Abstract 012

TREATMENT-FREE REMISSION IN CHRONIC MYELOID LEUKEMIA: CURRENT EVIDENCE, PREDICTORS, AND FUTURE DIRECTIONS

Yunus Çatma

Istanbul University Faculty of Medicine, Türkiye

Background: The advent of tyrosine kinase inhibitors (TKIs) has revolutionized the management of chronic myeloid leukemia (CML), transforming it into a chronic condition with near-normal life expectancy. In this context, treatment-free remission (TFR)—defined as the maintenance of deep molecular response after discontinuation of TKIs—has emerged as a new therapeutic milestone beyond survival and disease control. While multiple clinical trials and real-world cohorts have demonstrated the feasibility and safety of TFR, several biological, molecular, and clinical factors continue to shape patient selection and long-term outcomes. **Content:** This presentation synthesizes evidence from pivotal discontinuation trials (STIM, EURO-SKI, ENESTfreedom, ENESTop, DASFREE, DESTINY) as well as real-world studies from Europe, Asia, and North America. Updated recommendations from international guidelines (ELN 2020/2025, NCCN 2025) are reviewed alongside emerging biological insights, including immune surveillance, transcript types, and microenvironmental regulation of leukemia stem cells. Novel approaches such as dose de-escalation, immunotherapy combinations, and predictive modeling are critically examined to delineate future directions in TFR research. **Results:** Clinical evidence consistently shows that sustained TFR is achievable in approximately **40–60%** of patients after ≥3 years of TKI therapy and ≥2 years of stable deep molecular response (DMR). Higher success rates have been reported in Japanese cohorts (up to 63%), underscoring the influence of patient selection and monitoring intensity. 1. **Relapse dynamics:** Most relapses occur within the first 6–12 months, with >95% of patients regaining major molecular response (MMR) after restarting TKIs. Late relapses are rare but underscore the necessity of lifelong molecular monitoring. 2. **Predictors of success:** Longer TKI duration (≥5 years), sustained MR4.5, and the e14a2 transcript type are consistently associated with improved outcomes. Immunological parameters, particularly increased NK cell activity and reduced regulatory T-cell frequencies, also correlate with durable remission. 3. **Therapeutic strategies:** Dose de-escalation (e.g., DESTINY trial) has been shown to reduce relapse risk and mitigate withdrawal symptoms. Second TFR attempts, as demonstrated in DAstop2, are feasible and safe for selected patients. 4. **Adverse effects:** Approximately 30–40% of patients experience musculoskeletal discomfort—termed "TKI withdrawal syndrome"—which is typically mild and self-limiting. **Discussion:** TFR represents a paradigm shift in CML care, reflecting both biological disease control and patient-centered goals such as quality of life and long-term safety. While most relapses are molecular and rapidly reversible, careful patient selection and standardized monitoring remain essential to ensure safety. Regional differences highlight the importance of infrastructure: countries with frequent PCR monitoring and strong patient compliance report superior outcomes. Immunological studies suggest that durable TFR depends on effective immune surveillance, with NK cells and T-cell subsets emerging as potential biomarkers. Moreover, mathematical modeling of leukemia stem cell–microenvironment interactions provides new insights into relapse biology. Future research will likely integrate these biomarkers into predictive algorithms to personalize TFR eligibility. Importantly, novel combinations—such as TKI with interferon-α or immune checkpoint blockade—are under active investigation and may enhance remission durability. **Conclusion:** TFR is now established as a safe and realistic treatment goal in selected CML patients, particularly those with prolonged TKI exposure and stable deep molecular responses. Success rates of 40–60% can be expected, with >95% of relapsed patients regaining response upon retreatment. Ongoing efforts should focus on refining patient selection through biomarkers, enhancing durability with immunotherapy-based combinations, and harmonizing monitoring practices globally.

Keywords: CML, TFR, Tyrosine Kinase Inhibitors, Deep Molecular Response, Immunotherapy.

https://doi.org/10.1016/j.htct.2025.106189

Abstract 013

THE PAST, PRESENT, AND FUTURE OF TRANSFUSION

Mahmut Bayık

Istanbul Academic Hospital, Türkiye

Blood has attracted human interest since the dawn of history. The human spirit, strength, and character have been identified with blood. The first known human-to-human blood transfusion (1492) was performed on Pope Innocent VIII with the aim of rejuvenating him, using blood from three young men. This procedure ended with the death of the Pope and the young donors. Initially, blood transfusions were attempted from animal to animal, followed by attempts at blood transfusions from animal to human. A blood transfusion from a lamb to a human was performed to calm a person with mental disorders, followed by attempts at blood transfusions from various animals to humans. Following acute hemolysis cases that ended in death, the Paris Medical Association declared this practice illegal and banned it. The first human-to-human transfusion was performed by American Dr. Philip Syng Physick. Another significant example in the field of transfusion is James Blundell's blood transfusions from husbands to women with postpartum hemorrhage. Five of the ten transfusions performed by Blundell were successful. The discovery of blood groups by Karl Landsteiner (1901) marks a turning point in the history of transfusion. The A, B, and O blood groups were discovered first, followed by the AB blood group a year later, and the Rh blood group in 1939. The subantigens of the Rh blood group were discovered in 1944. In 1942, Bernstein discovered that blood groups are inherited in humans according to Mendel's laws. In 1946, the Kell, Duffy,