

SUPPLEMENTAL INFORMATION

Choice of AML-MRC Classification system

The AML classification system used for analysis was the AML-MRC 2010 system. While previous CIBMTR studies have used the 2007 ECOG / SWOG classification system, this system does not classify patients based on 11q23 abnormalities. The 2017 European Leukemia Network (ELN) system was considered, however this system includes molecular abnormalities for classification. Reliable genomic data was not available for all patients in our retrospective cohort, reflecting the advent of the use of molecular data during the time period under study as well as different practice patterns at sites across the world who contribute to the database. As such, the 2010 AML-MRC system was used, which categorizes both t(9;11) and t(11;19) as intermediate risk, with all other 11q23 rearrangements considered adverse risk, and does not use molecular data. Of note, this system also considers complex karyotype as ≥ 4 abnormalities and does not include the designation of monosomal karyotype.

Supplemental Table 1. Patient selection

Selection Criteria (CRF Sep 2017)	Excluded:	Remaining:
Inclusion:		
First Allo Tx for AML from 2007-2016 in adults 18-70	APML (n=79)	8630
Disease status prior to HCT: CR1	CR2 (n=1656) CR3+(n=122) PIF (n=1108) Relapse (n=848) Missing (n=24)	4872
Cytogenetics: Poor/KMT2A/Intermediate	Favorable cytogenetics (n=120) Unknown cytogenetics (n=369)	4383
Exclusion		
Syngeneic Twins	(n=22)	4361
Consent	(n=97)	4264
Embargoed Centers	(n=88)	4176
Forms selection	Missing disease specific forms (n=29) Missing 100 day forms (n=13) Missing Baseline forms (n=3) Missing 2200/2300 follow up form (n=23)	4108
Additional exclusions		
Donor types	Mis-matched unrelated ($\leq 6/8$) (n=17) Multi-donor (n=39) Unrelated (matching unknown) (n=53)	3999
Cytogenetics after review (ECOG-ACRIN)	Favorable cytogenetics (n=86) Not classifiable (n=9)	3904
Ex-vivo TCD/ CD34 selection	N=125	3779

Supplemental Table 2.

Completeness of Follow-up

(set date: 06/01/17)	KMT2A (N = 434), %	Intermediate (N = 2466), %	Poor (N = 1004), %
1-year	97	96	98
2-year	93	92	94
3-year	90	90	91

Supplemental Table 3. Multivariate analysis for comparison between translocation partner

Covariates	HR (95% CI)	p-value stepdown Bonferroni
<u>NRM</u>		
t(9;11) vs. remaining KMT2A	0.96 (0.58-1.60)	1.00
t(11;19) vs. remaining KMT2A	0.74 (0.38-1.46)	1.00
t(9;11) and t(11;19) vs. remaining KMT2A	0.80 (0.48-1.32)	1.00
<u>Relapse</u>		
	Reference	
t(9;11) vs. remaining KMT2A	0.76 (0.49-1.18)	0.69
t(11;19) vs. remaining KMT2A	1.10 (0.68-1.77)	0.85
t(9;11) and t(11;19) vs. remaining KMT2A	0.84 (0.55-1.26)	0.85
<u>LFS</u>		
	Reference	
t(9;11) vs. remaining KMT2A	0.78 (0.56-1.08)	0.34
t(11;19) vs. remaining KMT2A	1.00 (0.68-1.47)	0.94
t(9;11) and t(11;19) vs. remaining KMT2A	0.78 (0.57-1.07)	0.34
<u>OS</u>		
	Reference	
t(9;11) vs. remaining KMT2A	0.84 (0.60-1.19)	0.42
t(11;19) vs. remaining KMT2A	0.76 (0.49-1.17)	0.42
t(9;11) and t(11;19) vs. remaining KMT2A	0.71 (0.51-0.99)	0.13

Supplemental Table 4. Repeat main analyses for *KMT2A* with / without additional abnormalities

Covariates	Original model		KMT2A without additional abnorm.		KMT2A with additional abnorm.	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
<u>NRM</u>						
Main effect		0.11		0.08		0.15
Intermediate	Reference		Reference		Reference	
KMT2A	1.15 (0.92-1.44)	0.21	1.22 (0.94-1.58)	0.14	1.05 (0.73-1.52)	0.78
Adverse	1.17 (1.00-1.38)	0.05	1.18 (1.00-1.38)	0.05	1.17 (1.00-1.38)	0.05
<u>Relapse</u>						
Main effect		< 0.001		< 0.001		< 0.001
Intermediate	Reference		Reference		Reference	
KMT2A	1.21 (1.01-1.46)	0.04	1.30 (1.05-1.61)	0.02	1.04 (0.76-1.42)	0.81
Adverse	1.68 (1.49-1.91)	< 0.001	1.68 (1.48-1.90)	< 0.001	1.67 (1.47-1.89)	< 0.001
<u>LFS</u>						
Main effect		< 0.001		< 0.001		< 0.001
Intermediate	Reference		Reference		Reference	
KMT2A	1.22 (1.06-1.41)	0.007	1.30 (1.10-1.54)	0.002	1.08 (0.85-1.37)	0.54
Adverse	1.46 (1.32-1.61)	< 0.001	1.46 (1.32-1.61)	< 0.001	1.45 (1.32-1.61)	< 0.001
<u>OS</u>						
Main effect		< 0.001		< 0.001		< 0.001
Intermediate	Reference		Reference		Reference	
KMT2A	1.32 (1.13-1.53)	< 0.001	1.39 (1.17-1.66)	< 0.001	1.18 (0.92-1.52)	0.19
Adverse	1.45 (1.31-1.61)	< 0.001	1.45 (1.30-1.61)	< 0.001	1.45 (1.30-1.61)	< 0.001

Note: same adjusting factors were selected for the additional 2 analyses but only the main effect is presented in the table.

Supplemental Table 5. Univariate Analysis of Outcomes in *KMT2A* with Complex Karyotype (4 or more abnormalities) vs. Not

Outcomes	Complex karyotype				P Value
	No (N = 397)		Yes (N = 29)		
	N	Prob (95% CI)	N	Prob (95% CI)	
Relapse	397		29		0.223
1-year	210	25 (21-29)%	17	24 (10-41)%	0.933
Treatment related mortality	397		29		0.765
1-year	210	16 (13-20)%	17	17 (6-33)%	0.866
Disease free survival	397		29		0.341
1-year	209	59 (54-64)%	16	59 (41-76)%	0.954
Overall survival	397		29		0.183
1-year	242	68 (64-73)%	17	62 (44-78)%	0.489

Operational definition of MRD at time of HCT for AML/ALL

Positive: if answered “no” to molecular or cytogenetic or flow remission prior to HCT, or disease detected in BM or blood by flow prior to HCT, or “positive” to following molecular test prior to HCT: CEBPA, FLT3 D835, FLT3 ITD, IDH1, IDH2, KIT, NPM1, BCR/ABL, TEL-AML, other

Negative: if not classified as MRD positive, and answered “yes” to molecular or cytogenetic or flow remission prior to HCT, or disease not detected in BM or blood by flow prior to HCT

Missing: if not identified as either positive or negative