ABO mismatching and haploidentical hematopoietic stem cell transplantation in acute myeloid leukemia: a report from the ALWP of the EBMT

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Table 1
Early-onset viral infections and IPS*

	Total Patients n = 741	IPS (%) n = 41	No IPS (%) n = 700	P
Any viral	229	19 (46)	210 (30)	.04
CMV	116	4 (10)	112 (16)	0.38
EBV	27	4 (10)	23 (3)	.06
HHV-6	54	7 (17)	47 (7)	**.02**
HSV	6	2 (5)	4 (1)	.04
CAV	26	2 (5)	24 (3)	0.65

* Viral infections (excluding BK virus) within first 100 days post-HSCT.

Table 2
Early onset viral infection and BOS*

	Total Patients n = 741	BOS (%) n = 49	No BOS (%) n = 692	P
Any viral	242	22 (45)	220 (32)	.08
CMV	126	14 (29)	112 (16)	**.03**
EBV	27	2 (4)	25 (4)	0.70
HHV-6	56	5 (10)	51 (7)	0.41
HSV	7	1 (2)	6 (1)	0.21
CAV	26	0 (0)	26 (4)	0.17

* Viral infections (excluding BK virus) within first 100 days post-HSCT.

increased risk of developing IPS (P = .04), and trended towards significance for the development of BOS (P = .08). Nineteen of 41(46%) patients with IPS, and 22 of 49(45%) patients with BOS had a preceding EOVI (Tables 1 and 2). Early-onset HHV6 infections occurred in 7 of 41 (17%) patients with IPS versus 47 of 700 (7%) patients without IPS respectively, P = .02. There was no association between early-onset CMV or community acquired viral (CAV) infections and IPS. In contrast, early-onset CMV infections were associated with an increased risk of developing BOS post-HSCT (P = .03), with no association between early-onset EBV, HHV6, HSV, CAV infections and BOS noted. The median duration from viral infection to the onset of IPS was 25 days (range, 1-335 days) and the median duration from viral infection to the onset of BOS was 465 days (range, 76-1168).

Conclusion: HHV-6 infections within the first 100 days post-HSCT are associated with an increased risk of developing IPS, whereas CMV infections occurring during this 'early' post-HSCT period are associated with an increased risk for the development of BOS.

ALTERNATIVE DONORS

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ABO Mismatching and Haploidentical Hematopoietic Stem Cell Transplantation in Acute Myeloid Leukemia—a Report from the ALWP of the EBMT

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Background: About 30-50% of HLA-matched hematopoietic stem cell transplantation (HCT) are performed with ABOmismatch (ABO-MM) donor, which can be classified as either major, minor or bidirectional. The impact of ABO-MM on clinical outcome after HCT remains controversial and no large series is available to study the impact of ABO-MM in patients (pts) receiving haploidentical-HCT (haplo-HCT).

Methods: 837 pts with AML that underwent haplo-HCT from January 2005 to December 2014 were analyzed to study the long term impact of ABO-mismatching in haplo-HCT. The comparative analysis was performed between pts receiving ABO-matched vs. ABO-MM for common outcome variables.

Results: 522 (62%) pts received ABO-matched whereas 315 (38%) underwentABO-MMhaplo-HCT including 150 (18%) minor ABOMM (minor-A, 75 [50%]), 127 (15%) major ABO-MM (major-O, 98 [77%]) and 38 (5%) bidirectional ABO-MM (Bidirectional-A, 20 [53%]). Median agewas 42 years (range, 18-77) andwas not significantly different between ABO groups (P = .67). The median follow-up period was 36 months (IQR, 23-53). Median year of transplantationwas 2011. More than half of ptswere in CR1 and nearly one third of pts were with active disease prior to transplantation. 497 (59%) pts received ablative and 340 (41%) reduced intensity or non-ablative conditioning regimen. 219 (26%) of pts received BM, 240 (29%)BM+PB, 378 (45%) PB alone and 123 (15%) ex-vivo T-cell depleted grafts. There were no significant differences in distributions of pts and transplant characteristics among ABO- groups. 771 (94%) pts engrafted and the percentage of engraftmentwas lower in the major mismatch group (88% vs 95% in other group, P = .007). The cumulative incidences (CI) of day 100 grade II-IV acute GVHDwas 31% (III-IV, 10%) and the 3-year CI of chronic GVHD was 31% (95% CI, 27-34), and were not significantly different between the ABO-groups (P = .124 and .392). There was no differences in OS, RI, and NRM between ABOgroups. Bidirectional ABO-group had improved 3-year LFS (67%) and GFRS (54%) compared to other ABO-group in univariate analysis. Therewas no impact of ABO-MM when T-cells replete and T-depleted groups analyzed separately. In multivariate analysis, our data showed no significant differences in OS, LFS, RI, NRM, and chronic GVHD between ABO-groups. The analyses were performed separately for pts receiving PB and BM+/-PB grafts. There was no statistical difference between ABO-groups for OS, LFS, RI, NRM, GFRS and chronic GVHD in pts receiving PB grafts. However,

among BM group, pts with minor ABO-MM recipients had significantly higher acute GVHD (HR 2; 95% CI, 1-4; *P* = .048) without impacting other transplant outcome.

Conclusion: Despite the limitation of a retrospective registry based study, our large series shows no significant long term outcome difference between ABO matched and mismatched groups after haplo-HCT in current era.

LEUKEMIA

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Outcomes of Allogeneic Hematopoietic Cell Transplantation for AML with Complex Karyotypes: A Retrospective Study From the Acute Leukemia Working Party of the European Society for Blood and Marrow Transplantation and MD Anderson Cancer Center

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Introduction: Allogeneic hematopoietic stem cell transplantation (AHSCT) is the only curative treatment for CK AML which otherwise has dismal outcomes. Here we aimed to identify prognostic factors associated with post-transplant survival in patients with CK AML using combined data from the EBMT and MDACC.

Methods: A total 1342 consecutively transplanted patients with CK (≥3 cytogenetic abnormalities) AML reported to EBMT (N = 1118) and at MDACC (N = 224) between 01/2000-12/2015 were included. The median age was 52 years (range 18-76 years). Seven hundred and twenty-nine patients (54.3%) were male, 239 patients (17.8%) had secondary AML. Disease status before transplant was CR1, CR2 and active disease in 877 (65.3%), 77 (5.7%) and 388 (29%), respectively. Donors were MRD, MUD and MMUD in 749 (55.8%), 513 (38.2%) and 80 (6%), respectively. Conditioning regimens were various, mostly either busulfan-based (53.7%) or TBI-based (26.7%). Seven hundred and thirty-nine patients (55%) received MAC. The main stem cell source was PB (81%). Median follow-up duration was 35.5 months (range 8-174 months).
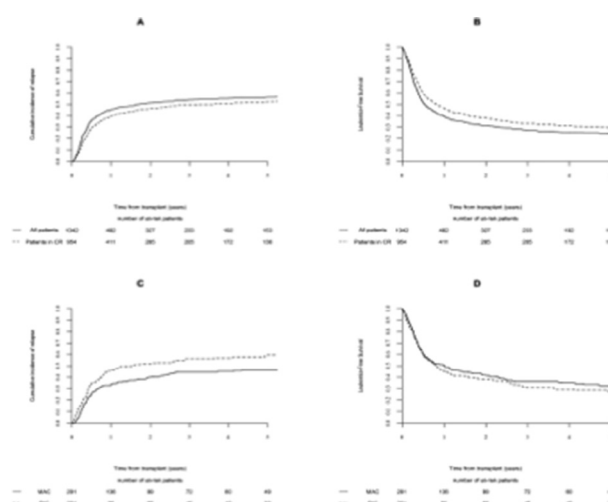

Figure 1. (A) CI of relapse for all patients and patients in CR; (B) LFS for all patients and patients in CR; (C) CI of relapse for patients age 40-60 years in CR with MAC, RIC; (D) LFS for all patients age 40-60 years in CR with MAC, RIC.

Results: Engraftment occurred in 96.3% and 69.7% had full donor chimerism. The cumulative incidence (CI) of acute GVHD grade II-IV and grade III-IV at 2 years was 26.3% and 8.4%, respectively, whereas CI of chronic GVHD was 30.9% with extensive chronic GVHD 17.8%. LFS, OS, CI of relapse, NRM at 2 years for the whole group was 31.3%, 36.8%, 51.1% and 17.6%, respectively, while 2-year GVHD-free, relapse-free survival (GRFS) was 19.8%. LFS, OS, GRFS, CI of relapse and NRM at 2 years for patients transplanted in CR1 was 38.4%, 44.5%, 23.8%, 46% and 15.7%, respectively (Figure 1A,B). Patients age 40-60 years transplanted in CR1 with MAC demonstrated lower relapse compared with RIC (40.2% versus 51%, *P* = .005), offset by a higher NRM (18.2% versus 9.8%, *P* = .037), associated with higher incidence of acute GVHD, and a non-significant difference in LFS (Figure 1C,D).

In multivariable analysis, advanced age, transplantation in active disease, secondary AML and presence of deletion or monosomy 5 or 7 predicted poor LFS and OS. All of these factors as well as year of transplant (before 2010) also predicted poor GRFS. Prognostic factors for relapse were age, secondary AML, active disease at transplant and presence of deletion or monosomy 5, while prognostic factors for NRM were older age, active disease, use of a mismatched unrelated donor and deletion or monosomy 7.

Conclusions: In this largest analysis of complex karyotypes AML patients, relapse remains the most common cause of treatment failure with 45% for patients in CR1 and 63.5% for patients not in remission relapsing after transplant. The only modifiable factors at this time are performing transplantation in CR1 as soon as the donor is available. Novel approaches are needed to decrease relapse rate and improve survival in these patients.

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Analysis of Transplantation Rate and Overall Treatment Efficacy by Age for Patients Aged 60 to 75 with Untreated Secondary Acute Myeloid Leukemia (AML) Given CPX-351 Liposome Injection Versus Conventional Cytarabine and Daunorubicin in a Phase III Trial

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