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REVIEW ARTICLE

Therapeutic Strategies in Acute Myeloid Leukemia: Current Advances and Future Directions

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Abstract

Acute Myeloid Leukemia (AML) is a clinically aggressive and molecularly heterogeneous hematologic malignancy characterized by poor long-term outcomes, largely due to high rates of relapse and therapeutic resistance. For decades, standard treatment has relied on cytotoxic chemotherapy and allogeneic hematopoietic stem cell transplantation; however, these approaches are limited by toxicity and incomplete disease eradication. Advances in genomic and molecular profiling have substantially reshaped the therapeutic landscape, enabling the development of targeted agents directed against key oncogenic drivers, including FLT3 and IDH1/2 mutations, as well as the anti-apoptotic protein BCL-2. These therapies, often used in combination with hypomethylating agents, have improved response rates, particularly in older or unfit patients. In parallel, immunotherapeutic strategies, such as antibody–drug conjugates, bispecific T-cell engagers, and cellular therapies, have been explored, although their efficacy in AML remains constrained by antigen heterogeneity and an immunosuppressive bone marrow microenvironment. Importantly, durable responses are frequently undermined by resistance mechanisms involving leukemia stem cell persistence, clonal evolution, metabolic reprogramming, and niche-mediated protection. Emerging therapeutic strategies emphasize rational combination regimens, targeting metabolic dependencies, and the integration of precision medicine approaches guided by multi-omics profiling and minimal residual disease assessment. In this review, we provide an integrated overview of current therapeutic strategies in AML, with a particular focus on mechanistic insights, resistance pathways, and future directions for improving clinical outcomes.

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Introduction

Acute Myeloid Leukemia(AML) is a biologically heterogeneous and clinically aggressive hematologic malignancy characterized by the clonal expansion of immature myeloid progenitors in the bone marrow, peripheral blood, and occasionally extramedullary tissues [1]. Despite decades of research, AML remains associated with high morbidity and mortality, particularly in older adults, who constitute the majority of affected patients. The clinical course of AML is highly variable, reflecting a complex interplay of genetic mutations, epigenetic alterations, and dysregulated cellular signaling pathways that collectively drive leukemogenesis and disease progression [2]. Advances in next-generation sequencing have substantially refined the molecular classification of AML, identifying recurrent mutations in genes such as FLT3, NPM1, IDH1/2, and TP53, which not only provide prognostic information but also serve as actionable therapeutic targets [3].

For several decades, the standard treatment paradigm for AML was dominated by intensive cytotoxic chemotherapy, most notably the combination of cytarabine and an anthracycline, commonly referred to as the "7+3" regimen [4]. While this approach can induce complete remission in a subset of patients, its efficacy is often limited by treatment-related toxicity, particularly in elderly or unfit individuals, and by a high rate of disease relapse. Allogeneic Hematopoietic Stem Cell Transplantation (HSCT) has been employed as a potentially curative strategy for selected patients, leveraging graft-versus-leukemia effects to eradicate residual disease [5]. However, its application is constrained by donor availability, treatment-related complications, and the persistent risk of relapse, underscoring the need for more effective and less toxic therapeutic approaches.

In recent years, the therapeutic landscape of AML has undergone a profound transformation with the advent of targeted therapies and mechanism-based treatment strategies [6]. Small-molecule inhibitors directed against mutant kinases, metabolic enzymes, and anti-apoptotic proteins have demonstrated clinical efficacy and have been incorporated into standard treatment regimens [7]. Agents targeting FLT3 mutations, IDH1/2-driven metabolic reprogramming, and BCL-2-mediated apoptotic pathways exemplify this shift toward precision medicine. In parallel, hypomethylating agents have gained prominence, particularly in combination with targeted drugs, offering improved outcomes for patients who are ineligible for intensive chemotherapy. These developments reflect a broader conceptual transition from nonspecific cytotoxicity to therapies tailored to the molecular and cellular dependencies of leukemic cells.

Nevertheless, durable remission remains elusive for many patients, as therapeutic resistance and disease relapse continue to pose major clinical challenges. Increasing evidence suggests that resistance arises from a multifaceted network of mechanisms, including the persistence of leukemia stem cells, clonal evolution under therapeutic pressure, metabolic reprogramming, and protective interactions within the bone marrow microenvironment [8]. These factors not only limit the efficacy of existing therapies but also complicate the development of novel treatment strategies. Furthermore, immunotherapeutic approaches, which have revolutionized the management of several solid and hematologic malignancies, have shown comparatively modest success in AML, highlighting the unique biological barriers inherent to this disease.

In this context, a comprehensive and integrative understanding of AML therapy is essential. This review provides an overview of current therapeutic strategies in AML, emphasizing the mechanistic basis of established and emerging treatments, the

challenges posed by therapeutic resistance, and future directions aimed at achieving more durable and personalized clinical outcomes.

Therapeutic landscape: From cytotoxic backbone to targeted intervention

The therapeutic framework for Acute Myeloid Leukemia (AML) has historically been anchored in cytotoxic chemotherapy, which for decades served as the principal modality for inducing remission. The combination of cytarabine and an anthracycline, commonly referred to as the "7+3" regimen, remains a foundational approach, particularly for younger and fit patients [9]. Mechanistically, cytarabine functions as a nucleoside analog that interferes with DNA synthesis [10], while anthracyclines induce DNA damage through intercalation and topoisomerase II inhibition [11]. Together, these agents promote leukemic cell death by exploiting the high proliferative rate of malignant blasts. Although this regimen achieves complete remission in a substantial proportion of patients, especially those with favorable-risk cytogenetics, its efficacy is frequently undermined by significant toxicity and a high incidence of relapse. Importantly, older patients and those with comorbidities often cannot tolerate intensive chemotherapy, highlighting a critical limitation of this conventional paradigm.

In parallel with induction chemotherapy, allogeneic Hematopoietic Stem Cell Transplantation (HSCT) has been established as a potentially curative strategy, particularly for patients with intermediate- or high-risk disease. The therapeutic benefit of HSCT extends beyond high-dose conditioning regimens, relying significantly on the immunologically mediated Graft-Versus-Leukemia (GVL) effect, whereby donor immune cells recognize and eliminate residual leukemic clones [12]. This approach has improved long-term survival in selected patient populations; however, its broader application is restricted by several factors, including donor availability, transplant-related morbidity and mortality, and the risk of Graft-Versus-Host Disease (GVHD). Moreover, relapse after transplantation remains a major cause of treatment failure, underscoring the persistence of therapy-resistant leukemic cells even in the context of intensive immunologic pressure.

The limitations of cytotoxic chemotherapy and HSCT have catalyzed the development of targeted therapies that exploit specific molecular vulnerabilities in AML [13]. Advances in genomic profiling have enabled the identification of recurrent driver mutations and dysregulated signaling pathways, providing a rational basis for precision medicine approaches. Among these, mutations in the FMS-Like Tyrosine kinase 3 (FLT3) gene represent one of the most common and clinically significant alterations, often associated with aggressive disease and poor prognosis. The introduction of FLT3 inhibitors, such as midostaurin in the frontline setting and gilteritinib in relapsed or refractory AML, has demonstrated improved clinical outcomes when combined with conventional chemotherapy or used as monotherapy. These agents function by inhibiting constitutively active FLT3 signaling, thereby suppressing downstream proliferative and survival pathways. However, resistance frequently emerges through secondary kinase domain mutations or activation of alternative signaling networks, limiting the durability of responses.

In addition to kinase-driven leukemogenesis, metabolic reprogramming has emerged as a critical hallmark of AML, exemplified by mutations in isocitrate dehydrogenase 1 and 2 (IDH1/2). These mutations confer neomorphic enzymatic activity, leading to the accumulation of the oncometabolite 2-hydroxyglutarate, which disrupts epigenetic regulation and blocks normal hematopoietic differentiation [14]. Targeted inhibitors such as ivosidenib and enasidenib have been developed to specifically

inhibit mutant IDH enzymes, thereby restoring differentiation and reducing leukemic burden [15]. Unlike conventional cytotoxic agents, these therapies induce a differentiation-based response rather than direct cytotoxicity, representing a distinct therapeutic paradigm. Nevertheless, clinical responses are often partial, and resistance mechanisms-including isoform switching and co-occurring mutations-can attenuate treatment efficacy.

Another major advance in AML therapy is the targeting of apoptotic pathways, particularly through inhibition of the anti-apoptotic protein B-Cell Lymphoma 2 (BCL-2). Venetoclax [16], a selective BCL-2 inhibitor, has shown remarkable efficacy when combined with hypomethylating agents such as azacitidine or decitabine, especially in older or unfit patients. By disrupting mitochondrial apoptotic regulation, venetoclax lowers the threshold for leukemic cell death and enhances the cytotoxic effects of partner agents. This combination has significantly improved response rates and overall survival in previously underserved patient populations. However, resistance to venetoclax-based regimens is increasingly recognized and is often associated with upregulation of alternative anti-apoptotic proteins such as MCL-1, as well as metabolic adaptations that sustain mitochondrial function.

Epigenetic therapies, particularly hypomethylating agents, have also played a central role in the evolving treatment landscape of AML. These agents act by inhibiting DNA methyl transferases, leading to reactivation of silenced tumor suppressor genes and modulation of gene expression programs [17]. While their single-agent activity is modest, their incorporation into combination regimens has enhanced therapeutic efficacy and broadened treatment options for patient's ineligible for intensive therapy. More recently, efforts to target additional epigenetic regulators, including histone modifiers and chromatin remodeling complexes, are underway, reflecting the growing recognition of epigenetic dysregulation as a key driver of AML pathogenesis.

Collectively, these developments illustrate a paradigm shift in AML therapy from a reliance on nonspecific cytotoxic agents toward mechanism-based and molecularly targeted interventions. Despite these advances, the clinical benefit of targeted therapies is often limited by incomplete responses and the emergence of resistance, emphasizing the need for continued refinement of therapeutic strategies and the integration of combination approaches to achieve more durable disease control.

Immunotherapeutic strategies and the constraints

The success of immunotherapy in a range of solid tumors and lymphoid malignancies has stimulated considerable interest in its application to Acute Myeloid Leukemia (AML) [18]. However, translating immunotherapeutic strategies into effective AML treatments has proven substantially more challenging, reflecting the unique biological and immunological features of this disease. Unlike B-cell malignancies, where lineage-specific antigens such as CD19 provide clear and relatively safe therapeutic targets [19], AML lacks universally expressed, leukemia-specific surface markers. Instead, most candidate antigens, including CD33 and CD123 [20], are also expressed on normal hematopoietic progenitors, raising concerns regarding on-target, off-tumor toxicity and limiting the therapeutic window.

Antibody-based therapies represent one of the earliest and most clinically advanced forms of immunotherapy in AML. Gemtuzumab ozogamicin, an antibody–drug conjugate targeting CD33, delivers a cytotoxic payload directly to leukemic cells upon antigen binding and internalization [21]. Clinical studies have demonstrated that the addition of this agent to conventional chemotherapy can improve

outcomes in selected patient subsets, particularly those with favorable or intermediate-risk disease. Nevertheless, its use is constrained by hepatotoxicity, including the risk of sinusoidal obstruction syndrome, and by variable efficacy across molecular subtypes. These limitations highlight the challenges of achieving both specificity and tolerability in AML-directed immunotherapy.

More recently, bispecific T-cell engagers have been developed to redirect cytotoxic T lymphocytes toward leukemic cells by simultaneously binding CD3 on T cells and tumor-associated antigens such as CD33 or CD123 [22]. This approach bypasses the need for endogenous antigen presentation and can induce potent, antigen-dependent T-cell activation and target cell lysis. Early-phase clinical studies have demonstrated promising antileukemic activity; however, these agents are frequently associated with cytokine release syndrome and neurotoxicity, necessitating careful dose optimization and clinical monitoring [23]. In addition, their efficacy may be compromised by T-cell exhaustion, antigen downregulation, or the immunosuppressive milieu of the bone marrow microenvironment.

Adoptive cellular therapies, particularly Chimeric Antigen Receptor (CAR)-T cells, have revolutionized the treatment of certain hematologic malignancies, yet their application in AML remains in an early and challenging stage [24]. The development of CAR-T therapies for AML is complicated by the lack of leukemia-specific antigens and the potential for prolonged myelosuppression due to targeting of shared antigens on normal hematopoietic cells. Strategies to mitigate these risks, including transient CAR expression, dual-targeting constructs, and incorporation of safety switches, are under active investigation. Despite these innovations, clinical responses have been variable, and durable remissions remain relatively uncommon.

Immune checkpoint inhibition, which has transformed the management of multiple solid tumors, has shown comparatively modest efficacy in AML. Agents targeting programmed cell death protein 1 (PD-1) or its ligand (PD-L1) have demonstrated limited activity as monotherapy, likely reflecting the relatively low mutational burden of AML and the absence of robust neoantigen-driven immune responses [25]. Combination approaches, particularly with hypomethylating agents, have been explored to enhance immunogenicity and overcome immune evasion, but clinical benefits have thus far been incremental [26]. These findings underscore fundamental differences between AML and more immunotherapy-responsive malignancies.

A central barrier to effective immunotherapy in AML is the highly specialized and immunosuppressive bone marrow microenvironment [27]. Leukemic cells actively remodel this niche through the secretion of cytokines, chemokines, and metabolic factors that inhibit effector T-cell function and promote regulatory immune populations. Additionally, metabolic competition within the microenvironment, including depletion of essential nutrients and accumulation of inhibitory metabolites, further impairs antitumor immunity. These factors collectively create a context in which even highly immune effector mechanisms may be insufficient to achieve sustained disease control.

Taken together, while immunotherapeutic strategies hold significant promise for AML, their clinical translation is constrained by antigenic heterogeneity, toxicity, immune evasion, and microenvironmental resistance. Overcoming these barriers will likely require the integration of immunotherapy with other treatment modalities, as well as a deeper understanding of the interactions between leukemic cells and the immune system within the bone marrow niche.

Mechanisms of therapeutic resistance in acute myeloid leukemia

Therapeutic resistance remains the central obstacle to achieving durable remission in Acute Myeloid Leukemia (AML), arising from a complex and dynamic interplay of cell-intrinsic adaptations and microenvironmental influences. Despite initial responses to chemotherapy, targeted agents, or combination regimens, a substantial proportion of patients ultimately experience relapse, underscoring the persistence of residual leukemic populations that evade therapeutic eradication. Increasing evidence suggests that resistance in AML is not driven by a single dominant mechanism, but rather by an integrated network encompassing leukemia stem cell biology, clonal evolution, metabolic reprogramming, and protective signals from the bone marrow niche.

A fundamental contributor to therapeutic resistance is the presence of Leukemia Stem Cells (LSCs), a subpopulation of self-renewing cells with the capacity to sustain disease propagation [28]. LSCs are typically characterized by a quiescent or slow-cycling state, rendering them intrinsically less susceptible to cytotoxic agents that preferentially target proliferating cells. In addition to cell cycle–mediated protection, LSCs exhibit enhanced DNA damage response pathways [29], elevated expression of drug efflux transporters [30], and resistance to apoptosis [31], collectively enabling their survival under therapeutic pressure. Importantly, LSCs are not static entities but display considerable phenotypic and functional heterogeneity, complicating efforts to identify universal therapeutic targets. Their persistence following treatment provides a reservoir for disease recurrence and highlights the limitations of therapies that fail to effectively eradicate this compartment.

Closely linked to LSC-driven resistance is the process of clonal evolution, whereby genetically distinct subclones within the leukemic population are differentially selected during therapy [32]. AML is characterized by substantial genetic heterogeneity at diagnosis, with multiple coexisting subclonal populations harboring distinct mutational profiles. Therapeutic interventions impose selective pressure that can eliminate sensitive clones while allowing resistant subclones to expand. In some cases, resistance arises through the acquisition of new mutations, such as secondary kinase domain alterations in FLT3 or mutations affecting signaling and epigenetic regulators [33]. In other instances, pre-existing minor subclones with intrinsic resistance properties become dominant following treatment [34]. This dynamic evolutionary process not only drives relapse but also contributes to increased disease aggressiveness and therapeutic refractoriness.

Beyond genetic alterations, metabolic reprogramming has emerged as a critical and increasingly recognized mechanism of resistance in AML [35]. Leukemic cells, particularly LSCs, exhibit a heightened dependence on mitochondrial Oxidative Phosphorylation (OXPHOS) for energy production and survival, in contrast to the glycolytic bias observed in many solid tumors. This reliance on mitochondrial metabolism confers a survival advantage under conditions of therapeutic stress and has been implicated in resistance to both conventional chemotherapy and targeted agents [36]. For example, resistance to BCL-2 inhibition by venetoclax has been associated with metabolic adaptations that restore mitochondrial function, including increased fatty acid oxidation and upregulation of alternative anti-apoptotic proteins such as MCL-1 [37]. These findings highlight the tight coupling between metabolic state and apoptotic sensitivity, suggesting that metabolic plasticity enables leukemic cells to circumvent targeted disruptions of cell survival pathways.

In addition to bioenergetic adaptations, mitochondrial dynamics and redox homeostasis

play important roles in mediating resistance [38]. AML cells often maintain a finely tuned balance of Reactive Oxygen Species (ROS), which can promote proliferation and survival at moderate levels while avoiding cytotoxic oxidative damage. Enhanced antioxidant capacity and regulation of mitochondrial integrity allow leukemic cells to withstand therapy-induced oxidative stress. Moreover, alterations in mitochondrial biogenesis and turnover can further support cellular adaptation to therapeutic challenges [39]. These features collectively underscore the central role of mitochondrial function as both a driver of leukemic cell survival and a barrier to effective treatment.

The bone marrow microenvironment provides an additional and critical layer of protection that contributes to therapeutic resistance [40]. Leukemic cells reside within a highly specialized niche composed of stromal cells, endothelial cells, immune cells, and extracellular matrix components, all of which interact to create a supportive and often immunosuppressive milieu. Stromal cells can directly promote leukemic cell survival through cell–cell contact and the secretion of cytokines and growth factors, such as CXCL12 and interleukins, which activate pro-survival signaling pathways. Hypoxic conditions within the bone marrow further enhance resistance by stabilizing hypoxia-inducible factors and promoting metabolic adaptations that favor cell survival. Additionally, the microenvironment can limit drug penetration and alter drug metabolism, reducing the effective concentration of therapeutic agents at the site of disease [41].

Metabolic interactions within the microenvironment further reinforce resistance mechanisms. For instance, stromal cells can supply metabolic substrates, including amino acids and lipids, that support leukemic cell survival and proliferation [42]. This metabolic crosstalk enables leukemic cells to adapt to nutrient stress and maintain mitochondrial function even in the presence of targeted metabolic inhibitors. At the same time, competition for nutrients and the accumulation of inhibitory metabolites can impair the function of antitumor immune cells, thereby indirectly facilitating immune evasion and disease persistence.

An additional layer of resistance is provided by disruptions in protein homeostasis, or proteostasis, which allows leukemic cells to cope with the proteotoxic stress induced by rapid proliferation and therapeutic intervention [43]. Activation of stress response pathways, including the unfolded protein response and endoplasmic reticulum stress signaling, can enhance cell survival by promoting adaptive mechanisms such as increased protein folding capacity and degradation of misfolded proteins. These pathways not only support leukemic cell viability under stress conditions but may also contribute to resistance against therapies that induce cellular stress or disrupt protein function.

Collectively, these mechanisms illustrate that therapeutic resistance in AML is a multifactorial and highly adaptive process, driven by the integration of cellular heterogeneity, metabolic flexibility, and microenvironmental support. The interplay between LSC persistence, clonal evolution, mitochondrial dependence, and niche-mediated protection creates a robust and resilient system that enables leukemic cells to evade therapeutic eradication. Addressing this complexity will require the development of combinatorial strategies that simultaneously target multiple resistance pathways, as well as the incorporation of dynamic biomarkers to monitor disease evolution and guide treatment decisions.

Emerging therapeutic strategies and future directions

The evolving understanding of Acute Myeloid Leukemia (AML) biology has catalyzed the development of next-generation therapeutic

strategies that move beyond single-agent approaches toward integrated, mechanism-driven interventions [44]. A central theme in current clinical and translational research is the rational design of combination therapies aimed at simultaneously targeting multiple, nonredundant pathways that sustain leukemic cell survival. Among these, venetoclax-based regimens have emerged as a cornerstone in the treatment of older or unfit patients, particularly in combination with hypomethylating agents or low-dose cytarabine [45]. Building on this foundation, ongoing efforts are exploring combinations of BCL-2 inhibition with kinase inhibitors, epigenetic modulators, and immune-based therapies to overcome resistance mediated by apoptotic escape and metabolic adaptation. Early clinical data suggest that such combinatorial approaches can deepen responses and potentially delay relapse, although challenges related to toxicity and optimal scheduling remain.

Targeting metabolic dependencies represents another promising avenue for therapeutic innovation in AML [46]. Increasing evidence indicates that leukemic cells, especially leukemia stem cells, rely heavily on mitochondrial Oxidative Phosphorylation (OXPHOS) and associated metabolic pathways for energy production and survival [47]. This metabolic vulnerability has prompted the development of agents that disrupt mitochondrial function, inhibit electron transport chain components, or interfere with substrate utilization such as fatty acid oxidation [48]. Importantly, these approaches may synergize with existing therapies, including venetoclax, by lowering the apoptotic threshold and impairing the metabolic flexibility that underlies drug resistance. However, given the essential role of mitochondrial function in normal hematopoiesis, achieving therapeutic selectivity remains a critical consideration.

Advances in precision medicine are also reshaping the therapeutic landscape of AML, driven by the integration of multi-omics technologies and increasingly sophisticated biomarker platforms [49]. Genomic, transcriptomic, and proteomic profiling now enable more refined risk stratification and facilitate the identification of actionable molecular alterations [50]. In parallel, single-cell sequencing technologies are providing unprecedented insights into intratumoral heterogeneity, clonal architecture, and the dynamic evolution of leukemic populations. These approaches hold significant promise for guiding individualized therapy selection, monitoring Minimal Residual Disease (MRD), and detecting early signs of relapse. The incorporation of MRD assessment into clinical decision-making represents a particularly important advance, allowing for treatment intensification or modification based on residual disease burden rather than conventional morphological criteria.

Immunotherapeutic strategies are also being re-envisioned within combination frameworks to enhance their efficacy in AML [51]. Rather than relying on single-agent immune checkpoint inhibitors or cellular therapies, current approaches increasingly focus on integrating immunotherapy with targeted agents or epigenetic modulators to overcome immune evasion and augment antitumor responses. For example, hypomethylating agents may enhance tumor immunogenicity by upregulating antigen expression and modulating the tumor microenvironment, thereby sensitizing leukemic cells to immune-mediated clearance [52]. Similarly, strategies that target the immunosuppressive bone marrow niche, including modulation of cytokine signaling or metabolic constraints, may further improve the effectiveness of immunotherapeutic interventions.

Beyond targeting leukemic cells directly, emerging strategies are increasingly directed toward the bone marrow microenvironment

and its role in disease persistence and therapy resistance [53]. Disrupting the interactions between leukemic cells and stromal components, inhibiting chemokine-mediated homing and retention, and altering the metabolic and hypoxic conditions of the niche represent potential avenues for enhancing therapeutic efficacy. These approaches reflect a broader shift toward viewing AML not solely as a cell-intrinsic disease but as a dynamic system shaped by its surrounding environment.

Looking forward, the future of AML therapy is likely to be defined by the convergence of precision medicine, systems biology, and adaptive treatment strategies [54]. Rather than applying uniform treatment regimens, emerging paradigms emphasize tailoring therapy based on the molecular and functional characteristics of each patient's disease. This includes the use of real-time biomarkers to guide treatment selection, the deployment of combination therapies to preempt or overcome resistance, and the integration of longitudinal monitoring to dynamically adjust therapeutic interventions [55]. Despite these advances, significant challenges remain, including the need to balance efficacy with toxicity, to ensure accessibility of complex diagnostic and therapeutic platforms, and to translate mechanistic insights into clinically meaningful outcomes.

Collectively, these emerging strategies underscore a fundamental transition in AML therapy from static, one-dimensional treatment approaches toward a more adaptive and multidimensional framework. By integrating advances in molecular biology, metabolism, immunology, and microenvironmental research, future therapeutic paradigms hold the potential to achieve more durable remissions and ultimately improve survival outcomes for patients with AML.

Conclusion

The therapeutic landscape of Acute Myeloid Leukemia (AML) has undergone a substantial transformation over recent years, evolving from a reliance on intensive cytotoxic chemotherapy toward a more nuanced, mechanism-based and precision-oriented framework. The integration of targeted therapies, epigenetic modulators, and emerging immunotherapeutic approaches has expanded treatment options and improved outcomes for selected patient populations, particularly those previously considered ineligible for intensive regimens [56]. Nevertheless, despite these advances, durable remission remains a major clinical challenge, with relapse and therapeutic resistance continuing to limit long-term survival.

A central theme emerging from current research is that AML is not driven by a single dominant pathway, but rather by a complex and adaptive network involving genetic heterogeneity, leukemia stem cell persistence, metabolic plasticity, and microenvironmental support. These interconnected factors collectively enable leukemic cells to evade therapeutic pressure and re-establish disease. As such, strategies that target only one aspect of AML biology are unlikely to achieve sustained efficacy. Instead, there is a growing consensus that combinatorial approaches, designed to simultaneously disrupt multiple survival mechanisms, will be essential for overcoming resistance and improving clinical outcomes.

Looking forward, the future of AML therapy will likely be defined by increasingly personalized and dynamic treatment paradigms. Advances in multi-omics technologies, single-cell analysis, and minimal residual disease monitoring are providing powerful tools to refine risk stratification, guide therapeutic decision-making, and track disease evolution in real time [57]. These innovations offer the potential to move beyond static treatment algorithms toward adaptive strategies that are tailored to the evolving biological landscape of each patient's disease. At the same time,

continued efforts to better understand the interactions between leukemic cells and the bone marrow microenvironment, as well as the metabolic and immunological determinants of therapy response, will be critical for identifying new therapeutic vulnerabilities.

In summary, while significant progress has been made in the treatment of AML, substantial challenges remain. Bridging the gap between mechanistic insights and clinical application will require coordinated advances in translational research, clinical trial design, and biomarker development. Through the integration of targeted therapies, rational combination strategies, and precision medicine approaches, there is a realistic prospect of achieving more durable remissions and ultimately improving survival for patients with this complex and aggressive disease.

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The authors declare no conflicts of interest.

References

1. Gilbert JS, Milano F. Conditioning for acute myeloid leukemia: looking beyond intensity. Haematologica. 2026 Apr 9 [Epub ahead of print]. doi:10.3324/haematol.2026.300787. PMID:41952631.
2. Zhang H, Zhang J. Comprehensive omics profiling in acute myeloid leukemia: from molecular landscape to clinical translation. Curr Proteomics. 2025;22(3):100028. doi:10.1016/j.curpro.2025.100028.
3. Chen P, Cao J, Chen L, Gao G, Xu Y, Jia P, et al. Prognostic value of an eighteen-gene panel in acute myeloid leukemia by analyzing TARGET and TCGA databases. Cancer Biomark. 2023;36(4):287-298. doi:10.3233/CBM-220179. PMID:36938728.
4. Shaikh MR, Singh B, Halder R, Singh R, Shaikh MR, Agarwal N, et al. FLAG-based vs standard 3+7 induction therapy in treatment-naïve acute myeloid leukemia: time to think beyond anthracyclines. Leuk Res. 2023;132:107346. Epub 2023 Jun 28. doi:10.1016/j.leukres.2023.107346. PMID:37467566.
5. Shimomura Y, Komukai S, Kitamura T, Sobue T, Yamasaki S, Kondo T, et al. The optimal conditioning intensity of stem cell transplantation for acute myeloid leukemia in complete remission. Ann Hematol. 2026;105(4):124. Epub 2026 Feb 19. doi:10.1007/s00277-026-06881-w. PMID:41711974; PMCID:PMC12920725.
6. Cao S, Wang Q, Zhu G. From chemotherapy to targeted therapy: unraveling resistance in acute myeloid leukemia through genetic and non-genetic insights. Int J Mol Sci. 2025;26(9):4005. Epub 2025 Apr 24. doi:10.3390/ijms26094005. PMID:40362245; PMCID:PMC12071668.
7. Lap CJ, Abrahim MS, Nassereddine S. Perspectives and challenges of small molecule inhibitor therapy for FLT3-mutated acute myeloid leukemia. Ann Hematol. 2024;103(7):2215-2229. Epub 2023 Nov 17. doi:10.1007/s00277-023-05545-3. PMID:37975931.
8. Titah S, Guillemette A, Lewuillon C, Shaik FA, Berthon C, Goursaud L, et al. Pre-therapeutic bone marrow-resident leukemic cells in acute myeloid leukemia exhibit a distinct dysregulated calcium signature and stem-like profile reflecting minimal residual disease precursors. J Exp Clin Cancer Res. 2026;45(1):55. Epub 2026 Jan 9. doi:10.1186/s13046-025-03634-x. PMID:41508052; PMCID:PMC12911078.
9. Hsiao TH, Wang RC, Lu TJ, Shih CH, Su YC, Tsai JR, et al. Chemoresponse of de novo acute myeloid leukemia to "7+3" induction can be predicted by c-Myc-facilitated cytogenetics. Front Pharmacol. 2021;12:649267. Epub 2021 Apr 8. doi:10.3389/fphar.2021.649267. PMID:33897436; PMCID:PMC8061304.
10. Marrero RJ, Shastri VM, Nicolet D, Mrózek K, Walker CJ, Blum WG, et al. Cytarabine pharmacogenomics and outcomes among children and young adults with acute myeloid leukemia. JAMA Netw Open. 2025;8(6):e2516296. Epub 2025 Jun 2. doi:10.1001/jamanetworkopen.2025.16296. PMID:40549387; PMCID:PMC12186577.
11. Mishra SV, Banerjee A, Sarkar D, Thangarathnam V, Bagal B, Hasan SK, et al. DNA-PKcs-mediated transcriptional

regulation of TOP2B drives chemoresistance in acute myeloid leukemia. J Cell Sci. 2024;137(3). Epub 2024 Feb 13. doi:10.1242/jcs.261931. PMID:38240344.

12. Werk J, Baden D, Shaforostova I, Mikesch JH, Reicherts C, Marx J, et al. Beta-blocker use and outcome after allogeneic hematopoietic stem cell transplantation in acute myeloid leukemia. Ann Hematol. 2026;105(4). Epub 2026 Mar 25. doi:10.1007/s00277-026-06962-w. PMID:41876878; PMCID:PMC13013103.

13. Vasu S, Caligiuri MA. Targeted immunotherapy for acute myeloid leukemia. Best Pract Res Clin Haematol. 2011;24(4):533-540. Epub 2011 Nov 11. doi:10.1016/j.beha.2011.09.001. PMID:22127317; PMCID:PMC4083700.

14. Wakita S, Yamaguchi H, Omori I, Terada K, Ueda T, Manabe E, et al. Mutations of epigenetics-modifying genes (DNMT3A, TET2, IDH1/2) at diagnosis may induce FLT3-ITD at relapse in de novo acute myeloid leukemia. Leukemia. 2013;27(5):1044-1052. Epub 2012 Nov 8. doi:10.1038/leu.2012.317. PMID:23135354.

15. Wang L, Song J, Xiao X, Li D, Liu T, He X. Comparison of venetoclax and ivosidenib/enasidenib for unfit newly diagnosed patients with acute myeloid leukemia and IDH1/2 mutation: a network meta-analysis. J Chemother. 2024;36(3):202-207. Epub 2023 Aug 20. doi:10.1080/1120009X.2023.2247200. PMID:37599456.

16. Niscola P, Catalano G, Pasqualini G, Piccioni D, Giovannini M, Noguera NI. Venetoclax and new BCL-2 inhibitors in acute myeloid leukemia. Expert Opin Pharmacother. 2025;26(16):1725-1739. Epub 2025 Nov 2. doi:10.1080/14656566.2025.2582022. PMID:41143709.

17. Baer MR, Kogan AA, Bentzen SM, Mi T, Lapidus RG, Duong VH, et al. Phase I clinical trial of DNA methyltransferase inhibitor decitabine and PARP inhibitor talazoparib combination therapy in relapsed/refractory acute myeloid leukemia. Clin Cancer Res. 2022;28(7):1313-1322. doi:10.1158/1078-0432.CCR-21-3729. PMID:35091444; PMCID:PMC8976746.

18. Lin H, Wang T, Wei J. Strategic innovations: tackling challenges of immunotherapy in acute myeloid leukemia. Chin J Cancer Res. 2025;37(4):490-504. doi:10.21147/j.issn.1000-9604.2025.04.02. PMID:40979658; PMCID:PMC12444347.

19. Ma G, Wang Y, Ahmed T, Zaslav AL, Hogan L, Avila C, et al. Anti-CD19 chimeric antigen receptor targeting of CD19+ acute myeloid leukemia. Leuk Res Rep. 2018;9:42-44. Epub 2018 Mar 27. doi:10.1016/j.lrr.2018.03.002. PMID:29892548; PMCID:PMC5993359.

20. Jin F, Wei X, Liu Y, Tang L, Ren J, Yang J, et al. Engineered cell membrane vesicles loaded with lysosomophilic drug for acute myeloid leukemia therapy via organ-cell-organelle cascade-targeting. Biomaterials. 2025;317:123091. Epub 2025 Jan 3. doi:10.1016/j.biomaterials.2025.123091. PMID:39778270.

21. Chen L, Duan H, Huang C, Xu Y, Wang Z, Huang H. Humanized anti-CD33 CAR-T cells and antibody-drug conjugates for targeted therapy in acute myeloid leukemia. Front Med (Lausanne). 2026;13:1691417. Epub 2026 Jan 26. doi:10.3389/fmed.2026.1691417. PMID:41669343; PMCID:PMC12884322.

22. Liegel J, Stroopinsky D, Cheloni G, Karagkouni D, Nahas M, Ma Y, et al. Vaccine-educated T cells and a CD123 bispecific T-cell engager for treatment of acute myeloid leukemia. Blood Adv. 2025;9(21):5585-5597. doi:10.1182/bloodadvances.2024015449. PMID:40811786; PMCID:PMC12630361.

23. Uckun FM, Lin TL, Mims AS, Patel P, Lee C, Shahidzadeh A, et al. A clinical phase 1B study of the CD3xCD123 bispecific antibody APVO436 in patients with relapsed/refractory acute myeloid leukemia or myelodysplastic syndrome. Cancers (Basel). 2021;13(16):4113. Epub 2021 Aug 15. doi:10.3390/cancers13164113. PMID:34439266; PMCID:PMC8394899.

24. Zanetti LC, Tomaz V, de Souza IF, Campregher PV, Hamerschlak N, Kerbauy LN. Precision medicine with CAR cells in acute myeloid leukemia: where are we? Front Immunol. 2025;16:1653350. Epub 2025 Nov 6. doi:10.3389/fimmu.2025.1653350. PMID:41280924; PMCID:PMC12631394.

25. Reinhardt C, Ochsenbein AF. Immune checkpoints regulate acute myeloid leukemia stem cells. Leukemia. 2025;39(6):1277-1293. Epub 2025 Apr 2. doi:10.1038/s41375-025-02566-x. PMID:40175626; PMCID:PMC12133569.

26. Zhou HS, Su YF, Wang J, Hu YL, Wang A, Xu L, et al. Updates from a single-center phase 2 study of PD-1 inhibitor combined with hypomethylating agent plus CAG regimen in patients with relapsed/refractory acute myeloid leukemia. Front Immunol. 2025;16:1533467. Epub 2025 Apr 17. doi:10.3389/fimmu.2025.1533467. PMID:40313949; PMCID:PMC12043577.

27. Zha C, Yang X, Yang J, Zhang Y, Huang R. Immunosuppressive microenvironment in acute myeloid leukemia: overview, therapeutic targets and corresponding strategies. Ann Hematol. 2024;103(12):4883-4899. Epub 2024 Nov 28. doi:10.1007/s00277-024-06117-9. PMID:39607487.

28. Ngai LL, Reuvekamp T, Hanekamp D, Janssen F, Marsbergen LO, Carbaat-Ham J, et al. Different features of acute myeloid leukemia stem cell quantification in intensively treated patients. Haematologica. 2025;110(12):2942-2953. Epub 2025 Apr 30. doi:10.3324/haematol.2024.287090. PMID:40304060; PMCID:PMC12666270.

29. Boila LD, Ghosh S, Bandyopadhyay SK, Jin L, Murison A, Zeng AGX, et al. KDM6 demethylases integrate DNA repair gene regulation and loss of KDM6A sensitizes human acute myeloid leukemia to PARP and BCL2 inhibition. Leukemia. 2023;37(4):751-764. Epub 2023 Jan 31. doi:10.1038/s41375-023-01833-z. PMID:36720973.

30. Damiani D, Tiribelli M. ABCG2 in acute myeloid leukemia: old and new perspectives. Int J Mol Sci. 2023;24(8):7147. Epub 2023 Apr 12. doi:10.3390/ijms24087147. PMID:37108308; PMCID:PMC10138346.

31. Gu H, Chen C, Hou ZS, He XD, Xie S, Ni J, et al. PI3Kγ maintains the self-renewal of acute myeloid leukemia stem cells by regulating the pentose phosphate pathway. Blood. 2024;143(19):1965-1979. doi:10.1182/blood.2023022202. PMID:38271660; PMCID:PMC11103183.

32. Peroni E, Randi ML, Rosato A, Cagnin S. Acute myeloid leukemia: from NGS through scRNA-seq to CAR-T, dissect cancer heterogeneity and tailor the treatment. J Exp Clin Cancer Res. 2023;42(1):259. Epub 2023 Oct 6. doi:10.1186/s13046-023-02841-8. PMID:37803464; PMCID:PMC10557350.

33. Cauchy P, James SR, Zacarias-Cabeza J, Ptasinska A, Imperato MR, Assi SA, et al. Chronic FLT3-ITD signaling in acute myeloid leukemia is connected to a specific chromatin signature. Cell Rep. 2015;12(5):821-836. Epub 2015 Jul 23. doi:10.1016/j.celrep.2015.06.069. PMID:26212328; PMCID:PMC4726916.

34. Kawashima N, Ishikawa Y, Kim JH, Ushijima Y, Akashi A, Yamaguchi Y, et al. Comparison of clonal architecture between primary and immunodeficient mouse-engrafted acute myeloid leukemia cells. Nat Commun. 2022;13(1):1624. Epub 2022 Mar 25. doi:10.1038/s41467-022-29304-6. PMID:35338146; PMCID:PMC8956585.

35. Fu YH, Ng KM, Tseng CY, Huang AC, Tu CH, Chen WC, et al. Modulating metabolic signatures to mitigate cabozantinib resistance in FLT3-ITD acute myeloid leukemia cell models. Cell Death Discov. 2026;12(1):98. Epub 2026 Feb 17. doi:10.1038/s41420-026-02957-8. PMID:41702887; PMCID:PMC12920922.

36. Liao X, Dai W, Xu X, Cai D, Tan M, Wang Z, et al. Marrow leptin-LEPR signaling rewires mitochondrial oxidative metabolism to confer chemoresistance in acute myeloid leukemia. Cell Death Dis. 2026;17(1). Epub 2026 Feb 23. doi:10.1038/s41419-026-08528-0. PMID:41730833; PMCID:PMC12966444.

37. Pan M, Jiao C, Sun M, Jin D, Wang Y, Wu H, et al. Venetoclax synergizes with Wnt/β-catenin inhibitor C-82 in acute myeloid leukemia by increasing the degradation of Mcl-1 protein. Cancer Cell Int. 2025;25(1):197. Epub 2025 May 29. doi:10.1186/s12935-025-03825-8. PMID:40442688; PMCID:PMC12121061.

38. Costa RGA, Silva SLR, Dias I, Oliveira MS, Rodrigues A, Dias RB, et al. Emerging drugs targeting cellular redox homeostasis to eliminate acute myeloid leukemia stem cells. Redox Biol. 2023;62:102692. Epub 2023 Apr 2. doi:10.1016/j.redox.2023.102692. PMID:37031536; PMCID:PMC10119960.

39. Aroua N, Boet E, Ghisi M, Nicolau-Travers ML, Saland E, Gwilliam R, et al. Extracellular ATP and CD39 activate cAMP-mediated mitochondrial stress response to promote cytarabine resistance in acute myeloid leukemia. Cancer Discov. 2020;10(10):1544-1565. Epub 2020 Jul 8. doi:10.1158/2159-8290.CD-19-1008. PMID:32641297.

40. Guarnera L, Santinelli E, Galossi E, Cristiano A, Fabiani E, Falconi G, et al. Microenvironment in acute myeloid leukemia: focus on senescence mechanisms, therapeutic interactions, and future directions. Exp Hematol. 2024;129:104118. Epub 2023 Sep 22. doi:10.1016/j.exphem.2023.09.005. PMID:37741607.

41. Gabellier L, Bosetta E, Heiblig M, Sarry JE. Metabolism and therapeutic response in acute myeloid leukemia with IDH1/2 mutations. Trends Cancer. 2025;11(5):475-490. Epub 2025 Feb 17. doi:10.1016/j.trecan.2025.01.011. PMID:39955197.

42. Liu W, Ming X, Wu J, Yan S, Su S, Zheng R, et al. AML-derived bone mesenchymal stem cell exosomal METTL14 promotes AML cell growth and glycolysis by HOXA3/WNT7B axis. Cell Biol Toxicol. 2026;42(1):27. Epub 2026 Jan 29. doi:10.1007/s10565-026-10143-w. PMID:41609866; PMCID:PMC12894161.

43. Lam K, Kim YJ, Tan EL, Ong CM, Liu AZ, Zhou FJ, et al. The proteostasis network is a therapeutic target in acute myeloid leukemia. Blood. 2026;147(5):557-572. doi:10.1182/blood.2024026749. PMID:41111393; PMCID:PMC12883865.

44. Tang Y, Li J, Ye W, Du Y, Zhang Y, Ye Y, et al. Overcoming therapeutic challenges in acute myeloid leukemia: active targeting strategies by nano-drug delivery systems. J Transl Med. 2026;24(1). Epub 2026 Feb 7.

doi:10.1186/s12967-026-07792-0. PMID:41654885; PMCID:PMC12977839.

45. Fathima S, Rokach L, Ghosoun N, Rezasoltani M, Ilyas R, Alsugair A, et al. CPX-351 versus venetoclax plus hypomethylating agent therapy in newly diagnosed acute myeloid leukemia: a retrospective comparison involving 600 Mayo Clinic patients. Blood Cancer J. 2026 Apr 6 [Epub ahead of print]. doi:10.1038/s41408-026-01495-x. PMID:41942467.

46. Cruz-Rodriguez N. Exploiting metabolic dependencies in acute myeloid leukemia: DHODH inhibition meets lipid and cholesterol metabolism. Haematologica. 2026 Feb 26 [Epub ahead of print]. doi:10.3324/haematol.2026.300677. PMID:41742882.

47. Da Ros A, Peloso A, Longo G, Benetton M, Indio V, Cairo S, et al. Advancing precision therapy in pediatric acute myeloid leukemia through PDX models and mitochondrial targeting. Blood Adv. 2026;10(7):2153-2167. doi:10.1182/bloodadvances.2025018002. PMID:41576348; PMCID:PMC13049648.

48. Parfenova EN, Vrdoljak N, Mosca D, Aristizabal-Henao JJ, Kiebish MA, Minden MD, et al. Targeting ABCD1 inhibits peroxisomal fatty acid oxidation to selectively eliminate acute myeloid leukemia cells. Blood. 2026 Feb 26 [Epub ahead of print]. doi:10.1182/blood.2025031202. PMID:41746867.

49. Wu X, Zhang J. Multi-omics approaches to understanding therapy resistance in acute lymphoblastic leukemia. Lymphatics. 2026;4(1):8. doi:10.3390/lymphatics4010008.

50. Chen P, Gao G, Xu Y, Jia P, Li Y, Li Y, et al. Novel gene signature reveals prognostic model in acute lymphoblastic leukemia. Front Cell Dev Biol. 2022;10:1036312. Epub 2022 Nov 3. doi:10.3389/fcell.2022.1036312. PMID:36407095; PMCID:PMC9669305.

51. Bawek S, Gurusinghe S, Burwinkel M, Przespolewski A. Updates in novel immunotherapeutic strategies for relapsed/refractory AML. Front Oncol. 2024;14:1374963. Epub 2024 Dec 4. doi:10.3389/fonc.2024.1374963. PMID:39697225; PMCID:PMC11652486.

52. Tang J, Ye X, Xu Z, Min T, Tian Z, Ma L, et al. Epigenetic mechanisms of drug resistance in acute myeloid leukemia: advances in small-molecule targeted therapy. Front Pharmacol. 2025;16:1672524. Epub 2025 Oct 20. doi:10.3389/fphar.2025.1672524. PMID:41199817; PMCID:PMC12587329.

53. Zhu Y, Liu J, Qiu F, You Z, Liu Z, Zeng J, et al. The tumor microenvironment in leukemia: molecular pathways of immune evasion. Front Immunol. 2026;17:1743920. Epub 2026 Feb 6. doi:10.3389/fimmu.2026.1743920. PMID:41727472; PMCID:PMC12920481.

54. Pirouzbakht M, Hamzeh S, Soleimani Samarkhazan H. Beyond single biomarkers: multi-omics strategies to predict immunotherapy outcomes in blood cancers. Clin Exp Med. 2025;25(1):355. Epub 2025 Nov 6. doi:10.1007/s10238-025-01902-w. PMID:41193778; PMCID:PMC12589271.

55. Zhuang J, Li Y, Zhang Y, Huang Y, Han Y, Lin N, et al. Mechanisms, treatment strategies and predictive biomarkers of drug resistance in acute myeloid leukemia. Mutat Res Rev Mutat Res. 2025;797:108578. Epub 2025 Dec 8. doi:10.1016/j.mrrev.2025.108578. PMID:41371488.

56. Rautenberg C, Stelljes M, Bug G, Holtick U, Jost E, Jennrich S, et al. Pretransplantation hypomethylating agents and venetoclax in acute myeloid leukemia patients: a real-world analysis from the cooperative transplant study group. Transplant Cell Ther. 2025 Dec 15 [Epub ahead of print]. doi:10.1016/j.jtct.2025.12.943. PMID:41407010.

57. Zheng T, Chen P, Xu Y, Jia P, Li Y, Li Y, et al. Comprehensive analysis of thirteen-gene panel with prognostic value in multiple myeloma. Cancer Biomark. 2023;38(4):583-593. doi:10.3233/CBM-230115. PMID:37980648.