

Risk Assessment in Myelodysplastic Syndromes: The Importance of IPSS and IPSS-R

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DESCRIPTION

Myelodysplastic Syndromes (MDS) are a heterogeneous group of hematological disorders characterized by ineffective hematopoiesis, resulting in cytopenias (low blood cell counts) and an increased risk of progression to Acute Myeloid Leukemia (AML). The treatment strategy for MDS is complex and depends largely on the risk stratification of the disease, patient characteristics, and overall prognosis. While the standard approach often focuses on supportive care, immunosuppressive therapy, or hypomethylating agents, the role of aggressive chemotherapy in MDS remains a subject of debate.

Historically, aggressive chemotherapy has been reserved for those patients with high-risk disease, particularly those with high-risk cytogenetics or those who have transformed into AML. However, the application of intensive chemotherapy in MDS is not without controversy. This article will show the evolving role of aggressive chemotherapy in the treatment of MDS, its indications, challenges, and future prospects.

MDS encompasses a range of clonal hematopoietic disorders that primarily affect older adults. Patients with MDS typically present with symptoms related to anemia, neutropenia, and thrombocytopenia, and may experience fatigue, bleeding, or frequent infections. The risk of progression to acute leukemia, particularly in higher-risk cases, is a major concern, and it is often this progression that drives the decision-making process around treatment options.

Risk assessment in MDS is largely guided by the International Prognostic Scoring System (IPSS) or its updated version, the IPSS-R, which takes into account factors such as cytogenetic abnormalities, bone marrow blast percentage, and the degree of cytopenias. Patients are classified into low-, intermediate-, or high-risk categories, with high-risk patients having a much poorer prognosis and an increased likelihood of progression to AML.

Traditional treatment approaches

For most patients with MDS, particularly those in the low- to intermediate-risk categories, the first-line treatments are focused on supportive care and disease-modifying therapies such as hypomethylating agents (e.g., azacitidine, decitabine) or immunosuppressive therapy. These therapies can help improve blood counts, delay progression, and reduce the risk of transformation to AML. Bone Marrow Transplantation (BMT) offers curative potential for a subset of patients, but its use is limited by age, comorbidities, and donor availability.

However, aggressive chemotherapy often consisting of intensive regimens used in AML has historically been employed in high-risk MDS cases, particularly those with significant bone marrow blast infiltration or transformation into AML. Chemotherapy regimens such as the standard "7+3" (cytarabine and an anthracycline) are frequently used in these patients.

For high-risk MDS patients, chemotherapy remains a cornerstone of treatment, particularly when the disease transforms into AML or when the blast percentage in the bone marrow is above 20%. Intensive chemotherapy can induce remission and improve survival in this group of patients. However, the outcomes are often less favorable than in *de novo* AML, with a higher rate of relapse and complications such as infections, organ toxicity, and prolonged cytopenias.

Recent data indicate that, while chemotherapy may offer short-term remission in high-risk MDS, the overall survival benefit is marginal. A key challenge is the increased frailty and comorbidities present in the MDS patient population, which often limits the ability to tolerate aggressive treatments. Moreover, the risk of treatment-related mortality can be high, especially in older patients or those with poor performance status.

One of the major concerns with aggressive chemotherapy in MDS is the potential for clonal evolution and resistance to

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treatment. While intensive chemotherapy can initially control the disease, the recurrence of leukemia or the development of chemoresistant clones remains a significant issue. This is compounded by the fact that many MDS patients already have complex cytogenetic abnormalities at diagnosis, which can make them less responsive to chemotherapy

Despite its potential role in high-risk MDS, aggressive chemotherapy is associated with several limitations. First and foremost is the inability to achieve long-term remission in a substantial proportion of patients. While some patients achieve remission following intensive chemotherapy, many relapse, and survival rates remain suboptimal compared to those with de novo AML. Furthermore, the side effects of chemotherapy, including myelosuppression, infections, and organ toxicity, are particularly pronounced in the older MDS population.

The heterogeneity of MDS also poses challenges. MDS is not a single disease but rather a spectrum of disorders, and the response to chemotherapy can vary widely based on the underlying genetic mutations, the presence of blasts, and other

individual factors. For instance, patients with specific chromosomal abnormalities (such as complex karyotypes or mutations in *TP53*) may fare worse with chemotherapy and are more likely to experience relapse.

CONCLUSION

Chemotherapy plays a role in the treatment of high-risk myelodysplastic syndromes, especially in patients who have transformed into AML or have high blast counts. However, the benefits of chemotherapy in MDS are limited by the disease's heterogeneity, the patient's ability to tolerate intensive treatments, and the risk of relapse. As our understanding of MDS deepens and new therapies emerge, the role of chemotherapy may become more targeted and personalized. Future treatment strategies will likely involve a combination of chemotherapy, targeted agents, and stem cell transplantation to optimize outcomes and minimize the toxicities associated with aggressive therapy.