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.

https://doi.org/10.1016/j.htct.2025.106214

Abstract 038

HIGH-RISK MDS TREATMENT AND INNOVATIONS

Mehmet Çelik

Manisa City Hospital, Türkiye

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 ≥10% blasts as MDS/AML, would potentially allow the use of AML-approved drugs also in higher-risk MDS

https://doi.org/10.1016/j.htct.2025.106215

Abstract 039

CURATIVE TREATMENT OPTIONS IN SICKLE CELL DISEASE

Merve Yahşi

Osmaniye State Hospital, Türkiye

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)

any young patient with symptomatic SCD who has an HLA-identical sibling donor should be transplanted as early as possible, preferably at preschool age; (2)bone marrow and umbilical cord blood from HLA-identical sibling donors are the recommended stem cell sources;(3)for patients who need to use an alternate donor source,more stringent indications are still recommended, and these patients should only have HSCT under a clinical trial and at a center where the staff are experienced in the procedure(3). DONOR SELECTION AND STEM CELL SOURCES Current recommendations by the National Marrow Donor Program recommend high-level matching at the HLA-A,HLA-B,HLA-C and HLA-DRB1 loci for unrelated donors.20 Matching in all the loci is referred to as an 8/8 match (3).Unfortunately, <%20 of patients have HLA-matched donors.In the absence of a matched sibling donor, HLA-matched unrelated donors,HLA-identical sibling cord blood donors and haploidentical donors are alternatives.Two trials, Sickle Cell Transplant To Prevent Disease Exacerbation (STRIDE) and Sickle Cell Unrelated Transplant trial (SCURT), are evaluating the use of matched unrelated donors in different age groups and with different conditioning regimens.The STRIDE trial started in 2012 for reduced intensity myeloablative transplantation in patients with SCD aged 15-40 years and reported excellent outcomes (OS and EFS of %95) at 12-month follow-up.32 The SCURT trial opened in 2008 and demonstrated no difference in graft rejection rates with matched unrelated donors compared to HLA-identical sibling donors; however, significant morbidity from chronic GVHD (%62) was reported. CONDITIONING REGIMENS Conditioning regimens are categorized as being myeloablative,reduced intensity,or nonmyeloablative. **Myeloablative Conditioning Regimen** The most commonly used myeloablative conditioning regimen for SCD consists of busulfan 14-16 mg/kg and cyclophosphamide 200 mg/kg ± ATG.Cryopreservation of sperm and ovarian tissue is recommended in these types of HSCT(1). **Reduced Intensity and Nonmyeloablative Conditioning Regimens** Reports of SCD symptoms resolving even in patients with mixed chimerism suggest that complete donor chimerism is not necessary and have led to interest in using reduced intensity and nonmyeloablative conditioning regimens for this population(3).

https://doi.org/10.1016/j.htct.2025.106216

Abstract 040

DİAGNOSİS AND TREATMENT OF PAROXYSMAL NOCTURNAL HEMOGLOBİNURİA

Tahsin Yüksel

Mehmet Akif Inan Training and Research Hospital, Türkiye

Background: Paroxysmal nocturnal hemoglobinuria (PNH) is a rare, life-threatening clonal hematopoietic stem cell disorder characterized by hemolytic anemia, bone marrow failure, and thrombosis. The absence of glycosylphosphatidylinositol (GPI)-anchored complement regulatory proteins, such as CD55 and CD59, leads to uncontrolled complement activation, chronic intravascular hemolysis, and severe complications. Thrombosis remains the leading cause of mortality, accounting for 40–67% of deaths in PNH patients. **Diagnosis:** High-sensitivity flow cytometry is the gold standard for detecting GPI-deficient cell populations and remains essential for both diagnosis and follow-up. Laboratory evaluation includes complete blood count, hemolysis parameters (LDH, bilirubin, haptoglobin, reticulocytes), and bone marrow examination. Clinical indications for testing are hemolysis, cytopenias, unexplained anemia, aplastic anemia, and thrombosis in atypical sites such as hepatic or cerebral veins. International guidelines (IPIG, ICCS, BCSH) recommend screening all patients with aplastic anemia for PNH clones at diagnosis. **Treatment and Follow-up:** Regular monitoring of hemolysis-related parameters is critical to identify high disease activity, defined as LDH ≥1.5 × ULN plus at least one symptom (fatigue, dyspnea, abdominal pain, hemoglobinuria, anemia, thrombosis). Eculizumab, a C5 inhibitor, was the first targeted therapy to significantly reduce intravascular hemolysis and thrombotic risk. Vaccination against Neisseria meningitidis is mandatory before treatment initiation. Ravulizumab, a long-acting C5 inhibitor, offers extended dosing intervals with comparable efficacy. **Novel Therapies:** Recent therapeutic advances are transforming PNH management. Crovalimab, a next-generation C5 inhibitor, allows subcutaneous administration with longer dosing intervals. Biosimilar eculizumab (Bkemv) improves treatment accessibility. Proximal complement inhibitors, including iptacopan (oral Factor B inhibitor), danicopan (Factor D inhibitor), and pegcetacoplan (C3 inhibitor), target both intravascular and extravascular hemolysis, improving hemoglobin stabilization, transfusion independence, and quality of life. These agents are increasingly incorporated into personalized treatment strategies. **Bone Marrow Transplantation:** Allogeneic hematopoietic stem cell transplantation (HSCT) remains the only curative option but is associated with high treatment-related mortality. It should be reserved for patients with severe bone marrow failure or refractory disease when risks outweigh potential benefits. **Conclusion:** The therapeutic landscape of PNH is undergoing a paradigm shift, with novel long-acting and oral complement inhibitors improving disease control and patient convenience. Early diagnosis through flow cytometry and individualized treatment selection remain essential for optimal outcomes. Although HSCT offers potential cure, complement inhibitors currently represent the cornerstone of PNH management.

https://doi.org/10.1016/j.htct.2025.106217

Abstract 041

ALL IN ADOLESCENT AND YOUNG ADULTS

Mesut Tahta

İzmir City Hospital, Türkiye

Recent advances in the treatment of adolescents and young adults (AYA) with acute lymphoblastic leukemia (ALL) highlight the critical role of pediatric-inspired regimens, molecular stratification, and novel immunotherapies. Historically, outcomes for AYA lagged behind children due to greater