



Outcomes of Allogeneic SC transplant in Hematological Malignancy Patients using Busulfan 3 (9.6 mg/kg) based conditioning regimen

Majed Altareb, Yazeed Bajuaifer, Walid Rasheed
King Faisal Specialist Hospital & Research Center, Riyadh, Saudi Arabia



Introduction

Allogeneic stem-cell transplantation (SCT) is a potentially curative therapy for malignant hematological disease. Busulfan is often used in myeloablative conditioning (MAC) regimen in hematological malignancies at an IV dose of 12.8 mg/kg (BU4). Reduced intensity regimen using 6.4 mg/kg (BU2) is commonly used in older patients or those with comorbidity diseases. The optimal Busulfan dose depends on age, patient comorbidities, disease activity and the graft source. Data on using BU3 (9.6mg/kg) based regimen are limited. At King Faisal Specialist Hospital and Research Center (KFSHRC), patients who can not tolerate full MAC regimen, would receive BU2 or BU3 based conditioning regimen depending on age and comorbidities profile.

Objective

To study the outcomes of Allo-SCT in patients with hematological malignancy who received BU3 (9.6 mg/kg) based conditioning from matched related or unrelated donors.

Materials & Methods

This is a retrospective analysis of KFSHRC- BMT Database. We identified 65 patients who underwent Allo-SCT between October 2005 and December 2019, using BU3 based condition regimen. Stem cell source included HLA matched related or unrelated donors. We excluded Mismatched MUD, Cord & Haplo-identical Stem Cell sources.

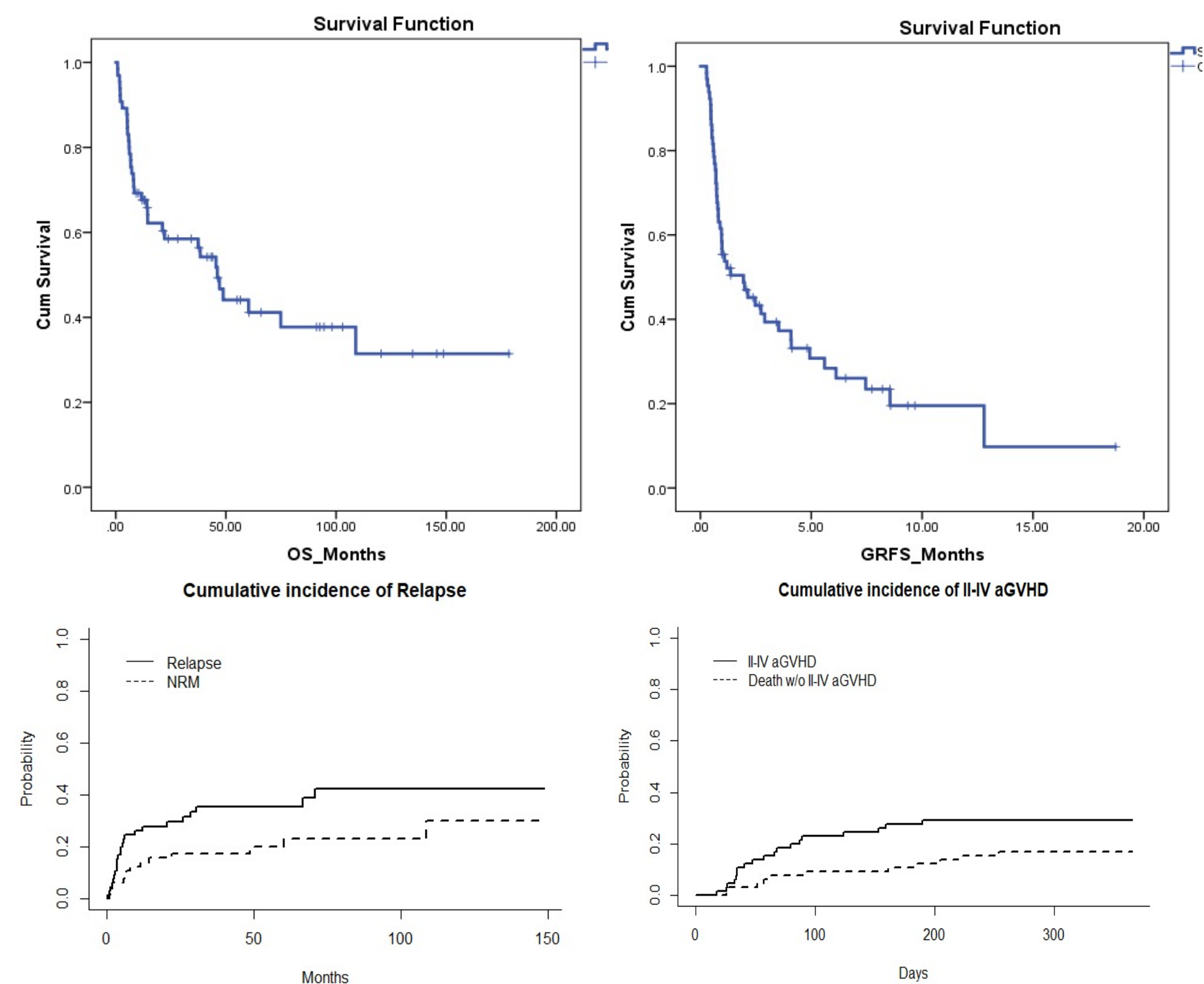
Results

Disease categories included: 47 AML (72.3%), 8 MDS (12.3%), 8 Myelofibrosis (12.3%) & 2 CML (3.1%) patients. Median age at Allo-SCT was 52 years (16-66); 35 (54%) were males. Pre-transplant status showed 37 (57%) were in CR1, 11 (17%) in CR2 and 2 (3%) not in CR. Fifty seven (88%) patients received PBSC, 6 (9%) received BM source & 2 (3%) received both PBSC & BM from HLA matched related [N= 61 (93%)] or unrelated [N=4 (7%)] donors.

Patients Characteristic	Study Population (N: 65)	%
Patient age, median (range), y	52	16-66 (50)
Sex:		
Male	35	53.8
Female	30	46.2
Diagnosis:		
AML	47	72.3
MDS	8	12.3
MF	8	12.3
CML	2	3.1
Disease status:		
CR1	37	56.9
> CR1	11	16.9
Not CR	2	3
Comorbidity:		
No	13	20
Yes	52	80
Sorror score (CI):		
1-2	29	44.6
>2	23	35.4
Conditioning regimen:		
IVBU12/FLU	40	61.5
IVBU12/CY	14	21.5
IVBU12/CY/ATG	4	6.2
IVBU12/FLU/ATG	7	10.8
ABO Compatibilities:		
Compatible	46	70.8
Major	6	9.8
Minor	9	13.8
Bidirectional	4	6.2
CD34 median (range):	7	1-9
Stem cell source:		
Bone marrow	6	9
PBSC	57	88
Both	2	3
Donor type:		
HLA identical sibling	61	93
HLA match unrelated donor	4	7
Reason for using BU3:		
Age > 55	4	6.2
Comorbidities	39	60
Infection	11	16.9
Physician preferences	11	16.9
	Study Population (N: 65)	100 %

Table 1: Patients Characteristic.

Forty (61.5%) patients received Bu/Flu conditioning regimen, 14 (21.5%) received Bu/Cy; 7 (10.8%) received Bu/Flu/ATG & 4 (6.2) received Bu/Cy/ATG. GVHD prophylaxis consisted of Cyclosporine and Methotrexate for all patients. Rabbit Antithymocyte Globulin (rATG, *Thymoglobulin*) was used in all transplants from unrelated donors (n=4). 52 (80%) patients had comorbidities with comorbidity index (Sorror Score) between 1-2 in 29 (44.6%) patients while more than 2 in 23 (35.4%). Median CD34 cell dose was 7 (1-9)x10⁶/kg. Sixty two (95%) patients engrafted; median time for neutrophil & platelets engraftment was 18 days.



Results (Continue)

Acute GvHD grade II-IV and III-IV occurred in 29% and 14% respectively. Chronic GvHD occurred in 55% and was extensive in 24% of patients. With Median follow-up 60.5 months, 2 years and 5 years OS were 58.5 % and 44.1% respectively. The 2 years and 5 years DFS were 52.9% and 44.5% respectively. Cumulative incidence of relapse at 2-years were 29.5%. Day +100 TRM was 10.7% and 2 year Non-Relapse Mortality was 17.4%.

Conclusion

Allogeneic HCT using BU3 based regimen appears feasible to use in patients who are not suitable for fully myeloablative (BU4) regimen. TRM, DFS & OS rates were comparable to reports from studies using BU4 based regimen, warranting prospective studies in this setting.

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