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REVIEW OPEN ACCESS

Combination Treatment Strategies in Acute Myeloid Leukemia: A Literature Review

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Abstract

Introduction: Acute Myeloid Leukemia is a hematologic malignancy with high relapse rates and poor long-term survival, largely due to the persistence of leukemic stem cells that resist conventional treatments. This study reviews combination treatment strategies aimed at targeting these stem cells to improve patient outcomes.

Methods: A comprehensive literature search was performed using major scientific databases to identify peer-reviewed articles, clinical trials, and preclinical studies published between January 2010 and January 2025. Titles and abstracts were screened for relevance, followed by full-text review by both authors. The search focused on studies evaluating combination therapies (the use of ≥2 therapeutic modalities with the intent of synergistic efficacy in AML) in AML patients involving targeted agents, such as inhibitors of FLT3 and BCL-2, and other treatment modalities, including hypomethylating agents, chemotherapy, metabolic inhibitors, and immunotherapeutic approaches. Both clinical outcomes and mechanistic insights were analyzed to assess the efficacy of strategies that simultaneously target leukemic blasts and stem cells and are reported in this review

Results: Findings indicate that combination therapies yield significant improvements over single-agent approaches. FLT3 inhibitors combined with chemotherapy or hypomethylating agents have demonstrated enhanced remission rates and survival in patients with FLT3-mutated disease. Similarly, regimens incorporating BCL-2 inhibitors with low-intensity agents have shown promising results, particularly in older or unfit patients. Emerging data also suggest that targeting metabolic dependencies and employing immunotherapy can further sensitize resistant leukemic stem cells (LSCs), leading to more durable remissions.

Discussion: The analysis underscores that the dual targeting of proliferating leukemic cells and quiescent stem cells is crucial for overcoming resistance and reducing relapse. Despite the advances observed with targeted combination regimens, challenges such as treatment resistance, metabolic plasticity, and toxicity remain. These issues highlight the need for continued investigation into multi-faceted therapeutic approaches.

Conclusion: This review supports the clinical potential of combination treatment strategies in Acute Myeloid Leukemia, advocating for personalized regimens that address disease heterogeneity and resistance mechanisms. Future research should focus on refining these approaches to enhance efficacy while minimizing adverse effects, ultimately paving the way for improved long-term outcomes.

Keywords: acute myeloid leukemia; leukemic stem cells; combination therapy; FLT3 inhibitors; BCL-2 inhibitors

Introduction

Acute Myeloid Leukemia (AML) is a hematological malignancy characterized by clonal proliferation of myeloid progenitor cells, leading to bone marrow burnout and poor clinical outcomes. AML caused over 10, 000 U.S. deaths in 2019, with global incidence rising from 79, 372 in 1990 to 144, 645 in 2021 [1, 2]. AML primarily affects older adults, with a median age at diagnosis of 68 years old [3].

AML arises from a combination of genetic predisposition, pre-existing hematologic conditions, environmental exposures, and prior cancer treatments. Moreover, extensive genetic heterogeneity is a hallmark of AML [4], which reflects the diverse molecular and cytogenetic landscapes underlying this disease. This transformation is often signaled by declining blood counts and an increase in peripheral blasts [3]. Therapy-related AML is another significant risk factor, particularly in individuals who have previously received chemotherapy or radiation for other malignancies. Environmental exposures such as tobacco smoke or radiation further contribute to AML risk, but despite these risk factors, most AML cases arise de novo [3].

Significant progress has been made in the treatment of AML, transforming it into an illness with improved survival rates. With the development of intensive chemotherapy regimens in the 1970s, the "3+7" combination of 7 days of

cytarabine and 3 days of an anthracycline became the standard of care [5]. This regimen, however is not well-suited for older patients with limited tolerability [6]. Despite advances in chemotherapy and supportive care, the 5-year survival rate remains below 30% in older patients [6]. Relapse is a major driver of poor prognosis in advanced AML[7]. As AML progresses, remission becomes harder to achieve due to limited treatment options. Therapies now aim to prevent relapse and progression early. Older adults are at particularly high risk, with this condition's relapse rates increasing from approximately 30-35% in younger patients to 70–80% in patients over 60 [8].

Current literature is looking into the factors contributing to relapse and therapeutic failure in AML, with a key focus on the persistence of leukemic stem cells (LSCs) [7]. LSCs are a self-renewing population of pluripotent cells that are resistant to conventional treatments, making them a major obstacle to achieving long-term remission. Unlike normal hematopoietic stem cells (HSCs), LSCs exhibit unique metabolic dependencies, aberrant signaling pathways, and maintain a quiescent state that allows them to survive therapeutic intervention [9, 10]. For example, while HSCs are typically activated by cytokine signals and enter the cell cycle before chemotherapy, LSCs often remain in a dormant (G_0) phase, thereby evading cell cycle–dependent drugs [11]. In addition, LSCs upregulate drug efflux transporters and anti-apoptotic mechanisms, which further protect them from chemotherapy-induced cell death [12, 13]. Moreover, LSCs can regenerate leukemic blasts more effectively than HSCs because their dysregulated differentiation program enables continuous propagation of the malignant clone [14]. Therefore, developing therapies that specifically target LSCs is crucial to consistently achieve durable, long-term remission. This review examines the recent advancements in combination therapies in studies from 2010-2025.

Methods

A literature search was conducted using PubMed, Scopus, Web of Science, and Google Scholar to identify peer-reviewed articles, clinical trials, and abstracts published between January 2010 and January 2025. These databases were selected to ensure comprehensive coverage: PubMed for biomedical and clinical literature, Scopus and Web of Science for broader multidisciplinary scientific coverage and citation tracking, and Google Scholar to capture grey literature and additional relevant citations. Combination therapy was defined as the use of two or more therapeutic modalities with the intent of achieving synergistic efficacy in AML. Drug resistance mechanisms were defined as genetic, epigenetic, or metabolic adaptations that reduce treatment efficacy. Search terms included "acute myeloid leukemia" AND ("leukemic stem cell*" OR LSC) AND ("combination therap*" OR "targeted therap*") AND ("FLT3 inhibitor*" OR "BCL-2 inhibitor*" OR "hypomethylating agent*"). Boolean operators (AND, OR) were used to combine synonyms and related concepts, and truncation (*) allowed inclusion of variations in word endings. Filters applied included restriction to English-language publications, human studies, and adult AML populations; studies focusing exclusively on pediatric AML or non-AML leukemias were excluded. Inclusion criteria prioritized studies evaluating:

1. LSC-specific mechanisms (e.g., metabolic dependencies, survival pathways).
2. Combination therapies involving FLT3 (FMS-like tyrosine kinase 3) inhibitors (midostaurin, gilteritinib), BCL-2 (B-cell lymphoma 2) inhibitors (venetoclax), hypomethylating agents (HMAs) (azacitidine), or novel agents (ruxolitinib, ulixertinib).
3. Clinical outcomes (response rates, survival) and toxicity profiles.
4. Drug resistance mechanisms (genetic, epigenetic, or metabolic adaptations that reduce treatment efficacy) and strategies to overcome them.

In this review, 'novel agents' refers to emerging targeted drugs under investigation in clinical trials or preclinical studies, regardless of FDA approval status; both approved and experimental therapies were considered if they demonstrated relevance to AML or leukemic stem cell biology. Exclusion criteria excluded studies focused solely on pediatric AML or non-AML leukemias, as well as editorials, letters, and other non-peer-reviewed publications. Study selection was performed in two stages. First, titles and abstracts were screened for relevance, followed by full-text review of potentially eligible studies. Both authors independently conducted the screening process. Any disagreements regarding inclusion were resolved through discussion until consensus was reached. From each included study, data were extracted on study characteristics (authors, year, country, study design, sample size, and patient population), intervention details (therapies and combinations tested), and key outcomes of interest (response rates, survival, toxicity, mechanistic findings, and resistance pathways). Data were collected by both authors independently and cross-verified to ensure accuracy. Findings were synthesized using a narrative review approach. Studies were grouped and summarized thematically according to therapeutic mechanism or strategy (e.g., FLT3 inhibition, BCL-2 inhibition, metabolic targeting, immunotherapy), allowing for integration of both clinical and preclinical evidence. No formal quality appraisal or risk-of-bias tool was applied, as this was not conducted as a systematic review. However, preference was given to high-impact peer-reviewed studies, clinical trial data, and widely cited preclinical investigations, and findings were interpreted with consideration of study design and potential limitations.

Results

The review of recent studies reveals that combination therapies in AML have significant improvements over single-agent approaches by simultaneously targeting leukemic blasts and the resilient LSCs.

1. FLT3 Inhibitors and Combinations

One of the most well-characterized molecular aberrations in AML involves mutations in FMS-like tyrosine kinase 3 (FLT3), a receptor tyrosine kinase that plays a crucial role in hematopoiesis. FLT3 mutations, particularly internal tandem duplications (FLT3-ITD), are present in about 30% of AML cases and lead to LSC growth and can be used as a predictor of low survival and high relapse rates [15]. Stone et al. demonstrated that the addition of midostaurin, a first-generation multi-kinase inhibitor targeting FLT3, to standard chemotherapy significantly improved overall survival in AML patients with mutated FLT3, marking an advancement in targeted therapy [16]. Targeting FLT3 reduces LSC burden and improves outcomes. In addition to FLT3, midostaurin inhibits the proto-oncogene c-KIT, (KIT), another receptor tyrosine kinase that, when mutated, is implicated as a risk factor for relapse and diminished survival rates in AML patients [17]. While midostaurin marked an important first step, the drive for enhanced therapeutic outcomes has spurred the development of next-generation inhibitors with more refined target specificity. As noted by Perl et al., Midostaurin has failed to achieve clinical benefits for patients with relapsed or refractory FLT3-mutated AML, signifying the need for the development of new drugs [17]. Perl et al. also reported that gilteritinib, a next-generation FLT3 inhibitor, effectively managed relapsed or refractory FLT3-mutated AML. The trial found longer survival rates and higher percentages of patients with remission than chemotherapy in individuals with relapsed or refractory FLT3-mutated AML [18]. Gilteritinib's success shows the value of targeted agents across AML stages. The PrECOG 0905 trial directly compared gilteritinib to midostaurin in newly diagnosed FLT3-mutated AML patients and found that gilteritinib resulted in higher remission rates [19].

Recent clinical trials further explored the utility of combining FLT3 inhibitors with other therapies in AML. Exploring combinations with other agents, a phase 1 study of CPX-351 (a liposomal formulation of cytarabine and daunorubicin, two chemotherapy drugs used for AML patients) plus gilteritinib in relapsed/refractory FLT3-mutated AML showed a promising complete remission (CR)/CR with incomplete blood count recovery (CRi) rate of 46.2% and a high minimal residual disease (MRD) negativity rate [20].

2. BCL-2 Inhibitors and Venetoclax-Based Combinations

B-cell lymphoma 2 (BCL-2) is an anti-apoptotic protein that plays a key role in cell survival by preventing apoptosis [21]. LSCs often exhibit high BCL-2 expression, enabling them to evade apoptosis and sustain disease progression. Targeting BCL-2 has therefore emerged as a promising therapeutic strategy, particularly in patients who are ineligible for intensive chemotherapy. Venetoclax is a highly selective inhibitor of BCL-2 that restores apoptosis in leukemic cells by disrupting their survival mechanisms [21]. DiNardo et al. (2019) reported that combining venetoclax with hypomethylating agents (HMA) decitabine or azacitidine, significantly improved outcomes in treatment-naïve elderly AML patients. Hypomethylating agents work by reversing aberrant DNA methylation patterns and reactivating tumor suppressor genes [22]. This combination is now standard of care, improving response and survival over HMA alone [23]. Complementing this, Pollyea et al. (2018) provided evidence that venetoclax disrupts energy metabolism in LSCs, thereby enhancing apoptosis and reducing disease burden [24]. Additionally, Wei et al. (2019) demonstrated that the combination of venetoclax with low-dose cytarabine offers clinical benefits for patients ineligible for intensive chemotherapy, further supporting the efficacy of BCL-2 targeting in AML treatment. Patients receiving venetoclax plus low-dose cytarabine (LDAC) achieved a CR/CRi rate of 54%, the median overall survival (OS) was 10.1 months [25]. Notably, patients without prior HMA exposure had improved outcomes, with a 62% CR/CRi rate and a median OS of 13.5 months. These outcomes surpass historical LDAC monotherapy rates (11–19%), reinforcing venetoclax-LDAC's value for older or unfit patients [25]. HMAs and low-dose cytarabine can induce differentiation in AML cells, making them more reliant on BCL-2 for survival and thus more susceptible to the apoptotic effects of venetoclax [23].

Despite the advances with venetoclax-based therapies, resistance remains a concern. It has been observed that FLT3-ITD mutations can serve as an adaptive resistance mechanism to venetoclax-based therapy [26]. To overcome this, a triplet regimen incorporating venetoclax, azacitidine, and gilteritinib was used in a study involving 52 patients with FLT3-mutated AML. The results of the study were promising with 72% 18-month OS and 71% relapse-free survival [27].

3. Novel Agents and Metabolic Targeting

Targeting metabolic pathways that are essential for the survival and proliferation of AML cells, particularly LSCs, has emerged as a promising strategy to overcome drug resistance. For the purposes of this review, 'novel agents' include both FDA-approved and experimental drugs under clinical or preclinical investigation, provided they target relevant pathways in AML or leukemic stem cells. Jones et al. (2018) found that inhibition of amino acid metabolism selectively compromises LSC viability, providing a rationale for integrating metabolic inhibitors into treatment protocols [28]. Their study demonstrated that LSCs from de novo AML patients show elevated amino acid uptake, catabolism, and dependency on amino acid metabolism for oxidative phosphorylation and survival. Pharmacological inhibition of this pathway effectively reduced oxidative phosphorylation and induced cell death in these LSCs. However, LSCs from relapsed AML

patients displayed metabolic plasticity, shifting reliance to fatty acid metabolism, which may contribute to treatment

resistance. These findings highlight amino acid metabolism as a potential therapeutic vulnerability in newly diagnosed AML, supporting the development of metabolic-targeted therapies for LSC eradication [28]. Stevens et al. (2020) extended these findings by illustrating that alterations in fatty acid metabolism contribute to resistance against venetoclax [29]. Their study found that resistance to venetoclax with azacitidine (ven/aza) arises through upregulation of fatty acid oxidation (FAO), particularly in relapsed AML or cases with RAS pathway mutations. This metabolic shift allows leukemic cells to bypass their reliance on amino acid metabolism, thereby negating ven/aza's efficacy. Importantly, pharmacological inhibition of FAO was shown to restore sensitivity to ven/aza in drug-resistant AML cells, highlighting FAO as a potential therapeutic target to overcome treatment resistance. Pei et al. (2020) further identified resistance mechanisms linked to metabolic adaptations in monocytic subclones, highlighting the need for combinatorial approaches to mitigate these escape pathways [30]. Monocytic subclones are a subset of AML cells that have undergone differentiation into a monocytic lineage, which alters their gene expression and metabolic dependencies [31]. Their study found that AML cells with monocytic differentiation exhibit inherent resistance to ven/aza, driven by distinct transcriptomic and metabolic properties. Unlike primitive AML cells, which depend on BCL-2, monocytic subclones lose expression of BCL-2 and instead rely on MCL-1 [30], another anti-apoptotic protein [32]. This shift in metabolic dependence allows monocytic subpopulations to persist and expand, particularly at relapse, where ven/aza treatment appears to select for these resistant clones [29]. Importantly, pharmacological inhibition of MCL-1 restored sensitivity to ven/aza in resistant AML cells, suggesting that targeting MCL-1 alongside venetoclax could improve treatment efficacy and prevent disease progression [29].

4. Immunotherapies Targeting LSCs

Immunotherapeutic approaches are being actively explored to target LSC-specific antigens. Riether et al. (2020) demonstrated that cusatuzumab, an anti-CD70 antibody, effectively eliminates leukemia stem cells (LSCs) when combined with hypomethylating agents (HMAs) [33]. CD70 is a tumor necrosis factor family ligand that plays a role in immune regulation and is overexpressed on LSCs, where it interacts with CD27 to promote survival and treatment resistance [33]. Their study found that LSCs upregulate CD70 in response to HMA treatment, leading to increased CD70/CD27 signaling, which supports LSC persistence. Blocking this pathway with cusatuzumab, a monoclonal antibody, effectively eliminated LSCs in vitro and in xenotransplantation models. A phase 1/2 clinical trial in previously untreated older AML patients showed promising hematologic responses, with 12 out of 12 patients achieving complete or partial remission and 4 reaching minimal residual disease negativity. Cusatuzumab was well tolerated, and treatment led to significant reductions in LSCs while promoting myeloid differentiation and apoptosis, supporting its potential as a targeted therapeutic strategy in AML [33]. Additionally, Kenderian et al. (2015) provided preclinical evidence that CD33-specific chimeric antigen receptor (CAR) T cells exhibit potent anti-leukemic activity, suggesting a promising role for cellular immunotherapies in AML [34]. CD33 is a transmembrane receptor expressed on AML blasts and normal myeloid progenitor cells, making it a key target for immunotherapy. Their study demonstrated that CD33-targeting CAR-T (Chimeric Antigen Receptor T-cell) cells (CART33) exhibited strong effector functions in vitro, effectively eradicating leukemia and prolonging survival in AML xenograft models. However, CART33 also led to human lineage cytopenias and depletion of myeloid progenitors, raising concerns about long-term toxicity. To mitigate this, the researchers developed a transiently expressed mRNA-based CART33, which maintained potent but self-limited anti-leukemic activity, reducing the risk of prolonged myelosuppression [33].

Other immune-based strategies are also under investigation. PRAME (preferentially expressed antigen in melanoma) is abnormally expressed in AML and on LSCs but not in normal hematopoietic cells, making it a potential target for vaccination and adoptive T-cell therapy [35]. Clinical trials with PRAME-specific T cells and dendritic cell-based PRAME vaccines have shown some promise in eliciting immunological responses in AML patients. Bispecific and trispecific antibodies, as well as other therapeutic vaccines, are also being explored as potential immunotherapeutic options in AML [36]. Despite the progress, significant challenges remain in the field of immunotherapy for AML. Identifying truly LSC-specific antigens that do not cross-react with normal stem/progenitor cells remains a critical hurdle [37].

5. Emerging Strategies and Future Directions

The comprehensive genomic analysis of AML has illuminated potential novel targets within the AML genomic landscape. The emphasis on utilizing molecular technologies has led to improved understanding, prognosis, and treatment strategies for AML [38]. Techniques such as Whole-Genome Sequencing (WGS) and Whole-Exome Sequencing (WES) are increasingly used to identify critical translocations and mutations in genes like DNMT3A, NPM1, and FLT3, which are central to AML pathogenesis [39]. These analyses aid in understanding clonal evolution, treatment resistance, and identifying genetic alterations that can be targeted by specific therapies [39]. Studies using next-generation sequencing have analyzed the molecular genetic profiles of high-risk AML patients, revealing genetic abnormalities associated with treatment outcomes [40]. These developments can be contextualized within the broader therapeutic landscape; a timeline of key advances in AML combination therapy is presented in Figure 1

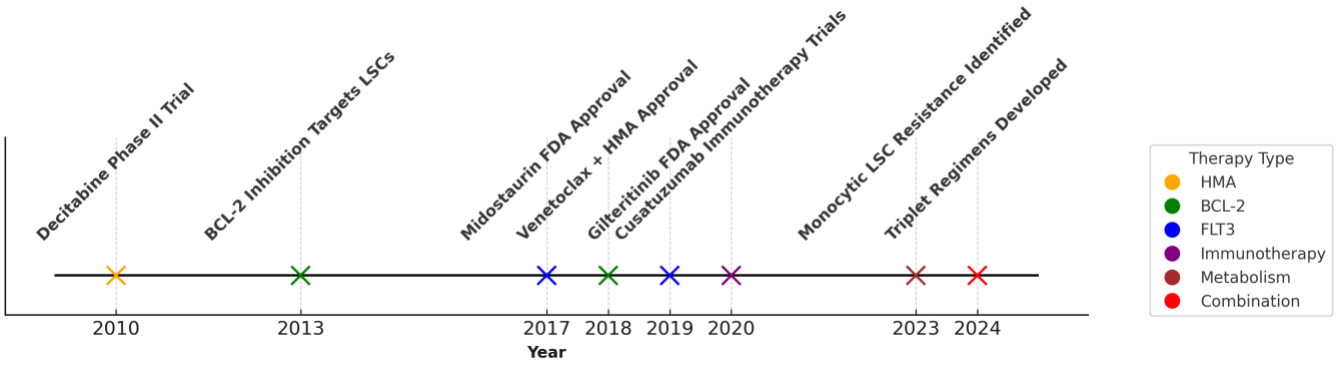

Figure 1. Timeline of Key Advances in AML Combination Therapy (2010–2024).

Discussion

Major therapeutic milestones are shown, color-coded by class: hypomethylating agents (orange), BCL-2 inhibitors (green), FLT3 inhibitors (blue), immunotherapies (purple), metabolic approaches (brown), and combination regimens (red). The timeline illustrates the progression from early hypomethylating agent studies to the emergence of triplet regimens targeting leukemic stem cell resistance. Figure created by authors using Python (matplotlib)

The introduction of FLT3 inhibitors has marked a significant advancement in the treatment of FLT3-mutated AML. First-generation inhibitors like midostaurin have improved survival in newly diagnosed patients, but their efficacy in relapsed or refractory AML is limited, necessitating the development of next-generation inhibitors like gilteritinib, which has demonstrated superior outcomes in this setting [16, 18]. FLT3 inhibition alone fails to eliminate LSCs, which use alternative survival pathways. The observed efficacy of combining FLT3 inhibitors with hypomethylating agents or chemotherapy suggests a synergistic approach, wherein FLT3 inhibition targets proliferating leukemic blasts while other agents may indirectly sensitize LSCs to apoptosis [18].

Similarly, the success of venetoclax-based regimens in elderly and unfit AML patients represents a paradigm shift in the treatment of these high-risk populations [21, 23]. The ability of LSCs to evade standard chemotherapy while remaining dependent on BCL-2 suggests that venetoclax-based strategies could serve as an effective approach to eliminating these resistant cell populations. However, emerging resistance mechanisms, such as the upregulation of alternative anti-apoptotic proteins like MCL-1 and the presence of FLT3-ITD mutations, highlight the need for combination strategies to prevent disease recurrence [25, 26]. The promising outcomes of triplet regimens incorporating venetoclax, azacitidine, and FLT3 inhibitors suggest that a multi-targeted approach may be necessary to overcome resistance and achieve deeper, more durable remissions [26].

Beyond genetic mutations, the metabolic adaptations of LSCs present a significant barrier to long-term remission [27]. LSCs rely on distinct metabolic pathways, including heightened amino acid and fatty acid metabolism, to maintain their survival [28]. This metabolic plasticity allows LSCs to adapt to therapeutic pressure, shifting their energy reliance when faced with targeted metabolic inhibitors. The observation that LSCs from relapsed AML patients preferentially utilize fatty acid oxidation as a resistance mechanism against venetoclax [28] suggests that single-agent metabolic inhibition may be insufficient. Instead, dual metabolic could provide a more effective strategy for eliminating LSCs [28].

The role of monocytic differentiation in venetoclax resistance further complicates AML treatment. Studies have shown that AML subpopulations with monocytic lineage differentiation exhibit reduced BCL-2 dependency, relying instead on MCL-1 for survival [31]. This finding suggests that AML is not a static disease but rather an evolving malignancy capable of escaping therapeutic pressure through lineage plasticity.

Immunotherapy is another approach for AML treatment; however, its application in AML has been less successful due to the lack of highly specific LSC antigens. The promising early results of cusatuzumab, an anti-CD70 antibody, highlight the potential for targeting LSC-specific markers in AML [33]. However, challenges remain in distinguishing LSCs from normal hematopoietic progenitors, as many target antigens are shared between malignant and healthy stem cells. This raises toxicity concerns, especially with CAR T therapies targeting CD33/CD123, which risk prolonged cytopenias [33]. Emerging immunotherapeutic approaches, including PRAME-targeted therapies and bispecific antibodies, may help overcome some of these challenges [35, 34]. However, the high degree of AML heterogeneity suggests that personalized immunotherapy strategies, guided by genomic and proteomic profiling, will be necessary to achieve meaningful clinical benefit.

This review synthesized findings from a wide range of high-impact biomedical databases, incorporating both clinical and preclinical evidence, which allowed for a comprehensive perspective on combination strategies targeting leukemic stem cells. Including diverse study

designs and mechanisms enhanced the breadth of analysis. However, this review was not conducted as a formal systematic review; therefore, the search and screening processes were not registered or protocolized, which may increase the risk of publication bias. Limiting inclusion to English-language publications may have excluded relevant studies in other languages. Additionally, the heterogeneity of study designs and endpoints precluded meta-analysis, and the reliance on narrative synthesis may limit the generalizability of conclusions. Furthermore, we excluded case reports, editorials, letters, and other non–peer-reviewed publications, which may have limited the breadth of perspectives but improved the overall rigor and reliability of the evidence base included. Additionally, study screening and selection were performed by two reviewers without formal arbitration, which may introduce some risk of selection bias despite efforts to reach consensus. Another limitation is that no formal quality appraisal of included studies was conducted; instead, we relied on peer-reviewed clinical trials, observational studies, and widely cited preclinical investigations, interpreting findings with consideration of study design and potential biases.

Conclusions

Despite significant progress, several challenges remain in optimizing AML treatment. First, AML is an extremely heterogeneous disease, with patients exhibiting diverse genetic, metabolic, and immunologic profiles that influence treatment response. Advances in molecular profiling, such as whole-genome and whole-exome sequencing, are providing new insights into the genetic landscape of AML, identifying potential therapeutic targets and predicting response to treatment [38, 39]. The integration of these technologies into clinical practice could enable more precise treatment selection, reduce the risk of unnecessary toxicity while maximizing efficacy. Second, resistance remains a major challenge. While combination therapies have improved outcomes, AML often develops adaptive survival mechanisms to evade treatment. Understanding these resistance pathways will be essential for developing next-generation therapies. Finally, translating these findings into clinical practice requires overcoming logistical and financial barriers. Many of the most promising targeted therapies, including FLT3 and BCL-2 inhibitors, remain expensive and may not be accessible to all patients. Cumulative toxicity from multi-agent regimens requires careful patient selection and monitoring. Future research should balance efficacy and tolerability, especially in older patients.

List of Abbreviations

ABC: ATP-Binding Cassette (as in ABC Transporters)
AML: Acute Myeloid Leukemia
BCL-2: B-Cell Lymphoma 2
CAR-T: Chimeric Antigen Receptor T-Cell
CART33: CD33-Specific Chimeric Antigen Receptor T Cells
CD27: Cluster of Differentiation 27
CD70: Cluster of Differentiation 70
CR: Complete Remission
CRI: Complete Remission with Incomplete Blood Count Recovery
FAO: Fatty Acid Oxidation
FLT3: FMS-like Tyrosine Kinase 3
G_0: G-zero phase (Quiescence)
HMA: Hypomethylating Agents
HSCs: Hematopoietic Stem Cells
KIT: A Receptor Tyrosine Kinase (often referenced by its gene symbol)
LAC: Low-Dose Cytarabine
LSCs: Leukemic Stem Cells
MCL-1: Myeloid Cell Leukemia-1
MDS: Myelodysplastic Syndromes
MPN: Myeloproliferative Neoplasms
MRD: Minimal Residual Disease
mRNA: Messenger RNA
OS: Overall Survival
PRAME: Preferentially Expressed Antigen in Melanoma
WES: Whole Exome Sequencing
WGS: Whole Genome Sequencing

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Ethics Approval and/or Participant Consent

Not applicable. This article is a literature review and does not involve human participants.

Authors' Contributions

BR: Made substantial contributions to the conception and design of the study, collected and analyzed data, drafted the manuscript, and gave final approval of the version to be published.
AS: Made substantial contributions to the conception and design of the study, collected and analyzed data, critically revised the manuscript for important intellectual content, and gave final approval of the version to be published.

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