Acute Myeloid Leukemia in Community Oncology: IDH1 Testing and Treatment Insights

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A recent Cornerstone Specialty Network survey (Q3-2025) of over 100 U.S.-based community oncologists revealed both the promise and the hurdles of treating patients with *IDH1*-mutated (m*IDH1*) 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.

INTRODUCTION

Acute myeloid leukemia (AML) is an aggressive hematologic malignancy characterized by the clonal proliferation of immature myeloid cells in the bone marrow, leading to impaired hematopoiesis and cytopenias. Management of AML has evolved significantly with the introduction of targeted therapies which are increasingly adopted in frontline settings, reflecting a shift toward precision medicine.

Molecular Profiling and Testing Practices

Molecular profiling, particularly multi-panel next-generation sequencing (NGS), is considered by most community oncologists central to AML treatment planning. Routine *IDH1* assessment with multi-gene NGS testing is widely adopted, although most community oncologists surveyed only occasionally encounter patients with m*IDH1* AML (approximately 5–10% of their AML cases) reflective of the incidence of m*IDH1* at approximately 6 – 10% of patients with AML [1]. *IDH1* testing is essential to enable initiation of mutation positive targeted therapy such as ivosidenib or olutasidenib (m*IDH1* inhibitors) and can benefit patient outcomes.

Turnaround Time & Workflow: NGS multi-panel results typically take between **one to two weeks turnaround time** and is considered important in the **timing of initiation of m*IDH1* targeted therapy.** Testing is almost always performed though external vendors with CARIS the most utilized out of many vendors with limited in-house testing.

Integration Challenges: Most community oncologists have to **manually upload PDF report test results** into EMRs (with no one standard EMR system utilized), highlighting the need for better **integration and interface** with testing vendors including the need for increased automated **flagging of actionable mutations** to help with timely identification of patients eligible for targeted therapy.

Timing of Treatment: While molecular testing results can guide therapy selection, only one quarter of community oncologists **always 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].

Mutation Monitoring: While **almost all** community oncologists are routinely **testing for** *IDH1* **mutations** in all patients with AML **at diagnosis,** repeat *IDH1* testing at relapse is not yet standard, underscoring the need for **consistent mutation monitoring** throughout disease progression to identify all patients with m*IDH1* AML eligible for targeted therapy.

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Treatment Landscape for *IDH1*-Mutated AML

Treatment of m*IDH1* AML in the community oncology setting aligns closely with NCCN Guidelines.

Frontline Therapy: Treatment selection is primarily based on performance status, disease characteristics including cytogenetics and molecular profile, and patient age. In general, fit patients typically receive intensive induction therapy, while older or unfit patients are treated with low-intensity regimens or targeted agents.

Targeted Therapy Adoption:

- **Ivosidenib** is the **predominant utilized *IDH1* inhibitor** in the community oncology setting across both **newly diagnosed** and **relapsed/refractory** (R/R) disease. Olutasidenib sees limited use, largely due to insufficient experience.

- **Doublet Regimens: Ivosidenib + azacitidine** is sometimes utilized by community oncologists for newly diagnosed AML with the combination preferred for older patients or patients unfit for intensive chemotherapy with strong efficacy over azacitidine alone (long-term follow-up [median 28.6 months] OS: 29.3 months vs 7.9 months, respectively, HR=0.42, P <0.001; 47% CR rate vs 15% CR rate, respectively) [3]. Indirect treatment comparisons and real-world studies suggest that **ivosidenib + azacitidine** provides **greater benefit with lower side effects such as cytopenias** when compared to venetoclax + azacitidine (ivosidenib plus azacitidine provides numerical OS benefit although not significant improvement compared to venetoclax + azacitidine, HR=0.74) and should be prioritized for patient's ineligible for standard induction chemotherapy [4, 5].

- **Triplet Regimens:** There is growing awareness and support among community oncologists for triplet combinations such as **azacitidine + venetoclax + ivosidenib or decitabine + venetoclax + ivosidenib** based on reported beneficial outcomes for patients' ineligible for intensive chemotherapy with m*IDH1* AML [6].

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Key Insights and Takeaways

- Continued standardization of molecular testing for *IDH1* and integration into EMRs is critical with a need for real-time actionable mutation alerts to guide precision treatment. Mutation monitoring at relapse should become standard practice.
- Delaying treatment until return of NGS test results supports informed treatment decisions, provides an opportunity for utilization of a targeted agent such as ivosidenib for newly diagnosed patients, and can improve patient outcomes.
- Doublet therapy such as ivosidenib + azacitidine should be the preferred regimen for patients that are ineligible for standard induction chemotherapy as it may provide greater benefit and lower toxicity than alternative regimens such as venetoclax + azacitidine.
- Ivosidenib (Tibsovo) is FDA-approved for patients with a susceptible *IDH1* mutation to treat newly diagnosed AML—either as monotherapy or in combination with azacitidine—as well as for relapsed or refractory AML, myelodysplastic syndromes (MDS), and locally advanced or metastatic cholangiocarcinoma.

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