup>7</sup>

1 National Evidence-based Healthcare Collaborating Agency

2 Department of Internal Medicine, Seoul National University

3 Department of Hemato-Oncology, Kyungpook National University Hospital

4 Hematologic Malignancy Branch, National Cancer Center

5 Hemato-Oncology, School of Medicine, Sungkyunkwan University

6 Hemato-Oncology, School of Medicine, Yonsei University

7 KAIST Graduate School of Medical Science and Engineering

#### Background

There are many occasions wherein stem cell transplantations are required for complete remission in patients diagnosed with blood disorders. When there is no domestic donor with a full match for a patient with a blood disorder, transplantation has been traditionally performed from an overseas donor. Recently, haploidentical stem cell transplantations have been actively performed. As the current trend shows that number of haploidentical stem cell transplantations is continuously increasing, it becomes necessary to create evidence of how actively transplantations need to be performed from overseas donors.

#### Objective

The objective of this study is to compare the clinical efficacy and economical result of allogeneic stem cell transplantations from domestic donors with those from overseas donors in each major blood disorder.

Through this study, a domestic evidence on the clinical efficacy and economical result of allogeneic stem cell transplantations from domestic and overseas donors could be created.

## □ Methods

### I. Survey on preferred donor for stem cell transplantation

A survey was conducted to investigate the preference of domestic hematologists on donors. For the four blood disorders (acute myeloid leukemia, acute lymphoblastic leukemia, chronic myeloid leukemia, and aplastic anemia) that frequently require stem cell transplantations, hypothetical scenarios were given, and the respondents were asked to choose the best donor and the reason of their choice for each scenario. This survey was conducted on participants during the spring meeting of the Korean Society of Hematology (29th to 30th May 2015).

### II. Clinical result of comparison between stem cell transplantation donors through a retrospective medical record study

To compare a patient group that has received stem cell transplantations from domestic donors with a patient group that has received stem cell transplantations from overseas donors, a multicenter retrospective chart review was conducted. Six hundred and sixty-one patients who received stem cell transplantations in five domestic medical centers (Seoul National University Hospital, Severance Hospital, Samsung Medical Center, Kyungpook National University Hospital, and National Cancer Center) from 1st January 2005 to 30th April 2015 were selected. Through the 1st CRF investigation, the information of recipients and donors and the conditions during the transplantations were collected. Based on these data, a tendency score matching (sex, age, HLA matching, and CD34) was conducted. For the 269 patients who have been matched, the results of transplantation treatments (overall survival, relapse-free survival, GvHD, and infection) were investigated. The risk of death or recurrence due to nationality (domestic or overseas) of the stem cell transplantation donors was confirmed using the Cox's proportional hazards model and Kaplan-Meier survival curve.

### III. Treatment cost comparison between stem cell transplantation donors through health insurance claims data

Among the patients collected through the retrospective chart review, we identify the treatment cost differences among donors linked with the National Health Insurance Service claims data (NHIS-2016-1-053) in 159 patients who have received stem cell transplantations from national and public medical centers (Seoul National University Hospital, Kyungpook National University Hospital, and National Cancer Center). The cost that patients had to pay to find donors, which was not claimed as part of their health insurance, was included through a calculation based on the data of the stem cell transplantation society of each country. When a donor was available, the Wilcoxon rank-sum test was used to see whether the total cost, which included the cost that patients had to pay, was significantly different between two groups.

#### Results

- So far, domestic hematologists prefer overseas donors with full match due to the clinical efficacy.
- The clinical comparison between stem cell transplantations from domestic and overseas donors shows that the transplantation results are similar in terms of survival rate, adverse effect, etc.
- In acute myeloid leukemia, the comparison between haploidentical transplantations and transplantations from overseas donors confirms that the transplantation results are similar.
- The medical cost comparison between donors for allogeneic stem cell transplantations shows that receiving a transplantation from an overseas donor due to donor unavailability costs approximately KRW 51,590,000.

## **I. Survey on preferred donor for stem cell transplantation**

The survey result shows that more than half of the respondents in each case prefer overseas donors whose human leukocyte antigen (HLA) types are fully matched. The reason is that it is expected to have the best clinical efficacy when a transplantation is performed from a donor with a full match. Although the reports that show the haploidentical transplantations have good results are continually produced, domestic hematologists still prefer overseas donors with a full match.

## **II. Clinical result of the comparison between stem cell transplantation donors through a retrospective medical record study**

The comparison between stem cell transplantations from domestic and overseas donors while the disease and transplantation condition are matched shows that: 1) the results of the allogeneic stem cell transplantations from overseas donors are similar to the transplantations from the Korea Marrow Donor Program (KMDP). The results are not only similar in acute leukemia, but also in aplastic anemia, which is a benign blood disorder. 2) The number of the graft-versus-host disease (GvHD) occurrences that were thought to possibly occur between races did not increase significantly, and the number of deaths related to the transplantations in 30 days did not also increase significantly.

The retrospective study that analyzed the haploidentical transplantations and transplantations from overseas donors shows that they have similar results in the overall survival rate and patient groups with acute leukemia. There was no significant difference in rejection and infection, which are complications after a transplantation. In patient groups with acute leukemia, there was no significant difference in occurrences of chronic GvHD.

## **III. Medical cost comparison between stem cell transplantation donors through health insurance claims**

The medical cost, including the transplantation for one year, was calculated and it was found that a patient who received a transplantation

from a domestic donor paid KRW 38,080,000, while a patient who received a transplantation from an overseas donor paid KRW 89,670,000. Therefore, a patient who received a transplantation due to the unavailability of a domestic donor paid approximately KRW 51,590,000. For the entire follow-up period, the cost was approximately KRW 59,290,000 so that the difference between the two groups became larger.

## Conclusions

When there was no domestic donor with a full match or a KMDP donor, a transplantation from an overseas donor caused an additional cost of about KRW 60 million, but it was a useful method that induced a long-term survival of 30-40% in terms of the clinical efficacy. It is thought that the result of the haploidentical transplantations is not too behind compared with the transplantations from overseas donors. However, the conclusion of which transplantation is advantageous in terms of clinical efficacy and cost can be determined by additional studies. Therefore, a survey of the haploidentical transplantation cost and joint study with the Korean Blood and Marrow Transplant Registry (KBMTR) are necessary as a follow-up study.

## Acknowledgement

This research was supported by National Evidence-based Healthcare Collaborating Agency (NECA) funded by the Ministry of Health and welfare (grant number: NC15-005, NC16-001).

## **Key words**

: overseas donor, allogeneic stem cell transplantation, comparative-effectiveness