Abstract 012

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

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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.

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Abstract 013

THE PAST, PRESENT, AND FUTURE OF TRANSFUSION

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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,

and Kidd blood group systems were discovered. Today, there are over 360 different blood group antigens within 48 blood group system. Landsteiner won the Nobel Prize in 1930 for his discovery of blood groups. In 1907, it was recognized that blood group compatibility between donor and patient was necessary, and the first cross-matching tests were performed by Ruben Ottenberg. With these studies, Ottenberg demonstrated that the O blood group is a universal donor. A milestone in blood banking was the use of sodium citrate, an anticoagulant, in blood transfusions (1914-1915) (Hustin, Agote, Levishon). Prior to this discovery, transfusions were performed by transferring blood from the donor to the patient using syringes or vascular anastomoses. However, with the ability to store blood without clotting, transfusions began to be performed by transferring blood from the donor into a glass bottle containing citrate and then to the patient. The world's first blood bank was established in England in 1921 by Oliver Percy. Later, with the addition of dextrose, phosphate, adenine, and mannitol mixtures, blood could be stored for up to 42 days in four-degree blood refrigerators. In 1930, Russian Shamov performed the first transfusion of cadaver blood to a living person. In the following years, transfusions were performed on 2,500 people using this method. In 1935, the International Society of Blood Transfusion (ISBT) was founded. At its 1937 congress, the ISBT adopted the ABO terminology for blood grouping. In 1950, plastic blood bags were developed. In 1953, blood components were obtained using a refrigerated centrifuge method. In 1968, the first apheresis devices were developed. In Turkey, the first human-to-human transfusion was performed at Haydarpaşa Numune Hospital in 1932. Starting in 1945, small blood units were established in some hospitals. In 1957, Red Crescent blood banks were established first in Ankara and then in Istanbul. In 1983, Law No. 2857 on Blood and Blood Products was enacted in Turkey. In ....., a new blood law and related regulations were enacted in light of scientific developments. Accordingly, Red Crescent Regional Blood Centers and Hospital Transfusion Centers were established. Guidelines were developed. Mandatory screening tests were initiated for diseases transmitted through transfusion, including HBV, syphilis, malaria, HIV, and most recently HCV. In 1996, the Blood Centers and Transfusion Association (KMTD) was established. In 1997, a donor screening form was created and its use was made mandatory throughout Turkey. When KMTD was established, whole blood usage in Turkey was over 95%. KMTD, in collaboration with the Ministry of Health, held 118 educational meetings in 74 provinces, explaining blood components, transfusion indications and complications, and blood bank-clinic relationships. As a result, component usage was adopted throughout the country. Annual courses and conferences were held to keep pace with developments worldwide and in Turkey. Recently, training has focused particularly on Hemovigilance (blood monitoring system) and Patient Blood Management. Currently, components are used not only for component requirements but also for various treatment options. For this purpose, platelets, mesenchymal stem cells, and plasma are used in regenerative medicine and wound healing. In light of scientific and technological developments, the following developments are expected in the field of transfusion in the future: Artificial blood (oxygen-carrying hemoglobin derivatives and engineered products), Universal blood production and conversion of erythrocytes from various blood groups to O-type erythrocytes (cell tissue engineering), digital and automation systems, and artificial intelligence will enable fast and accurate data analysis, reduction of human error, reduction of infection risk, and the use of advanced bioprinters.

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Abstract 014

PLATELET FUNCTION DISORDERS: CONTEMPORARY INSIGHTS AND FUTURE DIRECTIONS

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Platelet function disorders (PFDs) represent a diverse group of qualitative platelet defects that often remain underdiagnosed despite normal platelet counts. Their clinical relevance extends beyond hematology, as undetected PFDs contribute to perioperative bleeding, complications in oncology, and challenges in balancing hemostasis with cardiovascular protection during antiplatelet therapy. For hematologists, timely recognition of these disorders is critical for optimal patient care. Inherited PFDs (IPFDs) include Glanzmann thrombasthenia, Bernard–Soulier syndrome, and RUNX1-associated familial platelet disorder, each characterized by distinct receptor or signaling abnormalities. These range from impaired fibrinogen binding (αIIbβ3 defects) to defective adhesion (GPIb–IX–V complex deficiencies). Syndromic forms such as Wiskott–Aldrich syndrome illustrate the intersection of platelet dysfunction, immune dysregulation, and malignancy predisposition. The spectrum of bleeding can vary considerably. Acquired PFDs are more frequent and clinically impactful. Drugs such as aspirin and P2Y12 inhibitors, uremia, advanced liver disease, myeloproliferative neoplasms, and xtracorporeal circulation all compromise platelet activation or secretion. Given their prevalence, distinguishing pharmacologic platelet inhibition from true dysfunction is a practical challenge in routine hematology. Diagnosis requires a structured, tiered approach. Clinical history and bleeding scores remain the foundation, but must be complemented by laboratory assays. Initial testing should exclude von Willebrand disease, while light transmission aggregometry, flow cytometry, and secretion assays provide functional insights. Next-generation sequencing now allows precise molecular classification of many IPFDs, though accessibility remains uneven. Novel technologies, including microfluidics and whole-blood shear assays, ... Therapeutic strategies depend on etiology and severity. Antifibrinolytics and desmopressin are often sufficient for mild bleeding; platelet transfusions and recombinant factor VIIa are mainstays for severe inherited forms, particularly Glanzmann thrombasthenia complicated by alloimmunization. Hematopoietic stem cell transplantation offers curative potential in selected syndromic disorders. In acquired dysfunction, correcting underlying disease or adjusting medications is essential. Personalized perioperative