guided by a combination of mutational status and comorbidities. Specific mutations confer resistance to certain TKIs, making mutation-directed sequencing essential. At the same time, patient comorbidities such as cardiovascular, pulmonary, or metabolic disease influence drug tolerability and safety, thereby shaping the optimal therapeutic choice [1,7]. **Beyond TKIs:** For patients failing multiple TKIs, allogeneic hematopoietic stem cell transplantation (allo-HSCT) remains the only potentially curative approach, particularly in younger and high-risk patients [1,2]. Novel strategies under investigation include rational TKI combinations (e.g., asciminib plus ponatinib), immunotherapeutic approaches, and targeted inhibition of epigenetic regulators [8]. **Conclusion:** Refractory CML reflects the biological and clinical complexity of disease progression beyond BCR::ABL1 dependence. While ponatinib and asciminib have redefined therapeutic opportunities, additional high-risk mutations highlight the need for precision medicine strategies. Tailored TKI sequencing, integration of comorbidity profiles, and timely transplantation remain central pillars, while ongoing translational research promises to expand future options [7,8].

https://doi.org/10.1016/j.htct.2025.106185

Abstract 009

HYPERCOAGULABILITY: ETIOLOGY, DIAGNOSIS AND TREATMENT PRINCIPLES

Tanju Atamer

Istanbul University Faculty of Medicine, Türkiye

Thrombosis occurs when the delicate balance between prothrombotic and anticoagulant forces is impaired. It usually develops due to multiple factors. When multiple risk factors come together, the anticoagulant systems cannot resist procoagulant forces and thrombosis may develop as a result. Thrombosis due to hypercoagulability is usually seen clinically as venous thromboembolism (VTE) and rarely as arterial thrombosis. VTE can be seen as deep vein thrombosis (DVT) or pulmonary embolism. DVT most often manifests itself in the legs and rarely in the abdominal or intra-pelvic veins. The hereditary or acquired factors are involved in the etiology of venous thromboembolism. Clinically, VTE is observed in those who are due to hereditary factors, while venous or arterial thromboses may be observed in those who are due to acquired causes. Hypercoagulability due to acquired causes is observed more often (70%) and they have a greater risk of thrombosis. Venous thromboembolism is reported to occur in 1/10,000 people per year under the age of 40 and 1/1000 people per year over the age of 75. Hereditary thrombophilia causes are rare in the population. Although different rates are reported according to the world geography, The R506Q mutation in coagulation factor V, also known as the Factor V Leiden (FVL) mutation is the most common among them (3-8%). It is rare in far east countries. FVL mutation is the most common cause among hereditary hypercoagulabilities (50%). Clinically, young age, idiopathic thrombosis, thrombosis in an unusual place (upper extremity, mesenteric vein, portal vein, renal vein, cerebral vein) are noteworthy. Recurrence of thrombosis and a family history of venous thromboembolism are common. Since the findings are not specific in the diagnosis of venous thromboembolism, the patient's medical history, family history and examination findings should be evaluated together. Determination of thrombosis risk scores, D-Dimer test, blood chemistry, lung X-ray and ECG are included as the first examinations in the patient. In patients with a negative D-Dimer test, a further examination is usually not needed. The subject of which tests to perform and when to perform in VTE cases requires expertise. In cases of idiopathic thrombosis, occurring at a young age, or recurrent, genetic or coagulation tests may be planned. Since test results may be misleading during the acute thrombosis period, it is more appropriate to schedule the tests a few weeks later or after the end of treatment. In patients with a high thrombosis risk score and elevated D-dimer levels, extremity vein Doppler ultrasonography and computed pulmonary angiography are used as imaging studies. Oral or parenteral anticoagulants are used in the treatment of venous thromboembolism. These include low molecular weight heparin, FXa inhibitors (apixaban, rivaroxaban), and vitamin K antagonist (warfarin). The most commonly used are low-molecular-weight heparin, FXa inhibitors (apixaban, rivaroxaban), and vitamin K antagonists (warfarin). Anticoagulant therapy should last at least 3 months, after which patients should be evaluated based on their risk status. Anticoagulant therapy should be longer-term in patients with ongoing diseases or conditions that trigger thrombosis (such as antiphospholipid syndrome, active autoimmune disease, cancer). Patients should be carefully monitored for bleeding during anticoagulant therapy. Thrombolytic or interventional treatments may be administered to patients presenting with acute heart failure and hypotension. Patients should continue to be monitored after anticoagulant therapy, and physical therapy should be provided for patients with postthrombotic syndrome.

Key words: Hypecoagulability, venous tromboembolism, anticoagulant therapy.

https://doi.org/10.1016/j.htct.2025.106186

Abstract 010

THE PLACE OF IMMUNOTHERAPY IN ALL

Mehmet Bakırtaş

Tekirdag City Hospital, Türkiye

In patients with acute lymphoblastic leukemia (ALL), although 80-90% of adult patients achieve a complete response (CR), cure rates are only 40% with initial treatment and 10%-20% with subsequent salvage treatments. Ten percent of patients are refractory to initial treatment, and 40%-70% relapse. Allo-HCT is the standard of care for a fit and eligible group. Immunotherapies are an important choice in improving treatment success and reducing side effects. The primary immunotherapies include bispecific antibodies (BsAbs), antibody-drug conjugates, CAR T-cell, and CAR NK-cell therapies. Blinatumomab activates T cells by binding to

CD19 on B-ALL cells and CD3 on T cells, leading to polyclonal expansion of cytotoxic T cells, T-cell activation, and the release of cytokines and cytotoxic granules. thus causing lysis of CD19+ lymphoblasts. It is approved for the treatment of Ph (-) Relapsed/Refractory (R/R) B-ALL and has received FDA approval for consolidation therapy in patients with MRD-positive disease and for MRD-independent consolidation therapy. The Alcantara study demonstrated sustained responses in patients with Ph(+) R/R ALL. Inotuzumab is an antibody-drug conjugate containing calicheamicin, an anti-CD22-targeted, DNA-binding cytotoxic antibiotic. It received FDA approval after inotuzumab monotherapy demonstrated superiority over standard chemotherapy for relapsed/refractory CD22(+) B-ALL. The most common Grade ≥3 adverse events were hematologic and liver-related and included an 11% VOD, mostly seen after sequential allo-HSCT. Inotuzumab monotherapy has shown high CR and MRD negativity rates when used in combination with reduced-intensity chemotherapy in the first-line setting in elderly patients. Cell-based therapies have demonstrated efficacy in R/RB-ALL with CD19-targeted therapies such as tisagen-lecleucel (tisa-cel) for patients aged ≤25 years and brexucabtagene autoleucel for adults, despite the side effects that limit CAR T cells. Side effects include cytokine release syndrome, immune effector cell-associated neurotoxicity syndrome (ICANS), and B-cell aplasia. Studies of CD5-CART, CD7-CART, and NS7CAR are ongoing for relapsed/refractory T-cell leukemia. Although experimental, CAR-NK therapies, which use NK cells isolated from peripheral blood and do not pose a risk of GVHD, show promise with fewer side effects, fewer relapses, and longer survival. Studies of immune checkpoint inhibitors combined with other immunotherapies may be important for B-ALL, while combinations of BCL-2 and BCL-XL inhibitors with chemotherapy may be important for T-ALL, for which no antibody therapy is currently available. Difficulties continue to arise in the treatment of T-ALL and Ph-like ALL. Immunotherapy and cellular therapies are being studied in optimal combinations.

https://doi.org/10.1016/j.htct.2025.106187

Abstract 011

DIAGNOSIS AND MANAGEMENT OF EOSINOPHILIA

Esra Cengiz

Bilkent City Hospital, Türkiye

Eosinophilia is defined as an absolute eosinophil count greater than 500/μL in peripheral blood and is characterized by a broad clinical spectrum, ranging from transient, benign processes to severe, life-threatening hematologic malignancies. The severity of eosinophilia has been classified into three categories: mild (500–1,500/μL), moderate (1,500–5,000/μL), and severe (>5,000/μL). Persistent elevations above 1,500/μL, particularly when accompanied by tissue infiltration, are defined as hypereosinophilia. This condition can progress to hypereosinophilic syndromes (HES), with multisystem organ damage. The most frequently involved are the skin, lungs, gastrointestinal tract, cardiovascular system, and central nervous system. A stepwise and comprehensive diagnostic approach is essential for the evaluation of eosinophilia. A comprehensive medical history and physical examination should address the following: allergic and atopic disorders, travel to endemic regions for parasitic diseases, drug exposures, and family history suggestive of hereditary conditions. Initial laboratory evaluation includes complete blood count and peripheral smear to verify eosinophilia and identify dysplastic features. The diagnostic evaluation should begin with the exclusion of secondary causes, which comprise parasitic and fungal infections, allergic or atopic conditions (e.g., asthma, atopic dermatitis), drug hypersensitivity, autoimmune/connective tissue diseases, and certain solid tumors. When secondary causes are excluded, primary or clonal eosinophilia must be considered. Bone marrow aspiration/biopsy, cytogenetic analyses, flow cytometry, and molecular assays (e.g., FIP1L1–PDGFRA, PDGFRB, FGFR1, JAK2, BCR-ABL mutations) are essential for differentiating neoplastic eosinophilia. When organ involvement is clinically suspected, assessment often includes imaging modalities (CT, MRI), echocardiography, pulmonary function testing, and endoscopic procedures. The approach to treatment depends on the underlying pathology, disease severity, and the presence or absence of organ involvement. In secondary eosinophilia, management includes targeted therapy such as anti-parasitic agents, discontinuation of causative drugs, or treatment of underlying autoimmune or malignant disorders. Systemic corticosteroids remain the first-line intervention for many patients, particularly those with symptomatic hypereosinophilia or organ-threatening disease, due to their rapid effect in lowering eosinophil counts and mitigating tissue injury. In primary or clonal eosinophilia, treatment varies with molecular findings. Patients with FIP1L1–PDGFRA–positive myeloproliferative variants typically respond dramatically to tyrosine kinase inhibitors such as imatinib. Other cytoreductive agents, including hydroxyurea and interferon-α, may be used in refractory or steroid-intolerant cases. In acute eosinophilic leukemia, intensive chemotherapy or hematopoietic stem cell transplantation may be indicated. Monoclonal antibodies directed against interleukin-5 (mepolizumab, reslizumab) or its receptor (benralizumab) have demonstrated significant efficacy in reducing blood and tissue eosinophil counts, improving clinical outcomes in HES, eosinophilic asthma, and other eosinophil-mediated disorders. These agents provide a more targeted approach with fewer systemic toxicities compared to traditional immunosuppressants, representing a paradigm shift in long-term disease management. In conclusion, eosinophilia is not a diagnosis in itself but a clinical finding requiring careful evaluation to distinguish reactive from clonal causes. Early recognition of hypereosinophilia and prompt assessment of target organ involvement are vital to prevent irreversible complications. Advances in molecular diagnostics and targeted biologic therapies have markedly improved the ability to personalize treatment and enhance prognosis. Future research will likely further explain the causes of the disease and expand the available treatments, which will in turn improve long-term results for patients with eosinophilia.

https://doi.org/10.1016/j.htct.2025.106188