therapies, phenotype-specific treatments, and curative strategies. Allogeneic hematopoietic stem cell transplantation and the recently approved gene therapies based on CRISPR-Cas9 (Exa-cel) and lentiviral vectors (Lovo-cel) have ushered in a new era, offering curative potential for eligible patients. The future therapeutic algorithm is anticipated to become even more personalized through the integration of these revolutionary treatments.

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Abstract 007

WALDENSTRÖM MACROGLOBULINEMIA

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Waldenström Macroglobulinemia (WM) is a rare disease. The median age at diagnosis is 70 years and approximately 60 percent of patients are male. The etiology of WM is not fully understood. Approximately 90-95% of WM patients have mutations in the MYD88 L265P gene and 40% have recurrent mutations in the CXCR4 gene. The clonal B cell population leads to abnormal monoclonal IgM production. The pentameric configuration of IgM molecules increases serum viscosity, slowing blood flow through capillaries. In patients with WM, clonal B cells can directly infiltrate hematopoietic tissues, causing cytopenias (e.g., anemia, thrombocytopenia, neutropenia), lymphadenopathy, hepatomegaly, and/or splenomegaly. Rarely, plasmacytoid lymphocytes may infiltrate the central nervous system or meninges. Most patients with WM present with nonspecific constitutional symptoms but up to a quarter of patients may be asymptomatic at diagnosis. Common symptoms include weakness, fatigue, weight loss, and nose and gum bleeding. Bone marrow aspiration and biopsy demonstrating lymphoplasmacytic lymphoma is an important component of the diagnosis of WM. The biopsy specimen is usually hypercellular and densely infiltrated with lymphoid and plasmacytoid cells. Intranuclear vacuoles containing IgM monoclonal protein (Dutcher bodies) are common in the malignant cells of WM. The following criteria must be met for a diagnosis of WM: • IgM monoclonal gammopathy (any level) must be present in the serum. • ≥10% of the bone marrow biopsy specimen must show infiltration by small lymphocytes with plasmacytoid or plasma cell differentiation (lymphoplasmacytic features or lymphoplasmacytic lymphoma) and an intertrabecular pattern. • The infiltrate should express a typical immunophenotype (e.g., surface IgM +, CD5-/+, CD10-, CD11c-, CD19+, CD20+, CD22+, CD23-, CD25 +, FMC7+, CD103-, CD138-). The plasmacytic component will be CD138+, CD38+, and CD45- or less prominent. The differential diagnosis includes chronic lymphocytic leukemia, marginal zone and mantle cell lymphoma. Not every VM patient requires treatment. For asymptomatic patients, follow-up without treatment every 3-6 months is recommended. Treatment is indicated for patients with symptomatic WM if any of the following are attributable to WM: • Systemic symptoms: B symptoms such as recurrent fever, severe night sweats, fatigue and/or unintentional weight loss • Cytopenias: Hemoglobin ≤10 g/dL or platelet count <100,000/microL; cold agglutinin anemia, immune hemolytic anemia, and/or thrombocytopenia • Symptomatic or large (≥5 cm) lymphadenopathy, symptomatic splenomegaly and/or tissue infiltration • End-organ damage: Hyperviscosity, peripheral neuropathy, immunoglobulin light chain (AL) amyloidosis with organ dysfunction, symptomatic cryoglobulinemia, pleural effusions or nephropathy due to WM Symptomatic hyperviscosity in a patient with an indication for treatment requires urgent plasmapheresis. Signs and symptoms associated with hyperviscosity include oronasal hemorrhage, blurred vision, headache, dizziness, paresthesia, retinal vein occlusion, papilledema, stupor, and coma. In patients with treatment indications but without symptoms of hyperviscosity, options include rituximab plus bendamustine or Bruton's tyrosine kinase inhibitors (such as ibrutinib, zanubrutinib, or acalabrutinib). Treatment of relapsed or refractory disease may include Bruton's tyrosine kinase inhibitors, bendamustine plus rituximab, nucleosome analog-based regimens, and venetoclax, if not previously used. High-dose chemotherapy and autologous or allogeneic hematopoietic cell transplantation (HCT) are rarely used in the treatment of WM.

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Abstract 008

REFRACTORY CHRONIC MYELOID LEUKEMIA: A REVIEW OF CURRENT THERAPEUTIC LANDSCAPE AND EMERGING CHALLENGES

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Chronic myeloid leukemia (CML) has become a paradigm of targeted therapy success; however, a proportion of patients develop refractory disease, marked by failure or intolerance to multiple TKIs. Optimal management requires integrating molecular, clinical, and patient-related factors into therapeutic decision-making [1,2]. **Mechanisms of Resistance and Genetic Complexity:** Resistance is commonly mediated by BCR::ABL1 kinase domain mutations. While second-generation TKIs (dasatinib, nilotinib, bosutinib) address many resistant clones, the T315I substitution remains uniquely sensitive to ponatinib [3,4]. Beyond kinase domain changes, clonal evolution with mutations in ASXL1, RUNX1, IKZF1, TP53, and DNMT3A has been increasingly recognized. These lesions, frequently encountered in advanced phases, are associated with poor response to TKIs, higher risk of progression, and inferior survival [5,6]. **Current Therapeutic Approaches:** Ponatinib remains the agent of choice for patients harboring T315I or compound mutations, with careful risk management to mitigate vascular events [4]. Asciminib, a first-in-class STAMP inhibitor targeting the myristoyl pocket of BCR::ABL1, has emerged as a major advance. By restoring kinase autoinhibition, asciminib demonstrated superior efficacy and tolerability over bosutinib in the ASCEMBL trial [3] and has shown promising results in real-world refractory populations. **TKI Selection Considerations:** In clinical practice, TKI selection is

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].

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Abstract 009

HYPERCOAGULABILITY: ETIOLOGY, DIAGNOSIS AND TREATMENT PRINCIPLES

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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.

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Abstract 010

THE PLACE OF IMMUNOTHERAPY IN ALL

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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