Predictors of Outcomes in Patients with *MECOM EVI1* rearranged AML or MDS

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INTRODUCTION

- MDS/AML with inv(3) (and other cryptic *EVI1* rearrangements) are rare myeloid malignancies refractory to conventional regimens and associated with poor outcomes.
- Factors that influence prognosis are not well known.
- Retrospective analysis of *MECOM (EVI1)* AML or MDS to associate clinicopathologic variables w/ prognosis.

METHODS

- IRB approval through Mayo Clinic Institutional Review Board (IRB)
- Electronic health record (EHR) review of ≥18 years of age between January 2012 and December 2022 with a myeloid neoplasm (MDS/AML) and *MECOM EVI1* .
- .Response was defined by ELN 2022 criteria. Intensive chemotherapy was defined as 7+3 or high dose cytarabine. Non-intensive chemotherapy included hypomethylating agents with or without venetoclax.
- Overall survival (OS) & leukemia free survival (LFS) were estimated using the Kaplan-Meier method.
- Outcome differences between sub-groups & univariate analyses were assessed w/ Cox regression.

Table 1. Baseline characteristics of 60 patients included.

Age at diagnosis – Median (range), years	67.8 (56 – 75)
Male – n (%)	38 (63%)
Diagnosis, n (%)	
AML	48 (80%)
MDS	11 (18%)
MDS/MPN	1 (2%)
De-novo, n (%)	20 (33%)
Secondary, n (%)	40 (67%)
Number of HSCT prior to DX	
0	1 (2%)
1	53 (88%)
2	5 (8%)
3	1 (2%)
Cytogenetics	
Inv(3)/t(3;3)	39 (65%)
t(3;21)	6 (10%)
t(3;12)	2 (3.3%)
Other	13 (22%)
Additional Cytogenetic Abnormalities	
None	17 (28%)
Monosomy 7	16 (27%)
Del 7q	9 (15%)
Del 11q	5 (8%)
Del 5q	4 (7%)
Complex (≥3 abnormalities)	3 (5%)
Additional Mutations, n (%)	
No additional mutations	5 (16%)
1-2	12 (37%)
≥3	15 (47%)
SF3B1	10 (31%)
KRAS	6 (19%)
JAK2	4 (12%)
BCOR	4 (12%)
RUNX1	4 (12%)
ASXL1	4 (12%)
NRAS	4 (12%)
TP53	4 (12%)
Treatment Regimen	
Intensive	23 (38%)
Non-intensive	29 (48%)
Observation	8 (13%)

Table 2. Comparison of response by intensity of treatment received.

	Intensive (n=23)	Non-intensive (n=29)	Total (n=52)	P value
Response				0.007[1]
CR	8 (36%)	1 (4%)	9 (19%)	
PD	14 (64%)	25 (96%)	39 (81%)	
Missing	1	3	4	

RESULTS

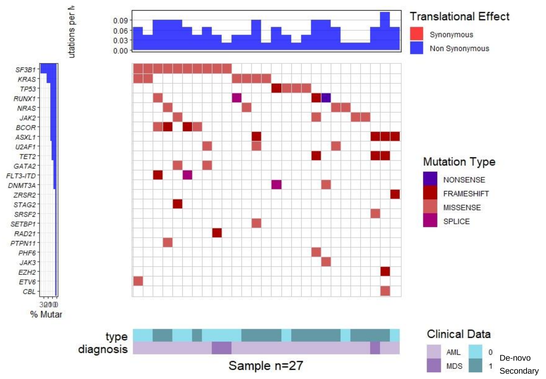


Figure 1. Pathogenic mutations detected at diagnosis. Thirty-two patients had NGS data available at diagnosis. Five patients had no mutations identified. Among those with mutations, *SF3B1* was the most common in 31%, followed by *KRAS* in 19%.

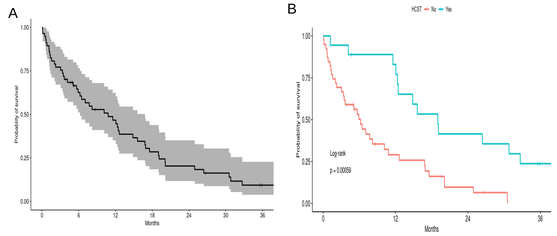


Figure 2. A) Kaplan Meier curve for the probability of OS over time in entire cohort. Median OS was 11 months (95% CI 6.2, 17). B) Kaplan Meier curve as stratified by HSCT, median OS was 19 months with HSCT vs 6.2 months without, p=0.001 (HR 0.31, 95% CI 0.15, 0.62).

- N=60
- 67% of cases were secondary MDS/AML
- SF3B1 and KRAS were the most common mutations
- Monosomy 7 or 7q deletion were the most common CG abnormalities, not significantly associated with OS or LFS.
- Intensive chemotherapy were more likely to achieve a CR/CRi (p=0.007). However, treatment intensity did not significantly impact OS in our cohort.
- HSCT was a significant prognostic factor for OS. The median OS in those with a HSCT was 19 months compared to 6.2 months for those without (p=0.001).
- AML-MRC was a significant negative prognostic factor with a hazard ratio of 4.23 (95% CI 1.02-17.5, p=0.047).

DISCUSSION

- MECOM-rearrangement MDS/AML is associated with poor outcomes, regardless treatment intensity
- Compared to other studies, out cohort had high frequency of secondary MDS/AML, and had history of transplant prior to diagnosis
- No differences in outcomes according to molecular of CG category.
- Compared to chemotherapy only, HSCT improved survival outcomes.
- Novel therapies are urgently needed for these patients.

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