Clofarabine and Total Body Irradiation (TBI) as Conditioning Regimen for Allogeneic Stem Cell Transplantation in High Risk Acute Leukemia

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Introduction

- Clofarabine is an immunosuppressive purine analog that may have better ant-leukemic activity than fludarabine as a conditioning regimen for stem cell transplant in acute leukemia.
- The addition of TBI to conditioning regimens have been widely investigated. However, the use of single agent clofarabine in combination with higher doses of TBI ranging from 4 to 8 Gy has not been studied.

Objective

- The aim of this study is to identify the outcome of patients with hematological malignancies who underwent allogeneic stem cell transplant from full matched or haplo-identical donors and received Clofarabine and TBI as conditioning regimen.

Methods

- This is a double center, observational, retrospective study of patients diagnosed with high risk acute leukemia (2015-2020) and treated at the American University of Beirut Medical Center in Lebanon and Saint-Antoine Hospital in Paris France.
- Data regarding patient baseline characteristics, disease-related factors, transplant outcomes including progression free survival (PFS) , overall survival (OS), graft versus host disease (GvHD) and transplant related mortality (TRM) were collected

Table 1. Patients and disease charateristics

CR: Complete Remission

TBI: Total Body Irradiation

GvHD: Graft-versus-host disease

Results

Number of Patients Included in Study	N=23
Institution	
AUBMC	12 (52%)
St. Antoine	11 (48%)
Gender	
Male	14 (61%)
Female	9 (39%)
Median age at transplant in years (range)	43.3 (21.5-77.8)
Disease	
AML/MDS	11 (48%)
ALL	11 (48%)
B-Lymphoblastic lymphoma	1 (4%)
EBMT risk score	
0	11 (48%)
1	2 (9%)
2	5 (22%)
≥ 3	5 (21%)
DRI score	
Intermediate	9 (39%)
High	10 (44%)
Very High	4 (17%)
Disease Status at Transplant[1]	
CR	14 (61%)
Refractory	8 (35%)
Untreated	1 (4%)
Donor Type	
MR	9 (39%)
Haplo	8 (35%)
MUD 10/10	4 (17%)
UCB	2 (9%)
Number of Transplant	
1	18 (78%)
2	5 (22%)
Conditioning regimen	
Clofarabine	23 (100%)
TBI[2]	23 (100%)
Total Dose (Gy)	
4	20 (87%)
8	3 (13%)
ATG 2.5mg/kg for 1 Day	15 (65%)
Immunosuppression	
Csa	23 (100%)
MMF	22 (96%)
PTCy	8 (35%)
aGVHD[3]	12 (52%)
aGVHD grade	
II - III	11 (48%)
IV	1 (4%)
aGVHD onset mean in days (range)	59 (20-132)
cGVHD	2 (9%)
Relapse/Progression	4 (17%)
Death	10 (44%)
Death cause	
Disease	5 (22%)
TRM	5 (22%)
Median Follow-up in months (range)	22.4 (0.6-110)

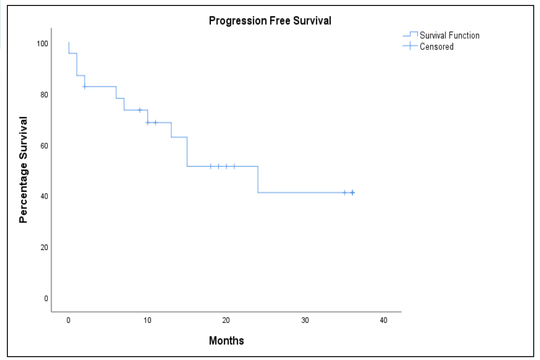


Figure 1. Kaplan Mayer Curve for PFS

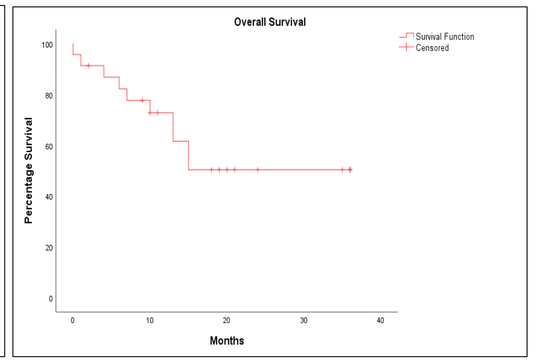


Figure 2. Kaplan Mayer Curve for OS

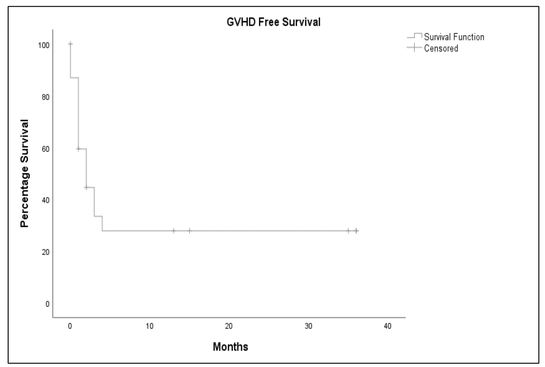


Figure 3. Kaplan Mayer Curve for GvHD Free Survival

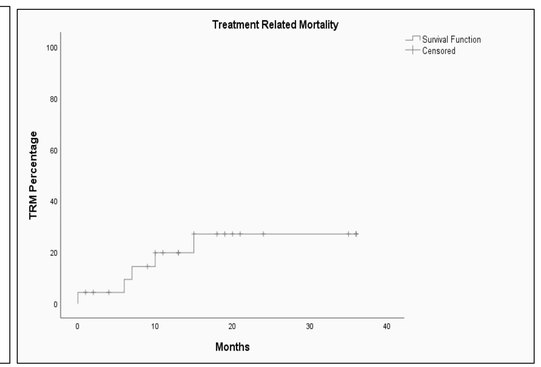


Figure 4. Kaplan Mayer Curve for treatment-related mortality

Discussion

- In a phase I/II trial using clofarabine and low dose TBI of 2 Gy in patients with AML, it was shown that this regimen has lower rates of overall mortality, disease progression, morphologic relapse compared to historical cohort of high risk patients treated with fludarabine 90 mg/m2 with 2 Gy TBI.
- In our study, the use of Clofarabine in combination with TBI as conditioning regimen for allogeneic stem cell transplant in high risk acute leukemia confers disease control with low transplant-related mortality. However, larger trials are required to confirm these results

References

- Krakow, E.F., et al., *Phase I/II multisite trial of optimally dosed clofarabine and low-dose TBI for hematopoietic cell transplantation in acute myeloid leukemia.* Am J Hematol, 2020. **95**(1): p. 48-56.