ELSEVIER

Blood 142 (2023) 4960–4961

The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

723.ALLOGENEIC TRANSPLANTATION: LONG-TERM FOLLOW-UP AND DISEASE RECURRENCE

Is Allogeneic Hematopoietic Stem Cell Transplant (HCT) in First Remission Beneficial to Acute Myeloid Leukemia (AML) Patients with Isocitrate Dehydrogenase(IDH) Mutations?

Ayman Sayyed, MD[1], Taehyung Simon Kim[1], Silvia Park[2], Jae-Sook Ahn[3], Aly Karsan, MD[4], Marie-France Gagnon, MD[5], Julie Bergeron, MD[5], Hyeoung-Joon Kim[3], Heeje Kim, MDPhD[6], David Sanford, MD FRCPC[7], Andre C. Schuh, MD FRCPC[1], Dennis Dong Hwan Kim, MD PhD[1]

[1]Department of Medical Oncology and Hematology, Princess Margaret Cancer Centre, University Health Network, Toronto, Canada
[2]Department of Hematology, Catholic Hematology Hospital, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South)
[3]Chonnam National University Hwasun Hospital, Hwasun, Korea, Republic of (South)
[4]BC Cancer Research Institute, University of British Columbia, Vancouver, CAN
[5]CEMTL, installation Maisonneuve-Rosemont, Montreal, Canada
[6]Department of Hematology, Seoul St. Mary's Hospital, College of Medicine, The Catholic University of Korea, Seoul, Korea, Republic of (South)
[7]Leukemia/Bone Marrow Transplant Program of BC, British Columbia Cancer Agency, University of British Columbia, Vancouver, BC, Vancouver, Canada

Introduction

Somatic mutations in the isocitrate dehydrogenase 1 and 2 genes (IDH1 and IDH2) are relatively frequent in acute myeloid leukemia (AML) but with heterogeneous prognoses. The prognostic impact of this AML subtype with IDH mutations may be influenced by the comutational status with other somatic mutation, the specific types of IDH1/2 mutation (ie, IDH1 R132, IDH2 R140, and IDH2 R172).

Allogeneic stem cell transplant allogeneic HCT represents a curative option for subgroups of AML patients (pts), but not for all subtypes. Transplant referral is made based on the ELN risk group classified into favorable, intermediate, and adverse risk. Although many AML pts with IDH1/2 mutations are referred to allogeneic hematopoietic stem cell transplantation (HCT) and transplanted, however it is not fully elucidated whether allogeneic HCT brings definite survival benefit to this group of the pts.

Statistical attention is to be paid to the time to HCT from CR1 achievement. Before HCT, the case should be counted as a case of no HCT, while after HCT this case can be accounted as the case received HCT using the Mantel-Byar test (MBT). To handle immortal time bias, the Mantel-Byar method was used to depict outcomes during the follow-up period. Kaplan-Meier curves were avoided as they can introduce immortal bias, considering the period of time before treatment as part of the treatment arm. Instead, the MBT and landmark methods were employed to address this issue. Allogeneic HCT was treated as a time-dependent variable to prevent immortal bias. The aim of the present study is to identify if AML pts with IDH mutations obtain survival benefit from allogeneic HCT in CR1 using HCT as a time-dependent covariate with using Mantel-Byar test.

Patients & Method

We conducted a retrospective study that included 1,228 adult pts who were diagnosed with AML and achieved CR1 in 5 centers (Toronto, Vancouver, and Montreal, Canada; Hwasun and Seoul, South Korea) from January 1997 to January 2020. Next-generation sequencing was performed in each institution according to their own standard targeted sequencing panel. We considered allogeneic HCT in CR1 as a time-dependent covariate and used a Mantel-Byar test to avoid immortal bias. Relapse-free survival (RFS) was selected for the primary endpoint, defined as the time from CR1 to relapse or death from any cause. EZR software version 1.41 was used throughout the study for statistical analysis.

Results

Out of 1228, a total of 238 pts (19.4%) was found to have IDH1/2 mutation, among whom 92 pts (38.6%) had isolated IDH1 mutations, 140 pts (58.8%), isolated IDH2 mutations, and 6 pts (2.5%) having coexistence of IDH1 and IDH2 mutations.

With a median follow-up duration of 20.8 months (mo) (1-194.3 mo) among survivors after achieving CR1, 91 pts died while 115 pts experienced relapse. One hundred twenty-one pts received HCT in CR1, and 44 pts relapsed after HCT. The 2-year overall survival of those 238 pts was 58.9% (51.3-65.6), and 2-yr RFS was48.9% (41.6-55.8)

Between the HCT (n=121) vs non-HCT group (n=117), there were no differences in sex, cytogenetic risk or other somatic mutation except NPM1 mutation which was more frequently detected in the non-HCT group (p =0.002). As expected, the HCT group was younger (55 years (15-74 yrs)) than non-HCT group (62 years (27-82 yrs), p<0.001).

First, the RFS and OS was compared between HCT vs non-HCT groups considering HCT as non-time dependent covariate. The 2-year RFS rate was higher in the HCT group (61.0%) compared to the non-HCT group (37.0%, p= 0.0002). However, it was not translated into superior OS in the HCT group: 2-year OS rate, 64.4% in the HCT group vs 53.7% in the non-HCT group, p=0.1).

We have conducted time-dependent analysis taking taken HCT in CR1 into account as a time-dependent (td) covariate using MBT. The trend of superior RFS in HCT group was reproduced in MBT: HCT in CR1 was found to improve RFS (Hazard ratio [(HR) of 0.62, (95% C.I. [0.42-0.92]; p=0.02)] as shown in Fig.1B utilizing Simon-Makuch plot. However, Multivariate analysis (MVA) for RFS did not confirm HCT in CR1 as an independent prognostic factor for RFS, while Following factors were found to be associated with RFS adversely: age > 60 years, presence of DNMT3A mutation, and presence of IDH1 mutation.

Conclusion

Allogeneic HCT in CR1 could bring some survival benefit on RFS in AML pts with IDH1/2 mutation, but not confirmed in MVA. Further study is warranted to reach a clearer conclusion with larger number of

Disclosures Bergeron: *BMS:* Honoraria; *Amgen:* Honoraria; *Abbvie:* Honoraria; *Jazz:* Honoraria; *Gilead:* Honoraria; *Taiho:* Honoraria; *Pfizer:* Honoraria. **Sanford:** *AbbVie:* Honoraria; *Astellas:* Honoraria. **Schuh:** *Bristol Myers Squibb:* Honoraria, Research Funding; *Astellas:* Honoraria, Research Funding; *Glycomimetics:* Research Funding; *Abbvie:* Honoraria, Research Funding; *Agios:* Honoraria, Research Funding; *Amgen:* Honoraria, Research Funding; *Kite/Gilead:* Research Funding; *Pfizer:* Consultancy, Honoraria; *Servier:* Honoraria, Research Funding; *Teva:* Consultancy, Honoraria. **Kim:** *Paladin:* Research Funding; *Pfizer:* Honoraria, Research Funding; *BMS:* Research Funding; *Novartis:* Consultancy, Honoraria, Research Funding.

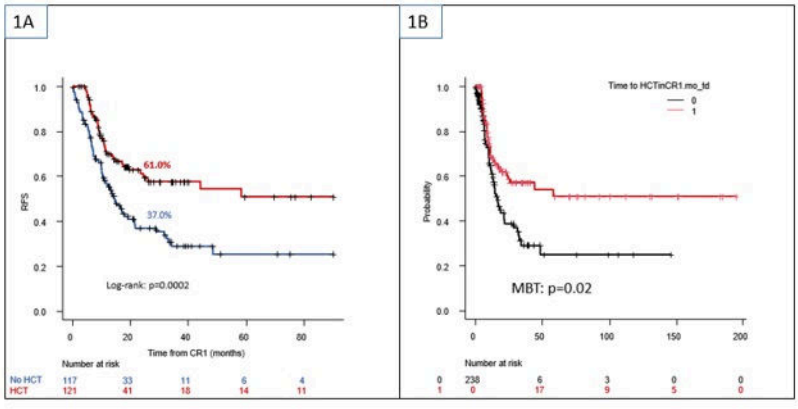

Fig.1. A: Kaplan-Meier plot of RFS, non-time-dependent HCT vs No HCT. B: Simon-Makuch plot of time-dependent allogeneic HCT on RFS.

Figure 1

https://doi.org/10.1182/blood-2023-191113