haematologica
Journal of the Ferrata Storti Foundation

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Received: March 30, 2026.
Accepted: April 1, 2026.

Martin Bornhäuser. FLT3 inhibition after transplantation: real-world evidence confirms common practice. Haematologica. 2026 Apr 9. doi: 10.3324/haematol.2026.300884 [Epub ahead of print]

FLT3 inhibition after transplantation: real-world evidence confirms common practice

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Disclosures: MBo has received lecture fees and travel grants from Jazz Pharmaceuticals and research funding from Abbvie. He has served in an advisory board for ActiTrexx.

For patients with FLT3-mutated acute myeloid leukemia (AML), relapse after allogeneic hematopoietic cell transplantation (allo-HCT) remains the central obstacle to cure. Despite advances in induction therapy and improved transplant strategies, post-transplant relapse continues to cause the majority of treatment failures. The introduction of FLT3 inhibitors has fundamentally reshaped the treatment algorithms of FLT3-mutated AML, but has raised an increasingly relevant clinical question: can sustained FLT3 inhibition after transplantation prevent relapse—and if so, for how long should therapy be continued?

In this issue of Haematologica, Massoud and colleagues provide important real-world evidence addressing the first part of this question.[1] Using data from the German Registry for Hematopoietic Stem Cell Transplantation and Cell Therapy, the authors analyzed outcomes in 523 patients with FLT3-ITD AML who underwent allo-HCT in first complete remission. In this large multicenter cohort, FLT3 inhibitor maintenance therapy was associated with significantly improved overall survival and relapse-free survival compared with no maintenance therapy.[1] Notably, sorafenib—the most frequently used inhibitor in the study—was associated with particularly favorable long-term outcomes, with exploratory analyses suggesting 5-year survival approaching 85%.[1]

These findings extend prior prospective trial results into routine clinical practice and reinforce the growing role of FLT3 inhibitor maintenance as a strategy for relapse prevention after transplantation. At the same time, they highlight several key questions that remain unresolved in this rapidly evolving field: which patients benefit most from maintenance therapy, which FLT3 inhibitor should be preferred, and perhaps most importantly, how long treatment should be continued.

From proof of concept to real-world validation. The rationale for FLT3 inhibitor maintenance after transplantation is biologically compelling. Even in patients who achieve complete remission and undergo allo-HCT, small populations of residual leukemic cells frequently persist and may eventually lead to relapse. Targeted inhibition of FLT3 signaling offers a mechanism to suppress these clones and potentially prolong remission. Prospective clinical

trials have provided proof of concept. The randomized SORMAIN trial demonstrated significantly improved relapse-free survival with sorafenib maintenance compared with placebo in patients with FLT3-ITD AML undergoing allo-HCT.[2] Similarly, a randomized multicenter study from China confirmed that sorafenib maintenance significantly reduced relapse incidence and improved survival following transplantation.[3] Together, these studies established sorafenib as a prototype for post-transplant FLT3 inhibitor maintenance.

However, prospective trials typically enroll highly selected patient populations under tightly controlled conditions. Real-world analyses therefore play an important role in determining whether these benefits translate into routine clinical practice. The registry study reported by Massoud and colleagues provides such validation. Across 13 transplant centers, FLT3 inhibitor maintenance was associated with superior survival outcomes compared with no maintenance therapy.[1] While the retrospective nature of the analysis introduces potential sources of bias, the consistency between these findings and prior randomized trials strengthens the overall evidence supporting FLT3 inhibitor maintenance as an effective post-transplant strategy.

Measurable residual disease and relapse risk. A critical element in post-transplant relapse prevention is the assessment of measurable residual disease (MRD). Besides fluorescence-activated cell sorting (FACS)-based MRD monitoring, increasingly sensitive molecular monitoring techniques now allow detection of minimal leukemic burden and provide valuable prognostic information regarding relapse risk[4]. In the analysis by Massoud et al., FLT3 inhibitor maintenance improved survival outcomes in both MRD-positive and MRD-negative patients at the time of transplantation.[1] While MRD-positive patients are generally considered at particularly high risk for relapse, these findings suggest that maintenance therapy may also provide benefit even in patients who appear to be in deep remission.

This observation highlights an important limitation of current MRD assays. Even highly sensitive molecular techniques may fail to detect rare leukemic stem cells that persist below the threshold of detection. Consequently, MRD negativity does not necessarily equate with

complete eradication of the disease. Maintenance therapy may therefore function not only as treatment for measurable residual disease but also as prophylaxis against the expansion of occult leukemic clones.

Synergy with graft-versus-leukemia effects. Beyond direct kinase inhibition, FLT3 inhibitors may also interact with immune-mediated graft-versus-leukemia (GVL) effects after transplantation. Experimental studies have demonstrated that sorafenib can enhance antileukemic immune responses by promoting interleukin-15 production and stimulating donor-derived T-cell and natural killer cell activity.[4]

These findings suggest that the clinical benefit of FLT3 inhibitor maintenance may not solely reflect suppression of leukemic proliferation but also amplification of immune-mediated antileukemic surveillance. In the post-transplant environment, where donor-derived immune responses are central to long-term disease control, such immunologic interactions may contribute significantly to sustained remission. Importantly, these effects should be considered when evaluating newer FLT3 inhibitors in the maintenance setting. Agents with similar kinase inhibition profiles may differ in their capacity to enhance—or potentially interfere with—immune-mediated antileukemic responses.

The unanswered question: duration of therapy. While the evidence supporting FLT3 inhibitor maintenance continues to grow, the optimal duration of therapy remains uncertain. Most clinical trials have employed fixed treatment periods of approximately two years, and many clinicians currently recommend maintenance therapy for two to three years following transplantation. However, clinical observations increasingly suggest that this duration may not be adequate for all patients. Relapse after discontinuation of prolonged FLT3 inhibitor therapy has been described even after sustained molecular remission, raising the possibility that continued suppression of residual leukemic clones may be required in selected cases.[6] The optimal duration of therapy is likely influenced by several factors, including MRD status, the clonal architecture of the leukemia, prior FLT3 inhibitor exposure, and the strength of the

graft-versus-leukemia effect. Future studies incorporating dynamic MRD monitoring may help define individualized strategies for both the initiation and duration of maintenance therapy.

An evolving therapeutic landscape. The treatment landscape of FLT3-mutated AML continues to evolve rapidly. In addition to sorafenib and midostaurin, newer inhibitors such as gilteritinib and quizartinib are increasingly incorporated into treatment algorithms. As these agents move earlier in the disease course, the post-transplant setting will increasingly involve patients previously exposed to targeted therapy. This shift raises important questions regarding resistance mechanisms, optimal sequencing of FLT3 inhibitors, and the most effective maintenance strategies after transplantation.

Looking ahead. The registry analysis by Massoud and colleagues provides compelling real-world evidence supporting the use of FLT3 inhibitor maintenance after allo-HCT in patients with FLT3-ITD AML.[1] Taken together with existing randomized trials, these findings bring clinical practice closer to recognizing post-transplant FLT3 inhibition as an important component of relapse prevention in this high-risk disease. Nevertheless, key questions remain regarding the optimal inhibitor, patient selection, and duration of therapy. Addressing these issues will require prospective studies integrating molecular monitoring, targeted therapy, and immune-based approaches. The next challenge for the field is not whether to maintain FLT3 inhibition after transplantation, but when it is safe to stop.

References

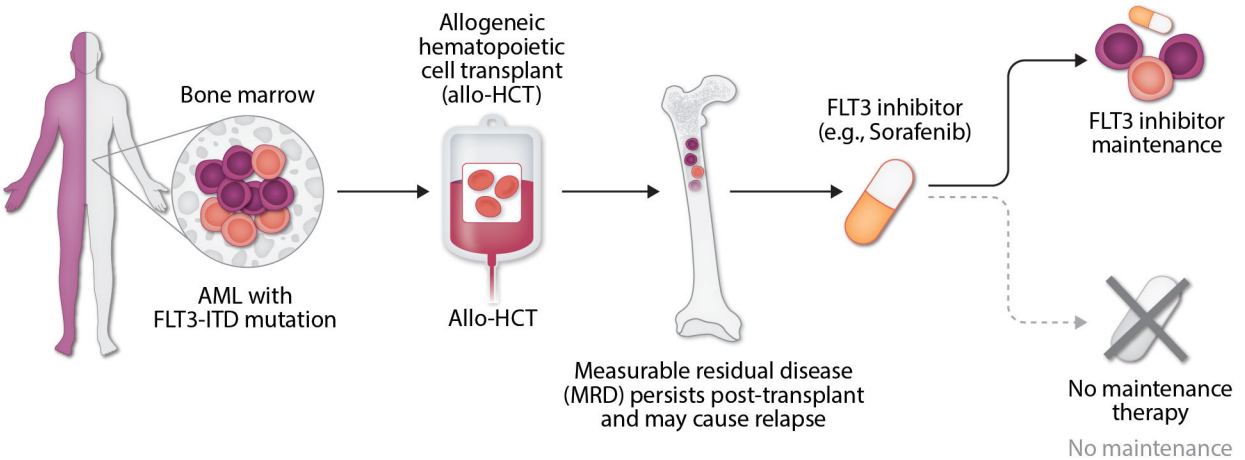
1. Massoud R, Flossdorf S, Hanke F, et al. Impact of FMS-like tyrosine kinase 3 inhibitor maintenance on post-transplant outcomes in acute myeloid leukemia with FMS-like tyrosine kinase 3 mutations: a real-world German registry analysis highlighting sorafenib. Haematologica. xxx
2. Burchert A, Bug G, Fritz LV, et al. Sorafenib maintenance after allogeneic hematopoietic stem cell transplantation for FLT3-ITD acute myeloid leukemia (SORMAIN). J Clin Oncol. 2020;38(26):2993-3002.
3. Xuan L, Wang Y, Huang F, et al. Sorafenib maintenance in patients with FLT3-ITD acute myeloid leukemia undergoing allogeneic hematopoietic stem-cell transplantation: an open-label, multicentre, randomized phase 3 trial. Lancet Oncol. 2020;21(9):1201-1212.
4. Cloos J, Valk PJM, Thiede C, et al. 2025 update on measurable residual disease in acute myeloid leukemia: a consensus document from the ELN-DAVID MRD Working Party. Blood. 2026;147(11):1147-1167.
5. Mathew NR, Baumgartner F, Braun L, et al. Sorafenib promotes graft-versus-leukemia activity through interleukin-15 production. Nat Med. 2018;24(3):282-291.
6. Georgi JA, Röllig C, Schetelig J, et al. Relapse following FLT3 inhibitor cessation in FLT3-ITD-positive acute myeloid leukemia: lessons from two clinical cases. Ann Hematol. 2026;105(3):82.

Figure 1:

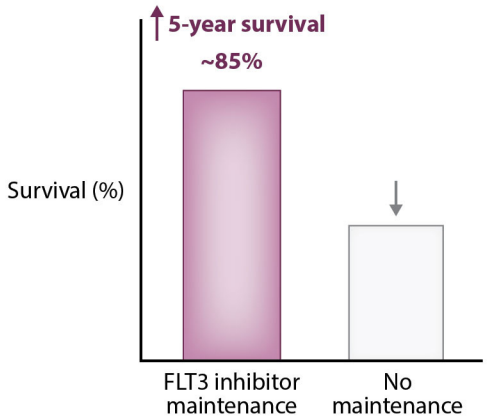
Real-world evidence supports FLT3 inhibitor maintenance after allogeneic hematopoietic cell transplant (allo-HCT) in FLT3-ITD AML

Disease and therapy pathway

Maintenance intervention



Outcome/survival data



FLT3 inhibitor maintenance improves overall and relapse-free survival

All data real-world registry, German centers, Mossoud *et al.*, 2006

Key unanswered questions

- Who benefits most?
- Which inhibitor is optimal?
- How long should therapy continue?
- Role of MRD, immune effects?