How to Optimize CML Treatment in 2026. ELN 2025 and Molecular Guidance

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The survival of patients with chronic myeloid leukemia (CML) has improved markedly since the advent of the BCR::ABL1 tyrosine kinase inhibitors (TKIs). With TKIs and proper management, the expected survival of patients with CML in chronic phase (CML-CP) is approaching that of the normal age-adjusted population. Any of the five TKIs, (imatinib, dasatinib, nilotinib, bosutinib, asciminib) approved for frontline therapy of CML-CP may be selected. Second-generation TKIs and asciminib are superior to imatinib in achieving faster and deeper molecular responses, but survival is similar because of the availability of effective TKI salvage therapies. Factors considered in choosing frontline TKI therapy include the goal of therapy, patient age, existing comorbidities, CML risk score, and cost of treatment. The ABL1 kinase domain mutation and ABL1 myristoyl mutation profiles play no role in selecting the initial TKI but become relevant in relapse. Most TKIs are reasonably well tolerated with close observation and supportive care. However, each TKI has a distinct toxicity profile that should be considered when deciding on therapy. In patients with intolerance to TKI therapy, the TKI dose should be reduced or modified before switching to a different TKI, unless the toxicity is prohibitive. With the availability of generic imatinib and generic second-generation TKIs, all patients with CML should have access to effective therapies. Allogeneic stem cell transplantation should be considered in patients with CML who progress to accelerated or blast phase (in combination with chemotherapy) after TKI therapy failure and those who have CML resistance to second- or third-generation TKIs while still in chronic phase.