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AML-261: Clinical Outcomes of Nucleophosmin (NPM1) Mutant Acute Myeloid Leukemia (AML): A Single-Institution Experience

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INTRODUCTION

- Mutant *NPM1* is recognized as a distinct entity in the WHO classification of hematopoietic neoplasms.
- One-third of AML patients have mutations in the *NPM1* gene.
- Although therapies specifically directed against the *NPM1* mutant or downstream signaling pathways are not yet available, a venetoclax-based regimen may be particularly effective in *NPM1*-mutated AML.

AIMS

- To identify the incidence of *NPM1*-mutated AML among acute leukemia patients treated at our institution..
- To analyze the clinical outcomes of *NPM1*-mutant AML patients treated with various induction therapy regimens at our institution.

METHOD

- Design: Single-center retrospective study of all *NPM1*-mutant AML patients treated at Memorial Hermann Hospital, Texas Medical Center, from January 1, 2013, to December 31, 2020.
- Setting: General community, academic hospital.
- Study participants: Adults with *NPM1*-mutant AML undergoing various induction therapy regimens.
- Main outcome measures: rate of composite complete remission (CCR; complete response [CR] + CR with incomplete hematologic recovery [CRi]), and median overall survival (OS).

RESULTS

- 120 patients with AML were analyzed.
- Young and fit individuals received dose-intense chemotherapy:
  - Fludarabine, idarubicin, and cytarabine (FIA; n=13) and
  - Standard 3+7 regimen with idarubicin and cytarabine (n=2).
- FLT3 mutation was seen in 14 patients, and 2 received FLT3 inhibitors and induction therapy.
- Older/unfit patients were treated with:
  - Hypomethylating agents (HMAs) alone (n=2) or
  - HMAs plus venetoclax (n=3).

	N=20
Age, years (median, range)	**58.5 (31-82)**
WBC count x10^3/µl (median)	**67**
ELN risk stratification	
Favorable risk, n (%)	**6 (30)**
Intermediate risk, n (%)	**14 (70)**
Induction regimen	
FIA, n (%)	**13 (65)**
3+7, n (%)	**2 (10)**
HMA + venetoclax, n (%)	**3 (15)**
HMA alone, n (%)	**2 (10)**
FLT3 mutation, n (%)	**13 (65)**
Outcome	
CR in the dose-intense chemo group	**13 (86)**
CCR in the dose-intense chemo group	**15 (100)**
30 days induction mortality, n (%)	**1 (5)**
Median OS, dose-intense chemo	**66.5 months**
Median OS, HMA + venetoclax group	**20.5 months**

- The CR and CCR in patients treated with dose-intense chemotherapy were 86% (13/15) and 100% (15/15), respectively.
- In the HMA plus venetoclax group, all 3 patients achieved CCR, whereas neither patient treated with HMA alone responded.
- The 30-day induction mortality rate was 5%.
- Two patients treated with dose-intense chemotherapy underwent allogenic stem cell transplant in the first CR, and both are alive with a follow-up of 4 years.
- The median OS in the dose-intense chemotherapy group was 66.5 months
- The median OS in the HMA plus venetoclax group was 20.5 months

CONCLUSIONS

- *NPM1*-mutant AML patients treated with dose-intense chemotherapy had a favorable long-term outcome with a median OS of 66.5 months.
- Older/unfit patients treated with HMA plus venetoclax also showed impressive results with a median OS of 20.5 months
- Due to the high sensitivity of *NPM1* to venetoclax, there may be a role for incorporating venetoclax into dose-intense chemotherapy.

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