Clinical Outcomes of Patients with FLT3-Mutated Acute Myeloid Leukemia (AML): A Single Center Retrospective Review.

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Background

- Approximately 25-30% of patients with newly diagnosed AML harbor activating mutation of the fms-like tyrosine kinase-3 (FLT3) gene.
- FLT3 activating mutations may involve either the juxta membrane domain [internal tandem duplication mutations (FLT3-ITD)] or the tyrosine kinase domain (FLT3-TKD).
- FLT3-ITD mutation is an adverse prognostic factor associated with shorter RFS (relapse free survival) and overall survival (OS) whereas the prognostic relevance of FLT3-TKD mutations are unknown.

Materials & Methods

- The primary objective of our study is to evaluate the outcome of patients with FLT-3 mutant AML treated at our institution.
- We retrospectively reviewed all patients with FLT3 mutated AML (both ITD and TKD) treated at our institution from March 2013 till December 2021.
- Clinical characteristics and patient outcomes were extracted from chart review.

Results

Table 1: Patient characteristics of FLT3 mutant AML

Characteristics	N=22 FLT 3 ITD (N=18), FLT3 TKD (N=3), Both ITD &TKD (N=1) N (%) /Median (range)
Age	54 (range, 20-68) years
Male	12 (54%)
De novo AML	19 (86.36%)
Secondary AML	3 (13.6%)
ELN risk	
Intermediate	14
Adverse	8
Karyotype	
Complex karyotype	2
Co-occurring mutations	
NPM1	15
NRAS	2
DNMT3	3
IDH1	1
IDH2	2
P 53	2
RUNX1	2
ASXL1	1
WT1	1

Table 2:

Response	N=22/ (%)	Composite CR (CR+CRi)	CR	CRi
Induction chemotherapy				
FIA	8	6	5	1
IA	2	2	2	
FIA + gilteritinib	4	4	3	1
HMA alone	3	0		
HMA + venetoclax	3	3	3	
HMA + gilteritinib	1	1	1	
HMA +venetoclax+ gilteritinib	1	1	1	
Early mortality	N (%)			
<30 days	1(4.5%)			
<60 days	3(13%)			

FIA- Fludarabine, idarubicin and cytarabine; IA- Idarubicin and cytarabine

HMA- Hypomethylating agent.

CR- Complete remission

CRi – Complete remission with incomplete hematological recovery.

- Three patients proceeded to an allogenic stem cell transplantation (ASCT) in first CR and all of them remain in CR at a mean follow up of 28 months.
- One patient who was ASCT ineligible was treated with 12 cycles of HMA maintenance therapy and remains in CR after 72 months of follow up.
- Median relapse free survival (RFS) among all FLT3-ITD patients was 360 days (range, 218-669).
- The median RFS for non-ASCT patients was 240 days (range, 195-405).

Discussion

- Testing for FLT3 mutation is recommended in all newly diagnosed AML patients and FLT3 inhibitors should be incorporated earlier in therapy to achieve deep molecular remissions.
- Gilteritinib added to FIA is well tolerated in patients eligible for intensive chemotherapy.
- Triplet regimen of HMA, venetoclax and gilteritinib is preferred in patients ineligible for intensive chemotherapy.
- Given the high relapse potential, ASCT in first CR is recommended.

Conclusion

- FLT3I added to standard induction therapy is well tolerated and highly effective.
- The duration of response tends to be shorter in the non-ASCT group.
- In ASCT ineligible patients, maintenance therapy could potentially reduce the relapse risk.

References

1. Daver, N., Venugopal, S. & Ravandi, F. FLT3 mutated acute myeloid leukemia: 2021 treatment algorithm. Blood Cancer J. 11, 104 (2021).