AML Treatment Strategies: Optimising Outcomes in a Complex Disease

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Acute myeloid leukemia (AML) remains a heterogeneous and aggressive haematological malignancy, necessitating precise, risk-adapted treatment strategies to improve patient outcomes. The complexity of AML, driven by diverse genetic and molecular aberrations, often complicates treatment selection, particularly in older or unfit patients. This review examines established and emerging approaches to guide therapeutic decisions in AML, focusing on optimising patient benefit.

KEY TAKEAWAYS

- The Pivot: AML treatment increasingly relies on molecular profiling to inform targeted therapy selection, moving beyond age and fitness alone.
- The Data: While specific trial data are not provided, the principle of integrating cytogenetic and molecular risk stratification is paramount for guiding induction and post-remission therapy.
- The Action: Clinicians should incorporate comprehensive molecular diagnostics into routine AML workup to tailor treatment, including targeted agents where appropriate, and consider allogeneic stem cell transplantation for eligible patients.

Acute myeloid leukemia (AML) is characterised by the rapid proliferation of abnormal myeloid blasts in the bone marrow and peripheral blood. The disease primarily affects older adults, with a median age at diagnosis of approximately 68 years.1 Prognosis varies widely, influenced by patient age, performance status, and critically, the underlying cytogenetic and molecular abnormalities.2 Accurate risk stratification is fundamental to treatment planning, guiding decisions regarding intensive chemotherapy, targeted therapies, and allogeneic hematopoietic stem cell transplantation (allo-HSCT).3

Initial diagnostic workup for AML requires bone marrow aspiration and biopsy, flow cytometry, cytogenetics, and molecular testing.4 These comprehensive analyses are crucial for distinguishing AML from other myeloid neoplasms and for identifying specific genetic alterations that drive disease progression and influence therapeutic response. Key molecular markers, such as mutations in FLT3, NPM1, CEBPA, IDH1/2, and translocations like t(8;21), inv(16), and t(15;17), are essential for risk classification and therapeutic targeting.5 For instance, patients with core-binding factor AML (CBF-AML), characterised by t(8;21) or inv(16), generally have a more favourable prognosis and respond well to intensive chemotherapy.6 Conversely, mutations in FLT3-ITD, particularly with a high allelic ratio, are associated with a higher risk of relapse and often necessitate the incorporation of FLT3 inhibitors.7 The identification of these specific mutations allows for a more personalised approach to treatment, moving beyond a one-size-fits-all strategy.

Treatment Strategies and Patient Outcomes

Treatment for AML is typically divided into induction and post-remission (consolidation) phases. The goal of induction therapy is to achieve a complete remission (CR), defined by less than 5% blasts in the bone marrow, absence of extramedullary disease, and recovery of peripheral blood counts.8 For younger, fit patients, intensive induction chemotherapy, typically with a '7+3' regimen (cytarabine for 7 days, daunorubicin or idarubicin for 3 days), remains the standard of care.9 This regimen aims to rapidly reduce the leukemic blast burden. However, the advent of targeted therapies has expanded options, particularly for specific genetic subsets. For example, gilteritinib, a FLT3 inhibitor, is approved for relapsed/refractory AML with a FLT3 mutation.10 Its mechanism involves inhibiting the FLT3 receptor tyrosine kinase, thereby disrupting downstream signaling pathways critical for leukemic cell survival. Similarly, venetoclax, a BCL-2 inhibitor, in combination with hypomethylating agents (HMAs) or low-dose cytarabine, has significantly improved outcomes for older or unfit patients who cannot tolerate intensive chemotherapy.11 Venetoclax selectively inhibits the anti-apoptotic protein BCL-2, leading to the restoration of apoptosis in AML cells.

Post-remission therapy aims to eradicate minimal residual disease (MRD) and prevent relapse. For many patients, especially those with intermediate or adverse risk features, allo-HSCT offers the best chance for long-term cure.12 The decision for allo-HSCT is complex, balancing the potential for cure against treatment-related mortality and morbidity. Factors such as donor availability, patient age, comorbidities, and disease risk stratification influence this decision.13 For patients not proceeding to allo-HSCT, consolidation typically involves additional cycles of chemotherapy, often with high-dose cytarabine, or maintenance therapy with targeted agents where applicable.14 For example, oral azacitidine has demonstrated a survival benefit in patients with AML in CR after intensive chemotherapy who are not candidates for allo-HSCT.15 This maintenance approach aims to sustain remission and delay relapse.

The management of relapsed or refractory AML presents a significant challenge. Treatment options include re-induction chemotherapy, targeted agents, and clinical trial participation.16 The choice of therapy depends on the patient's prior treatments, duration of remission, and current disease characteristics. For patients with IDH1/2 mutations, inhibitors such as ivosidenib and enasidenib offer targeted options in both newly diagnosed and relapsed/refractory settings.17 These inhibitors block the mutant IDH enzymes, which produce the oncometabolite 2-hydroxyglutarate, thereby restoring normal hematopoietic differentiation. The evolving landscape of AML treatment underscores the importance of continuous molecular monitoring and adapting therapeutic strategies based on disease response and emerging resistance mechanisms.18 Despite advancements, a significant proportion of patients still experience relapse, highlighting the ongoing need for novel therapeutic approaches and improved understanding of resistance pathways.

For a comprehensive understanding of current practices and emerging strategies in managing complex haematological conditions, consult the Oxford Handbook of Clinical Haematology.

> **CLINICAL IMPLICATIONS**
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> The EHA 2026 session on AML treatment strategies highlights a critical shift in haematological oncology: the move from a one-size-fits-all approach to highly individualised, molecularly-driven therapy. For clinicians, this means that a comprehensive molecular diagnostic panel is no longer an optional extra but a foundational component of AML management. Relying solely on morphology and basic cytogenetics risks suboptimal treatment selection, particularly given the expanding armamentarium of targeted agents like FLT3 inhibitors

(e.g., gilteritinib), IDH inhibitors (e.g., ivosidenib), and BCL-2 inhibitors (e.g., venetoclax). The industry's investment in these targeted therapies underscores the commercial imperative to identify specific patient populations, thereby driving the need for precise diagnostic tools.

The increasing complexity of AML treatment also places a greater burden on multidisciplinary teams. Integrating the expertise of haematologists, pathologists, and molecular geneticists is essential to interpret complex genomic data and translate it into actionable treatment plans. This collaborative approach is particularly pertinent when considering the timing and eligibility for allogeneic stem cell transplantation, which remains the only curative option for many high-risk patients. Furthermore, the financial implications of these advanced diagnostics and therapies are substantial, necessitating careful consideration of cost-effectiveness and equitable access, especially in healthcare systems with finite resources.

For patients, this evolution offers the promise of improved outcomes and reduced toxicity compared to traditional intensive chemotherapy, particularly for older or frail individuals. However, it also demands a more informed engagement with their treatment journey, understanding the rationale behind molecular testing and the implications of specific genetic mutations. The rapid pace of drug development in AML means that treatment guidelines from bodies like the European LeukemiaNet (ELN) and NCCN require frequent updates, and clinicians must remain vigilant in incorporating the latest evidence. The eha 2026 session serves as a timely reminder that staying abreast of these developments is not merely academic, but directly impacts patient survival and quality of life.

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