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NPM1-MUTATED MYELOID NEOPLASMS IRRESPECTIVE OF BLAST COUNT ARE ASSOCIATED WITH BETTER OUTCOMES WITH ACUTE MYELOID LEUKEMIA TREATMENT APPROACH

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INTRODUCTION

Myeloid neoplasms (MNs) specifically MDS and CMML harboring *NPM1* mutation at diagnosis are rare with an incidence of ~1%. According to WHO (5th edition),[1] *NPM1* is a defining genetic abnormality of AML, irrespective of marrow blasts, while the ICC (2022)[2] requires ≥10% blasts to diagnose *NPM1*-mutated AML. The classification and management of *NPM1*-mutated MNs with <10% blasts remain controversial. Here, we evaluate the clinical outcomes in patients at our institution with *NPM1*-mutated MNs.

AIM

This study aims to provide supporting evidence that *NPM1*-mutated MNs, regardless of blast count, are consistent with AML and benefit from an AML treatment approach.

METHOD

We retrospectively evaluated 40 patients with *NPM1*-mutated MDS (n=30) and CMML (n=10) treated at the Moffitt Cancer Center from 2009-2022. Patients were stratified by intensity of frontline treatment: intensive (cytarabine-based regimen) vs non-intensive (HMA-based regimen; none received HMA/venetoclax). Univariate, multivariate, and survival analyses were performed using standard statistical methods.

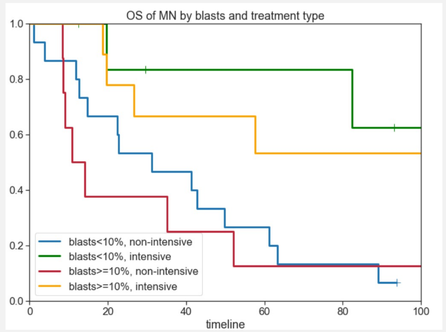
RESULTS

Of the 40 patients (24M/16F), 17 (42.5%) were treated with intensive therapy. Median age (68 years) between intensive and non-intensive were comparable (P=0.472).

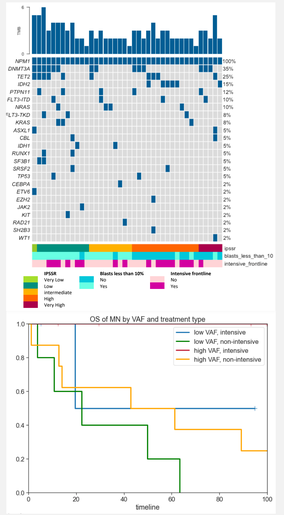
There were 22 (55%) and 18 (45%) patients with marrow blasts <10% and ≥10% at diagnosis, respectively. Nineteen patients (47.5%) had high-/very high-risk disease by IPSS-R. For those transformed into AML (85%), 47.5% occurred within 3 months.

Common co-mutations included DNMT3A (35%), TET2 (25%), IDH1/2 (20 %), FLT3-ITD/TKD (17.5%), and PTPN11 (12.5%).

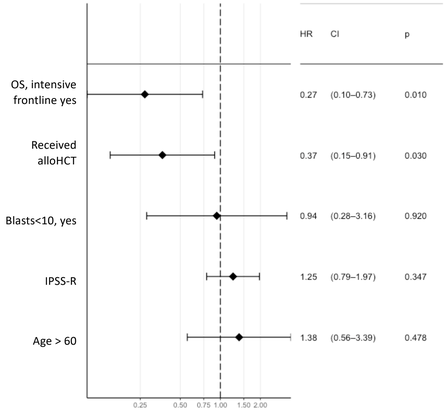
Sixteen patients (40%) underwent allogeneic hematopoietic cell transplant (HCT).



Median overall survival (mOS) was longer for the intensive group (63 vs 35.2 months, *P*=0.0295). Among patients with blasts ≥10%, intensive cohort (n=10) had better mOS vs. non-intensive (n=8) (mOS NR vs. 14.1 months, *P*=0.030). Even in patients with blasts <10%, similar findings were observed (intensive [n=7] mOS NR vs. non-intensive [n=15] mOS 31.2 months, *P*=0.020).



Multivariate Analysis



Multivariate regression using covariates including age, IPSS-R, blasts, treatment intensity, and HCT confirmed survival impact (intensive, HR 0.25; 95% CI, 0.10-0.62; P=0.003; HCT, HR 0.30; 95% CI, 0.13-0.71; P=0.006).

CONCLUSIONS

Our data add to the supporting evidence that *NPM1*-mutated MNs, even with low marrow blasts, are consistent with AML and benefit from an AML treatment approach. Evaluation of larger data sets that confirm these observations may help guide future treatment recommendations for these patients.

REFERENCES

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