

## **SUPPLEMENTAL MATERIAL**

### **Supplemental Material 1.**

Definitions and statistical methods used to measure outcomes of interest.

- Primary outcome: Progression-free survival (PFS)
- Secondary outcome: GVHD-free relapse-free survival (GRFS), relapse incidence, non-relapse mortality (NRM)

Demographic and clinical characteristics of patients in each conditioning group were summarized with descriptive statistics. The comparisons of baseline characteristics between groups were done using the Fisher's exact test for categorical variables and the Kruskal–Wallis equality-of-populations rank test for continuous data.

The Kaplan-Meier method was used to estimate all survival measures. Differences in survival between groups were assessed using the log-rank test. Associations between survival outcomes and potential prognostic factors were determined using univariable and multivariable Cox proportional hazards regression models. All variables of interest were tested for the proportional hazard assumption and interaction terms.

The cumulative incidence of relapse and NRM were evaluated by the competing risks method where death was the competing risk for relapse and relapse was the competing risk for NRM. Differences in cumulative incidence between subgroups were assessed using Gray's test. The associations between measures of interest and the cumulative incidence outcomes were determined using the proportional subdistribution hazards regression models.

The analyses were done using the complete-case method without data imputation. All statistical calculations were carried out using STATA 13.1 (Stata Corp., College Station TX, USA). P-values <0.05 were considered significant. All tests were two-sided.

### **Multiple propensity score calculation**

Multiple propensity score was calculated using multinomial logistic regression analysis with all variables related to the probabilities of receiving each type of conditioning regimen as independent variables and type of conditioning regimen as dependent variable. Because in our study we compared

4 conditioning types, we have estimated 4 multiple PSs. Since all these PSs add up to 1 and are complementary, only 3 out of 4 multiple PSs are needed in a further analysis. Factors included in the propensity score calculation were age (continuous), sex, Karnofsky performance status (continuous), secondary AML, ELN2017 genetic risk<sup>19</sup>, remission status before transplant (CR with MRD negative vs. CR with MRD positive vs. CR with unknown MRD status vs. active disease), induction failure, donor type (matched-related vs. matched-unrelated vs. mismatched-related/haploidentical vs. mismatched-unrelated), stem cell source (peripheral blood vs. bone marrow), patient and donor CMV serostatus, and transplant protocol (treatment on clinical trial vs. standard of care). After creating propensity scores, overlap among the treatment groups was checked to demonstrate that the groups were comparable.

The similarity of baseline characteristics was then tested using the ANCOVA (for continuous variables), logistic (for dichotomous variables) or multinomial logistic regression (for nominal variables) with 3 out of 4 multiple PSs as covariate.

Multiple PS was then used as a covariate in a multivariable Cox regression model to adjust the impact of conditioning type on survival outcomes.

**Supplemental Table 1s.** Patients and transplant characteristics in each conditioning group and P value before and after multiple propensity score adjustment

	<b>Total (N=404)</b>	<b>FM100 (N=89)</b>	<b>FM140 (N=78)</b>	<b>Bu≥20000 (N=131)</b>	<b>Bu16000 (N=106)</b>	<b>P value before multiple PS adjustme nt</b>	<b>P value after multiple PS adjustme nt</b>
Sex: female (%)	171 (42.3)	36 (40.5)	34 (43.6)	57 (43.5)	44 (41.5)	0.97	1.00
Age at transplant in year; median	65 (60-79)	67 (60-79)	64 (60-76)	64 (60-73)	65 (60-77)	0.001	0.08
Cytogenetic (%)						0.69	0.79
• Favorable	19 (4.7)	7 (7.9)	2 (2.6)	7 (5.3)	3 (8.7)		
• Intermediate	239 (59.3)	51 (57.3)	47 (60.3)	80 (60.1)	61. (58.1)		
• Unfavorable	145 (36.0)	31 (34.8)	29 (37.2)	44 (33.6)	41 (39.1)		
Diagnosis (%)						<0.001	0.67
• De novo AML	290 (71.8)	70 (78.7)	43 (55.1)	106 (80.9)	71 (67.0)		
• Secondary AML	114 (28.2)	19 (21.4)	35 (44.9)	25 (19.1)	35 (33.0)		
Prior autologous transplantation (%)	4 (0.9)	0	2 (2.6)	1 (0.7)	1 (0.9)	0.56	0.99
Remission status (%)							
• CR/hypoplastic marrow/marrow CR	299 (74.0)	78 (87.6)	42 (53.6)	107 (81.7)	72 (67.9)	<0.001	0.84
• CR1/2	172 (42.6)	43 (48.3)	21 (26.9)	64 (48.9)	44 (41.5)	0.01	0.59
MRD status (%)						<0.001	1.00
• CR with MRD negative	46 (11.4)	12 (13.5)	2 (2.6)	21 (16.0)	11 (10.4)		
• CR with MRD positive	110 (27.2)	37 (41.6)	3 (3.9)	42 (32.1)	28 (26.4)		
• CR with unknown MRD status	143 (35.4)	29 (32.6)	37 (47.4)	44 (33.6)	33 (31.1)		
• Active disease	105 (26.0)	11 (12.4)	36 (46.2)	24 (18.3)	34 (32.1)		
Induction failure (%)	148 (36.6)	29 (32.6)	30 (38.5)	49 (37.4)	40 (37.7)	0.85	0.99
ELN 2017 genetic risk (%)						0.17	0.77
• Favorable	58 (14.4)	15 (16.9)	5 (6.4)	24 (18.3)	14 (13.2)		
• Intermediate	149 (36.9)	29 (32.6)	36 (46.2)	42 (32.1)	42 (39.6)		
• Adverse	197 (48.8)	45 (50.6)	37 (47.4)	65 (49.6)	50 (47.2)		

HCT-CI; median	3 (0-11)	3 (0-9)	3 (0-8)	3 (0-9)	3 (0-10)	0.33	1.00
HCT-CI $\geq$ 3 (%)	246 (60.9)	51 (57.3)	48 (61.5)	73 (55.7)	74 (69.8)	0.13	1.00
Median Kanofsky performance status	90 (60-100)	80 (60-100)	80 (70-100)	90 (70-100)	90 (80-100)	<0.001	0.65
Kanofsky performance status $\leq$ 90 (%)	125 (30.9)	40 (50.6)	25 (32.1)	34 (27.4)	26 (26.8)	<0.001	0.98
DRI (N=1407) (%)						<0.001	0.77
• Low	18 (4.5)	7 (7.9)	1 (1.2)	7 (5.3)	3 (2.9)		
• Intermediate	180 (44.7)	45 (50.6)	24 (30.8)	63 (48.1)	48 (45.7)		
• High	161 (40.0)	32 (36.0)	42 (53.9)	54 (41.2)	33 (31.4)		
• Very high	44 (10.9)	5 (5.6)	11 (14.1)	7 (5.3)	21 (20.0)		
Donor type (%)						<0.001	0.94
• Matched-related	126 (31.2)	17 (19.1)	23 (27.5)	51 (38.9)	35 (33.0)		
• Matched-unrelated	218 (54.0)	39 (43.8)	43 (55.1)	71 (54.2)	65 (61.3)		
• Mismatched-related/Haploidentical	40 (9.9)	30 (33.7)	8 (10.3)	2 (1.5)	0		
• Mismatched-unrelated	20 (5.0)	3 (3.4)	4 (5.1)	7 (5.3)	6 (5.7)		
Cell source (%)						0.001	1.00
• Peripheral blood	243 (60.1)	41 (46.1)	53 (68.0)	88 (67.2)	61 (57.6)		
• Bone marrow	161 (39.9)	48 (53.9)	25 (32.1)	43 (32.9)	45 (42.5)		
Transplant protocol (%)						<0.001	1.00
• Standard of care	181 (44.8)	65 (73.0)	50 (64.1)	33 (25.2)	33 (31.1)		
• On clinical trial	223 (55.2)	24 (27.0)	28 (35.9)	98 (74.8)	73 (68.9)		
Patient CMV positive (%)	361 (89.4)	80 (89.9)	70 (89.7)	121 (92.4)	90 (84.9)	0.34	0.99
Donor CMV positive (%)	191 (47.3)	38 (42.7)	39 (50.0)	64 (48.9)	50 (47.2)	0.78	0.99
Median follow up of all patients (month)	7.8 (1-145)	11.3 (1-145)	9.7 (1-144)	12.4 (1-140)	9.1 (1-109)	0.77	0.93
Median follow up of survivors (month)	32.5 (1.5-144) (N=166)	40 (1.5-108.4)	74.2 (1.9-144.1)	30.0 (2.4-140.4)	43.6 (3.4-109.3)	0.06	0.45
<p><b>Abbreviations:</b> Bu16000: fludarabine+IV busulfan x 4 days with Bu AUC 4,000/day; Bu<math>\geq</math>20000: fludarabine+IV busulfan x 4 days with Bu AUC<math>\geq</math>5,000/day; FM100: fludarabine+melfalan 100mg/m<sup>2</sup>; FM140: fludarabine+melfalan 140mg/m<sup>2</sup>; AML: acute myeloid leukemia; CR: complete remission; CR1/2: 1<sup>st</sup> or 2<sup>nd</sup> complete remission; MRD: minimal residual disease; ELN: the European LeukemiaNet; HCT-CI: Hematopoietic cell transplant comorbidity index; CMV: cytomegalovirus</p>							