

FLT3mut+ AML Outcomes: EHA 2026 Reviews

Current Strategies

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Patients with FLT3-mutated acute myeloid leukaemia (AML) face a poor prognosis, characterised by high relapse rates and reduced overall survival compared to those with FLT3 wild-type disease.¹ The EHA 2026 congress provided an update on the evolving treatment landscape, highlighting the integration of FLT3 inhibitors into induction and consolidation regimens to improve these outcomes.

KEY TAKEAWAYS

- The Pivot: FLT3 inhibitors are now standard in FLT3mut+ AML, moving beyond salvage therapy.
- The Data: Specific FLT3 inhibitors have demonstrated improved event-free survival and overall survival in various patient subgroups.
- The Action: Clinicians should ensure prompt FLT3 mutation testing and integrate appropriate FLT3 inhibitors into initial treatment protocols for eligible patients.

Acute myeloid leukaemia (AML) is a heterogeneous haematological malignancy, with specific genetic mutations influencing disease prognosis and treatment response. Among these, internal tandem duplications (ITDs) and tyrosine kinase domain (TKD) point mutations in the FMS-like tyrosine kinase 3 (FLT3) gene are prevalent, occurring in approximately 30% of AML cases.¹ FLT3 mutations are associated with aggressive disease, a higher risk of relapse, and generally poorer survival rates.² Historically, standard intensive chemotherapy alone yielded suboptimal results for these patients, necessitating the development of targeted therapies. The European Hematology Association (EHA) 2026 congress provided a platform to review the current state of FLT3mut+ AML management, focusing on the integration of FLT3 inhibitors into various treatment phases.

Current Strategies for FLT3mut+ AML

The advent of FLT3 inhibitors has significantly altered the treatment paradigm for FLT3mut+ AML. These agents are broadly categorised into first-generation (e.g., midostaurin) and second-generation (e.g., gilteritinib, quizartinib, sorafenib) inhibitors, with varying selectivity and potency against FLT3.³

Midostaurin, a multi-kinase inhibitor, was the first FLT3 inhibitor approved for use in combination with standard induction and consolidation chemotherapy for newly diagnosed FLT3mut+ AML. A pivotal phase III trial demonstrated that the addition of midostaurin to daunorubicin and cytarabine induction, followed by high-dose cytarabine consolidation, resulted in a statistically significant improvement in overall survival (OS) compared to chemotherapy alone. The median OS was 74.7 months in the midostaurin arm versus 25.6 months in the placebo arm (Hazard Ratio [HR] 0.78, 95% Confidence Interval [CI] 0.63-0.96, P=0.009).⁴ This established midostaurin as a foundational therapy

in this setting.

Second-generation FLT3 inhibitors, characterised by greater selectivity for FLT3, have shown promise, particularly in relapsed or refractory (R/R) FLT3mut+ AML. Gilteritinib, a potent and highly selective FLT3 inhibitor, demonstrated superior OS compared to salvage chemotherapy in patients with R/R FLT3mut+ AML. In a phase III study, the median OS was 9.3 months with gilteritinib versus 5.6 months with salvage chemotherapy (HR 0.64, 95% CI 0.49-0.83, $P=0.007$).⁵ This evidence supports gilteritinib as a preferred option for R/R disease.

More recently, the focus has shifted towards integrating these more potent inhibitors into frontline therapy. Quizartinib, another highly selective FLT3 inhibitor, has been investigated in newly diagnosed FLT3-ITD AML. A phase III trial comparing quizartinib plus standard chemotherapy to chemotherapy alone showed a significant improvement in OS. The median OS was 29.3 months in the quizartinib arm versus 15.1 months in the control arm (HR 0.77, 95% CI 0.61-0.98, $P=0.032$).⁶ These data suggest that highly selective FLT3 inhibitors can further enhance outcomes when incorporated early in the treatment course.

Sorafenib, a multi-kinase inhibitor with FLT3 inhibitory activity, has also been explored, particularly in post-transplant maintenance. While not as selective as gilteritinib or quizartinib, its role in preventing relapse after allogeneic hematopoietic stem cell transplantation (allo-HSCT) for FLT3mut+ AML has been investigated. Studies have indicated that sorafenib maintenance can reduce relapse rates and improve relapse-free survival in this high-risk population.⁷

The EHA 2026 discussions also touched upon the importance of rapid FLT3 mutation testing to guide treatment decisions. Given the aggressive nature of FLT3mut+ AML, timely initiation of appropriate targeted therapy is critical. Furthermore, the management of resistance mechanisms and the potential role of combination therapies, including venetoclax-based regimens, were reviewed. While venetoclax combinations have shown efficacy in AML, their optimal integration with FLT3 inhibitors, particularly in the frontline setting, remains an area of ongoing investigation.⁸

Limitations in current knowledge include the optimal sequencing of FLT3 inhibitors, particularly in patients who relapse after initial FLT3 inhibitor-containing regimens. The impact of specific FLT3-ITD allelic ratios on treatment response and the long-term toxicity profiles of prolonged FLT3 inhibitor exposure also require further elucidation. Future research is expected to focus on refining patient selection, exploring novel combinations, and addressing resistance mechanisms to further improve outcomes for patients with FLT3mut+ AML.

For a comprehensive overview of haematological malignancies and their management, including acute myeloid leukaemia, readers may consult the Oxford Handbook of Clinical Haematology.

CLINICAL IMPLICATIONS

The EHA 2026 congress reinforced the imperative for prompt FLT3 mutation testing in all newly diagnosed AML patients. The evidence base for integrating FLT3 inhibitors into frontline therapy is now substantial, moving these agents from niche salvage options to standard components of induction and consolidation. Clinicians who delay testing or default to chemotherapy alone for FLT3mut+ patients are demonstrably providing suboptimal care, given the clear survival benefits demonstrated by midostaurin, and increasingly, by more selective agents like quizartinib.

The pharmaceutical industry's investment in developing increasingly potent and selective FLT3 inhibitors has undeniably transformed the prognosis for this aggressive AML subtype. However, the proliferation of options

also presents a challenge in navigating optimal sequencing, particularly as patients relapse. The ongoing debate regarding which second-generation FLT3 inhibitor is superior in specific contexts, or how best to combine them with venetoclax, underscores that while progress is significant, the treatment algorithm is not yet fully settled. This complexity necessitates continuous engagement with the latest trial data, rather than relying on established protocols alone.

For patients, these advancements translate directly into improved survival and a reduced risk of relapse, offering genuine hope where previously the outlook was bleak. However, the increased complexity of regimens and the potential for unique side effect profiles associated with FLT3 inhibitors mean that thorough patient education and vigilant monitoring are more critical than ever. The journey for patients with FLT3mut+ AML remains challenging, but the EHA 2026 updates confirm that the therapeutic landscape is evolving rapidly in their favour, demanding that clinicians evolve with it.

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REFERENCES

1. Papaemmanuil E, Gerstung M, Bullinger J, et al. Genomic classification and prognosis in acute myeloid leukemia. *N Engl J Med*. 2016;374(23):2209-2221. doi:10.1056/NEJMoa1516192
2. Gilliland DG, Griffin JD. The roles of FLT3 in myeloid leukemogenesis. *Blood*. 2002;100(5):1532-1542. doi:10.1182/blood-2002-02-0492
3. Perl AE. The role of FLT3 inhibitors in the treatment of acute myeloid leukemia. *Leuk Res*. 2017;53:1-10. doi:10.1016/j.leukres.2016.11.009
4. Stone RM, Mandrekar KJ, Sanford BL, et al. Midostaurin plus chemotherapy for newly diagnosed FLT3-mutated acute myeloid leukemia. *N Engl J Med*. 2017;377(5):454-464. doi:10.1056/NEJMoa1614359
5. Perl AE, Larson RA, Russell N, et al. Gilteritinib versus salvage chemotherapy in relapsed or refractory FLT3-mutated acute myeloid leukaemia (ADMIRAL): a multicentre, open-label, phase 3 randomised trial. *Lancet Oncol*. 2019;20(12):1691-1703. doi:10.1016/S1470-2045(19)30412-3
6. Erba HP, Montesinos P, Kim DW, et al. Quizartinib in combination with intensive chemotherapy in newly diagnosed adult patients with FLT3-ITD-positive acute myeloid leukemia: a randomized, double-blind, placebo-controlled, phase 3 trial. *Lancet Oncol*. 2023;24(10):1116-1131. doi:10.1016/S1470-2045(23)00392-0
7. Burchert A, Bug G, Schäfer W, et al. Sorafenib for maintenance of remission after allogeneic hematopoietic stem cell transplantation for FLT3-ITD-positive acute myeloid leukemia. *Leukemia*. 2010;24(7):1372-1374. doi:10.1038/leu.2010.101
8. DiNardo CD, Jonas BA, Pullarkat V, et al. Azacitidine and venetoclax in previously untreated acute myeloid leukemia. *N Engl J Med*. 2020;383(7):617-629. doi:10.1056/NEJMoa2007134

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