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LIMITED TOXICITY AND IMPRESSIVE OUTCOMES OF UPFRONT FLAG-BASED INDUCTION IN NEWLY DIAGNOSED ACUTE MYELOID LEUKEMIA: AN INDIAN SCENARIO

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INTRODUCTION

Young patients with newly diagnosed acute myeloid leukemia (AML) in LMICs like India face high induction mortality (≈20%) due to factors like drug-resistant bacteremia, fungal pneumonia, and poor tolerance to anthracyclines. The common '3+7' induction regimen has significant complications, while the FLAG regimen (fludarabine, cytarabine, and GCSF) is suggested as an anthracycline-free alternative. Further investigation is needed to assess FLAG's effectiveness and safety in these high-risk settings.

AIM

The aim of the study is to assess upfront FLAG's effectiveness and safety in AML.

Endpoints:

- Overall composite complete response (CRc), which includes complete remission (CR) and CR with incomplete counts recovery (CRi) was primary endpoint.
- Incidence of induction mortality was secondary endpoint.

METHOD

- Retrospective analysis of patients with newly diagnosed AML, aged 18-60 years, treated between May 2021 and February 2024.
- All patients received a 4-day FLAG-based induction therapy.
- Addition of Midostaurin, ponatinib, or venetoclax was determined based on AML genomics, though availability limited their use.

RESULTS

54 patients included (median age 39 years).

- Response to Induction Therapy:

- CRc rate of 76% (41/54) after 1 cycle of induction.

- CRc rates by risk group:

- Favorable-risk: 90%
- Intermediate-risk: 84%
- Adverse-risk: 43%

- Consolidation Therapy:

- 80% (33/41) consolidated with intensive chemotherapy.
- 12% (5/41) with low-intensity therapy.
- 7% (3/41) underwent allogenic stem cell transplantation.

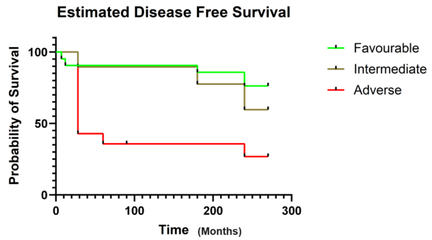


Fig:1 Kaplan Meier Curve depicting Disease Free Survival (DFS)

- Survival Outcomes:

- Median overall survival (OS) and relapse-free survival (RFS) at 9 months were not reached for responders.
- Estimated 9-month RFS by risk group:
  - Favorable-risk: 76%
  - Intermediate-risk: 59%
  - Adverse-risk: 27%

Table 1. Baseline characteristics of 54 AML patients

Characteristic	N (%)
Total number of patients	54
Median age, years (range)	39 (19–59)
Gender	
Male	30 (55.5%)
Female	24 (44.4%)
ECOG	
• 0-1	22
• 2	22
• 3	10
Baseline median WBC (× 10^9/L) count	10.9 (0.11–268)
Baseline median platelet count, (× 10^9/L) count	49.5 (7–262)

Table 2. Adverse events during induction

Haematological adverse events, Grade ≥ 3	
Neutropenia	100% (54/54)
Anaemia	100% (54/54)
Thrombocytopenia	100% (54/54)
Non-haematological adverse events	
Respiratory Tract infection	38.8% (21/54)
Skin and soft tissue infection	9.2% (5/54)
Gastro-Intestinal infection	14.8% (8/54)
CNS infection	3.7% (2/54)
Invasive Fungal infection, Probable	35% (19/54)
Probable	29.6% (16/54)
Proven	5.5% (3/54)
Blood Culture Positivity	38.8% (21/54)
Gram positive bacteremia	11.1% (6/54)
Gram negative bacteremia	27.7% (15/54)
Carbapenem Resistance Enterobacteremia	7.4% (4/54)
Induction mortality	
At 4 weeks	3.7% (2/54)
At 6 weeks	Nil
At 8 weeks	Nil

CONCLUSIONS

Anthracycline-free FLAG-based regimen with or without a third agent shows promising induction outcomes. This warrants further evaluation in settings with high induction morbidity and mortality.

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