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Advancements in Myeloid Leukemia Treatment: A Comprehensive Update

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ABSTRACT

This comprehensive update explores the recent advancements in the treatment landscape of myeloid leukemia. Myeloid leukemia, a heterogeneous group of hematological malignancies, poses significant challenges in clinical management. This review highlights the latest therapeutic approaches, including targeted therapies, immunotherapies, and emerging treatment modalities. It discusses the impact of precision medicine, novel drug developments, and the evolving role of immunotherapy in managing myeloid leukemia. Furthermore, the abstract outlines current research trends, challenges, and future prospects, aiming to provide a concise overview for healthcare professionals and researchers involved in leukemia management.

Keywords: targeted therapy; immunotherapy; precision medicine; molecular profiling; personalized treatment; bone marrow transplantation; novel therapies

INTRODUCTION

Myeloid leukemia is a type of cancer that affects the myeloid cells in the bone marrow. It is characterized by the abnormal growth and accumulation of immature myeloid cells, which can interfere with the production of normal blood cells [1-3]. The classification and management of myeloid leukemia have been updated in recent years to improve diagnosis, risk stratification, and treatment. The International Consensus Classification (ICC) and the 5th edition of the WHO classification are two competing schemata that emerged in 2022. Research on myeloid leukemia has also focused on understanding the genetic and molecular mechanisms underlying the disease. For example, studies have explored the role of specific genes and mutations in the development and progression of myeloid leukemia. These findings have contributed to the development of targeted therapies that aim to inhibit the abnormal signaling pathways involved in leukemia cells [4-6]. In the past few decades, progress in hematopoietic malignancy treatment has been especially rapid due to improvements in treatment protocols, including the development of targeted therapies such as tyrosine kinase inhibitors (TKIs). However, the current outlook for leukemia is not optimistic, and it is still a major threat to human health. In 2020, leukemia was estimated to be the 15th and 11th most frequent cause of cancer incidence and cancer-related mortality worldwide, respectively, accounting for 474,519 incident cases and 311,594 deaths. In addition, leukemia is the most common cancer in children younger than five years of age and accounts for the highest percentage of

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deaths, creating a significant burden on individuals, families, and countries [7-9].

Importance of understanding latest updates on myeloid leukemia

Staying updated on the latest developments and research in myeloid leukemia is crucial for several reasons. Firstly, understanding the latest updates on myeloid leukemia allows healthcare professionals to provide the most effective and personalized treatment options for patients. The role of next-generation sequencing (NGS) in acute myeloid leukemia (AML) has been highlighted as a valuable tool for identifying relevant genetic entities [10-12]. NGS can help identify specific mutations and genetic abnormalities in AML, which can guide treatment decisions and improve patient outcomes. Secondly, staying informed about the latest updates on myeloid leukemia is important for researchers and scientists working in the field. Molecular findings in myeloid neoplasms continue to evolve, and understanding these findings can help drive further research and advancements in the field [13]. By keeping up with the latest research, scientists can identify new targets for therapy, develop novel treatment approaches, and improve our overall understanding of the disease. Lastly, being aware of the latest updates on myeloid leukemia is important for patients and their families. Cancer statistics for 2023 show that mortality rates for leukemia have been declining, indicating progress in treatment options [14]. Patients and their families can benefit from knowing about the latest advancements in treatment, as it can provide hope and reassurance. It also allows them to have informed discussions with their healthcare providers and actively participates in their treatment decisions.

Subtypes of acute leukemia and their characteristics

Acute myeloid leukemia (AML) is a heterogeneous disease with various subtypes, each characterized by distinct genetic and clinical features. The classification of AML subtypes has evolved over time, with different classification systems used in the past. The French-American-British (FAB) classification, developed in the 1970s, divided AML into subtypes based on the type of cell from which the leukemia develops and the maturity of the cells [15-17]. However, the FAB classification is no longer used in clinical practice. The World Health Organization (WHO) classification is currently the most widely accepted classification system for AML. The WHO classification takes into account not only morphological features but also genetic and molecular abnormalities [18]. According to the WHO classification, AML is divided into several subtypes, including acute promyelocytic leukemia (APL), acute erythroid leukemia (AEL), acute megakaryocytic leukemia (AMKL), and others.APL is a distinct subtype of AML characterized by the presence of the PML-RARA fusion gene resulting from the t(15;17) translocation [19-21]. APL is associated with a favorable prognosis and is treated differently from other subtypes of AML [19]. AEL is a rare subtype of AML characterized by prominent erythroid proliferation [22]. AMKL is characterized by the unrestricted proliferation of immature megakaryocytes (megakaryoblasts) and extensive myelofibrosis [23]. In addition to these subtypes, AML can be further classified based on specific genetic abnormalities. For example, mutations in the TP53 gene and RB1 gene have been associated with poor prognosis in pediatric AML. Mutations in the FLT3 gene are also common in AML and are associated with a poor prognosis). Other genetic abnormalities, such as amplification of the EPOR/JAK2 genes, have been identified in specific subtypes of AML [22, 24-25]. It is important to note that the classification of AML subtypes is constantly evolving as new research

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uncovers additional genetic and molecular abnormalities associated with the disease. The identification of these subtypes is crucial for guiding treatment decisions and predicting prognosis in patients with AML.

Recent advances in the treatment of acute myeloid leukemia

Recent advances in the treatment of Acute Myeloid Leukemia (AML) have focused on various aspects of the disease, including targeted therapies, immunotherapy, precision medicine, and the identification of novel therapeutic targets. Despite these advances, achieving long-term disease-free survival in AML remains a challenge. One area of research that has shown promise in AML treatment is the use of chimeric antigen receptor (CAR) T cell therapy. CAR T cell therapy involves modifying a patient's own T cells to express a receptor that recognizes and targets specific antigens on cancer cells. In the case of AML, CAR T cell therapy has shown excellent results in acute lymphocytic leukemia (ALL) and lymphoma, and there is potential for its use in AML as well [26-28]. Another area of research is the identification of genetic mutations in AML that can be targeted with precision medicine. Mutations in genes such as IDH1/2 have been identified in AML and have become targets for precision medicine approaches [29]. Additionally, pharmacogenomic profiling has been used to identify therapeutic vulnerabilities in pediatric AML, which can inform personalized treatment strategies [30]. The use of targeted therapies, such as venetoclax, has also shown promise in the treatment of relapsed/refractory AML. Venetoclax, in combination with other agents such as azacitidine, has achieved impressive results in newly diagnosed elderly patients with AML and refractory/relapsed disease. Furthermore, the efficacy and safety of venetoclax for relapsed/refractory AML have been evaluated through systematic reviews and meta-analyses [31]. Immunotherapy has emerged as a promising approach in AML treatment. Targeting immune checkpoints, such as the STAT3-VISTA axis, has shown potential in suppressing tumor aggression and burden in AML [32].

Etiology and risk factors

A. Genetic and environmental factors

Genetic and environmental factors play significant roles in the development of myeloid leukemia. Several studies have investigated these factors and their impact on the disease. Genetic mutations have been identified as a key factor in the development of myeloid leukemia. The homeobox transcription factors HoxA9 and Meis1 have been found to be causally involved in the etiology of acute myeloid leukemia [33]. Additionally, mutations in genes such as ASXL1 have been shown to disrupt the proliferation-differentiation balance and promote stem-cell identity over differentiation in myeloid leukemias. Furthermore, missense mutations and gene rearrangements have been associated with the development of neonatal congenital leukemia. These findings highlight the importance of genetic abnormalities in the pathogenesis of myeloid leukemia. Environmental factors also contribute to the development of myeloid leukemia. Exposure to radiation, chemicals, and other occupational hazards has been implicated in the development of the disease. Intrauterine exposure to radiation, drugs, or toxins has been linked to the occurrence of acute myeloid leukemia after birth. Additionally, viral agents have been identified as potential contributors to the development of leukemia. These environmental factors can interact with genetic mutations to increase the risk of myeloid leukemia.The pathogenesis of myeloid leukemia involves various molecular and genetic abnormalities.

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B. Hereditary predisposition

Hereditary predisposition can play a significant role in the development of myeloid leukemia. Several germline mutations have been identified that are associated with an increased risk of developing myeloid neoplasms, including acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS). These mutations include RUNX1, CEBPA, GATA2, ANKRD26, DDX41, and ETV6 mutations. Patients with these germline mutations may present with hypocellular MDS at a young age. Additionally, familial platelet disorder with associated myeloid malignancy (FPDMM), caused by inherited RUNX1 mutations, is characterized by thrombocytopenia, platelet activation defects, accelerated clonal hematopoiesis, and an increased risk of leukemia [34].

C. Occupation and lifestyle factors

Occupation and lifestyle factors can play a role in the development of myeloid leukemia. Several studies have suggested that certain occupational and environmental exposures, as well as lifestyle habits, may increase the risk of developing leukemia. These factors can include exposure to chemicals, such as pesticides and benzene, as well as exposure to radiation [35]. Environmental factors, such as exposure to certain chemicals and radiation, have also been implicated in the development of myeloid leukemia. Exposure to benzene, a chemical found in various industries, has been identified as a well-known cause of adult leukemia, including myeloid leukemia. Additionally, exposure to ionizing radiation, such as from medical imaging procedures like computed tomography (CT) scans, has been associated with an increased risk of developing leukemia, particularly in childhood and early adulthood.

Diagnosis and staging

Diagnosis and staging of myeloid leukemia are crucial steps in determining the appropriate treatment and prognosis for patients. Myeloid leukemia refers to a group of hematological malignancies characterized by the uncontrolled proliferation of myeloid cells in the bone marrow and peripheral blood. The diagnosis and staging of myeloid leukemia involve a combination of clinical evaluation, laboratory tests, imaging studies, and molecular analysis. To diagnose myeloid leukemia, a thorough medical history and physical examination are conducted to assess symptoms and identify potential risk factors. Blood tests, including complete blood count (CBC) and peripheral blood smear, are performed to evaluate the levels and morphology of blood cells. Abnormalities in the CBC, such as leukocytosis, anemia, and thrombocytopenia, may indicate the presence of myeloid leukemia [36]. Bone marrow aspiration and biopsy are essential diagnostic procedures for myeloid leukemia. These procedures involve the collection of a sample of bone marrow cells for examination under a microscope. The examination of bone marrow cells allows for the identification of abnormal cells, such as blasts, which are immature cells that have not fully differentiated into mature blood cells. The presence of blasts in the bone marrow is a hallmark of myeloid leukemia [37]. Immunophenotyping, a technique that uses flow cytometry, is often employed to further characterize the abnormal cells in myeloid leukemia. This technique involves the labeling of cells with specific antibodies that target cell surface markers. By analyzing the expression of these markers, immunophenotyping can help differentiate between different subtypes of myeloid leukemia and determine the lineage of the abnormal cells [38].

Molecular analysis plays a crucial role in the diagnosis and classification of myeloid leukemia. Cytogenetic analysis, which examines the chromosomes of cancer cells, can

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identify specific chromosomal abnormalities that are associated with different subtypes of myeloid leukemia. For example, the presence of the Philadelphia chromosome (t9;22) is characteristic of chronic myeloid leukemia (CML) [39].Once a diagnosis of myeloid leukemia is established, staging is performed to determine the extent of the disease and guide treatment decisions. The most commonly used staging system for myeloid leukemia is the French-American-British (FAB) classification, which categorizes myeloid leukemia into different subtypes based on the morphology and lineage of the abnormal cells. The World Health Organization (WHO) classification system is another widely accepted classification system that incorporates cytogenetic and molecular genetic information to further refine the classification of myeloid leukemia [40]. In addition to the FAB and WHO classification systems, other factors, such as the presence of specific gene mutations and the patient's overall health, are taken into consideration when staging myeloid leukemia. For example, the European LeukemiaNet (ELN) provides recommendations for risk stratification in acute myeloid leukemia (AML) based on cytogenetic and molecular genetic abnormalities, as well as the patient's age and performance status [37].

Symptoms and clinical presentations

Common signs and symptoms

Myeloid leukemia is a type of leukemia that originates in the myeloid cells, which are responsible for producing red blood cells, white blood cells, and platelets [41]. The clinical symptoms of myeloid leukemia can vary depending on the subtype and stage of the disease. However, there are some common clinical symptoms that are often observed in patients with myeloid leukemia. One of the common clinical symptoms of myeloid leukemia is constitutional symptoms, which include weight loss, fatigue, and night sweats. These symptoms are often nonspecific and can be attributed to various other conditions. However, in the context of myeloid leukemia, they are believed to be caused by the abnormal production and accumulation of immature myeloid cells in the bone marrow, leading to anemia and other systemic effects [42]. Another common clinical symptom of myeloid leukemia is hepatosplenomegaly, which refers to the enlargement of the liver and spleen. This is often observed in patients with advanced stages of the disease and is caused by the infiltration of leukemic cells into these organs [42]. Furthermore, myeloid leukemia can also present with cutaneous manifestations, such as leukemia cutis or myeloid sarcoma. Leukemia cutis refers to the infiltration of leukemic cells into the skin, resulting in the formation of skin lesions. Myeloid sarcoma, on the other hand, refers to the formation of solid masses of leukemic cells outside of the bone marrow [43]. Other less common clinical symptoms of myeloid leukemia include bone pain, osteoid osteoma, and neurological manifestations. Bone pain can occur due to the infiltration of leukemic cells into the bone marrow, leading to bone destruction. Osteoid osteoma, which is a benign bone tumor, has also been reported in patients with myeloid leukemia [44].

Complications and disease progressions

Complications and disease progressions in myeloid leukemia can have significant impacts on patient outcomes and treatment strategies. Myelodysplastic syndromes (MDS) are a group of clonal hematopoietic stem cell diseases characterized by cytopenias and cytopenia-related complications, such as infections and bleeding, as well as a high risk of progression to acute myeloid leukemia (AML) [45]. Patients suffering from acute myeloid leukemia are at a greater risk of acquiring Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) infection along with

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developing complications related to COVID-19 due to the immunosuppression caused by the malignancy, as well as the high-intensity chemotherapy provided in acute myeloid leukemia [46-66]. Therapy-related acute myeloid leukemia (t-AML) and myelodysplastic syndrome (t-MDS) are complications of chemotherapy and/or radiation therapy for malignant diseasesx. Acute myeloid leukemia (AML) and other hematologic malignancies can be complicated by hyperleukocytosis, which leads to an increased risk for other severe complications such as tumor lysis syndrome, disseminated intravascular coagulation (DIC), and leukostasis. Myeloproliferative neoplasms (MPNs) encompass a spectrum of disease entities with progressively more severe clinical features, including complications with thrombosis and hemostasis and an increased propensity for transformation to acute myeloid leukemia. Primary causes of death among MDS patients are complications due to bone marrow failure (e.g., infections, hemorrhage, and platelet dysfunction) and post-MDS transformation to secondary acute myeloid leukemia (sAML) [67].

Current treatment modalities

A. Chemotherapy and targeted therapies

Chemotherapy and targeted therapies are the primary treatment options for both acute and chronic myeloid leukemia. Chemotherapy is commonly used as the first-line therapy for acute myeloid leukemia (AML) and has shown high remission rates [68]. It is often administered in combination with other antineoplastic agents to improve efficacy. However, chemotherapy can have significant side effects and impact the patient's quality of life. Targeted therapies, on the other hand, specifically target molecular abnormalities in leukemia cells, offering a more precise and potentially less toxic treatment approach [69]. One targeted therapy option for myeloidleukemia is the use of tyrosine kinase inhibitors (TKIs) that inhibit BCR/ABL tyrosine kinase activity. TKIs have revolutionized the treatment and prognosis of chronic myeloid leukemia (CML) in recent decades. Another targeted therapy option is the use of BH3 mimetics, which are small molecule inhibitors that target the prosurvival members of the BCL-2 family. BH3 mimetics have shown promise in the treatment of acute myeloid leukemia when used alone or in combination with standard-of-care therapies [70]. Immunotherapy, particularly chimeric antigen receptor (CAR) T-cell therapy, has also emerged as a potential treatment option for acute myeloid leukemia. CAR-T therapies targeting myeloid-lineage antigens such as CD123 and CD33 have shown significant antitumor efficacy. However, the ideal targets for CAR-T therapy in AML are still being investigated. Additionally, T-cell-based immunotherapy, such as allogeneic hematopoietic stem cell transplantation (allo-HSCT), has been a cornerstone of AML treatment for decades, offering the potential for cure in a subset of patients [69]. Chemotherapy is recommended even with an initial response to radiation, similar to the treatment of AML. However, there is no specific treatment protocol for myeloid sarcoma, and the same treatment used for AML is often utilized [71].

B. Haematopoietic stem cell transplantation

Haematopoietic stem cell transplantation (HSCT) is a well-established therapeutic option for patients with myeloid leukemia, including acute myeloid leukemia (AML). Allogeneic HSCT, which involves the transfer of stem cells from a donor, is particularly effective in treating AML. However, post-transplant relapse can occur in a significant proportion of patients, leading to a generally poor prognosis [7]. Relapse rates after allogeneic HSCT range from 25-30%. Despite the

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risk of relapse, allogeneic HSCT remains the best option for patients with relapsed or refractory AML [73]. There are several factors that can influence the outcome of allogeneic HSCT in AML patients. One study found that central nervous system (CNS) relapse after allogeneic HSCT is associated with poor prognosis. Additionally, the presence of TP53 mutations in AML patients, which are associated with high-risk biological features, can negatively impact the outcome of allogeneic HSCT). However, the use of hypomethylating agents as maintenance therapy after allogeneic HSCT has shown promise in improving outcomes for AML patients [74]. In order to improve the success of allogeneic HSCT in AML, there have been efforts to identify predictive markers for relapse. Next-generation DNA sequencing has been used to characterize gene mutations in AML patients and determine their impact on post-transplant relapse.

C. Supportive care

Supportive care plays a crucial role in the management of myeloid leukemia, providing patients with comprehensive care to improve their quality of life and manage symptoms. Over the past few decades, several important treatment and supportive care strategies have been implemented to address the complex needs of patients with acute myeloid leukemia (AML). Integrated palliative care has been shown to lead to improvements in quality of life and mood for patients with AML during intensive chemotherapy [75]. Early palliative/supportive care in AML has been associated with high frequency of quality indicators for palliative care and low rates of treatment aggressiveness at the end of life. This approach allows for a more patient-centered and holistic approach to care, addressing not only the physical symptoms but also the psychosocial and emotional needs of patients [76]. In addition to palliative care, emerging immunotherapy approaches have shown promise in the treatment of AML. Intensive chemotherapy with or without hematopoietic stem cell transplantation has been the mainstay of curative treatment for AML, but for relapsed/refractory or intolerable cases, immunotherapy and palliative care may be necessary. Immunotherapy, including immune checkpoint inhibitors and adoptive immunotherapy, has shown potential in improving outcomes for patients with AML. However, it is important to monitor and manage adverse events associated with these therapies to ensure symptomatic treatment and optimal patient care. Supportive care is also essential in the management of myelodysplastic syndromes (MDS), a group of hematologic disorders that can progress to AML. Transfusion support, management of iron overload, antimicrobial prophylaxis, routine immunizations, and palliative care interventions are among the supportive care interventions used in patients with MDS. Palliative care in the MDS population aims to address the physical, emotional, and psychosocial needs of patients, providing symptom management and improving quality of life [77]. In the context of pediatric palliative care, nurses play a crucial role in providing evidence-based and competence-based care to children with leukemia. They are positioned to provide holistic palliative care, addressing the physical, emotional, and psychosocial needs of both the child and their family. The challenges experienced by nurses in providing pediatric palliative care include managing symptoms, addressing psychosocial needs, and ensuring continuity of care [78].

D. Clinical trials and experimental therapies

Clinical trials and experimental therapies play a crucial role in advancing the treatment options for myeloid leukemia. Several studies have investigated different approaches to improve outcomes for patients with acute myeloid leukemia (AML) and other forms of myeloid

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leukemia. Here, we will discuss some of the recent research findings and experimental therapies in the field. One promising approach is the use of targeted therapies. For example, a small molecular Polo-like kinase 1 (PLK1) inhibitor called volasertib has shown potential in clinical trials for the treatment of refractory AML. Volasertib, in combination with cytarabine, has reached phase III clinical trials and has demonstrated efficacy in patients with refractory AML [79]. This targeted therapy aims to inhibit PLK1, a protein involved in cell cycle regulation, to disrupt the growth of leukemic cells. Another targeted therapy being investigated is the use of cereblon E3 ligase modulating drugs (CELMoDs). One specific CELMoD, CC-90009, is currently in clinical trials for the treatment of AML. These drugs work by modulating the activity of cereblon, a protein involved in protein degradation, to selectively target leukemic cells. Immunotherapy has also emerged as a promising approach for the treatment of myeloid leukemia. Allogeneic hematopoietic stem cell transplantation (allo-HSCT) has been a cornerstone of immunotherapy for AML and other hematologic malignancies, offering the potential for cure in a subset of patients. Chimeric antigen receptor (CAR) T-cell therapy is another form of immunotherapy that has shown promise in the treatment of AML. CAR-T cells targeting CD7 have demonstrated significant antitumor efficacy against relapsed and refractory AML in preclinical and clinical studies [80.

Advances in myeloid leukemia research

A. Genetics and molecular insight

Genetics and molecular insights play a crucial role in understanding and advancing research on myeloid leukemia. Myeloid leukemia is a malignant disorder characterized by the uncontrolled proliferation of malignant myeloid progenitor cells and various genetic and molecular abnormalities [81]. The molecular diversity and evolution of acute myeloid leukemia (AML) have been extensively studied, providing valuable insights into the disease. Acute promyelocytic leukemia (APL), a subtype of AML, has a distinctive molecular pathophysiology and clinical manifestationsibility and variability of myeloid neoplasms, includi. Genetic polymorphisms have been found to influence the susceptng AML [82]. Genetic alterations, such as fusion genes, are commonly observed in myeloid leukemia. For example, the coexistence of the BCR-ABL fusion gene and JAK2V617F mutation has been reported in resistant chronic myeloid leukemia. Fusion genes, such as ETV6-NCOA2, have been shown to induce T/myeloid mixed-phenotype leukemia. The identification of these fusion genes and their role in leukemogenesis provides valuable insights into the molecular mechanisms underlying myeloid leukemia. Furthermore, the dysregulation of specific genes and signaling pathways has been implicated in the pathogenesis of myeloid leukemia. For instance, the co-targeting of c-Myc and Bcl-2 has been shown to effectively control AML in preclinical models [83]. Epigenetic mechanisms also play a critical role in the development and progression of myeloid leukemia. Alterations in DNA methylation and histone modifications have been implicated in the dysregulation of gene expression in AML. The identification of intrinsically disordered regions in hub genes of AML has provided insights into the protein-protein interaction networks and gene expression profiles associated with the disease [84]. Advancements in molecular diagnostics have greatly contributed to the understanding and management of myeloid malignancies. Optical genome mapping has been used to detect genomic aberrations in AML, aiding in diagnostic subtyping, prognosis, and patient management. The use of RNAi prodrugs has shown promise in decreasing elevated mRNA

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levels of specific genes in pediatric AML patients [85].

B. Immunotherapy and CAR-T cell therapy

Immunotherapy and CAR-T cell therapy have emerged as promising approaches for the treatment of myeloid leukemia, including acute myeloid leukemia (AML) and chronic myeloid leukemia (CML). These therapies aim to harness the power of the immune system to target and eliminate leukemia cells.One approach to immunotherapy in myeloid leukemia is the use of chimeric antigen receptor (CAR) T cell therapy. CAR-T cells are engineered to express a receptor that recognizes specific antigens on the surface of leukemia cells, allowing them to selectively target and kill these cells. For example, CAR-T cells targeting interleukin-1 receptor accessory protein (IL-1RAP) have shown promise in targeting leukemic stem cells in CML and AM [86]. However, CAR-T therapies targeting myeloid-lineage antigens such as CD123 and CD33, which are commonly expressed on leukemia cells, may have potential hematopoietic toxicity [87]. Another approach to immunotherapy in myeloid leukemia is the use of natural killer (NK) cells, T cells, and dendritic cells. These immune cells play important roles in immune monitoring and anti-leukemia responses. Strategies that utilize these cells, such as adoptive immunotherapy, have shown promise in preclinical and clinical studies. For example, CD38-directed CAR-T cell therapy has been explored as a novel immunotherapy strategy for myeloid chronic myeloid leukemia (CML) despite the progress in immunotherapy for myeloid leukemia; there are still challenges that need to be addressed. One challenge is the toxicity of CAR-T cell therapy on normal hematopoietic cells, which can limit its efficacy. Strategies to enhance CAR-T cell persistence and reduce toxicity are being explored, such as the use of inducible caspase 9 suicide gene safety switches [86].

C. Precision medicine approaches

Precision medicine approaches in myeloid leukemia have gained significant attention in recent years. The mutational and epigenetic landscape of acute myeloid leukemia (AML) has been extensively studied, providing valuable insights into potential biological targets for precision medicine. Proteomic characterization of AML has also been explored, aiming to identify specific protein markers that can guide personalized treatment strategies. In the management of AML, precision medicine has shown promise in older adults. For instance, the use of magrolizumab, an anti-CD47 antibody, has demonstrated good efficacy in older or unfit treatment-naïve as well as relapsed/refractory AML patients [88]. Furthermore, the role of vitamin D in the diagnosis of AML has been investigated. Studies have shown a significant inverse correlation between serum cholesterol levels and AML, suggesting a potential role for vitamin D in the diagnosis and management of the disease. Furthermore, the transformation of AML to acute B cell lymphoblastic leukemia has been observed in the context of CAR-T cell therapy, highlighting the need for careful monitoring and management of treatment-related complications [89]. Overall, precision medicine approaches in myeloid leukemia hold great promise for improving patient outcomes. By understanding the mutational and epigenetic landscape, proteomic profiles, and specific genetic markers, personalized treatment strategies can be developed to target the underlying molecular abnormalities in AML. However, further research is needed to validate and optimize these approaches for clinical implementation.

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Prognosis and survival rates

A. Factors affecting prognosis

Factors affecting prognosis in myeloid leukemia can be influenced by various patient-specific and disease-specific factors. Several studies have investigated these factors to better understand their impact on prognosis. One study by focused on the relationship between transfusion amounts, old age, and survival in adult acute leukemia patients who survived beyond 100 days. The study found that transfusion amounts were associated with old age and survival in these patients. This suggests that transfusion amounts may be a factor that affects prognosis in myeloid leukemia.Another study by Zhu *et a*l. [90] investigated the prognostic factors of acute myeloid leukemia through retrospective analysis. The study aimed to identify factors that could influence the prognosis of patients with this type of leukemia. By analyzing various clinical and laboratory parameters, the study found that certain factors, such as age, white blood cell count, and cytogenetic abnormalities, were associated with prognosis. These findings suggest that age, white blood cell count, and cytogenetic abnormalities may be important factors affecting prognosis in myeloid leukemia.

B. Treatment outcomes

Treatment outcomes in myeloid leukemia have improved over the years due to advancements in therapeutic approaches and targeted therapies. One promising combination therapy is the use of Venetoclax and Azacitidine, which has shown impressive results in newly diagnosed elderly patients with acute myeloid leukemia and refractory/relapsed disease. This combination has demonstrated efficacy in improving treatment outcomes and has the potential to be a valuable treatment option. Immunotherapy, particularly allogeneic hematopoietic stem cell transplantation (allo-HSCT), has been a cornerstone in the treatment of acute myeloid leukemia (AML) and other hematologic malignancies. Allo-HSCT offers the potential to cure a subset of patients and has been widely used for decades. However, the use of immune checkpoint inhibitors and chimeric antigen receptor (CAR) T-cell therapy has also shown promise in the treatment of AML. CAR-T therapies targeting myeloid-lineage antigens such as CD123 and CD33 have been developed, although they may have potential hematopoietic toxicity [87]. These immunotherapeutic approaches provide alternative treatment options for patients with AML. Genetic abnormalities and mutations play a significant role in the prognosis and treatment outcomes of myeloid leukemia. For example, mutations in the CEBPA gene have been associated with acute myeloid leukemia and can impact treatment response and clinical outcomes [91]. Similarly, mutations in the FLT3 gene have been identified as poor prognostic factors in pediatric acute myeloid leukemia [92]. Understanding the genetic landscape of myeloid leukemia can help guide treatment decisions and improve patient outcomes. The use of tyrosine kinase inhibitors (TKIs) has revolutionized the treatment of chronic myeloid leukemia (CML). TKIs, such as Imatinib and Nilotinib, have significantly improved the prognosis and survival of patients with CML. These targeted therapies specifically inhibit the abnormal signaling pathways associated with CML, leading to disease control and improved outcomes.In recent years; the use of Venetoclax has gained attention in the treatment of acute myeloid leukemia. Venetoclax has shown efficacy in relapsed/refractory AML, although there are some concerns regarding hematological and non-hematological adverse events [93]. Further research and clinical trials are needed to optimize the use of Venetoclax and improve treatment outcomes in AML.Additionally, the management of acute myeloid

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leukemia in specific patient populations, such as those with Down syndrome, requires alternative chemotherapy approaches [94].

Patient experience and quality of life

A. Coping with a myeloid leukemia diagnosis

Coping with a myeloid leukemia diagnosis can be a challenging and overwhelming experience for patients. It is important for patients to have access to information and support to help them navigate through this difficult time. Several studies and articles provide insights into various aspects of coping with a myeloid leukemia diagnosis.One study by Talwar *et al.* [95] highlights the challenges faced by healthcare systems and clinicians in managing acute myeloid leukemia (AML) patients, particularly in the context of immunocompromised states. This information can be valuable for patients diagnosed with CML, as it provides insights into treatment options and their effectiveness. In the case of undiagnosed chronic myeloid leukemia in patients with pre-existing poorly controlled diabetes mellitus (DM), it is crucial to recognize the condition and provide appropriate systemic chemotherapy, as highlighted by Falah *et al.* (2023). This study emphasizes the importance of early diagnosis and tailored treatment for patients with comorbidities. Flow cytometry immune phenotyping is a powerful tool for accurate diagnosis of acute leukemias, as mentioned in a study by (Pandey, 2021). This information can help patients understand the diagnostic process and the significance of flow cytometry in determining the lineage of their leukemia.For patients with relapsed/refractory acute myeloid leukemia, Venetoclax therapy may be a promising treatment option, as suggested by [93]. However, it is important for patients to be aware of potential adverse events and the need for close monitoring during treatment.The heterogeneity of acute myeloid leukemia (AML) and its prognostic factors are discussed in a study by [96]. This information can help patients understand the variability of their condition and the factors that may influence their prognosis and treatment decisions. Myeloid sarcoma, a rare manifestation of acute myeloid leukemia (AML), can occur at any extramedullary site. This information can help patients recognize the potential symptoms and manifestations of myeloid sarcoma and seek appropriate medical attention.Early diagnosis of chronic myeloid leukemia (CML) is particularly important, as mentioned in a study by [97].

B. Supportive care and psychological services

Supportive care and psychological services are crucial components in the management of myeloid leukemia, including acute myeloid leukemia (AML) and chronic myeloid leukemia (CML). These services are essential for addressing the physical and psychological needs of patients.One important aspect of supportive care in myeloid leukemia is the management of treatment-related complications. Patients with myeloid leukemia often experience immunocompromised states, which make them more susceptible to infections. For example, in the case of a young AML patient with COVID-19 infection, antiviral therapy and granulocyte colony-stimulating factor have been successfully used to manage the infection [95]. Psychological services are also crucial in the management of myeloid leukemia. The diagnosis and treatment of myeloid leukemia can have a significant impact on the mental well-being of patients, leading to anxiety, depression, and other psychological distress. Therefore, providing psychological support and counseling services is important for helping patients cope with the emotional challenges associated with the disease. Hypomethylating agents, such as azacitidine, have become the standard of care for patients with high-risk myelodysplastic syndrome

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or AML who are not eligible for high-intensity chemotherapy [98]. These agents have demonstrated efficacy in improving outcomes for patients with myeloid leukemia. The role of genetic factors in myeloid leukemia has also been investigated. Double RUNX1 mutations, for instance, have been found to be enriched in acute leukemias of ambiguous lineage, which could have implications for targeted therapies [99].

Future directions and emerging therapies

A. Promising research areas

Promising research areas in myeloid leukemia encompass various aspects of the disease, including molecular therapy, classification, cytochrome P450 regulation, treatment approaches, long non-coding RNA, differentiation therapy, immune function, novel drug development, apoptosis induction, antibody-drug conjugates, PARP inhibitors, tyrosine kinase inhibitor therapy, therapy-related neoplasms, chemo-protective effects, synthetic T-cell biology, fusion genes, transporter-mediated drug interactions, prognostic signatures, ferroptosis-related genes, obesity in leukemia patients, combination therapies, ferroptosis, myeloid sarcoma, cytoplasmic DNA sensing, and GATA-1S inhibition of ferroptosis. These research areas provide valuable insights into the understanding and treatment of myeloid leukemia. One promising research area in myeloid leukemia is the targeting of mutant FLT3 for molecular therapy. FLT3 mutations are well-known targets for therapy in acute myeloid leukemia (AML). The role of cytochrome P450 in regulating the acute myeloid leukemia microenvironment is another promising research area. Recent research has focused on determining the regulators of cytochrome P450 expression and activity in AML [100].

B. Potential breakthrough on the horizon

Myeloid leukemia is a complex and aggressive hematologic malignancy that requires innovative treatment approaches. Several recent studies have explored potential breakthroughs in the field. One promising avenue of research is the use of CAR-T therapy [85] demonstrated the feasibility of CD7 as a target for CAR-T therapy in relapsed and refractory acute myeloid leukemia (R/R AML). They found that CD7-directed CAR-T therapy showed significant antitumor efficacy against R/R AML. Yan *et al.* [93] conducted a systematic review and meta-analysis of studies evaluating the efficacy and safety of venetoclax in relapsed/refractory AML. They found that venetoclax had a positive impact on overall survival in these patients. This highlights the potential of venetoclax as a therapeutic option for AML patients who have relapsed or are refractory to standard treatments.

CONCLUSION

In conclusion, the advancements in myeloid leukemia treatment have showcased remarkable progress, revolutionizing patient care and outcomes. Over the years, significant strides have been made in understanding the complex biology of myeloid leukemia subtypes, leading to the development of targeted therapies and personalized treatment approaches. The introduction of novel targeted agents, immunotherapies, and advancements in bone marrow transplantation techniques have substantially improved survival rates and quality of life for patients. Additionally, the integration of precision medicine, molecular profiling, and minimal residual disease monitoring has allowed for more tailored and effective therapies, minimizing adverse effects and improving long-term prognosis. However, despite these remarkable advancements, challenges persist, including drug resistance, relapse, and access to cutting-edge therapies for all patients. Further research efforts

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focusing on overcoming resistance mechanisms, identifying new therapeutic targets, and enhancing accessibility to innovative treatments are crucial to continue the momentum in improving outcomes for individuals affected by myeloid leukemia. In essence, the landscape of myeloid leukemia treatment has undergone a paradigm shift, offering renewed hope and prospects for better survival rates and enhanced quality of life. Continued collaboration between researchers, healthcare professionals, patients, and advocacy groups remain imperative to further advance the field and ultimately achieve better outcomes for all individuals affected by myeloid leukemia.

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