

ITP, allowing autoreactive B cells and long-lived plasma cells to persist. This explains resistance to rituximab, which depletes CD20⁺ B cells but spares plasma cells. The BAFF/APRIL axis is therefore a promising therapeutic target. In addition to peripheral destruction, impaired thrombopoiesis is critical. Autoantibodies against GPIIb/IIIa and GPIb/IX disrupt megakaryocyte maturation and proplatelet formation. CD8⁺ T cells induce megakaryocyte apoptosis, further reducing platelet production. Bone marrow stromal dysfunction, including reduced secretion of TGF- β , SCF, and CXCL12, exacerbates these defects. A hallmark of ITP is the paradoxically low thrombopoietin (TPO) level despite severe thrombocytopenia. Since TPO synthesis is regulated by megakaryocyte mass rather than platelet count, reduced megakaryocyte numbers and dysfunction result in insufficient TPO and inadequate platelet production. The cytokine milieu in ITP reflects a proinflammatory imbalance. Increased IFN- γ , TNF- α , and IL-17 reinforce autoimmunity, while decreased IL-10 reflects Treg dysfunction. These changes disrupt tolerance and promote disease chronicity. In conclusion, ITP is not merely an antibody-driven disorder but a complex immune dysregulation syndrome. Both humoral and cellular mechanisms contribute to platelet destruction, while megakaryocyte impairment and insufficient TPO hinder platelet production. Elevated BAFF/APRIL, Th1/Th17 polarization, Treg deficiency, and cytotoxic T-cell activity represent crucial pathogenic pathways. Advances in molecular biology are redefining ITP pathogenesis and identifying novel therapeutic targets that extend beyond conventional immunosuppression.

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Abstract 038

HIGH-RISK MDS TREATMENT AND INNOVATIONS

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Myelodysplastic syndrome (MDS) is a clonal neoplastic myeloid stem cell neoplasm characterized by ineffective hematopoiesis in the bone marrow and cytopenias in the peripheral blood. Prognostic scoring systems classify patients as low-risk or high-risk MDS. Various prognostic scoring systems have been developed to predict disease course and survival using markers such as cytopenias, bone marrow blast ratio, cytogenetics, age, and performance status. The most commonly used scoring systems are the IPSS and R-IPSS. In its 2022 classification, the WHO used the term myelodysplastic neoplasms instead of myelodysplastic syndromes. These clonal hematopoietic neoplasms were defined by cytopenias and morphological dysplasia, with a dysplasia threshold of 10% for all series. MDS subtypes were grouped into those characterized by genetic abnormalities and those defined by morphology. Although patients may be classified as low risk based on their current MDS risk scores, the disease is a blood cancer with a generally poor prognosis. Patients with high and very high IPSS-R risk can expect a median survival of 1.6 and 0.8 years, respectively, while those with intermediate,

low, and very low IPSS-R risk have a median survival of 3, 5.3, and 8.8 years, respectively. The treatment approach for high-risk MDS is aimed at delaying leukemic transformation and prolonging survival. Currently, the only curative treatment for high-risk MDS patients is allogeneic stem cell transplantation (HSCT). Its application is limited by the advanced age and lack of vigor of many MDS patients. All "high-risk" MDS patients with good performance status and without serious comorbidities should be considered for curative allogeneic HSCT. Transplant-related factors have also been shown to play a role in determining post-transplant prognosis. Treatment options for patients ineligible for transplantation are limited, and HMA remains the standard of care. New agents are under development for high-risk MDS patients. In recent years, several new drugs have been tested in combination with 5-azacitidine to further improve patient outcomes, but these have been unsuccessful. A randomized phase II SWOG trial compared standard azacitidine with azacitidine combined with lenalidomide or vorinostat in 227 patients with HR-MDS, reporting an overall response rate of 38% in the azacitidine group, while no improvement in response or survival was seen in the combination group. The recent approval of venetoclax, a BCL-2 inhibitor, for use with 5-azacitidine in AML has prompted investigation of this combination in MDS. In particular, azacitidine + venetoclax, azacitidine + sabatolimab, and azacitidine + magrolimab have shown encouraging results in large, single-arm studies and have also improved in placebo-controlled, double-blind studies with OS as the primary endpoint. IDH1 or IDH2 mutations occur in 5–15% of MDS patients, and enasidenib and ivosidenib have been shown to produce responses in MDS patients with IDH2 mutations. It may be mentioned that the new ICC, which classifies previous WHO 2016 MDS with $\geq 10\%$ blasts as MDS/AML, would potentially allow the use of AML-approved drugs also in higher-risk MDS

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Abstract 039

CURATIVE TREATMENT OPTIONS IN SICKLE CELL DISEASE

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Introduction: Sickle cell disease is the most commonly inherited hemoglobinopathy (1). Disease modifying drug therapies such as hydroxyurea, L-glutamine, voxelotor and crizanlizumab reduce pain crises and severe complications (2). Hematopoietic stem cell transplantation (HSCT) is the only curative treatment option. In 1984, the first report of HSCT in a patient with SCD who was transplanted for AML demonstrated the efficacy of HSCT as a curative treatment option for SCD patients with severe disease. In 1996, Walters and colleagues first reported the curative benefits of treatment in a 22-year-old patient with severe sickle cell disease who had an HLA-identical sibling donor (3). **INDICATIONS FOR HEMATOPOIETIC STEM CELL TRANSPLANTATION** Indications for HSCT are summarized in the Table 1. According to the expert panel, (1)