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).

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Abstract 040

DİAGNOSİS AND TREATMENT OF PAROXYSMAL NOCTURNAL HEMOGLOBİNURİA

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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.

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Abstract 041

ALL IN ADOLESCENT AND YOUNG ADULTS

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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

treatment resistance and toxicity. However, intensification strategies adapted from pediatric protocols have significantly improved remission and survival rates. Despite this progress, survival in AYA remains inferior to pediatric patients, underscoring the need for more refined, biology-driven approaches (Siegel et al., 2018). One of the most important biological insights concerns the Philadelphia-like (Ph-like) ALL subtype, which is particularly prevalent in AYA (25–30%). Characterized by kinase-activating lesions, this subgroup exhibits high resistance to chemotherapy but offers opportunities for targeted therapy using tyrosine kinase inhibitors (TKIs) such as ruxolitinib or ABL-class inhibitors. Other genetic alterations, including MEF2D, ZNF384, and DUX4 fusions, also contribute to disease heterogeneity and prognosis. Identifying these lesions rapidly remains a major challenge, and the integration of genomic profiling with predictive algorithms and ex vivo drug sensitivity testing is expected to optimize individualized care (Pui et al., 2019). Minimal residual disease (MRD) monitoring has become a cornerstone of risk stratification in AYA ALL. Early MRD levels after induction and consolidation strongly predict relapse risk and guide decisions regarding allogeneic hematopoietic stem cell transplantation (allo-HSCT). Importantly, MRD thresholds differ between pediatric and adult-inspired protocols, highlighting the need for age-specific approaches. Furthermore, MRD is increasingly employed as a primary endpoint in clinical trials and as a trigger for introducing immunotherapies (Stock et al., 2019). Immunotherapeutic agents are transforming frontline therapy in AYA ALL. Inotuzumab ozogamicin (anti-CD22) and blinatumomab (CD3–CD19 bispecific antibody) have demonstrated superior response rates and MRD clearance compared with standard chemotherapy in relapsed/refractory settings. Both are now being evaluated earlier in therapy, particularly as consolidation strategies. Similarly, CD19-directed chimeric antigen receptor (CAR) T-cell therapy, notably tisagenlecleucel, has shown durable remissions in pediatric and AYA patients, although relapse due to antigen loss remains a challenge. Efforts are underway to improve CAR T-cell persistence and safety in this age group (Pui et al., 2019). Beyond targeted and immune-based therapies, novel small molecules such as BCL2 inhibitors (venetoclax, navitoclax) and menin inhibitors show promise in genetically defined subgroups. These agents may further reduce chemotherapy intensity while improving efficacy. Equally crucial is comprehensive supportive care for AYA patients. Fertility preservation, psychosocial support, and survivorship programs are essential to address long-term treatment burdens, particularly for those undergoing allo-HSCT. Late complications such as infertility, osteonecrosis, and prolonged immune dysfunction remain pressing issues that require multidisciplinary management (Siegel et al., 2018). In conclusion, the therapeutic landscape of AYA ALL is shifting from generalized intensification to precision medicine. Advances in understanding disease biology, the incorporation of MRD into decision-making, and the integration of immunotherapy and small molecules are reshaping standards of care. Future progress will depend on broad clinical trial participation and multidisciplinary support to optimize both survival and quality of life for AYA patients with ALL.

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Abstract 042

WHY I CHOSE HEMATOLOGY ?

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After graduating from Hacettepe University Faculty of Medicine in 1970, with the support of my professors I began corresponding with universities abroad to pursue residency training. During this period I met Prof. Faruk Özer, the head of the Hacettepe Faculty of Medicine Hematology Department, who made me love hematology and sparked my interest in the field., Türkiye On July 1, 1971, I started my straight medical internship at Newark Medical School Hospital/Jersey City Medical Center. At the beginning of 1972, I transferred to Thomas Jefferson University in Philadelphia (Jefferson Medical College), to which I had applied, and in 1974 I completed my internal medicine residency. While training in internal medicine, I met Prof. Allan J. Erslev, the head of the Hematology Department and director of the Cardeza Foundation for Hematologic Research, and I began attending the early-morning slide discussion sessions he organized for residents. He would put the peripheral smear and bone marrow slides of inpatients onto the microscope, have us read them, and ask us to interpret the findings. We received an excellent education in morphology. These morning sessions created a passion for hematology in me, because we could make diagnoses by directly examining morphology alongside the clinical and laboratory findings. No other subspecialty offered such a superb opportunity. This excited and motivated me., Türkiye With that excitement, I began my hematology fellowship in July 1974. Our department chair, Prof. Allan J. Erslev, had identified the hormone erythropoietin in 1953 while working at Harvard Medical School. In my second year as a clinical fellow, he suggested that I conduct research on erythropoietin. Thus, starting in 1976, I focused my research on extrarenal sources of erythropoietin and on immunology. One of Prof. Erslev's most important contributions to modern hematology is that the erythropoietin hormone he described was later produced recombinantly and is now widely used in clinical practice for many anemias, especially in chronic renal failure. At that time Prof. Allan J. Erslev was also preparing a new hematology textbook, and in 1972 he began serving as a co-editor—together with Williams, Rundles, and Beutler—of the book **HEMATOLOGY**, which went on to become the much-read **"Williams Hematology"**, now in its 10th edition. Prof. Erslev entrusted me with many tasks in the preparation of this book. I would go to the famous Saunders Publishing house next to Thomas Jefferson University and, working together with the responsible editors, proofread and revise the chapters I had corrected. This greatly contributed to my affection for hematology and to my training. Thus, even before the book's first edition in 1974, I had the opportunity to read the entirety of a very important text in hematology., Türkiye At the Hematology Department of Thomas Jefferson University, I had the opportunity to do both clinical and research fellowships until 1980. In my research, I examined the antigenic and immunologic characteristics of extrarenal erythropoietin. During this period, I received comprehensive