The 65th ASH Annual Meeting Abstracts

POSTER ABSTRACTS

721.ALLOGENEIC TRANSPLANTATION: CONDITIONING REGIMENS, ENGRAFTMENT AND ACUTE TOXICITIES

Fludarabine and Melphalan Reduced Toxicity Versus a Myeloablative Fludarabine and Busulfan Conditioning Regimen for Acute Myeloid Leukemia

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Introduction: The optimal induction regimen for an allogeneic hematopoietic cell transplant (allo-HCT) for a young adult patient diagnosed with acute myeloid leukemia (AML) remains to be defined. Among reduced intensity regimens (RIC), retrospective registry data from both CIBMTR and EBMT would suggest that a Fludarabine / Melphalan (Flu/Mel) regimen was superior to a Fludarabine / Busulfan x 2 (Flu/Bu2) regimen. The need for a myeloablative conditioning regimen over a RIC has been evaluated in at least six randomized clinical trials (RCT), and the results have yet to be uniform. Published meta-analysis suggests equipoise. The studies are further limited by including a heterogenous group of conditioning regimens, especially in the reduced intensity arm; they all come from developed countries, a mix of AML and MDS in most studies, and variation in age groups enrolled in them. In India and developing countries, there remain significant challenges with multi-drug resistant infections, financial constraints, and challenges with intensive care support. We hypothesize that in this setting, a reduced toxicity regimen, such as a combination of Fludarabine with Melphalan (140 mg/m^2) (Flu/Mel), may be preferable to a myeloablative regimen.

Methods: A single-center retrospective analysis was undertaken to study the impact of a reduced toxicity Flu/Mel regimen versus a myeloablative Fludarabine combined with Busulfan (130 mg/m^2/day x 4 days) regimen (Flu/Bu4). All consecutive patients in all age groups with a diagnosis of AML who underwent an allo-HCT between Jan 2005 and Dec 2021 were included in this analysis. The conditioning regimen used was as per physician discretion with a broad guideline within the department to use a myeloablative Flu/Bu4 regimen in a young fit patient with high-risk features such as high-risk ELN at diagnosis, CR2, and beyond, or requiring more than one cycle of induction chemotherapy to achieve a complete remission (CR).

Results: 439 patients underwent an allo-HCT for a diagnosis of AML at our center in the given time. The median age was 33 years (range: 1 - 63), and there were 267 (60.8%) males. The transplants were done in CR1 in 236 (54%), CR2 in 90 (20.5%), CR3 in 13 (3%), and in relapsed/refractory or with active disease in 100 (22.8%). The majority were matched sibling/related donors (MRD) in 284 (64.7%), followed by matched unrelated (MUD) in 75 (17.1%) and haploidentical in 80 (18.2%). The conditioning regimen used was Flu/Mel in 170 (38.7%), Flu/Bu4 in 185 (42.1%), and a mix of other regimens in 84 (19.1%). At an actuarial median follow-up of 4 years, the overall survival (OS) and event-free survival (EFS) of the entire cohort were 40.8% ± 3.0% and 38.6% ± 3.0%, respectively. The EFS of cases in CR1, CR≥2, and in relapsed/refractory/active disease were 47.7% ± 3.8%, 45.0% ± 5.5%, and 12.3% ± 3.6%, respectively. The baseline characteristics and clinical outcome of cases that received a Flu/Mel condition versus Flu/Bu4 conditioning are summarized in Table 1. In summary, baseline characteristics were comparable between the two groups, except that significantly more cases underwent a haploidentical transplant in the Flu/Bu4 group. In contrast, in the Flu/Mel group, there were significantly more cases in CR1, and the median age was also significantly older. The 5-year KM EFS of the Flu/Mel and Flu/Bu4 cohort was 51.7±3.9% and 43.9±3.9% (P-value = 0.297), respectively (Figure 1). On univariate analysis, only CR1 status before transplant and the presence of chronic GVHD impacted EFS positively, and on multivariate analysis, only CR1 status affected EFS.

Conclusion: In conclusion, in one of the most extensive retrospective studies comparing a uniform reduced toxicity conditioning regimen with Flu/Mel versus a standard myeloablative Flu/Bu4 conditioning regimen, we find no significant advantage of Flu/Bu4 over a Flu/Mel conditioning regimen.

Table 1: Baseline characteristics and key clinical outcome parameters between the Flu/Mel and the Flu/Bu4 cohort.

Variables	Flu / Mel (n=170)	Flu / Bu4 (n=185)	P- value
Patient Age	35 (3-63)	32 (1-59)	0.004
Patient Sex: Male	97 (57.1%)	118 (63.8%)	0.232
Female	73 (42.9%)	67 (36.2%)	
Type of Tx: MRD	136 (80%)	94(50.8%)	0.000
MUD	15(8.8%)	39 (21.1%)	
HAPLO	19(11.2%)	52 (28.1%)	
Cytogenetics:			
Standard	7(4.5%)	15(8.7%)	
Intermediate	111(71.6%)	107(61.8%)	0.120
High	37(23.9%)	51 (29.5%)	
Status @ TX:			
CR1	123(72.4%)	95(51.4%)	
Others	47(27.6%)	90(48.6%)	0.000
Type of product:			
PBSCT	170(100%)	184(99.5%)	
BM	-	1(0.5%)	1.000
Engraftment: Yes	158(92.9%)	174(94.1%)	0.674
No	12(7.1%)	11(5.9%)	
Acute GVHD: Yes	67(39.4%)	105(56.8%)	0.001
No	103(60.6%)	80(43.2%)	
Acute GVHD:			
Grade I	11(16.7%)	20(19.0%)	
Grade II	25(37.9%)	46(43.8%)	0.591
Grade III	13(19.7%)	13(12.4%)	
Grade IV	17(25.8%)	26(24.8%)	
Chronic GVHD:			
Yes	80(58.4%)	97(66.0%)	
No	57(41.6%)	50(34.0%)	0.221
TRM at 1 year	45(26.5%)	55(30.3%)	0.480
Relapse: Yes	33(19.4%)	44(23.8%)	0.367
No	137(80.6%)	141(76.2%)	
Dead: Yes	83(48.8%)	96(51.96%)	0.596
No	87(47.9%)	89(48.1%)	

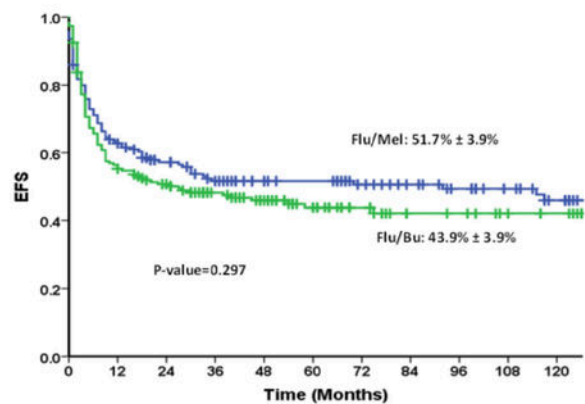**Figure 1:** 5-year KM event-free survival between the cohort that received a Flu/Mel versus a Flu/Bu4 conditioning.

Flu/Mel: 51.7% ± 3.9%

Flu/Bu: 43.9% ± 3.9%

P-value=0.297

Figure 1

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