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# POSTER ABSTRACTS

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

### Analysis of the Impact of Whole Blood and T-Cell Donor Chimerism after Allogeneic Stem Cell Transplant

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**Background**: Allogeneic stem cell transplant (alloSCT) is one of the few currently available therapies to cure acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). Positive outcomes are dependent on engraftment of donor cells to provide hematopoiesis as well as a graft-versus-tumor effect. Measurement of whole blood (WB) and T-cell (TC) chimerism at routine intervals post alloSCT allows for monitoring of engraftment. Development of mixed donor chimerism (MC) may indicate impending graft failure or disease relapse. The ideal frequency for chimerism measurements as well as the role of WB versus TC chimerism remains unclear. In this study, we analyzed the impact of WB versus TC mixed chimerism on survival outcomes in patients with AML and MDS. Furthermore, we studied baseline factors associated with the development of MC.
**Methods**: In this retrospective analysis, adults with AML or MDS who received an alloSCT between January 1, 2016 and February 1, 2022 that had at least 1 donor chimerism measured on Day 30 (D30), Day 60 (D60), Day 90 (D90) at Juravinski Hospital and Cancer Centre (Hamilton, ON, Canada). Baseline demographic and transplant-related characteristics were collected. AML and MDS diagnoses were based on WHO 2016 classification of myeloid neoplasm and acute leukemia. Conditioning intensities were classified according to CIBMTR definitions. A total of 271 transplants were completed during the study period for AML or MDS. 128 were excluded from the analysis (chimerism testing not performed (n=121), second transplants (n=7)). We analyzed a total of 143 patients with median age of 63 years (19 - 76) who were transplanted for AML (n=105) and MDS (n=38). Donors were HLA-matched siblings (MRD, n=26), unrelated donors (MUD (8/8 or 7/8), n=85) or haploidentical related donor (MMRD, n=32). All patients except one received peripheral blood stem cell grafts. For alloSCT, 20 % of patients received myeloablative conditioning (MAC) and 80% received reduced-intensity conditioning (RIC). Complete chimerism (CC) was defined as $\geq$95%, whereas MC was defined as $\leq$95%. All chimerism measurements were measured using a PowerPlex® 16 System (Promega) (Hamilton Regional Laboratory Medicine Program, Hamilton, ON).
**Results**: In our cohort, OS at 2 years was 57% and RFS 49%. Of the baseline factors, only disease-risk based on ELN 2022 for RFS with a hazard ratio (HR) of 1.43, 95% CI [0.83, 2.49] for adverse risk and HR 0.53 95% CI [0.23, 1.03] (p=0.03) for favourable risk. WB MC was detected in 22%, 22%, 23% of patients on D30, D60, and D90, respectively. TC MC was detected in 48%, 46%, and 43% of patients on D30, D60, and D90, respectively. WB MC had a strong negative impact on RFS, with a HR of 2.81, 95% CI [1.69, 4.66; p<0.001] on D30, 3.07, 95% CI [1.67, 5.66; p<0.001] on D60 and 4.77, 95% CI [2.47, 9.22; p<0.001] on D90. The influence of TC MC on RFS was also significant at all time points. Of 101 patients who were alive and did not have a relapse prior to D90 and had D30 chimerism and D90 chimerism evaluated, the patients who had a mixed WB and

TC chimerism on D90 had a HR of 6.13, 95% CI [2.23, 16.85] and HR 2.73, 95% CI [1.24, 5.98] for RFS, which was statistically significant even after adjusting for known information of D30 WB/TC chimerism status (Table 1). WB MC had a strong negative impact on OS with a HR of 2.67, 95% CI (1.54, 4.64; p=0.001) on D30, 2.81, 95% CI (1.47, 5.38; p=0.002) on D60 and 4.78, 95% CI (2.47, 9.24; p<0.001) on D90. Again, the later time points remained statistically significant, when adjusting for known D30 chimerism status. The influence of TC MC on OS was also significant at all time points, however only a non-significant trend remained at later time points when adjusting for D30 TC chimerism (Table 2). We analyzed baseline factors predictive for D30 chimerism. For WB chimerism, only donor source remained statistically significant (p=0.038) with MMRD having a lower HR for MC 0.39, 95% CI [0.11, 1.41] and MRD having a higher HR for MC 2.33, 95% CI [0.9 - 5.99].

**Conclusions**: Our data confirm that a mixed chimerism as early as D30 post-alloSCT can have a detrimental impact on outcomes (RFS and OS) in alloSCT. Patients receiving haploidentical alloSCT had a lower risk to develop mixed chimerism in our cohort. These dismal outcomes of patients with mixed chimerism in our cohort provides a strong rationale to study interventions such as novel maintenance strategies or donor-lymphocyte infusions in this patient group.

**Disclosures Garcia-Horton:** *BMS:* Honoraria; *Avir Pharma:* Honoraria. **Khalaf:** *Novartis:* Consultancy, Honoraria; *Pfizer:* Consultancy, Honoraria; *Paladin:* Consultancy, Honoraria; *Astellas:* Consultancy, Honoraria; *Jazz:* Consultancy, Honoraria; *Taiho:* Consultancy, Honoraria; *Abbvie:* Consultancy, Honoraria; *BMS:* Consultancy, Honoraria. **Walker:** *Sanofi:* Honoraria, Research Funding. **Leber:** *Gilead/KITE:* Honoraria, Speakers Bureau; *Treadwell:* Honoraria, Speakers Bureau; *Roche:* Honoraria, Speakers Bureau; *Celgene:* Honoraria, Speakers Bureau; *Otsuka:* Honoraria, Speakers Bureau; *Astellas:* Honoraria, Speakers Bureau; *Astex:* Honoraria, Speakers Bureau; *AMGEN:* Honoraria, Speakers Bureau; *Palladin Canada:* Honoraria, Speakers Bureau; *Jazz Canada:* Honoraria, Speakers Bureau; *Taiho Canada:* Honoraria; *Novartis Canada:* Consultancy, Honoraria, Speakers Bureau; *Janssen Canada:* Honoraria, Speakers Bureau; *Pfizer Canada:* Consultancy, Honoraria, Speakers Bureau; *Bristol Myers Squibb Canada:* Honoraria, Speakers Bureau; *Alexion Canada:* Honoraria, Speakers Bureau; *AbbVie Canada:* Consultancy, Honoraria, Speakers Bureau. **Lepic:** *Sanofi:* Honoraria. **Pond:** *Merck:* Consultancy; *Astra-Zeneca:* Consultancy; *Profound Medical:* Consultancy; *Takeda:* Honoraria, Membership on an entity's Board of Directors or advisory committees. **Berg:** *Incyte:* Other: Travel Funding; *Bristol Myers Squibb:* Honoraria; *AVIR Pharma:* Honoraria; *Jazz Pharmaceuticals:* Honoraria; *Riemser Pharma GmbH:* Honoraria; *Imago Biosciences (a subsidiary of Merck):* Research Funding; *Celgene:* Honoraria, Other: Travel Funding; *Takeda Pharma:* Honoraria; *Astellas:* Other: Travel Funding; *Abbvie:* Other: Travel Funding; *Alexion:* Other: Travel Funding.

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## Table 1. Impact of Donor Chimerism Status on Relapse-Free Survival

| | Classification | HR (95 % CI) | p-value |
|---|---|---|---|
| **Univariate Analysis** | | | |
| Day 30 WB | Mixed vs Complete | 2.81 (1.69, 4.66) | <0.001 |
| Day 30 TC | Mixed vs Complete | 2.49 (1.51, 4.09) | <0.001 |
| Day 60 WB (n=101) | Mixed vs Complete | 3.07 (1.67, 5.66) | <0.001 |
| Day 60 TC (n=101) | Mixed vs Complete | 2.46 (1.35, 4.49) | 0.003 |
| Day 90 WB (n=107) | Mixed vs Complete | 4.77 (2.47, 9.22) | <0.001 |
| Day 90 TC (n=107) | Mixed vs Complete | 2.86 (1.51, 5.43) | 0.001 |
| **Adjusted for Day 30 Status** | | | |
| Day 60 WB (n=101) | Mixed vs Complete | 3.42 (1.03, 11.33) | 0.044 |
| Day 60 TC (n=101) | Mixed vs Complete | 2.74 (1.28, 5.86) | 0.010 |
| Day 90 WB (n=107) | Mixed vs Complete | 6.13 (2.23, 16.85) | <0.001 |
| Day 90 TC (n=107) | Mixed vs Complete | 2.73 (1.24, 5.98) | 0.012 |

## Table 2. Impact of Donor Chimerism Status on Overall Survival

| | Classification | HR (95 % CI) | p-value |
|---|---|---|---|
| **Univariate Analysis** | | | |
| Day 30 WB | Mixed vs Complete | 2.67 (1.54, 4.64) | 0.001 |
| Day 30 TC | Mixed vs Complete | 2.81 (1.47, 5.38) | <0.001 |
| Day 60 WB (n=102) | Mixed vs Complete | 3.07 (1.67, 5.66) | 0.002 |
| Day 60 TC (n=102) | Mixed vs Complete | 2.01 (1.04, 3.88) | 0.038 |
| Day 90 WB (n=107) | Mixed vs Complete | 4.78 (2.47, 9.24) | <0.001 |
| Day 90 TC (n=107) | Mixed vs Complete | 2.65 (1.34, 5.24) | 0.005 |
| **Adjusted for Day 30 Status** | | | |
| Day 60 WB (n=101) | Mixed vs Complete | 3.87 (1.16, 12.94) | 0.028 |
| Day 60 TC (n=101) | Mixed vs Complete | 1.80 (0.80, 4.06) | 0.15 |
| Day 90 WB (n=107) | Mixed vs Complete | 6.06 (2.55, 14.36) | <0.001 |
| Day 90 TC (n=107) | Mixed vs Complete | 1.89 (0.83, 4.26) | 0.13 |

**Figure 1**