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