Dynamics of FLT3 Mutations in Acute Myeloid Leukemia: A Systematic Review and Meta-analysis

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Introduction

FLT3 mutations are among the most frequent molecular abnormalities in AML, particularly FLT3-ITD. These mutations influence prognosis and therapeutic decisions. Emerging evidence suggests their status can change over time, impacting patient management and outcomes.

Aim

To evaluate the dynamics of FLT3 mutational status in adult AML patients by comparing findings at diagnosis and at relapse/refractory disease.

Objectives

>Determine the rate of FLT3 mutation shifts.
>Compare changes in FLT3-ITD and FLT3-TKD subtypes.
>Assess implications for molecular monitoring and therapy.
>Provide evidence-based recommendations for clinical practice.

Methods

Design: Systematic review and meta-analysis.
Databases: PubMed (searches in 2020 and updated in 2024).
Inclusion: Adult AML patients, studies reporting FLT3 status at both diagnosis and relapse, PCR-based methods.
Total studies included: 20
Total patients analyzed: 1,094

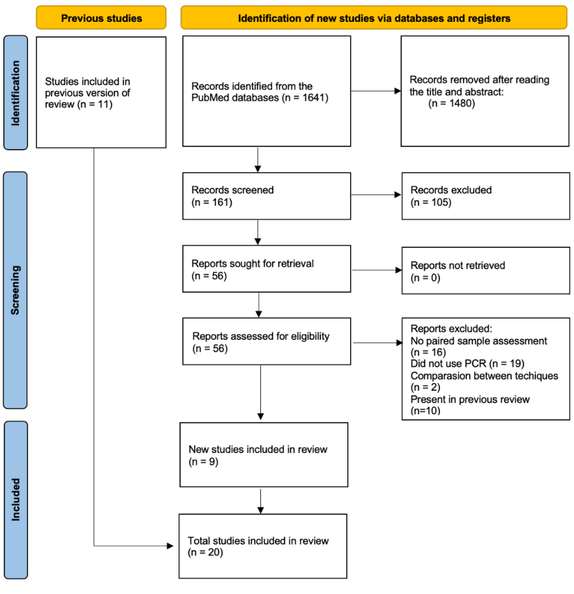


Figure 1. Flowchart of study selection and inclusion based on eligibility criteria for systematic review. Abbreviation: PCR: Polymerase chain reaction.

Results

FLT3 Mutation Dynamics:
Overall mutation shift rate: FLT3 mutation status changed in **147 patients (13%)**, indicating that approximately **1 in 7 AML patients** experiences a shift between diagnosis and relapse.
FLT3-ITD subgroup (n = 936 patients): 222 patients (24%) remained FLT3-ITD-positive, **46 patients (5%)** lost the ITD mutation, **73 patients (8%)** acquired the mutation at relapse → This corresponds to a **13% overall shift rate** for FLT3-ITD.
FLT3-TKD subgroup (n = 543 patients): 14 patients (2%) remained FLT3-TKD-positive, **3%** lost the TKD mutation, **3%** acquired the TKD mutation at relapse → Representing a **6% shift rate** for FLT3-TKD.

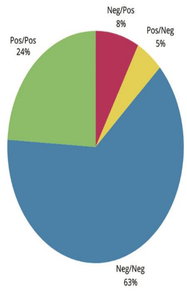


Figure 2. Change in *FLT3*-ITD mutational status between diagnosis and relapse/refractory disease

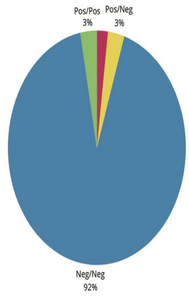


Figure 3. Change in *FLT3*-TKD mutational status between diagnosis and relapse/refractory disease

Discussion

Mutation dynamics may reflect subclonal evolution or treatment-induced selection.
These shifts have therapeutic consequences, especially in the era of FLT3 inhibitors (e.g., midostaurin, gilteritinib).
Many centers fail to perform routine molecular reassessment, particularly in public systems (e.g., SUS in Brazil).
The study emphasizes the need for re-testing at relapse to guide targeted therapy and transplantation decisions.

Conclusion

FLT3 mutation status can change during AML progression. Approximately 1 in 7 patients experience a shift. Routine reassessment is critical to ensure optimal therapy. PCR with fragment analysis is currently the most accessible and feasible method.

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