underscore the central role of hematology in the comprehensive management of this condition.

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Abstract 017

OPTIMIZATION OF TYROSINE KINASE INHIBITORS IN CHRONIC MYELOID LEUKEMIA

Nanişe Gizem Fener

Bozyaka Training And Research Hospital, Türkiye

In the treatment of chronic myeloid leukemia (CML), first-line tyrosine kinase inhibitor (TKI) choice should be individualized. According to current guidelines, not only risk scores (Sokal, Hasford, ELTS) but also patient-specific factors must be considered. In young patients with high-risk disease, second-generation TKIs (dasatinib, nilotinib, bosutinib) are recommended to achieve deeper and faster responses, thereby increasing the likelihood of future treatment-free remission (TFR). For elderly or low-risk patients, first-generation imatinib remains a safe and effective option.Comorbidities significantly influence drug choice The type of BCR-ABL1 transcript should also be considered; while common variants do not consistently affect outcomes, rare atypical transcripts may influence monitoring and drug selection.Molecular response must be closely monitored with RT-qPCR (international scale, %IS) every three months. Achieving BCR-ABL1 targets of ≤10% at 3 months, ≤1% at 6 months, and ≤0.1% at 12 months (major molecular response, MMR) strongly predicts better long-term outcomes and TFR achievement.BCR-ABL1 >10% at 3 months is considered a warning, while failure to achieve MMR by 12 months is an adverse prognostic sign. Once stable MMR is achieved, monitoring can be extended to every 3–6 months, but in potential TFR candidates or in cases of suspected relapse, more frequent testing is recommended.For patients with primary or secondary resistance, mutation analysis of the BCR-ABL1 kinase domain is strongly recommended. Mutations determine TKI sensitivity and guide therapeutic choices. The T315I “gatekeeper” mutation confers resistance to all first- and second-generation TKIs; in such cases, ponatinib or the novel allosteric inhibitor asciminib is preferred. Other mutations, such as P-loop (Y253H, E255K/V, F359), reduce nilotinib sensitivity but may still respond to dasatinib, bosutinib, or ponatinib. Conversely, mutations like F317L reduce dasatinib efficacy. Thus, therapy must be tailored to the patient’s mutational profile.In cases of intolerance, dose reduction is the first strategy rather than immediate drug substitution.Persistent grade 3–4 toxicities, however, necessitate switching to another TKI. Ponatinib should be initiated at the lowest effective dose, with further reductions once major molecular response is achieved, in order to mitigate cardiovascular risks. The favorable safety profile of asciminib makes it an important option for patients intolerant to multiple TKIs. TFR is feasible in patients with durable deep molecular responses (MR^4 or MR^4.5) after at least 4–5 years of TKI therapy. Eligibility criteria include:chronic-phase disease only, no history of accelerated/blast phase, no prior resistance, and reliable PCR monitoring. Following TKI discontinuation, BCR-ABL1 should be monitored monthly for the first 6–12 months and every 2–3 months thereafter. Loss of MMR (≥0.1%) requires immediate TKI reinitiation, and responses are typically regained quickly. Longer duration of TKI therapy and prolonged deep response increase the likelihood of durable TFR. TKI optimization in CML must be individualized, balancing risk scores, comorbidities, transcript types, molecular milestones, and mutation status. Intolerance can often be managed with dose reduction or switching to alternative TKIs, while TFR remains an attainable and important quality-of-life goal for appropriately selected patients.

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Abstract 018

Mastocytosis

Filiz Yavaşoğlu

Osmangazi University Faculty of Medicine, Türkiye

Mastocytosis is a rare, heterogeneous myeloid neoplasm characterized by clonal proliferation and abnormal accumulation of mast cells. It is classified into cutaneous mastocytosis (CM), systemic mastocytosis (SM), mast cell sarcoma (MCS), and extracutaneous mastocytoma. SM comprises indolent and smouldering variants as well as advanced forms, including aggressive SM and mast cell leukemia. Clinical manifestations range from asymptomatic disease to life-threatening presentations with cytopenia, malabsorption, hepatosplenomegaly, lymphadenopathy, ascites, or osteolytic bone lesions. Mediator-related symptoms such as flushing, diarrhea, and anaphylaxis are common. The KIT D816V gain-of-function mutation represents the central pathogenic driver, leading to ligand-independent KIT activation and uncontrolled mast cell proliferation. Diagnosis relies on WHO and ICC criteria, integrating histopathology, immunophenotyping, and KIT mutation analysis. Management depends on disease subtype: non-advanced forms are treated symptomatically with antihistamines, mast cell stabilizers, and trigger avoidance, while advanced SM requires cytoreductive agents and KIT inhibitors. Midostaurin and avapritinib, potent inhibitors of KIT D816V, have demonstrated significant improvements in mediator-related symptoms, overall survival, and quality of life, whereas imatinib is ineffective in D816V-positive patients but may benefit other KIT genotypes (e.g., K509I, V560G, F522C). Emerging inhibitors such as bezuclastinib and elenestinib show promising efficacy. Allogeneic hematopoietic stem cell transplantation remains the only curative option for aggressive SM. In summary, mastocytosis is a clinically heterogeneous disease in which early-stage treatment focuses on symptom control and anaphylaxis prevention, whereas advanced disease benefits from targeted therapy that has markedly improved prognosis.

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