

Upfront Triple Therapy With FLAG-Venetoclax backbone in Intensive Chemotherapy-Eligible FLT3-ITD AML patients:
Preliminary Results from a Retrospective Cohort

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INTRODUCTION

AML remains a challenging disease to treat in patients with non-favourable molecular and cytogenetic features.

Although venetoclax-based therapy has improved outcomes, evidence for upfront FLAG-Ven-based triplet therapy in newly diagnosed AML is still scarce

AIM

To evaluate the feasibility, response, and safety of upfront FLAG-Ven-based triplet therapy in newly diagnosed AML in a real-world cohort.

METHOD

Study design: Single-centre retrospective study.

Study duration: March 2023 – January 2026.

Inclusion: Newly diagnosed FLT3-positive AML patients.

Treatment: Upfront FLAG-Venetoclax-Midostaurin (Triplet)

Baseline characteristics, ELN 2022 risk, response at day 28, MRD status, hematologic recovery, transplant bridging, infections, organ toxicities, and mortality were collected.

CR and MRD negativity were assessed by marrow examination using flow cytometry as available.

Table 1: Baseline characteristics of the study patients

Characteristics	Result
Total Patients	14
Median age, years (range)	33.5 (18 – 52)
Age < 40 years	8 (57.1%)
Female	5 (35.7%)
Male	9 (64.3%)
ECOG	
0 – 1	2 (14.3%)
2 – 3	12 (85.7%)
3	3 (21.4%)
Median baseline TLC, /μL, range	99,555 (8690 – 3,40,000)
Hyperleukocytosis (>100,000/μL)	6 (42.9%)
Median baseline platelets, /μL, range	32,500 (10,000 – 83,000)
ELN 2022 Risk	
– Favorable	-
– Intermediate	10 (71.4%)
– Adverse	4 (28.6%)
Common molecular/cytogenetic features	
– FLT3 mutation present	14 (100%)
– DEK-NUP/ t (6;9)	4 (28.6%)
– RUNX1-RUNX1T1/ t (8;21)	1 (7.1%)
– NPM1	5 (35.7%)
– CEBPA	4 (28.6%)

RESULTS

This study included 14 patients (median age 33.5 years).

- ELN 2022 risk stratification:

- Favorable-risk: n=0
- Intermediate-risk: n=10
- Adverse-risk: n=4

- Response to Induction Therapy:

- The day 28 CR rate was 78.6% by intent-to-treat, with one primary induction failure and one induction death.
- Best MRD-negative response was achieved in 9/14 patients (64.3%).

Efficacy Outcomes

Day 28: complete remission (CR)	11 (78.6%)
Primary Induction Failure (PIF)	1 (7.1%)
Induction Mortality	1 (7.1%)
Lost to follow-up before assessment	1 (7.1%)
Day 28 MRD-negative among assessable patients (n=9)	4 (44.4%)
Best MRD-negative response overall	9 (64.3%)
Allogeneic HSCT performed	7 (50%)
MSD	3
MUD	2
Haplo	2
HSCT in CR1, (n=7)	7/7 (100%)
Post-HSCT relapse	2/7 (28.6%)
Any relapse event	2/14 (14.3%)
Deaths	2 (14.3%)

Table 2: Safety profile of the study patients

Safety/feasibility parameter	Result
Median ANC recovery to ≥500/μL, day+	18 (15 – 23)
Median platelet recovery to ≥20,000/μL, day+	18.5 (15 – 21)
ICU admission	4 (28.6%)
Median induction hospital stays (days), range	22 (9 – 35)
Any fungal infection (proven/probable)	6 (42.9%)
Proven fungal infection	2 (14.3%)
Probable fungal infection	4 (28.6%)
Any bacterial infection	8 (57.1%)
MDR organisms reported	3 (21.4%)
Cardiac/renal/hepatic toxicity	0 (0%)
Pancreatitis	1 (7.1%)
4-week mortality	1 (7.1%)
6-week mortality	0 (0%)
8-week mortality	0 (0%)

CONCLUSIONS

This single-centre experience suggests that upfront FLAG-Ven-based triple therapy is a feasible and active induction strategy for newly diagnosed AML, with promising remission and MRD-negative responses in a high-risk real-world population. Larger studies are needed to confirm the durability of response and define the safety profile.

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