Following the administration of induction chemotherapy, complete remission (CR) is observed in approximately 73% - 45% of patients in the ELN-2022 favorable-adverse risk groups, respectively. However, overall survival (OS) and progression-free survival (PFS) are not satisfactory despite current treatments. The five-year PFS was estimated at 52% - 16%, and the five-year OS was 55% - 15%, respectively. As the pathogenesis of AML becomes clearer, clinical trials on current targeted therapies are increasing, and being developed to accompany or replace standard AML treatments that have been similar for nearly 50 years. It is now evident that epigenetic-based treatments can lead to significant changes in the fundamental model that underpins therapeutic interventions. The combination of BCL2 inhibitor venetoclax with hypomethylating agents has significantly improved survival, particularly in elderly and unfit patients. Studies are ongoing to combine intensive therapies with induction and consolidation therapy. Three FLT3 inhibitors (midostaurin, gilteritinib, and quizartinib) have shown promising results in induction and consolidation therapies, salvage therapies, and follow-up therapies after allogeneic transplantation. A phase Ib-II trial of crenolinib, a potent type I second-generation FLT3 inhibitor, demonstrates that its use with intensive therapy in newly diagnosed AML patients under 60 years of age improves survival and results in higher rates of MRD negativity. In addition, ongoing trials are also evaluating the 7 + 3 + midostaurin versus 7 + 3 with gilteritinib (NCT04027309). Other targeted studies are ongoing with IDH inhibitors (ivosidenib and olutasidenib targeting IDH1 mutations; enasidenib targeting IDH2 mutations). Olutasidenib has been shown to provide better response rates and survival compared to ivosidenib in elderly, unfit patients, and combination with azacitidine also increases OS. Other promising studies for AML appear to be focused on menin inhibitors. The phase 1 trial of Revumenib (AUGMENT-101 trial) and Ziftomenib (KOMET-001 trial) (both studies in patients with KMT2A rearranged and NPM1m R/R AML) have yielded positive results, and phase 2 trials are eagerly awaited. A phase 1 trial evaluating a third oral Menin inhibitor, JNJ-75276617, results rates were similar to the other 2 inhibitors. Clinical trials are now ongoing these drugs in combination with additional low dose and high dose chemotherapy regimens (NCT05735184, NCT05886049). Another area is immunotherapy in AML. The success of allogeneic stem cell transplantation has demonstrated the potential for immunotherapy. Talacotuzumab and Pivekimab, targeted to CD123, appear to be particularly effective in relapsed-refractory (R/R) patients, and combination studies with FLAG-IDA are ongoing. Additionally, Tagraxofusp, a drug containing IL-3 ligand conjugated to the first 388 amino acids of diphtheria toxin, has been studied combination with Azacitidine/Venetoclax in newly diagnosed AML patients. MRD negativity was found in 71% of patients. Magrolimab, which acts on CD47, has promising results in patients with R/R AML. The potential of ongoing targeted therapies to provide new insights into the treatment of AML.

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Abstract 003

OLD TRADITIONS IN A NEW VILLAGE*... WHY ARE FACTORS STILL NECESSARY? CONTEMPORARY PARADİGMS İN HEMOPHILIA MANAGEMENT AND THE IRREPLACEABLE ROLE OF FACTOR REPLACEMENT

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Hemophilia is an X-linked recessive hereditary coagulation disorder characterized by a deficiency of factor VIII (hemophilia A) or factor IX (hemophilia B). Beginning in childhood, it constitutes a lifelong global health problem, associated with substantial morbidity, mortality, and treatment costs. While novel approaches—including gene therapies and non-factor-based biologic agents—are reshaping therapeutic strategies, factor replacement therapies remain the indispensable cornerstone of hemophilia management due to persistent clinical, biological, and economic limitations. **Gene Therapy:** Gene transfer techniques utilizing adeno-associated virus (AAV) vectors (e.g., valoctocogene roxaparvovec, etranacogene dezaparvovec) have shown promise in maintaining sustained factor levels in adults. However, in pediatric populations, hepatocyte proliferation inevitably leads to loss of transgene expression. In addition, immune responses, hepatotoxicity, and the inability to administer repeat dosing represent major barriers to safety and efficacy in children. Ethical concerns further complicate implementation. For these reasons, gene therapy does not appear to be a feasible treatment option for pediatric hemophilia in the near future. **Non–Factor-Based Agents:** Emicizumab, a bispecific antibody that mimics the bridging function of factor VIII, has significantly reduced bleeding frequency and revolutionized care, particularly in hemophilia A patients with inhibitors. Its subcutaneous administration enhances treatment adherence. Nevertheless, its inability to rapidly increase factor levels in emergencies such as major surgery or trauma is a critical limitation. Likewise, RNA interference (RNAi) therapies such as fitusiran and tissue factor pathway inhibitor (TFPI) inhibitors (concizumab, marstacimab) have shown encouraging results in clinical trials. However, thrombotic risks and uncertainties surrounding long-term safety restrict their use in pediatric populations. **Factor Replacement Therapy:** Standard and extended half-life (EHL) FVIII/FIX concentrates, supported by more than four decades of safety data, continue to form the foundation of prophylaxis in childhood. EHL products have reduced treatment burden with once- or twice-weekly dosing, while playing a vital role in maintaining joint health and preventing trauma-related bleeding episodes. Factor replacement therapy remains the gold standard for the management of acute bleeding. **Global Access and Health Economics:** Gene therapies and biologic agents are accessible almost exclusively in high-income countries due to their prohibitive costs (USD 2–3 million per treatment; emicizumab approximately USD 400,000 annually). In contrast, in low- and middle-

income countries, factor replacement remains the only feasible option, in line with World Federation of Hemophilia (WFH) recommendations. **Conclusion:** Despite recent paradigm shifts in the treatment of pediatric hemophilia, factor replacement remains indispensable. Gene therapies hold promise for the future, but biological and ethical constraints currently prevent their application in children. Non–factor-based agents have facilitated prophylaxis but are insufficient in emergencies and lack long-term safety data, particularly in major surgical procedures and severe acute bleeding episodes. Factor replacement therapies, with their proven efficacy, predictable pharmacokinetics, established safety, and global accessibility, continue to stand as the gold standard treatment option for both today and the foreseeable future. *"A reference to a Turkish idiomatic saying, originally 'Introducing a new custom to an old village' (bringing new ways to an old place), which means introducing a revolutionary, unusual, or unexpected innovation or behavior into a traditional, clichéd order or way of doing things."

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Abstract 004

IRON CHELATİON İN MYELODYSPLASTİC SYNDROMES: WHO AND WHEN?

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Red blood cell (RBC) transfusions are the cornerstone of supportive care in patients with myelodysplastic syndromes (MDS). While transfusions alleviate symptomatic anemia, they inevitably lead to progressive iron accumulation in patients. This transfusional iron overload may exert toxic effects on the heart, liver, endocrine system, ultimately contributing to increased morbidity and mortality. Timely initiation of iron chelation therapy has become an important consideration in the comprehensive management of MDS. Chelation is primarily indicated for patients with lower-risk MDS (IPSS low or Int-1) who are expected to have longer survival, who remain transfusion-dependent. In such patients, iron overload not only threatens organ function also worsens prognosis. Multiple studies have shown that transfusion dependence is a negative prognostic factor, and retrospective analyses suggest that iron chelation may improve overall survival. Chelation is also particularly important in patients who are candidates for allogeneic stem cell transplantation, since excess iron has been associated with inferior transplant outcomes. By reducing systemic iron burden, chelation help optimize organ function and improve transplant eligibility. The decision is usually guided by transfusion history and serum ferritin levels. Most guidelines recommend considering chelation after approximately 20–30 units of RBC transfusions or when serum ferritin persistently exceeds 2500 ng/mL. The therapeutic goal is to maintain ferritin below 1000 ng/mL, minimizing iron-mediated oxidative stress and tissue damage. While serum ferritin is an imperfect surrogate, it remains a practical marker. More advanced techniques such as MRI T2* or SQUID can provide direct estimates of hepatic iron, but their availability is limited. Three chelators are currently in clinical use. Deferoxamine, administered subcutaneously or intramuscularly, is effective but limited by its parenteral route. Deferasirox, an oral once-daily agent, has become the preferred choice in many cases and is FDA-approved for transfusion-related iron overload. Randomized trials in lower-risk MDS demonstrated that deferasirox reduced ferritin, improved event-free survival, and even enhanced hematologic response in some patients. However, renal, hepatic toxicity require careful monitoring. Deferiprone, another oral agent, is mainly approved for thalassemia, can be considered when other chelators fail, though its use in MDS remains limited due to risk of agranulocytosis. Chelation has been associated with improved overall survival in observational studies, prospective trials provide encouraging evidence. Beyond survival, reversal of some iron-related cardiac, hepatic damage has been documented, underscoring its importance. Monitoring should include serial ferritin, renal, liver function, vigilance for adverse events. Individualization is critical: patients with advanced or high-risk MDS, limited life expectancy are less likely to benefit, and chelation is generally not recommended in such settings. Iron chelation therapy plays a vital role in selected MDS patients. It should be considered in lower-risk individuals with substantial transfusion requirements and elevated ferritin, especially in those with preserved organ function or who are candidates for transplantation. As evidence grows, iron chelation continues to evolve from a supportive measure into a prognostically meaningful intervention in the management of MDS.

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Abstract 005

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP)

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Thrombotic thrombocytopenic purpura (TTP) is a rare but life-threatening thrombotic microangiopathy caused by severe ADAMTS-13 deficiency due to either autoantibodies (immune TTP, iTTP) or biallelic mutations (congenital TTP, cTTP). The first International Society on Thrombosis and Haemostasis (ISTH) guidelines were issued in 2020. Since then, substantial advances in therapeutic strategies and real-world evidence have prompted an ISTH 2025 focused update. The most significant change relates to cTTP prophylaxis. A new strong recommendation was issued in favor of recombinant ADAMTS-13 (rADAMTS-13) over fresh frozen plasma (FFP) in patients in remission. This decision, supported by a phase 3 randomized crossover trial, demonstrated that rADAMTS-13 provides higher and sustained ADAMTS-13 activity and fewer TTP-related manifestations, with a favorable safety profile [1]. Where rADAMTS-13 is unavailable, the panel conditionally recommends FFP over a watch-and-wait strategy, shifting from the neutral stance in 2020 [1,2]. Pregnancy-related cTTP remains a high-risk setting, and prophylactic therapy—preferably rADAMTS-13, or intensified FFP when rADAMTS-13 is