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.

https://doi.org/10.1016/j.htct.2025.106218

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

training in hematopoiesis and bone marrow physiology as well as cellular immunology. Encouraged by Prof. Erslev, I even completed a master's program in protein science at Temple University in my second fellowship year. Later, to better understand stem-cell biology, he arranged for me to work for a time at the Toronto Cancer Center, where Prof. Ernest McCulloch and Prof. James Till—who, in their 1961 publications, identified hematopoietic stem cells in mice—were based. All these experiences greatly helped me learn the fundamental principles of hematology in depth., Türkiye Together with my wife, Prof. Tülay Kansu, we completed our postgraduate training in Philadelphia between 1972 and 1980. During my years in Philadelphia, I had the opportunity to meet and work with many distinguished hematologists who made very significant contributions to the field. Prof. Peter C. Nowell of the University of Pennsylvania (who identified the Philadelphia chromosome), Prof. Sol Sherry of Temple University in the field of coagulation, Prof. Sandy Shapiro in antiphospholipid syndrome and Prof. James Holland the founder of CALGB, among many other esteemed hematologists. Through these collaborations, I gained highly valuable academic knowledge and experience from pioneers of the field., Türkiye Over the last 50 years, hematology has seen major scientific advances that have improved patients' quality of life and expanded treatment options. Among these are the development of cell-culture and genetic technologies; stem-cell transplantation; cancer immunotherapy and targeted therapies; checkpoint inhibitors; gene therapy; biotechnology; innovations in the treatment of sickle-cell disease and thalassemia and advances in imaging and diagnostic methods. In conclusion, I believe that the hematology subspecialty—which I chose with determination and affection in the final years of my internal medicine residency—has made very important contributions to my academic life. I sincerely recommend that our young colleagues choose hematology in their subspecialty training and academic careers.

https://doi.org/10.1016/j.htct.2025.106219

Abstract 043

DONOR SELECTION IN ALLOGENEIC HEMATOPOIETIC STEM CELL TRANSPLANTATION

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Allogeneic hematopoietic stem cell transplantation (HSCT) is a curative therapeutic option for various malignant and non-malignant hematological disorders. Donor selection remains the most critical factor affecting transplantation outcomes, with human leukocyte antigen (HLA) compatibility being the cornerstone of this process. The traditional donor hierarchy begins with HLA-matched sibling donors (MSD), who provide the best outcomes with the lowest risk of graft-versus-host disease (GVHD) and transplant-related mortality (TRM). For patients without an MSD, matched unrelated donors (MUD) with 10/10 HLA compatibility are the next preferred option. Recent advances in high-resolution HLA typing have improved outcomes with unrelated donors, approaching results comparable to those of MSD. When multiple compatible donors are available, non-HLA factors guide selection. Donor age significantly impacts outcomes, with younger donors (18-35 years) yielding better results. Cytomegalovirus serostatus concordance between donor and recipient is crucial to prevent post-transplant complications. Male donors are generally preferred over female donors, particularly for male recipients, due to the increased risk of chronic GVHD associated with female-to-male transplants. ABO blood group compatibility, while not affecting survival directly, influences the risk of immediate post-transplant complications. Alternative donor sources have expanded transplantation possibilities for patients lacking conventional donors. Haploidentical family donors have seen remarkable improvements in outcomes with the introduction of post-transplant cyclophosphamide (PTCy), challenging the traditional donor hierarchy. Umbilical cord blood units provide another alternative, particularly beneficial in pediatric patients, despite limitations in cell dose. Donor selection strategies differ between pediatric and adult populations. In pediatric patients, the focus remains on minimizing long-term complications, particularly chronic GVHD, which can severely impact growth and development. In adults, stronger graft-versus-leukemia effects may be prioritized in high-risk malignancies, making alternative donors with potential for enhanced alloreactivity more attractive. Disease-specific considerations also influence donor choice. Benign hematological disorders require complete HLA matching to minimize complications, while in malignant diseases, partial HLA mismatches might be accepted to enhance graft-versus-tumor effects. Hodgkin lymphoma patients demonstrate superior outcomes with haploidentical donors compared to MUDs, challenging conventional hierarchies. Donor exclusion criteria encompass medical conditions that may increase donation-related risks or compromise graft quality. These include cardiovascular, pulmonary, hematological, and immunological disorders, active infections, and malignancy history. As transplantation practices evolve, personalized donor selection algorithms incorporating disease characteristics, patient factors, donor availability, and center experience are replacing rigid hierarchies, ultimately improving outcomes for patients requiring allogeneic HSCT.

https://doi.org/10.1016/j.htct.2025.106220

Abstract 044

GENE THERAPY IN HEMOPHILIA

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Symptomatic or prophylactic treatment of hemophilia began in the 1960s with fresh frozen plasma therapy. Over the years, treatment evolved through plasma-derived products, recombinant therapies, extended half-life products, and