



## Mature T cell and Natural Killer Cell Tumor Allogeneic Hematopoietic Stem Cell Transplantation in the Kyoto Stem Cell Transplantation Group: Effect of Donor Source

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### Abstract

Although allogeneic hematopoietic stem cell transplantation (allo- HSCT) is the crucial strategy to cure cases with mature T and natural killer (NK) cell tubercles leukemia, especially those with regressed/ refractory conditions, there's no agreement strategy for patron selection. We retrospectively anatomized the issues of allo- HSCT in 111 cases in 15 Japanese institutions as amulti-institutional common exploration design. Thirty- nine cases entered bone gist or supplemental blood stem cell transplantation from affiliated benefactors (rBMT/ rPBSC), 37 entered BMT/ PBSC from unconnected benefactors (uBMT/ uPBSC), and 35 entered cord blood transplantation (CBT). Overall survival (zilches) and progression-free survival (PFS) at 4 times were 42 and 34, independently. The accretive frequentness of relapse and nonrelapse mortality was 43 and 25. In multivariate analysis, CBT showed similar zilches with rBMT/ rPBSC( rBMT/ rPBSC versus CBT hazard rate( HR),1.63; P = .264) and better zilches compared with uBMT/ uPBSC( HR,2.99; P = .010), with a trend toward a lower relapse rate( rBMT/ rPBSC versus CBT HR,2.60; P = .010; uBMT/ uPBSC versus CBT HR,2.05; P = .082). This superiority of CBT was more definite in on- complaint cases (zilches rBMT/ rPBSC versus CBT HR, 5.52; P = .021; uBMT/ uPBSC versus CBT HR, 6.80; P = .007). More complaint control was also explosively associated with better zilches and PFS with lower relapse rate. In conclusion, allo- HSCT is salutary for the survival of cases with mature T and NK cell tubercles leukemia if performed in a timely fashion. Since CBT showed favorable survival with a lower relapse threat, it could be a favored volition, especially in on- complaint cases.

**Keywords:** Mature T and NK cell neoplasms; T cell lymphomasNK cell tubercles leukemia; Allogenic hematopoietic stem cell transplantation; Cord blood transplantation; Donor source

### Introduction

Mature T cell and natural killer (NK) T cell tumors correspond of miscellaneous subtypes with different pathological, morphological, and clinical features. Since these subtypes are known to have a poor prognostic, original treatment strategies, except for grown-up T cell leukemia/ carcinoma or early- stage extra nodal NK/ T cell carcinoma, remain under discussion. In particular, control of regressed/ refractory conditions remains a major problem [1]. Although autologous hematopoietic stem cell transplantation (bus- HSCT) as an outspoken treatment or as a part of exertion treatment in first complete response (CR) has bettered clinical issues and is now recommended in some subtypes and in some technical cases, bus- HSCT is considered inadequate to profit overall survival (zilches), especially in regressed refractory or heavily treated mature T and NK cell tumors.

For utmost cases with regressed/ refractory conditions, allogeneic hematopoietic stem cell transplantation (allo- HSCT) is the sole strategy that can give long- term absolution of the carcinoma. The major goods of allo- HSCT are the high- cure chemotherapies used as conditioning rules and graft- versus- leukemia/ carcinoma (GVL) goods after transplantation, which enable durable defensive monitoring by all reactive lymphocytes against carcinoma relapse [2]. Owing to recent advances in allo- HSCT, similar as expanded patron sources with multiple HLA mismatches or cord blood (CB) units, advancements in conditioning through the use of nonmyeloablative rules and other probative strategies, allo- HSCT can be applied in a broader population. still, transplantation strategies for mature T NK cell tubercles, especially regarding patron selection, haven't yet been clarified, owing substantially to the small number of cases. Similar opinions still largely depend on an expert's opinion or the programs

at each transplantation center. Therefore, in this study, we anatomized data on allo- HSCT in several different Japanese institutions as amulti-institutional common exploration, to achieve better patron selection in allo- HSCT for cases with these rare carcinoma subtypes with poor prognostic [3].

### Material and Methods

#### Data Collection

All transplantation data in Japan are collected at the Japanese Data Center for Hematopoietic Cell Transplantation. These data are redistributed upon request from each transplant center or from eachmulti-institutional exploration group. In this study, we anatomized the data recaptured from the public registry to ormulti-institutional exploration group, Kyoto Stem Cell Transplantation Group, conforming of 15 Japanese transplantation centers. This study was approved by the Institutional Review Board of each transplantation center, including Kyoto University Hospital, where this study was organized [4].

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## Cases

This analysis included adult cases (age  $\geq 18$  times) that passed their first allogeneic HSCT for mature T and NK cell carcinoma/ leukemia between 1998 and 2016. Cases with adult T cell leukemia/ carcinoma were barred, because these are biologically distinct subtypes deduced from viral infection [5].

## Endpoints and Delineations

The primary endpoint of this study was OS. The secondary endpoints were progression-free survival (PFS), relapse, and nonrelapse mortality (NRM). Zilches were examined by calculating death from any cause after transplantation; survivors at last follow-up were censored. Relapse was defined as any relapse or progression of the complaint after transplantation. PFS was examined by calculating treatment failure; carcinoma progression/ relapse and death from any cause after stem cell infusion. NRM was defined as death without any substantiation of carcinoma progression/ relapse. Myeloablative exertion (MAC) or reduced-intensity exertion (RIC) rules were classified grounded on the report of the factory of the Center for International Blood and Marrow Transplant Research [6]. Carcinoma status at transplantation was defined according to the report of a transnational factory to regularize the response criteria for non-Hodgkin carcinoma or its revised interpretation. To determine the number of HLA mismatches, low-resolution typing ways for 6 loci (HLA-A, -B, and -DR) were used for bone marrow or supplemental blood stem cell transplantation from affiliated benefactors (rBMT/ rPBSTCT), and high-resolution typing ways for 8 loci (HLA-A, -B, -C, and -DR) were used for BMT/ PBSTCT from unconnected benefactors (uBMT/ uPBSTCT).

## Statistical Analysis

Descriptive statistics were used to epitomize variables related to patient characteristics. Zilches and PFS were estimated by Kaplan-Meier styles, and carcinoma relapse and NRM were calculated grounded on accretive prevalence curves. However, the missing data were included as a separate order in each analysis, if a variable had further than 5 missing values. A Cox retrogression hazards model and contending-threat retrogression model were used to perform multivariate analysis to assess the prognostic significance of each patron source (related benefactors, unconnected benefactors, cord blood units) on each endpoint. Covariates were named in an accretive manner with a variable retention criterion of  $P < .20$  before the multivariate analysis. Covariates assessed in the model were as follows: philanthropist's coitus, International Prognostic Index value, histological subtypes, number of chemotherapy rules entered before allo-HSCT, history of bus-HSCT, interval from carcinoma opinion to allo-HSCT, status of carcinoma control at transplantation (controlled or active conditions), center effect (number of allo-HSCTs for mature T and NK cell tubercles in each transplantation center), intensity of exertion authority (RIC or MAC), use of total body irradiation (TBI) as exertion, and GVHD prophylaxis (tacrolimus- or cyclosporine-grounded) [7]. Number of HLA mismatches wasn't entered into the model to assess the impact of patron sources, given the strong relationship between them. We performed a fresh analysis to assess the impact of HLA mismatches, using another order to classify affiliated and unconnected benefactors into 2 orders by the presence of HLA mismatch (HLA-MM) related benefactors (rBMT/ rPBSTCT) with or without HLA-MM and unconnected benefactors (uBMT/ uPBSTCT) with or without HLA-MM and CBT. The status of carcinoma control at transplantation was caught on as follows: the controlled complaint group included cases who achieved CR or partial response (PR) after the final chemotherapy;

the active complaint group included cases who presented with stable complaint, progressive complaint (PD), or regressed complaint (RD) after the final chemotherapy session and who passed transplantation without antedating induction remedy. All statistical analyses were performed with State interpretation 15 (StataCorp, College Station, TX) [8].

## Discussion

Our study reconfirmed that allo-HSCT is salutary for survival in certain patient groups with mature T and NK cell carcinoma/ leukemia if performed with applicable patron sources in a timely fashion. This result is compatible with former reports from a single center (30), the data from which were included in the present study.

Our results show that CB units were a favorable patron source for mature T and NK cell carcinoma/ leukemia cases that redounded in similar zilches and PFS to affiliated benefactors and supposedly superior zilches and PFS compared with unconnected benefactors, especially in those with unbridled complaint. Utmost CBTs in our cohort were performed using HLA-MM CB units, and these were associated with a lower prevalence of relapse compared with other patron sources, especially HLA-matched benefactors. This result might reflect the potent GVL goods deduced from HLA mismatches in CB units as reported in colorful myeloid conditions. Although the GVL effect has been suggested to be effective for mature T and NK carcinoma cells it's frequently neutralized by NRM relating to GVHD and is weakened by treatment for habitual GVHD. Our result suggested that it might be easier to balance the benefit of GVL and the threat of GVHD deduced from HLA-MM if we chose CB units as a patron source. Considering that unconnected patron HSCT showed inferior issues compared with CBT, CB units should be considered a favorable volition patron source when applicable affiliated benefactors aren't available. Also, for cases with unbridled mature T- and NK- cell lump, it could be considered as a preferred patron source [9].

In conclusion, in the present study, CBT showed favorable issues in mature T and NK cell tubercles leukemia. It had a lower prevalence rate of relapse compared with transplantation from other patron sources, performing in similar survival with rBMT/ rPBSTCT and superior survival to uBMT/ uPBSTCT. CBT could be a promising option with implicit GVL goods, especially for cases with unbridled tubercles. The achievement of better complaint control, at least PR, and acceptable patron selection at acceptable timing are crucial to performing effective allo-HSCT for cases with mature T and NK cell tumors [10].

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## Conflict of Interest

There are no conflicts of interest to report.

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