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POSTER ABSTRACTS

617.ACUTE MYELOID LEUKEMIAS: BIOMARKERS, MOLECULAR MARKERS AND MINIMAL RESIDUAL DISEASE IN DIAGNOSIS AND PROGNOSIS

Role of Measurable Residual Disease (MRD) Testing for the Prediction of Late Relapses Following Allogeneic Hematopoietic Cell Transplantation in Adult Acute Myeloid Leukemia

Naveed Ali, MBBS[1], *Othus Megan, PhD*[2], *Eduardo Rodríguez-Arbolí, MD*[3], *Corentin Orvain*[3], *Filippo Milano, MD*[3], *Brenda M. Sandmaier, MD*[3], *Chris Davis*[1], *Ryan S. Basom*[1], *Frederick R. Appelbaum, MD*[1], *Roland B. Walter, MDPhDMS*[4,5,6]

[1] Clinical Research Division, Fred Hutchinson Cancer Center, Seattle, WA
[2] Public Health Sciences Division, Fred Hutchinson Cancer Center, Seattle, WA
[3] Translational Science and Therapeutics Division, Fred Hutchinson Cancer Center, Seattle, WA
[4] Translational Science and Therapeutics Division, Fred Hutchinson Cancer Research Center, Seattle, WA
[5] Division of Hematology, Department of Medicine, University of Washington, Seattle, WA
[6] Department of Laboratory Medicine and Pathology, University of Washington, Seattle, WA

BACKGROUND: Measurable residual disease (MRD) before and/or shortly after allogeneic hematopoietic cell transplantation (HCT) is an independent indicator of high post-HCT relapse risk in acute myeloid leukemia (AML). However, many relapses, particularly among patients with MRD, occur within the first 3 months after allografting, and the role of MRD testing in the identification of patients at risk of relapses occurring at later times is unknown.
METHODS: To address this uncertainty, we studied all adults ≥18 years with AML or MDS/AML based on 2022 International Consensus Classification criteria who received a first allograft while in first or second morphologic remission at a single institution between 4/2006 and 3/2023 and underwent MRD testing via multiparameter flow cytometry during the pre-HCT evaluation. In line with the performance characteristics of the assay, any detectable MRD was considered positive.
RESULTS: One thousand two hundred and sixty-two patients with AML (n=1,112 [88%]) or MDS/AML (n=150 [12%])underwent allograft following myeloablative (n=732 [58%]) or non-myeloablative (n=530 [42%]) conditioning regimens. Of these, 260 (21%) tested positive for MRD during the pre-HCT evaluation. With a median follow-up of 60.6 (range: 1.9-196.3) months after HCT among survivors, there were 589 deaths, 381 relapses, and 259 NRM events contributing to the probability estimates for relapse, overall survival (OS), relapse-free survival (RFS), and non-relapse mortality (NRM) in this cohort. 239/1,262 patients (19%) experienced disease recurrence (n=181 [14%]) and/or death (n=89 [7%]) within the first 100 days after allografting. Relapse (P<0.001) and death (P=0.002) but not NRM (P=0.29) before day +100 were more common among patients with pre-HCT MRD. Of patients alive without relapse at day +100, 93% (954 of 1,023) underwent bone marrow restaging studies between day 70 and 100 post-HCT. Among these 954 patients, 146 (15%) had MRD before HCT, whereas only 25 (3%) had MRD at day +70-100 testing. The latter had a significantly higher 3-year relapse risk (37% *vs.* 18%; P=0.002), and worse RFS (17% *vs.* 68%; P<0.001) OS (16% *vs.* 72%; P<0.001) and NRM (46% *vs.* 14%; P<0.001) relative to the 929 patients without MRD; for results of univariate regression models, see Table 1. Importantly, however, while 130 of the 146 patients (89%) with MRD before HCT tested negative for MRD at day +70-100, their outcomes were substantially worse compared to patients who tested negative for MRD before HCT and at day +70-100, with 3-year relapse risk of 38% *vs.* 15% (P<0.001), 3-year RFS of 47% *vs.* 71% (P<0.001), and 3-year OS of 53% *vs.* 75% (P<0.001), whereas 3-year NRM estimates were similar (14% *vs.* 14% (P=0.21). Qualitatively similar results were obtained when the cohort was restricted to patients with AML, and also when comparing patients undergoing myeloablative conditioning with those undergoing non-myeloablative conditioning, with a statistically significantly higher relapse risk and lower RFS and OS but not NRM for patients with MRD before HCT but no MRD at day +70-100 compared to those who tested negative for MRD before HCT and at day +70-100 (Table 1).
CONCLUSION: For AML and MDS/AML patients alive without relapse at day +100 after allografting, MRD testing at day +70-100 post-HCT identifies patients at increased risk of relapse and worse survival, but only a small number of patients will test positive at this post-HCT timepoint. While a high proportion of patients with MRD before HCT will test negative for MRD at day +70-100, their outcomes are substantially inferior to patients without MRD both before and at day +70-100 after HCT. These data suggest that all patients with pre-HCT MRD should be considered for pre-emptive therapeutic strategies, ideally

in the setting of well-controlled clinical trials, given their high risk of disease recurrence regardless of the post-HCT MRD information.

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TABLE. Results from univariate regression models in entire study cohort and individual patient subsets

	Relapse		Relapse-free survival		Overall survival		Non-relapse mortality	
	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value	HR (95% CI)	*P*-value
Entire study cohort								
Pre-HCT MRD status								
MRD^{neg} (n=1002)	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
MRD^{pos} (n=260)	3.49 (2.84-4.30)	<0.001	2.64 (2.23-3.13)	<0.001	2.33 (1.96-2.78)	<0.001	1.58 (1.16-2.15)	0.004
Post-HCT MRD status								
MRD^{neg} (n=929)	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
MRD^{pos} (n=25)	3.31 (1.55-7.06)	<0.001	4.22 (2.58-6.89)	<0.001	5.06 (3.09-8.28)	<0.001	5.24 (2.74-9.99)	<0.001
Pre/post-HCT MRD dynamics								
MRD^{neg}/MRD^{neg} (n=799)	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
MRD^{pos}/MRD^{neg} (n=130)	3.15 (2.28-4.35)	<0.001	2.21 (1.71-2.86)	<0.001	2.10 (1.61-2.74)	<0.001	1.32 (0.85-2.06)	0.21
AML patients only								
Pre-HCT MRD status								
MRD^{neg} (n=905)	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
MRD^{pos} (n=207)	4.04 (3.23-5.05)	<0.001	2.93 (2.44-3.53)	<0.001	2.51 (2.07-3.04)	<0.001	1.55 (1.08-2.21)	0.016
Post-HCT MRD status								
MRD^{neg} (n=846)	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
MRD^{pos} (n=19)	4.41 (2.06-9.42)	<0.001	4.84 (2.87-8.18)	<0.001	5.58 (3.31-9.44)	<0.001	5.30 (2.58-10.91)	<0.001
Pre/post-HCT MRD dynamics								
MRD^{neg}/MRD^{neg} (n=745)	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
MRD^{pos}/MRD^{neg} (n=101)	3.47 (2.46-4.91)	<0.001	2.39 (1,81-3.16)	<0.001	2.24 (1.69-3.02)	<0.001	1.33 (0.80-2.20)	0.27
MAC only								
Pre-HCT MRD status								
MRD^{neg} (n=569)	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
MRD^{pos} (n=163)	4.35 (3.32-5.71)	<0.001	3.20 (2.55-4.01)	<0.001	2.78 (2.20-3.52)	<0.001	1.60 (1.02-2.50)	0.039
Post-HCT MRD status								
MRD^{neg} (n=564)	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
MRD^{pos} (n=14)	2.68 (0.85-8.45)	0.093	4.53 (2.31-8.91)	<0.001	5.39 (2.73-10.62)	<0.001	7.04 (3.00-16.50)	<0.001
Pre/post-HCT MRD dynamics								
MRD^{neg}/MRD^{neg} (n=478)	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
MRD^{pos}/MRD^{neg} (n=86)	3.75 (2.56-5.50)	<0.001	2.77 (2.01-3.82)	<0.001	2.64 (1.88-3.70)	<0.001	1.43 (0.75-2.72)	0.28
Non-MAC only								
Pre-HCT MRD status								
MRD^{neg} (n=433)	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
MRD^{pos} (n=97)	2.68 (1.92-3.74)	<0.001	2.19 (1.69-2.85)	<0.001	1.99 (1.52-2.60)	<0.001	1.64 (1.07-2.52)	0.023
Post-HCT MRD status								
MRD^{neg} (n=365)	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
MRD^{pos} (n=11)	3.92 (1.42-10.83)	0.009	3.85 (1.88-7.90)	<0.001	4.83 (2.34-9.98)	<0.001	3.78 (1.37-10.42)	0.010
Pre/post-HCT MRD dynamics								
MRD^{neg}/MRD^{neg} (n=321)	1 (Reference)		1 (Reference)		1 (Reference)		1 (Reference)	
MRD^{pos}/MRD^{neg} (n=44)	2.13 (1.14-4.00)	0.018	1.64 (1.06-2.53)	0.026	1.58 (1.01-2.47)	0.043	1.33 (0.73-2.44)	0.36

Figure 1

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