

Outcomes of Patients with Relapsed/Refractory Acute Myeloid Leukemia Undergoing Allogeneic Hematopoietic Cell Transplantation in Active Disease

Ali Atoui*, Ahmad AqeI, Ammar Zahreddine, Jean El Cheikh, Ali Bazarbach, and Iman Abou Dalle,MD

Division of Hematology-Oncology, American University of Beirut Medical Center, Beirut, Lebanon



Introduction

- Relapsed/ Refractory (R/R) acute myeloid leukemia (AML) remains an aggressive disease.
- Allogeneic hematopoietic stem cell transplantation (ASCT) represents a potentially curative approach for patients with R/R AML.
- The overall mortality post-ASCT in patients with active disease (R/R AML) is 68% with median overall survival (OS) of 8 months.¹
- Mortality is mostly related to transplant-related complications and is higher in the first 90 days of transplant.
- There is still a gray area where the highlights in patient's clinical managements with respect to a best therapeutic choice and side-effects control are the mainstay of this field.

Objective

- To evaluate the efficacy and safety of myeloablative conditioning followed by ASCT in patients with R/R AML in active disease.

Methods

- This is a single center, observational, retrospective study of patients diagnosed with R/R AML (2016-2020) and treated at the American University of Beirut Medical Center in Lebanon.
- Data regarding patient baseline characteristics, disease-related factors, transplant-related factors, survival and complications were collected.
- Univariate analysis was used to identify main independent predictors of OS at one year post transplant.

Results

- We screened the medical records of 200 patients and were able to identify 16 AML patients treated with ASCT in active disease at AUBMC with a median follow-up of 5.28 months.

Variable		Number of patients: 16
Age at transplant, median (range)		49 (37-75)
Gender	Male	8 (50%)
	Female	8 (50%)
AML	De novo AML	8 (50%)
	Secondary (MDS)	3 (19%)
	Relapsed	5 (31%)
ELN classification	Favorable	3 (19%)
	Intermediate	9 (56%)
	Adverse	4 (25%)
First induction regimen	IDA- AraC	10 (62%)
	FLAG- IDA	3 (19%)
	CLAG	3 (19%)
Second induction	FLAG- IDA	3 (19%)
	CLAG	3 (19%)
Response to first induction	Complete remission (CR)	5 (39%)
	Refractory	11 (69%)
Lines of treatment, median (range)		3 (1-5)
Donor type	MMRD	12 (75%)
	FMRD	4 (25%)
Stem cell source	Peripheral blood stem cell	16 (100%)
Conditioning regimen	TEC-RIC	13 (81%)
	Clofarabine – TBI	2 (13%)
	FB3 – ATG	1 (6%)
GVHD prophylaxis	Cyclosporine	16 (100%)
	MMF and PTCy	12 (75%)
Post transplant maintenance treatment	5- Azacitadine	7 (44%)
	Sorafenib	2 (13%)
	Donor lymphocyte infusion	5 (31%)

ELN: European Leukemia Network, IDA: Idarubicin, AraC: Cytarabine, MMRD: Mismatched related donor, FMRD: Full matched related donor, TBI: Total body irradiation, MMF: Mycophenolate mofetil, PTCy: Post-transplant cyclophosphamide,

Results	
Median follow up after ASCT	5.28 months (8 days – 27.5 months)
Neutrophil engraftment	14 (88%) Median time to engraftment: 14.5 days (10-23) days
Platelets engraftment	9 (56%) Median time to engraftment: 19 days (8-55) days
Survival at day 100	10 (63%)
Disease free with full donor chimerism at day 100	7 (44%)
Survival at one year	10 (63%)
Disease free with full donor chimerism at one year	7 (44%)
Median survival from ASCT to death	88 days (8 – 826 days)
Mortality and causes of death at last follow up	13 (81%) Relapsed/Refractory Disease: 8 (62%) Transplant Related Mortality: 4 (31%) Acute GVHD: 1 (8%)

- Four patients (25%) had a prolonged disease-free survival, median 441 days (403 – 589). All of them received stem cells from MMRD and post-transplant azacitidine (75% received DLI and had CMV reactivation).
- Effect of post-transplant maintenance azacitidine on survival at one year (odds ratio 20, P = 0.0350).
- Effect of post transplant DLI on survival at one year (odds Ratio 18, P = 0.0341).

Safety	
CMV reactivation	6 (38%)
BK Virus hemorrhagic cystitis	3 (19%)
EBV reactivation	1 (6%)
HHV-6 reactivation	0
Intensive care Transfer	7 (44%)
Acute GVHD	3 (19%)
Grade II	2
Grade IV	1
Chronic GVHD	0

Discussion

- Sequential conditioning followed by ASCT improves short-term survival in a subgroup of patients with R/R AML.
- Post-transplant use of Azacitidine is associated with increased survival one year after transplant.
- Factors that enhances GVT effect (MMRD and DLI infusion) tend to improve survival in those patients and might be confirmed by larger studies powered enough to detect this effect.
- Although sequential conditioning is associated with significant infectious complications, disease related complications remain the most observed cause of death.

Conclusions

- Myeloablative conditioning followed by allo-HCT for patients with R/R AML in active disease can confer a disease control in a subset of patients, with acceptable rate of transplant-related mortality.

Bibliography:

- De-Mello RA, Pinho-Vaz C, Branca R, Campilho F, Rosales M, Roncon S, et al. Outcomes of allogeneic stem cell transplantation among patients with acute myeloid leukemia presenting active disease: Experience of a single European Comprehensive Cancer Center. Revista da Associacao Medica Brasileira (1992). 2016;62(7):641-6.