

Review Article**Allogeneic Transplantation in Acute Myeloid Leukemia in the Era of Novel Therapies: Changing Indications and Dynamic Risk Assessment**

Simona Sica^{1,2}, Filippo Frioni^{1,2}, Matteo Breccia^{1,2} and Patrizia Chiusolo^{1,2}.

¹ Dipartimento di Scienze di Laboratorio ed Ematologiche, Fondazione Policlinico Universitario Agostino Gemelli-IRCCS, Roma.

² Sezione di Ematologia, Dipartimento di Scienze Radiologiche ed Ematologiche, Università Cattolica del Sacro Cuore, Roma.

Competing interests: The authors declare no competing interest.

Abstract. Allogeneic HSCT remains a major potentially curative treatment for patients with AML at high risk of relapse. However, the rapid development of targeted agents and novel non-intensive therapies has substantially changed the therapeutic landscape, raising questions regarding the optimal timing and indications for transplantation. In this narrative review, we discuss how recently introduced therapeutic strategies may influence transplant decision-making, with particular emphasis on disease risk, treatment response, measurable residual disease, and the integration of pharmacological therapy before and after allogeneic HSCT. Novel therapies have primarily modified rather than replaced the role of allogeneic HSCT. Venetoclax-based regimens may allow initially unfit patients to achieve remission and become transplant candidates. At the same time, targeted agents such as FLT3, IDH, and Menin inhibitors can provide effective disease control in molecularly defined AML, particularly in the relapsed/refractory setting. They may enable transplantation in patients with limited therapeutic options. Growing evidence also supports using selected targeted agents after allo-HSCT, particularly FLT3 inhibitors, while post-transplant maintenance with IDH or Menin inhibitors and hypomethylating agents remains investigational. Across these settings, MRD is emerging as an increasingly important tool for refining transplant decisions and identifying patients who may benefit from additional therapy. The role of allogeneic HSCT in AML is evolving from a decision based predominantly on baseline genetic risk toward a dynamic, response- and MRD-adapted strategy. Novel agents should not currently be viewed as alternatives to transplantation in patients with a substantial risk of relapse, but rather as complementary therapies that may improve disease control before HSCT and reduce relapse risk afterward. Prospective studies integrating targeted therapy, MRD assessment, and post-transplant maintenance are needed to define the optimal therapeutic sequence and identify patients who may safely avoid transplantation.

Keywords: Acute myeloid leukemia; Allogeneic hemopoietic Stem cell transplant; New drugs.

Citation: Sica S., Frioni F., Breccia M., Chiusolo P. Allogeneic transplantation in acute myeloid leukemia in the era of novel therapies: changing indications and dynamic risk assessment. *Mediterr J Hematol Infect Dis* 2026, 18(1): e2026088, <http://dx.doi.org/10.4084/MJHID.2026.088>

Published: November 01, 2026

Received: October 13, 2026

Accepted: October 19, 2026

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by-nc/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Correspondence to: Patrizia Chiusolo, MD, PhD. Sezione di Ematologia, Università Cattolica del Sacro Cuore, Largo Francesco Vito 1, 00168 Roma, Italy. Tel: +390630154180. E-mail: patrizia.chiusolo@unicatt.it

Introduction. Acute myeloid leukemia (AML) is a biologically heterogeneous clonal disorder of hematopoietic progenitor cells characterized by impaired differentiation and uncontrolled proliferation within the bone marrow microenvironment. Despite high rates of complete remission (CR) following intensive induction chemotherapy, disease relapse remains the leading cause of treatment failure, largely due to the persistence of chemo-resistant leukemic stem cells and measurable residual disease (MRD). Allogeneic hematopoietic stem cell transplantation (HSCT) remains the most effective, potentially curative, strategy for patients with AML at intermediate or adverse risk according to the European LeukemiaNet (ELN) recommendations.¹ By providing both high-dose antileukemic therapy and a graft-versus-leukemia effect, allogeneic HSCT substantially reduces relapse risk. However, this benefit must be balanced against transplant-related morbidity and mortality. Accordingly, in medically fit patients in whom the expected risk of relapse outweighs transplant-related risks, allogeneic HSCT is generally considered the preferred post-remission strategy. Similarly, patients with relapsed or refractory AML, or with MRD positivity, may be considered for HSCT regardless of their initial ELN risk category.²

In these settings, achieving the deepest possible response before transplantation is a major therapeutic goal, as disease burden and MRD status at allogeneic HSCT are among the most important determinants of post-transplant outcomes. Disease relapse following allo-HSCT remains the principal cause of treatment failure, occurring in approximately 30–50% of patients depending on disease status at transplantation and underlying disease characteristics³. The presence of MRD before transplantation is one of the strongest predictors of post-transplant relapse and inferior survival.^{3,4}

Over the last decade, novel targeted and non-targeted therapies have substantially changed the therapeutic landscape of AML. These agents have increased the likelihood of achieving deeper responses, including MRD negativity, before transplantation; provided new options for refractory disease; and expanded the role of pharmacological strategies after transplantation, as maintenance therapy and as treatment or pre-emptive intervention for molecular or overt relapse. In this rapidly evolving setting, the role of allogeneic HSCT is being progressively redefined. The availability of increasingly effective non-transplant therapies raises important questions regarding which patients derive the greatest benefit from transplantation, the optimal timing of allo-HSCT, and how molecular risk and MRD should be incorporated into transplant decision-making.⁵

This review reassesses the role and timing of allo-HSCT in AML in the era of targeted and novel non-transplant therapies, with particular emphasis on disease

risk, MRD status, response to novel agents, and the emerging role of maintenance and post-transplant strategies.

The Current Role of Allogeneic HSCT in AML: from Genetic Risk to Dynamic Risk Assessment. Allogeneic HSCT remains a major curative strategy for adults with AML, particularly those at high risk of relapse. However, its indication has progressively shifted from a genetic-risk-oriented approach to a more individualized, dynamic one. Current treatment algorithms integrate disease biology at diagnosis with therapy response, MRD, patient fitness, donor characteristics, and expected transplant-related morbidity and mortality.^{1,6}

The 2022 ELN recommendations provide the current framework for genetic risk stratification and post-remission treatment in AML.¹ Patients with favorable-risk AML generally have a relatively low probability of relapse following intensive chemotherapy and, in the absence of persistent MRD, are therefore not routinely considered candidates for allogeneic HSCT in first complete remission (CR1). Conversely, patients with adverse-risk AML have a substantial risk of relapse despite morphological remission and are generally considered candidates for allogeneic HSCT when medically eligible. The role of transplantation in intermediate-risk AML is less straightforward and requires individualized assessment, particularly in relation to MRD and patient- and transplant-related factors.^{1,6}

The ELN 2022 recommendations incorporated the increasing relevance of treatment response and MRD into risk-adapted therapeutic decisions.¹ This is particularly relevant in molecularly defined AML, such as NPM1-mutated disease, in which deep molecular response can substantially modify the estimated risk of relapse.³ Conversely, persistence of MRD may identify patients whose relapse risk is considerably higher than predicted by baseline genetic category alone.³

MRD prognostic relevance before allo-HSCT has been demonstrated across several studies and disease subgroups. A meta-analysis including patients with AML undergoing allo-HSCT showed that pre-transplant MRD positivity was associated with a significantly increased risk of relapse and inferior survival compared with MRD-negative disease.⁴

Patient- and transplant-related factors must also be incorporated. Age, performance status, comorbidities, frailty, donor availability, conditioning intensity, and expected non-relapse mortality (NRM) all contribute to the overall risk-benefit assessment. Current recommendations therefore emphasize an individualized comparison between relapse risk without transplantation and anticipated toxicity and NRM associated with the procedure.⁶

This approach has become increasingly important as novel therapies develop. Targeted agents and new combination regimens can increase the probability of deep responses in several AML subgroups and may modify the relapse risk initially estimated from genetic characteristics alone. They can also be used before transplantation to reduce disease burden and potentially achieve MRD negativity. Consequently, novel agents do not necessarily imply a reduced role for transplantation; rather, they may change how transplantation is integrated into the overall treatment strategy.

Changing the Therapeutic Landscape

Venetoclax-based regimens. The introduction of venetoclax, a selective BCL-2 inhibitor, combined with hypomethylating agents (HMAs), has substantially changed AML treatment, particularly for patients considered unsuitable for intensive chemotherapy⁷. The azacitidine-venetoclax combination demonstrated significantly higher response rates and improved survival than azacitidine alone in previously untreated patients ineligible for intensive chemotherapy.⁸

The main impact of venetoclax-based therapy has been in older patients and those with comorbidities or frailty precluding intensive induction and subsequent allo-HSCT. However, the distinction between “unfit” and “fit” patients becomes increasingly blurred when Venetoclax-based therapy is considered as a potential pathway to transplantation. Some patients initially considered unsuitable for intensive chemotherapy may subsequently achieve sufficient clinical and hematological recovery to become candidates for allogeneic HSCT⁹. Response to Venetoclax-based treatment may therefore provide an opportunity to reassess transplant eligibility after disease control has been achieved. Retrospective studies have demonstrated the feasibility of proceeding to HSCT after HMA-Venetoclax, with encouraging post-transplant outcomes in selected patients.⁹

HMA-Venetoclax can also induce deep responses. In VIALE-A, MRD negativity was documented in approximately 23% of patients in the experimental arm, compared with 7.6% in the azacitidine-alone arm⁸. More recent real-world data further support the prognostic value of MRD clearance with AZA-VEN.¹⁰ In the French VENAURA registry, cumulative MRD negativity among patients achieving remission was observed in approximately 62–67% of evaluable patients, and it was associated with significantly longer overall survival and lower relapse incidence.¹¹

Venetoclax-based salvage therapy may also represent a bridge to transplantation in relapsed/refractory AML. A propensity-matched analysis reported higher response rates with venetoclax-based salvage compared with physician's choice non-Venetoclax salvage therapy (62% vs. 42%), with a numerically higher proportion of

patients proceeding to allo-HSCT.¹² The bridge-to-transplant concept may be particularly relevant in molecularly defined AML. In NPM1-mutated AML with molecular persistence or relapse, Venetoclax-based regimen has been shown to induce substantial molecular responses and allow patients to proceed to transplantation while attempting to minimize the risk of overt hematological relapse. In one multicenter cohort, 84% of patients achieved at least a one-log reduction in MRD and 71% achieved MRD negativity; 41 patients were subsequently bridged to allo-HSCT.¹⁰

Despite these high response rates, venetoclax-based therapy lasts only a limited time in a substantial proportion of patients. In VIALE-A, the median duration of composite remission was 17.5 months, and median event-free survival was 9.8 months, highlighting the difference between inducing remission and maintaining long-term disease control.⁸

Consequently, in potentially transplant-eligible patients, achieving remission with HMA-Venetoclax should not automatically lead to continuing non-intensive therapy indefinitely. Instead, the finite durability of disease control supports considering allogeneic HSCT during the first remission in appropriately selected patients, particularly when disease biology predicts a high relapse risk. Conversely, in patients with favorable disease biology and sustained MRD-negative remission, particularly when transplant-related mortality is expected to be high, continued Venetoclax-based therapy may represent a reasonable alternative.

HMA-Venetoclax has also shown efficacy in post-transplant AML/MDS relapse, particularly in late relapse, ELN-favorable disease, and when administered in association with DLI.¹³ Furthermore, researchers are exploring combinations with molecularly targeted agents, including FLT3 and IDH1/2 inhibitors, which may further increase response depth and molecular remission rates in selected subgroups.

Overall, venetoclax-based therapy has substantially modified the therapeutic pathway toward allo-HSCT across different AML settings. In patients initially considered unfit for intensive chemotherapy, achievement of remission with venetoclax-based regimens may allow recovery of clinical fitness and subsequent reassessment for allogeneic transplantation. Moreover, venetoclax-based therapy can induce deep responses, including MRD-negative remission in some patients, which may improve disease control before transplantation and potentially contribute to more favorable post-transplant outcomes. In the relapsed/refractory setting, venetoclax-based regimens may also induce responses in patients who have failed conventional chemotherapy, providing an alternative salvage approach and, in selected cases, a bridge to allo-HSCT. Thus, rather than replacing transplantation,

venetoclax has expanded therapeutic opportunities to achieve a transplantable disease state and has made transplant eligibility and timing increasingly dynamic.

FLT3-target therapy. FLT3 mutations are among the most relevant molecular determinants of prognosis and therapeutic response in AML. FLT3-mutated AML, particularly FLT3-ITD disease, is characterized by constitutive FLT3 signaling that promotes leukemic proliferation and survival and has historically been associated with increased relapse risk and poorer survival.¹⁴ Treatment has evolved with the introduction of FLT3 inhibitors, first by adding midostaurin to intensive chemotherapy and later by using more potent, selective inhibitors such as gilteritinib and quizartinib. Their clinical role now extends from induction and consolidation to salvage treatment and post-transplant maintenance.

The first major demonstration that targeting FLT3 improves AML outcomes came from the RATIFY trial:¹⁵ adding midostaurin to intensive induction and consolidation chemotherapy significantly improved overall survival in FLT3-mutated AML, with benefit across FLT3 mutational subtypes.¹⁵ However, the study did not demonstrate that FLT3 inhibition could replace allogeneic HSCT. Transplantation remained an important component of post-remission therapy, and among patients undergoing allogeneic HSCT in first remission, treatment assignment showed no statistically significant survival difference.¹⁵ Midostaurin should therefore be viewed primarily as a strategy to improve disease control within a treatment pathway that may include transplantation in patients at appropriate relapse risk.

The development of quizartinib, a more potent and selective FLT3 inhibitor, further strengthened the role of targeted therapy in newly diagnosed FLT3-ITD-positive AML. In the phase III QuANTUM-First trial, adding quizartinib to induction and consolidation chemotherapy, followed by continuation therapy, significantly improved overall survival compared with chemotherapy alone.¹⁶ The trial included patients up to 75 years of age, extending evidence for FLT3-directed therapy beyond the younger population enrolled in RATIFY. Importantly, HSCT was permitted, and quizartinib was administered as maintenance after consolidation or transplantation, supporting a model in which targeted therapy and transplantation are complementary rather than mutually exclusive.¹⁶ Exploratory analyses suggested that the benefit of quizartinib maintenance may be less evident among patients undergoing allo-HCT.¹⁷

The role of FLT3 inhibition is particularly evident in relapse/refractory disease. In the phase III ADMIRAL trial, gilteritinib significantly improved response rates and overall survival compared with salvage chemotherapy in FLT3-mutated relapse/refractory

AML.¹⁸ Importantly for transplant decision-making, gilteritinib may function as a bridge to allo-HSCT. In a subsequent ADMIRAL analysis, 26% of patients in the gilteritinib arm underwent HSCT compared with 15% in the salvage chemotherapy arm,²⁰ among patients proceeding to transplantation, restarting gilteritinib after HSCT was feasible and associated with relatively low rates of post-transplant relapse in patients who had achieved remission before transplantation.¹⁹

Thus, in relapse/refractory FLT3-mutated AML, the objective of gilteritinib is not necessarily definitive disease control but conversion of active disease into transplantable remission. The integration of midostaurin and quizartinib into intensive therapy has improved outcomes, but available evidence does not support considering FLT3 inhibitors as substitutes for HSCT in patients with high relapse risk.

The development of FLT3 inhibitors has also changed the concept of allogeneic HSCT itself. Transplantation can now be followed by molecularly targeted maintenance to suppress residual FLT3-mutated leukemia. Two randomized trials evaluating sorafenib maintenance after allo-HSCT in FLT3-ITD AML demonstrated significant reductions in relapse and improved relapse-free survival.^{20,21} These findings provided proof of principle that FLT3 inhibition can complement the graft-versus-leukemia effect.

More recently, gilteritinib was evaluated in the randomized MORPHO trial.²² Although the primary analysis did not demonstrate a statistically significant improvement in relapse-free survival in the entire population, a prespecified subgroup analysis showed a significant benefit among patients with detectable peri-transplant FLT3-ITD MRD. Patients without detectable MRD did not appear to derive a similar benefit.²² Subsequent MRD analysis further supported this concept: in the placebo arm, 42.2% of patients with detectable MRD relapsed compared with 13.4% without detectable MRD, while gilteritinib improved relapse-free survival, particularly among patients with detectable peri-transplant MRD.²³

Triplet regimens combining an HMA, venetoclax, and a FLT3 inhibitor have also shown encouraging response and molecular response rates, supporting their potential role in selected patients considered for subsequent allo-HSCT, although prospective comparative data remain limited.²⁴

FLT3-mutated AML therefore represents a paradigm for how targeted therapy modifies the relationship between relapse risk and transplantation. FLT3 inhibitors can deepen remission before transplantation, facilitate transplantation in relapsed disease, and reduce post-transplant relapse. Sorafenib may also enhance the graft-versus-leukemia effect by inducing IL-15 production in FLT3-ITD-mutated leukemia cells, promoting expansion, cytotoxicity, and persistence of donor CD8⁺ T cells.²⁵

Targeted therapy and allo-HSCT should therefore be viewed as complementary strategies.

IDH inhibitors. Recurrent IDH1 and IDH2 mutations provide biologically defined therapeutic targets in AML. Mutant IDH enzymes acquire neomorphic activity leading to accumulation of 2-hydroxyglutarate (2-HG), epigenetic dysregulation, and impaired differentiation.²⁶ IDH inhibitors are relevant not only in relapsed or refractory disease but also as potential agents for disease control before allo-HSCT and, potentially, for post-transplant maintenance.

Ivosidenib is an oral selective inhibitor of mutant IDH1²⁷. Its activity in IDH1-mutated AML was initially demonstrated in pretreated AML, and induced meaningful CR and CRi rates, with evidence of differentiation rather than conventional cytotoxicity.²⁷ Its differentiation-based mechanism may be clinically relevant when the objective is to stabilize or reduce disease burden before transplantation. Ivosidenib has also been evaluated in newly diagnosed patients unsuitable for intensive chemotherapy, including in combination with azacitidine.²⁸ However, implications for transplant-eligible patients remain less clearly established.

Enasidenib is a selective oral inhibitor of mutant IDH2 and similarly suppresses 2-HG production and promotes differentiation. Its development has focused particularly on relapsed IDH2-mutated AML.^{29,30} Its role in frontline treatment of transplant-eligible patients is less well defined. Still, its relatively favorable non-intensive toxicity profile supports incorporating it into strategies aimed at reducing disease burden before allo-HSCT.³¹

IDH inhibitors are particularly relevant in relapsed AML patients with limited therapeutic options because of age, comorbidities, previous treatment exposure, or poor tolerance of intensive salvage. Researchers are also investigating combinations of HMA, venetoclax, and IDH inhibitors, with early studies suggesting improved response and MRD-negative remission rates. However, in transplant candidates, the therapeutic objective should extend beyond response to determine whether disease control is sufficient and durable enough to permit allo-HSCT.

Retrospective and post hoc analyses suggest that patients who achieve a response and subsequently undergo transplantation may derive meaningful long-term benefit.^{29,32} However, these observations are difficult to interpret because patients proceeding to transplant represent a selected population with adequate disease control and fitness. No prospective evidence currently shows that an IDH inhibitor-based strategy is superior to conventional salvage for improving post-transplant outcomes. Therefore, IDH inhibitors as a bridge to transplant may be particularly useful when

conventional salvage is ineffective or associated with unacceptable toxicity.

IDH inhibition may also play a role in post-HSCT maintenance. Persistence of molecularly detectable IDH-mutated clones after transplantation provides a biological rationale for continued mutant IDH inhibition to suppress residual leukemia while allowing the graft-versus-leukemia effect to operate. A multicenter phase I trial evaluating ivosidenib maintenance after allo-HCT in IDH1-mutated AML reported a 2-year cumulative relapse rate of 19%, with progression-free and overall survival of 81% and 88%, respectively.³³ Although encouraging, the small sample size and single-arm design preclude definitive conclusions. Enasidenib has similarly been investigated as post-HCT maintenance in IDH2-mutated myeloid malignancies³⁴. Therefore, post-HSCT IDH inhibition should remain investigational.

Menin inhibitors. Menin inhibitors represent a novel class of targeted agents with particular activity in AML characterized by KMT2A rearrangements or NPM1 mutations. Menin functions as a chromatin-associated scaffold within the KMT2A complex and contributes to transcriptional activation of leukemogenic programs, including HOXA and MEIS1. Pharmacologic disruption of the menin–KMT2A interaction promotes differentiation and impairs leukemic self-renewal in these molecular subsets.^{35,36,37}

Clinical development has initially focused on refractory disease, in which KMT2A-rearranged and NPM1-mutated disease is associated with limited therapeutic options and poor outcomes. Studies of agents such as revumenib and ziftomenib have demonstrated meaningful responses, including complete remissions, in heavily pretreated patients.^{38,39} Responses have also been observed after venetoclax-based therapy, supporting a potential role in overcoming resistance to established non-intensive regimens.

From a transplant perspective, the most relevant aspect of menin inhibition is its potential to convert difficult-to-treat chemoresistant AML into a remission suitable for allo-HSCT. In early studies, some responding patients proceeded to HSCT, suggesting menin inhibitors can be incorporated into treatment sequences that may lead to potentially curative transplantation. This may be particularly relevant for KMT2A-rearranged or NPM1-mutated AML in patients who cannot achieve an adequate response with conventional salvage or cannot tolerate intensive cytotoxic approaches.

The importance of menin inhibition may extend beyond morphological remission. NPM1-mutated AML provides a model in which molecular MRD can be quantified with high sensitivity. It remains unknown whether molecular responses induced by menin inhibitors translate into lower post-transplant relapse

rates. Nevertheless, their ability to induce differentiation and reduce leukemic burden without intensive chemotherapy may allow more patients to reach transplantation in a favorable disease state. Prospective studies are needed to determine whether molecular response should influence allo-HSCT timing and whether transplantation should occur after morphological remission or, preferably, after deeper molecular clearance.

Post-transplant maintenance with menin inhibitors is another potentially important but still investigational application. Residual leukemic cells in KMT2A-rearranged and NPM1-mutated AML may remain dependent on menin-mediated transcriptional programs after allo-HSCT, supporting continued inhibition to complement graft-versus-leukemia effects⁴⁰. Early experience with revumenib and other menin inhibitors has demonstrated feasibility of treatment after transplantation in selected patients, including those with persistent or subsequently detectable molecular disease⁴¹. However, these data derive from small non-randomized cohorts and cannot establish a survival benefit.

Preliminary real-world data presented in 2026 further support the feasibility of menin inhibitor maintenance after allo-HSCT, with encouraging relapse control reported in small cohorts of patients with KMT2A-rearranged, NPM1-mutated, and other genetically defined AML⁴².

The optimal timing and duration of maintenance, tolerability during graft-versus-host disease and immunosuppressive therapy, and the role of molecular MRD in selecting patients remain undefined.

Overall, menin inhibitors illustrate how molecularly targeted therapies may modify rather than eliminate the role of allo-HSCT. Their principal contribution may currently be to provide an effective salvage or bridging strategy for molecularly defined AML, increasing the likelihood that patients with otherwise refractory disease can reach transplantation. In the future, their role may extend across the transplant pathway, from response induction and molecular disease control before HSCT to MRD-guided maintenance after transplantation.

TP53-mutated AML: when the risk of relapse challenges the value of transplantation. TP53-mutated AML represents a particularly difficult transplant decision. It is frequently associated with complex cytogenetics, myelodysplasia-related disease, and profound resistance to conventional therapy. Contemporary analyses show that HMA-VEN can improve response rates compared with HMA alone in some patients, but responses are often short, and overall survival remains poor^{43,44}. Thus, morphological CR should not be equated with durable biological control in TP53-mutated disease. The role of allo-HSCT is controversial because the disease retains a very high relapse propensity even after transplantation.

A systematic review and meta-analysis reported poor pooled outcomes after allo-HSCT, including a two-year overall survival of approximately 30% and a relapse rate of approximately 61%. However, the available evidence is heterogeneous and observational⁴⁵. More recent studies continue to support the concept that transplant may offer the only realistic route to long-term survival for a selected minority. Still, outcomes remain strongly dependent on disease status, molecular burden, comorbidity and transplant-related risk^{46,47}.

The decision should therefore distinguish younger/fit patients who can achieve a meaningful remission and tolerate transplantation from older or frail patients in whom NRM may consume a substantial proportion of the limited expected benefit. In TP53-mutated AML, achieving morphological CR without molecular or biological control may be insufficient justification for an aggressive transplant strategy if the probability of early post-HSCT relapse is extremely high. Conversely, because durable non-transplant therapies remain limited, withholding transplantation solely because TP53 mutation predicts poor prognosis may also deny the only potentially curative approach in selected patients.

Oral Azacitidine and other post-transplant maintenance strategy. Maintenance therapy has emerged as an important strategy to reduce relapse after remission in AML, particularly in patients who are not candidates for allo-HSCT. Oral azacitidine (CC-486) is the most established non-targeted maintenance strategy for patients achieving remission after intensive chemotherapy but not proceeding to transplantation. In the QUAZAR AML-001 trial, oral azacitidine improved overall and relapse-free survival compared with placebo, establishing its role as a standard post-remission option in transplant-ineligible patients.⁴⁸

These findings do not directly inform patients who are candidates for allo-HSCT, as the trial excluded patients proceeding to transplantation.⁴⁹ Therefore, CC-486's relevance to transplant decision-making lies primarily in providing an effective alternative for patients in whom the expected benefit of allo-HSCT is outweighed by transplant-related risks, rather than defining a strategy that can replace transplantation in otherwise eligible patients.

In the post-HSCT setting, the rationale for hypomethylating-agent maintenance is based on their potential to suppress residual leukemia while preserving or potentially enhancing graft-versus-leukemia effects.^{50,51} Early studies of oral CC-486 after allo-HSCT have shown feasibility, with treatment generally initiated after hematologic recovery and manageable toxicity⁵². However, randomized studies have not established a definitive survival benefit, and this approach remains investigational.

Other strategies have focused on injectable azacitidine, either as routine post-transplant maintenance or as pre-emptive treatment guided by MRD^{53,54}. The RELAZA study demonstrated the feasibility of using azacitidine to delay hematologic relapse in patients with molecular evidence of impending relapse after allo-HSCT, supporting an MRD-guided rather than universal approach.⁵⁴

The distinction between maintenance in transplant-eligible patients and maintenance after allo-HSCT is therefore clinically important. Oral azacitidine has demonstrated a clear survival benefit in the former population. In contrast, after transplantation, hypomethylating-agent maintenance remains individualized or investigational, potentially guided by disease risk, pre- and post-transplant MRD, tolerability, and relapse risk.

CPX-351. CPX-351 is a liposomal formulation of cytarabine and daunorubicin developed for AML with myelodysplasia-related changes and therapy-related AML. Its relevance in the transplant era lies primarily in its ability to induce remission and facilitate subsequent allo-HSCT in patients with high-risk or secondary AML. In the pivotal phase III trial, CPX-351 improved remission rates and overall survival compared with conventional 7+3 chemotherapy in older adults with newly diagnosed high-risk or secondary AML.⁵⁵ Importantly, among patients undergoing allo-HSCT, CPX-351 was associated with improved post-transplant survival compared with 7+3, suggesting that its benefit may extend beyond induction and contribute to outcomes after transplantation.^{56,57}

Post hoc analyses showed that patients achieving CR or CRi after CPX-351 had a higher probability of proceeding to transplantation and experienced longer survival when outcomes were landmarked from the date of transplantation.⁵⁸ These findings suggest that CPX-351's principal value in transplant-eligible patients is not to replace allo-HSCT, but to increase the likelihood of achieving a remission suitable for transplantation and potentially improve disease control before HSCT.

The optimal timing of allo-HSCT after CPX-351 remains incompletely defined. Real-world data suggest that many responding patients proceed directly to transplantation after remission, while the benefit of additional consolidation remains uncertain⁵⁹. Thus, in transplant-eligible patients with AML-MR or therapy-related AML, CPX-351 should be viewed primarily as a remission-induction strategy to facilitate definitive consolidation with allo-HSCT.

Discussion. The increasing availability of effective non-transplant therapies is changing how allogeneic HSCT is considered in AML. Venetoclax-based regimens, molecularly targeted inhibitors, menin inhibitors, and

novel chemotherapy formulations have expanded the ability to induce remission in patients who previously had limited therapeutic options. However, these advances do not simply reduce the need for transplantation. Instead, they are changing the pathway to allogeneic HSCT, the disease status at transplantation, and the possibility of continuing pharmacological treatment after transplantation. The central question is therefore shifting from whether novel drugs can replace allo-HSCT to which patients should undergo transplantation, when it should be performed, and how pharmacological therapy should be integrated before and after the procedure.

One of the most important consequences of this therapeutic evolution is the transition from a static to a dynamic definition of transplant eligibility. Although baseline genetic risk remains fundamental, increasingly effective therapies may substantially modify the relapse risk initially predicted at diagnosis. Patients with adverse-risk AML may achieve deep responses with novel agents, whereas patients initially considered favorable or intermediate risk may demonstrate persistent MRD and consequently a higher relapse risk. Transplant decision-making should therefore integrate baseline biology with treatment response, MRD, patient fitness, and transplant-related risk.

This concept is particularly relevant to venetoclax-based therapy. Patients initially unsuitable for intensive chemotherapy may achieve remission and recover sufficiently to become candidates for allo-HSCT. Conversely, transplant-eligible patients may achieve rapid and deep responses with the HMA-Venetoclax combination, creating an opportunity to proceed to transplantation before prolonged treatment leads to resistance or relapse. Thus, remission achieved with a non-intensive regimen should not necessarily imply indefinite continuation of non-transplant therapy. In high-risk disease, HMA-Venetoclax may instead represent a therapeutic window for transplantation.

A similar principle applies to molecularly targeted therapies. FLT3 inhibitors provide the clearest example of drugs integrated throughout the transplant pathway. They can be used during frontline treatment, as salvage therapy to achieve a transplantable remission, and after HSCT to suppress residual disease. Their availability has not eliminated the rationale for transplantation in intermediate-risk FLT3-mutated AML, but it has created additional opportunities to control disease before and after HSCT. Gilteritinib in refractory or pretreated disease is particularly illustrative, as targeted therapy may convert active leukemia into a remission suitable for transplantation. At the same time, post-transplant treatment may further reduce relapse risk.

IDH and menin inhibitors may similarly expand access to transplantation in molecularly defined AML. Their ability to induce responses with relatively

favorable toxicity may be valuable when intensive salvage is ineffective or poorly tolerated. In these settings, the objective may be less about achieving definitive disease control with the targeted agent alone than about achieving sufficient disease reduction to allow HSCT. Thus, the clinical value of these agents should also be considered in the context of the subsequent treatment sequence.

At the same time, increasingly effective non-transplant therapies raise the question of whether transplantation can be safely avoided in selected patients. This may become particularly relevant in favorable-risk AML and in selected intermediate-risk patients achieving sustained deep molecular responses. However, there is currently insufficient evidence to define which patients can safely omit HSCT on the basis of response to novel therapies. MRD negativity is strongly associated with favorable outcome. Still, it does not eliminate relapse risk, while transplantation solely because of persistent low-level MRD may expose some patients to substantial treatment-related risks without sufficient benefit.

MRD is therefore likely to become increasingly central to individualized treatment. The relevant question may no longer be simply whether CR has been achieved, but whether the response is sufficiently deep and durable to justify continuing non-transplant therapy or whether transplantation should be pursued. This is particularly relevant in molecularly defined AML, such as NPM1-mutated disease, in which sensitive molecular monitoring allows dynamic assessment of residual disease. However, MRD should not be interpreted as a binary variable, as its prognostic significance depends on the molecular marker, assay sensitivity, timing, disease context, and kinetics of response. Importantly, delaying transplantation to achieve deeper molecular clearance must be balanced against the risk of disease progression or treatment resistance.

Another major implication of the new therapeutic landscape is the changing role of allogeneic HSCT in relapsed AML. Targeted agents may overcome one of the main limitations of transplantation in relapse, namely the inability to achieve sufficient disease control with conventional salvage chemotherapy. Even when a targeted agent provides limited long-term disease control, its ability to convert active disease into a transplantable remission may have substantial clinical value. Therefore, response rates and duration of response to FLT3, IDH, or menin inhibitors should be interpreted in the context of subsequent transplantation rather than in isolation.

Nevertheless, evidence linking novel therapies to HSCT remains limited. Much of the evidence derives from retrospective studies, post hoc analyses, or small prospective cohorts. Patients who respond and proceed to transplantation are inherently selected for favorable characteristics, including treatment sensitivity, adequate

organ function, performance status, donor availability, and clinical stability. Consequently, improved survival among transplanted responders cannot necessarily be attributed to the preceding drug, nor does a higher transplantation rate demonstrate superiority over continued non-transplant therapy.

The post-transplant setting represents another important area of change. Allogeneic HSCT is increasingly being incorporated into a broader continuum of pharmacological disease control rather than representing the final therapeutic step. The strongest evidence currently supports FLT3 inhibitors, particularly sorafenib, while emerging data on gilteritinib, IDH inhibitors, menin inhibitors, and hypomethylating agents suggest that post-HSCT maintenance may become increasingly relevant in selected patients. The rationale is that pharmacologically suppressing residual molecular disease may complement the graft-versus-leukemia effect and reduce the risk of overt relapse. **Table 1** displays selected post-HSCT pharmacological strategies in AML.

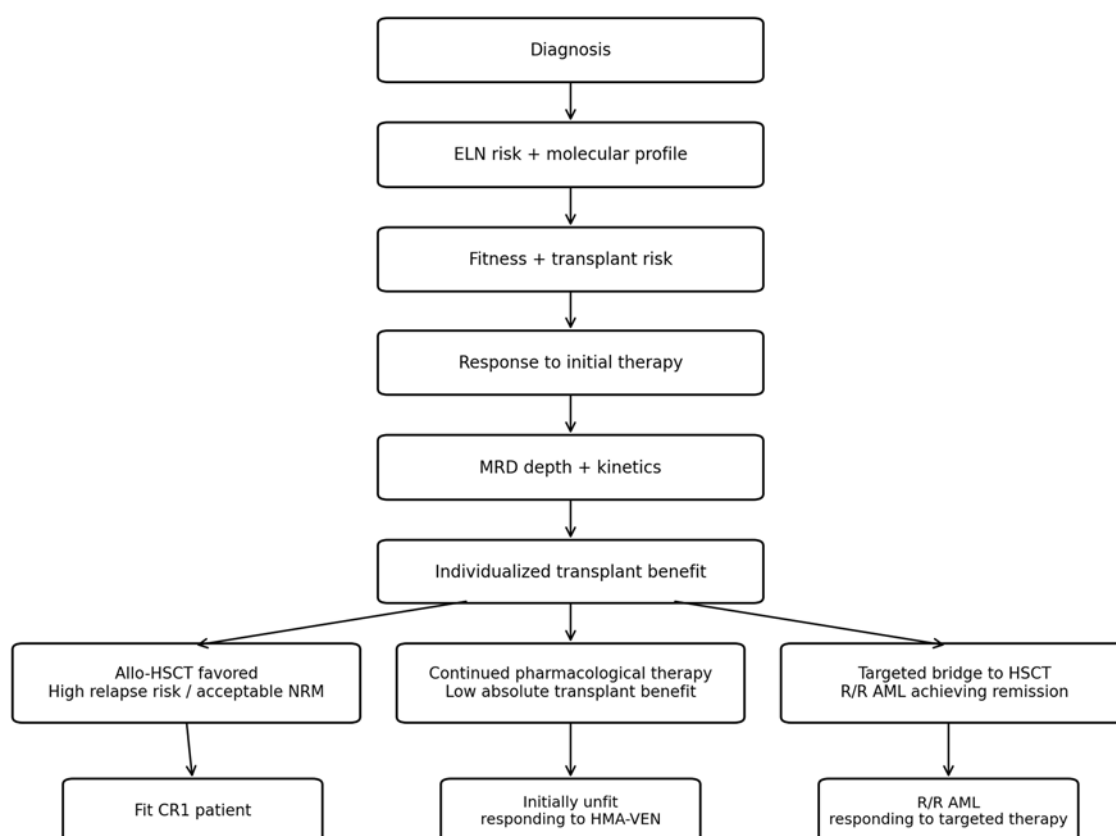
However, post-HSCT maintenance should not yet be generalized across all AML subgroups. Evidence varies substantially by drug and molecular disease, and many studies are limited by small sample sizes, heterogeneous populations, and non-randomized designs. Optimal timing, duration, and patient selection remain uncertain, particularly in the context of immunosuppression or graft-versus-host disease. Integration with molecular MRD monitoring may therefore be essential to identify patients most likely to benefit from maintenance.

Overall, novel drugs' impact on allo-HSCT is likely bidirectional. In some patients, more effective non-transplant therapy may reduce the absolute benefit of transplantation, particularly when sustained MRD negativity is achieved, and evaluation of transplant-related risk is substantial. In others, novel agents may increase the role and impact of transplantation by offering a realistic pathway to remission in otherwise refractory or relapsed disease. Thus, the same therapeutic innovation may reduce the need for transplantation in one subgroup while increasing access to transplantation in another.

This changing landscape emphasizes the importance of assessing transplant benefit in absolute rather than relative terms. As non-transplant therapies become more effective, the key question is not simply whether HSCT provides the lowest relapse risk, but whether its reduction in relapse risk outweighs NRM and long-term morbidity compared with contemporary pharmacological alternatives. This balance will increasingly depend on disease biology, MRD, age, comorbidities, donor characteristics, conditioning intensity, and the expected efficacy of available targeted therapies. A proposed algorithm is displayed in **Figure 1**.

Table 1. Selected post-HSCT pharmacological strategies in AML

Strategy	Subgroup	Evidence	Objective	Current status
Sorafenib	FLT3-ITD	Randomized phase 3 studies	Relapse prevention	Most consolidated targeted evidence
Gilteritinib	FLT3-ITD	Randomized; benefit concentrated by peri-transplant MRD	Maintenance/ MRD-guided strategy	Patient selection important
Ivosidenib	IDH1	Phase I, single-arm	Maintenance	Investigational
Enasidenib	IDH2	Early-phase study	Maintenance	Investigational
Menin inhibitors	KMT2A-rearranged/NPM1-mutated	Early studies and preliminary real-world/conference data	Maintenance/ molecular disease control	Investigational
Azacitidine/CC-486	Various high-risk AML/MDS	Heterogeneous randomized and non-randomized studies	Maintenance or pre-emptive therapy	Not a universal standard

**Figure 1.** Dynamic decision algorithm for transplantation in AML in the era of novel therapies.

The future therapeutic model may therefore shift toward increasingly MRD-guided, molecularly adapted treatment algorithms. Baseline genetic and clinical characteristics would provide an initial estimate of relapse risk, while treatment response and serial MRD measurements would dynamically update it. In this model, transplantation would remain a major curative intervention. Still, it would be deployed selectively, either when relapse risk without transplantation remains sufficiently high or when novel therapy creates an opportunity for transplantation in otherwise difficult-to-treat disease. Post-HSCT maintenance could then be reserved for patients with substantial residual relapse risk or persistent molecular targets.

Prospective studies are needed to determine whether molecular response to novel agents predicts differential benefit from allo-HSCT, when transplantation should be performed after targeted therapy, and whether maintenance should be universal or MRD-guided. Comparative studies are also required to establish whether selected patients with sustained deep responses can safely avoid transplantation without compromising cure rates.

Conclusions. Overall, novel AML therapies should be seen as an opportunity to refine, not diminish, the role of allogeneic HSCT. The challenge is to define the sequence and combination of therapies that maximize

durable disease control while minimizing cumulative toxicity. Allogeneic HSCT is increasingly becoming one component of an individualized therapeutic continuum

in which disease biology, MRD, targeted therapy, transplantation, and post-transplant intervention are integrated according to the evolving risk of each patient.

References:

- Döhner H, Wei AH, Appelbaum FR, et al. Diagnosis and management of AML in adults: 2022 recommendations from an international expert panel on behalf of the ELN. *Blood*. 2022;140(12):1345-1377. <https://doi.org/10.1182/blood.2022016867> PMID:35797463
- Yakoub-Agha I, et al. AML in Adults. In: The EBMT Handbook. 8th ed. Springer; 2024. https://doi.org/10.1007/978-3-031-44080-9_70 PMID:39437056
- Schuurhuis GJ, Heuser M, Freeman S, et al. Minimal/measurable residual disease in AML: a consensus document from the European LeukemiaNet MRD Working Party. *Blood*. 2018;131(12):1275-1291. <https://doi.org/10.1182/blood-2017-09-801498> PMID:29330221
- Buckley SA, Wood BL, Othus M, et al. Minimal residual disease prior to allogeneic hematopoietic cell transplantation in acute myeloid leukemia: a meta-analysis. *Bone Marrow Transplant*. 2017;52:24-32. <https://doi.org/10.3324/haematol.2016.159343> PMID:28126965
- Bazarbachi A, Schmid C, Labopin M, et al. Relapse of AML after hematopoietic stem cell transplantation: methods of monitoring and preventive strategies. *Bone Marrow Transplant*. 2016;51:1441-1450. <https://doi.org/10.3389/fonc.2021.793274> PMID:35047405
- Craddock C. AML in Adults. In: Carreras E, Duffy J, Kröger N, et al., editors. The EBMT Handbook: Hematopoietic Cell Transplantation and Cellular Therapies. 8th ed. Cham: Springer; 2024. https://doi.org/10.1007/978-3-031-44080-9_70 PMID:39437056
- DiNardo CD, Jonas BA, Pullarkat V, et al. Azacitidine and Venetoclax in Previously Untreated Acute Myeloid Leukemia. *N Engl J Med*. 2020;383:617-629. <https://doi.org/10.1182/blood-2020-134100>
- Pratz KW, Jonas BA, Pullarkat V, et al. Long-term follow-up of VIALE-A: Venetoclax and azacitidine in chemotherapy-ineligible untreated acute myeloid leukemia. *Am J Hematol*. 2024;99:615-624. <https://doi.org/10.1097/01.hs.9.0000968152.92514.0d> PMID:33079766
- Chen TT, Lin CC, Lo WJ, et al. Venetoclax Plus Azacitidine as a Bridge Treatment to Allogeneic Stem Cell Transplantation in Unfit Patients with Acute Myeloid Leukemia. *Cancers (Basel)*. 2024 Mar 7;16(6):1082. <https://doi.org/10.48095/cctahd202604>
- Sartor C, Brunetti L, Audisio E, et al. A venetoclax and azacitidine bridge-to-transplant strategy for NPM1-mutated acute myeloid leukaemia in molecular failure. *Br J Haematol*. 2023 Aug;202(3):599-607. <https://doi.org/10.1182/blood-2022-165914>
- Heiblig M, Gross Z, Belhabri A, et al. Prognostic impact of measurable residual disease in AML patients treated frontline with azacitidine and venetoclax: results from the French VENAURA registry. *Leukemia*. 2026 Jul 17. <https://doi.org/10.21203/rs.3.rs-7959681/v1> PMID:42899752
- Uhlmann JM, et al. Venetoclax-based salvage therapy as a bridge to transplant is feasible and effective in patients with relapsed/refractory AML. *Blood Advances*. 2025;9(2):375-385. <https://doi.org/10.1182/bloodadvances.2024013086> PMID:39293081
- Chiusolo P, Malagola M, Giglio F, et al. Venetoclax plus hypomethylating agents as first salvage therapy for myeloid malignancies relapsing after allogeneic HSCT. *Bone Marrow Transplant*. 2026 Jan;61(1):101-103. <https://doi.org/10.1038/s41409-025-02723-x> PMID:41120716
- Daver N, Schlenk RF, Russell NH, et al. Targeting FLT3 mutations in AML: review of current knowledge and evidence. *Leukemia*. 2019;33:299-312. <https://doi.org/10.1038/s41375-018-0357-9> PMID:30651634
- Stone RM, Mandrekar SJ, Sanford BL, et al. Midostaurin plus chemotherapy for acute myeloid leukemia with a FLT3 mutation. *N Engl J Med*. 2017;377(5):454-464. <https://doi.org/10.3410/f.727742055.793548553>
- Erba HP, Montesinos P, Kim HJ, et al.; QuANTUM-First Study Group. Quizartinib plus chemotherapy in newly diagnosed patients with FLT3-internal-tandem-duplication-positive acute myeloid leukaemia (QuANTUM-First): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2023;401(10388):1571-1583. [https://doi.org/10.1016/s0140-6736\(23\)00464-6](https://doi.org/10.1016/s0140-6736(23)00464-6) PMID:37116523
- Levis MJ, Erba HP, Montesinos P, et al. Quizartinib for patients with newly diagnosed FLT3-ITD-positive AML who received maintenance therapy in QuANTUM-First. *Blood Adv*. 2026;10(12):4144-4159. <https://doi.org/10.55788/d113a075>
- Perl AE, Martinelli G, Cortes JE, et al. Gilteritinib or Chemotherapy for Relapsed or Refractory FLT3-Mutated AML. *N Engl J Med*. 2019;381(18):1728-1740. <https://doi.org/10.1182/bloodadvances.2022009077> PMID:36378495
- Kurosawa S, et al. Outcomes in patients with FLT3-mutated relapsed/refractory acute myelogenous leukemia who underwent transplantation in the phase 3 ADMIRAL trial of gilteritinib versus salvage chemotherapy. *Transplant Cell Ther*. 2023;29(4):265.e1-265.e10. <https://doi.org/10.1002/hon.70107/v1/review2>
- Xuan L, Wang Y, Huang F, et al. Sorafenib maintenance in patients with FLT3-ITD acute myeloid leukaemia undergoing allogeneic haematopoietic stem-cell transplantation: an open-label, multicentre, randomised phase 3 trial. *Lancet Oncol*. 2020;21(9):1201-1212. https://doi.org/10.5353/th_b5108679
- Burchert A, Bug G, Fritz LV, et al. Sorafenib maintenance after allogeneic hematopoietic stem cell transplantation for acute myeloid leukemia with FLT3-internal tandem duplication mutation (SORMAIN). *J Clin Oncol*. 2020;38(26):2993-3002. <https://doi.org/10.1002/hon.70129/v1/review1>
- Levis MJ, Hamadani M, Logan B, et al. Gilteritinib as Post-Transplant Maintenance for AML With Internal Tandem Duplication Mutation of FLT3. *J Clin Oncol*. 2024;42(15):1766-1775. <https://doi.org/10.1182/blood-2019-124322>
- Levis MJ, Hamadani M, Logan B, et al. Measurable residual disease and posttransplantation gilteritinib maintenance for patients with FLT3-ITD-mutated AML. *Blood*. 2025;145(19):2138-2148. <https://doi.org/10.1017/s0143814x26101226.sm001> PMID:41292463
- Bataller A, Short NJ, Daver N, et al. Current Treatment Strategies for FLT3-Mutated Acute Myeloid Leukemia in Patients not Candidates for Intensive Chemotherapy. *Curr Oncol Rep*. 2025 Sep;27(9):1097-1105. <https://doi.org/10.1007/s11912-025-01709-8> PMID:40748523
- Mathew NR, Baumgartner F, Braun L, et al. Sorafenib promotes graft-versus-leukemia activity in mice and humans through IL-15 production in FLT3-ITD-mutant leukemia cells. *Nat Med*. 2018;24(3):282-291. <https://doi.org/10.1016/j.bbmt.2015.11.389> PMID:42574925
- Dang L, Su SM. Isocitrate dehydrogenase mutation and (R)-2-hydroxyglutarate: from basic discovery to therapeutics development. *Annu Rev Biochem*. 2017;86:305-331. <https://doi.org/10.1146/annurev-biochem-061516-044732> PMID:28375741
- DiNardo CD, Stein EM, de Botton S, et al. Durable Remissions with Ivosidenib in IDH1-Mutated Relapsed or Refractory AML. *N Engl J Med*. 2018;378(25):2386-2398. <https://doi.org/10.3410/f.733365365.793558675>
- Montesinos P, Recher C, Vives S, et al. Ivosidenib and Azacitidine in IDH1-Mutated Acute Myeloid Leukemia. *N Engl J Med*. 2022;386(16):1519-1531. <https://doi.org/10.1056/nejmoa2117344> PMID:35443108
- Stein EM, DiNardo CD, Pollyea DA, et al. Enasidenib in mutant IDH2 relapsed or refractory acute myeloid leukemia. *Blood*. 2017;130(6):722-731. <https://doi.org/10.3410/f.727693321.793558676>
- Amatangelo MD, Quek L, Shih A, et al. Enasidenib induces acute myeloid leukemia cell differentiation to promote clinical response. *Blood*. 2017;130(6):732-741. <https://doi.org/10.1182/blood-2017-04-779447> PMID:28588019
- DiNardo CD, Schuh AC, Stein EM, et al. Enasidenib plus azacitidine versus azacitidine alone in patients with newly diagnosed, mutant-IDH2 acute myeloid leukaemia (AG221-AML-005): a single-arm, phase 1b and randomised, phase 2 trial. *Lancet Oncol*. 2021;22(11):1597-1608. [https://doi.org/10.1016/s1470-2045\(21\)00494-0](https://doi.org/10.1016/s1470-2045(21)00494-0) PMID:34672961
- Farge T, et al. Real-life use of IDH inhibitors in patients with refractory or relapsed AML considered eligible for allogeneic stem cell transplantation. *Br J Haematol*. 2022. <https://doi.org/10.1002/hon.2803/v1/review2>
- Fathi AT, Kim HT, Soiffer RJ, et al. Multicenter Phase I Trial of Ivosidenib as Maintenance Treatment Following Allogeneic Hematopoietic Cell Transplantation for IDH1-Mutated Acute Myeloid Leukemia. *Clin Cancer Res*. 2023;29(11):2034-2042.

- <https://doi.org/10.1158/1078-0432.30707485> PMID:36230740
34. Fathi AT, Kim HT, Soiffer RJ, et al. Enasidenib as maintenance following allogeneic hematopoietic cell transplantation for IDH2-mutated myeloid malignancies. *Blood Adv*. 2022;6(22):5857-5865. <https://doi.org/10.1182/bloodadvances.2022008632> PMID:36150050
 35. Riedel SS, Ray D, Gerbing AK, et al. MLL1 inhibition and epigenetic regulation in MLL-rearranged leukemia. *Blood*. 2014;123(4):553-563. <https://doi.org/10.1016/j.exphem.2019.06.415> PMID:42574925
 36. Kühn MWM, Song E, Feng Z, et al. Targeting chromatin regulators inhibits leukemogenic gene expression in NPM1 mutant leukemia. *Cancer Discov*. 2016;6(10):1166-1181. <https://doi.org/10.1158/2159-8290.CD-16-0237> PMID:27535106
 37. Candoni A, Coppola G. A 2024 Update on Menin Inhibitors. A New Class of Target Agents against KMT2A-Rearranged and NPM1-Mutated Acute Myeloid Leukemia. *Hematology Reports*. 2024;16(2):24. <https://doi.org/10.3390/hematolrep16020024> PMID:38651453
 38. Issa GC, Aldoss I, Thirman MJ, et al. Menin Inhibition With Revumenib for KMT2A-Rearranged Relapsed or Refractory Acute Leukemia (AUGMENT-101). *J Clin Oncol*. 2025;43(1):75-84. <https://doi.org/10.1182/blood-2025-1657>
 39. Wang ES, Issa GC, Erba HP, et al. Ziftomenib in relapsed or refractory acute myeloid leukaemia (KOMET-001): a multicentre, open-label, multi-cohort, phase 1 trial. *Lancet Oncol*. 2024;25(10):1310-1324. <https://doi.org/10.70534/mlxm8716>
 40. Fetsch V, Schwöbel L, Ozyerli-Goknar E, et al. Menin inhibition enhances graft-versus-leukemia effects by T-cell activation and endogenous retrovirus induction in AML. *Blood*. 2026;147(5):584-601. <https://doi.org/10.1182/blood.2025029712> PMID:41144759
 41. Issa GC, Aldoss I, DiPersio J, et al. The menin inhibitor revumenib in KMT2A-rearranged or NPM1-mutant leukaemia. *Nature*. 2023;615:920-927. <https://doi.org/10.1182/blood-2025-1657>
 42. Goulart H, Okeleji O, Denton DiNardo C, et al. Revumenib as maintenance for AML following allogeneic stem cell transplantation. *J Clin Oncol*. 2026;44(16_suppl):6505. [https://doi.org/10.1016/s2152-2650\(26\)00586-0](https://doi.org/10.1016/s2152-2650(26)00586-0)
 43. DiNardo CD, Pratz KW, Pullarkat V, et al. Venetoclax combined with decitabine or azacitidine in treatment-naïve, elderly patients with acute myeloid leukemia. *Blood*. 2019;133:7-17. <https://doi.org/10.1182/blood-2018-08-868752> PMID:30361262
 44. Short NJ, Maiti A, Loghavi S, et al. Outcomes of patients with TP53-mutant acute myeloid leukemia with azacitidine and venetoclax. *Blood Adv*. 2020;4(24):644-649. <https://doi.org/10.1182/blood.2024027156> PMID:39946151
 45. Shahzad M, Amin MK, Daver NG, et al. Outcomes with allogeneic hematopoietic stem cell transplantation in TP53-mutated acute myeloid leukemia: a systematic review and meta-analysis. *Leuk Lymphoma*. 2022;63:2928-2936. <https://doi.org/10.1080/10428194.2022.2123228> PMID:36107118
 46. Ghimire B, Zimmer M, Donthireddy V. TP53-Mutated Acute Myeloid Leukemia: Review of Treatment and Challenges. *Eur J Haematol*. 2025;114(6):924-937. <https://doi.org/10.1111/ejh.14404> PMID:40035191
 47. Zhao Y, Cao W, Shi J, Cao Y, Lu Y, Luo Y, et al. Impact of TP53 variants and germline mutations on allogeneic stem cell transplantation outcomes in acute myeloid leukemia and myelodysplastic neoplasms. *Leukemia*. 2025;39(9):2292-2296. <https://doi.org/10.1038/s41375-025-02672-w>
 48. Wei AH, Döhner H, Pocock C, et al. Oral Azacitidine Maintenance Therapy for Acute Myeloid Leukemia in First Remission. *N Engl J Med*. 2020;383(26):2526-2537. [https://doi.org/10.1016/s2666-6367\(21\)00166-4](https://doi.org/10.1016/s2666-6367(21)00166-4)
 49. Bewersdorf JP, Prebet T, Gowda L. Azacitidine maintenance in AML post induction and posttransplant. *Curr Opin Hematol*. 2022;29(2):84-91. <https://doi.org/10.1097/moh.0000000000000700> PMID:35013047
 50. Craddock C, et al. A phase 3 randomized study of 5-azacitidine maintenance vs observation after transplant in high-risk AML and MDS patients. *Blood Advances*. 2020;4(21):5580-5588. <https://doi.org/10.1182/bloodadvances.2021004374> PMID:33755091
 51. Martino R, et al. Optimizing outcomes following allogeneic hematopoietic progenitor cell transplantation in AML: the role of hypomethylating agents. *Curr Pharm Des*. 2013;19(24):4184-4190. <https://doi.org/10.2174/15680096113139990005> PMID:23713435
 52. de Lima M, Giral S, Thall PF, et al. CC-486 Maintenance after Stem Cell Transplantation in Patients with Acute Myeloid Leukemia or Myelodysplastic Syndromes. *Biol Blood Marrow Transplant*. 2018;24(10):2017-2024. <https://doi.org/10.1016/j.bbmt.2018.06.016> PMID:29933073
 53. Craddock C, et al. A phase 3 randomized study of 5-azacitidine maintenance vs observation after transplant in high-risk AML and MDS patients. *Blood Advances*. 2020;4(21):5580-5588. <https://doi.org/10.1182/bloodadvances.2021004374> PMID:33755091
 54. Platzbecker U, Wermke M, Radke J, et al. Azacitidine for treatment of imminent relapse in patients with acute myeloid leukemia or myelodysplastic syndromes after allogeneic hematopoietic stem cell transplantation. *Leukemia*. 2012;26(3):381-389. <https://doi.org/10.1038/leu.2011.234> PMID:21886171
 55. Lancet JE, Uy GL, Cortes JE, et al. CPX-351 (cytarabine and daunorubicin) liposome for injection versus conventional cytarabine plus daunorubicin in older patients with newly diagnosed high-risk/secondary acute myeloid leukemia: a randomised, open-label, phase 3 trial. *Lancet*. 2018;391(10140):1185-1195. <https://doi.org/10.1200/jco.2017.77.6112> PMID:30024784
 56. Lancet JE, Uy GL, Newell LF, et al. Transplant outcomes after CPX-351 vs 7+3 in older adults with newly diagnosed high-risk and/or secondary AML. *Blood Advances*. 2022;6(17):4989-4997. <https://doi.org/10.1182/bloodadvances.2023010005> PMID:37318935
 57. Giammarco S, Chiusolo P, Metafuni E, et al. Feasibility of allogeneic stem cell transplantation (HSCT) in patients with acute myeloid leukemia previously treated with CPX-351: report from a single center. *Ann Hematol*. 2025;104(7):3855-3861. <https://doi.org/10.1002/hon.2826/v2/response1>
 58. Lin TL, Rizzieri DA, Ryan DH, et al. Older adults with newly diagnosed high-risk/secondary AML who achieved remission with CPX-351: phase 3 post hoc analyses. *Blood Advances*. 2021;5(6):1719-1728. <https://doi.org/10.1182/bloodadvances.2023010005> PMID:37318935
 59. Real World Study on the Best CPX-351 Treatment Duration and Timing for Allogeneic Stem Cell Transplantation. *American Journal of Hematology*. 2025. <https://doi.org/10.3324/haematol.2026.300845> PMID:42389813