Acute Myeloid Leukemia in Community Oncology: *FLT3* Testing and Treatment Insights

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INTRODUCTION

Acute myeloid leukemia (AML) is a rapidly progressive hematologic malignancy; mutation of the *FLT3* (Fms-like tyrosine kinase 3) gene is the most frequent genetic alteration and contributes to poor prognosis [1]. **A recent Cornerstone Specialty Network survey (Q2-2026) of 100 U.S.-based community oncologists revealed both the opportunities and the ongoing challenges of managing patients with *FLT3*-mutated (*FLT3*m) AML.** Respondents were mainly general hematologists / oncologists managing a modest volume of patients with AML somewhat limiting exposure and experience to AML-specific and targeted therapies.

Molecular Profiling and Testing Practices

Molecular profiling: Multi-panel next-generation sequencing (NGS), is considered central to AML treatment decision-making. **Routine *FLT3*m assessment** is consistently adopted in the community setting at initial diagnosis and is frequently **repeated on relapse.**

***FLT3* Mutation Monitoring:** Almost all community oncologists are testing for *FLT3* mutations with **internal tandem duplication (ITD) and tyrosine kinase domain (TKD) mutations** being assessed. There is some observation of ***FLT3* mutation loss or gain** at relapse highlighting the need for repeat testing, and identification of **co-mutations with *FLT3* mutations** driving **disease aggressiveness.**

Integration Challenges: Many community oncologists still manually upload PDF test results due to limited vendor / EMR integration. The absence of automated actionable mutation alerts highlights the **need for stronger genomic flagging** to reliably identify patients eligible for targeted therapy.

Timing of Treatment: Some community oncologists **do not delay treatment** until results are available, suggesting that initial treatment decisions are not always informed or optimal. The **Beat AML Master Trial supports the delay of treatment initiation** for genomic work-up to inform decision-making and is a feasible and relatively safe strategy that can improve overall survival [2].

Treatment Landscape for *FLT3*-Mutated AML

Treayment of *FLT3m* AML aligns closely with **NCCN Guidelines** with **performance status, molecular mutations, cytogenetic risk, and age** highly considered in treatment decision-making with fit patients typically receiving intensive induction therapy, while older or unfit patients are treated with low-intensity regimens.

Co-management of AML: In the community oncology setting, regular **co-management of AML with academic or hospital partners** is common throughout the patient journey, driven by transplant considerations and clinical complexity, with coordination of care considered effective although some **communication gaps** remain requiring **additional clarification** as patients transition between settings

Targeted Therapy in Frontline: Chemotherapy plus a *FLT3* inhibitor such as midostaurin [3] or quizartinib [4] is preferred (Table 1)

Targeted Therapy in Relapsed/Refractory: **Gilteritinib** is used as maintenance monotherapy in the post-transplant [5] and in the relapsed/ refractory setting [6] providing benefit, **irrespective of *FLT3-ITD, FLT3-TKD, and FLT3-ITD-TKD* mutation status** reflecting its broad approved indication; midostaurin should not be used in the relapsed or refractory AML setting (Table 1)

Future Considerations: **Investigations of combinations** such as venetoclax + azacitidine with or without a *FLT3* inhibitor [7] to **increase MRD negativity and achieve greater remission** in the relapsed / refractory setting are ongoing

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Table 1: Overview of FLT3 Inhibitors and Their Approved Uses

FLT3 inhibitor	Indication and Usage
Midostaurin (RYDAPT®)	Newly diagnosed AML that is FLT3 mutation positive, in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation
Quizartinib (VANFLYTA®)	Newly diagnosed AML that is FLT3 ITD-positive, in combination with standard cytarabine and anthracycline induction and cytarabine consolidation, and as maintenance monotherapy following consolidation chemotherapy
Gilteritinib (XOSPATA®)	Relapsed or refractory AML with a FLT3 mutation

Key Insights and Takeaways

- ✓ Continued standardization of testing and retesting for *FLT3* mutations is important due to gain and loss, while identification of co-mutations with *FLT3* can still be approached with a *FLT3* inhibitor
- ✓ 1L/maintenance: Quizartinib is indicated for *FLT3* ITD-positive newly diagnosed AML in combination with intensive chemotherapy and as a single-agent maintenance therapy
- ✓ R/R *FLT3* mutated AML: Gilteritinib is more broadly indicated for relapsed or refractory AML with a *FLT3* mutation irrespective of ITD or TKD status
- ✓ Optimal sequencing of *FLT3* inhibitors is yet to be determined with consideration of prior therapy and different mechanisms of action as key data gaps
- ✓ Consider adverse event profile when selecting treatment with gilteritinib generally more favorable than midostaurin and quizartinib which require monitoring and management of gastrointestinal and QTc prolongation / cardiac events.

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