venetoclax-azacitidine has become a first-line treatment for elderly AML patients worldwide who are unfit for intensive therapy. Similarly, the VIALE-C trial, which randomized patients to LDAC/venetoclax versus LDAC/placebo, demonstrated improved CR/Cri (48% vs 13%) and OS (8.4 vs 4.1 months) in the venetoclax arm.(8) The combination of HMAs with other agents, together with the establishment of genetic risk profiles and identification existing mutations, underscores the importance of individualized therapy. Among promising agents, Ivosidenib monotherapy or its combination with HMA has shown superiority in OS, CR/Cri, and EFS for IDH- 1mutated de novo AML (AGILE trail) (9). Patients with TP53 alterations, however, continue to experience significantly worse survival outcomes (10). The CD47 monoclonal antibody magrolimab has demonstrated clinical efficacy when combined with azacitidine or with azacitidine/venetoclax (11).Several multiple novel agents and combinations are under investigation, including fromtline FLT3i, oral HMAs, and triplets combining HMA, venetoclax and targeted agents (12). Considering that none of these regimens are curative, it remains a matter of debate whether dynamically assessing patient frailty and using non-intensive therapies can provide a bridge to allogenic stem cell transplantation.

https://doi.org/10.1016/j.htct.2025.106197

Abstract 021

HEPATIC VENO-OCCLUSIVE DISEASE

Barbaros Şahin Karagün

Adana City Training and Research Hospital, Türkiye

Hepatic veno-occlusive disease, also called sinusoidal obstruction syndrome (VOD/SOS), is a severe complication which usually occurs due to conditioning regimens used for hematopoietic stem cell transplantation (HSCT). It is characterized by hepatomegaly, hyperbilirubinemia, ascites and right upper quadrant pain and usually develops within the first 20-30 days after transplant. It is accepted to be a result of endothelium and hepatocyte damage caused by chemotherapy and radiotherapy of the conditioning regimen. Current studies suggest that the primary site of toxic injury is the hepatocyte, subsequently followed by damage to the central veins in zone 3 of the hepatic acinus and sinusoidal endothelial cells. Early changes include fibrin deposition, venous occlusion, progressive venous micro-thrombosis and sinusoidal occlusion. These changes lead to severe clinical problems including portal hypertension, hepatorenal syndrome and hepatocellular necrosis, which may ultimately result in multiorgan dysfunction (MOD) and death. Previously, the Baltimore and Seattle criteria were used for VOD/SOS diagnosis; however, the limitations of these criteria for VOD/SOS diagnosis (especially in anicteric children and those who have symptom onset after 21 days), led to establishment of the EBMT (European Society for Blood and Marrow Transplantation) 2017 VOD/SOS criteria which evaluates pediatric and adult patients separately. The EBMT 2017 criteria is comprised of laboratory and clinical findings such as transfusion-resistant thrombocytopenia, unexplained weight gain, hepatomegaly, ascites and elevation in bilirubin levels. Despite the advantages brought by this criteria, it is still difficult to diagnose VOD/SOS. Several approaches to prevent its development of VOD/SOS were put forth, including individualized dosing of chemotherapy, reduction of the intensity of the conditioning regimens, close monitoring of the levels of busulfan and cyclophosphamide and also reducing their use. Prostaglandin E1 and tissue-plasminogen activator with or without concurrent heparin have been explored in VOD/SOS treatment; however, these approaches have shown little success, as is the case with supportive treatments. Defibrotide (DF) emerged as the most promising medication for both prophylaxis and treatment in patients with VOD/SOS. DF is a single-stranded polydeoxyribonucleotide with anti-inflammatory, anti-ischemic, anti-thrombotic, and thrombolytic properties in addition to its protective effects on endothelial cells. DF is approved for adult and pediatric patients with VOD/SOS with renal or pulmonary dysfunction after HSCT in the United States, and for severe VOD/SOS post-HSCT in patients aged >1 month in the European Union. In addition, several studies have examined DF prophylaxis can reduce the incidence of VOD/SOS in high-risk patients. Although the literature is unanimous for the use of DF in patients diagnosed with VOD/SOS, its use as a prophylactic agent has not been approved; even though many studies have reported reduced VOD/SOS incidence and severity with DF prophylaxis.

https://doi.org/10.1016/j.htct.2025.106198

Abstract 022

TREATMENT OF RELAPSED/REFRACTORY DLBCL

Hakan Kalyon

Koç University Faculty Of Medicine, Türkiye

Fifteen percent of DLBCL patients are refractory to the first line of therapy, while 25% experience relapse after response. The management of these patients is planned according to the patient's suitability for high-dose chemotherapy and whether the disease is refractory/early relapse (BSH guideline, 2025). While HSCT provides long-term survival in patients who are suitable for treatment and are chemosensitive (CORAL study), long-term survival compared to HSCT has been achieved in non-chemosensitive patients with CAR-T therapies ZUMA-7 and TRANSFORM studies. CAR-T therapies are approved as first-line treatment for patients with refractory/early relapse. However, some r/r DLBCL patients are not suitable for HSCT and CAR-T treatments due to age and comorbidities, and some are resistant to these treatments or relapse after these treatments. Tafasitamab – Lenalidomide combination is approved for patients with relapsed DLBCL, NOS who are not eligible for HSCT or CAR-T therapies (L-MIND study). The efficacy of Glofitamab – GemOx has also been proven in patients with relapsed DLBCL, NOS who are not suitable for HSCT or CAR-T therapy in the STARGLO study. Loncastuximab is a single-agent ADC used in r/r DLBCL. Due to its cumulative toxicity, long-term use is not suitable, and a one year treatment was planned in the LOTIS-

2 study. This study also included a significant number of patients with refractory and high-grade lymphoma, making it one of the limited treatment options in this high-risk patient group. Polatuzumab-BR was compared with BR in a phase II trial. Pola-BR demonstrated superiority in r/r DLBCL patients who were not suitable for HSCT and CAR-T therapies, and it should be considered an option, particularly in patients with < 60 years, IPI<2, ABC phenotype, non-bulky, and relapsed patients.Glofitamab and epcoritamab are a treatment option for r/r DLBCL patients. CAR-T therapies are costly and have high side effects, leading to treatment delays, especially in patients with rapid progression, and requiring specialized centers. BiTE therapies, with fewer side effects, lower costs, and easier access, may be an alternative for patients unable to access CAR-T therapies. The inclusion of high-grade lymphoma cases in trials provides an alternative in this group with limited treatment options. Its use will also increase as an important part of combination treatments. The XPO1 inhibitor Selinexor has been tested in SADAL study in patients with R/R DLBC lymphoma who have no treatment options. Although response rates are low, it may increase the effectiveness of these treatments as part of combination therapies. The SADAL study demonstrated greater efficacy in the GCB phenotype. Since there are no randomized studies of TL, Loncastixumab, BiTE treatments, Pola-BR and XPO1 inhibitors with each other, the choice of these treatments can be determined based on subgroup analyses in the studies. Allogeneic stem cell transplantation, a treatment with high NRM and morbidity, remains an alternative treatment for DLBCL patients. Although prospective studies have not compared it with CAR-T therapies, retrospective studies have not found any significant differences (Blood 2020, Dreger et al)

https://doi.org/10.1016/j.htct.2025.106199

Abstract 023

MODULATION OF INEFFECTIVE ERYTHROPOIESIS IN THALASSEMIA

Şifa Şahin

Istanbul University Faculty Of Medicine, Türkiye

Introduction: Thalassemia comprises inherited disorders characterized by reduced globin chain synthesis, leading to an imbalance between α- and β-globin chains. Ineffective erythropoiesis (IE) is the long-term outcome of a complex interaction of molecular mechanisms, primarily involving the bone marrow and its intricate bidirectional communication with the liver, spleen, and gut, ultimately leading to the production of pathological RBCs. IE is the primary driver of thalassemia and the main contributor to most of the clinical manifestations of this disorder. In patients with β-thalassemia, the bone marrow contains approximately six times more erythroid precursors than in healthy individuals, and the rate of apoptotic cell death is nearly four times higher than normal (1). In thalassemia, the altered differentiation of erythroid progenitors appears to worsen IE, coupled with increased proliferation and apoptosis, ultimately leading to anemia, extramedullary hematopoiesis, splenomegaly, and systemic iron overload. Therefore, advanced characterization of the molecular foundations of these complex processes is crucial for developing effective disease-modifying therapies. Therapeutic approaches seek to modulate pathways that reduce iron absorption (for example, activating hepcidin through Tmprss6 antisense oligonucleotides—ASOs) or pathways that increase erythropoiesis (e.g., erythropoietin [EPO] administration or modulating red blood cell (RBC) synthesis via control of transferrin receptor 2 [Tfr2]) or activin II Receptor Ligand Traps (2). **Pathophysiology of Ineffective Erythropoiesis:** Erythropoiesis is a tightly regulated process producing billions of functional red blood cells (RBCs) daily. In thalassemia, this process is disrupted. The hallmark is the substantial expansion of early-stage erythroid precursors in the bone marrow in response to elevated erythropoietin, coupled with premature death of late-stage precursors, resulting in a low output of mature RBCs. Therapeutic Strategies Targeting IE Building on the mechanistic understanding of IE, therapies aim to address the underlying pathology rather than merely treating anemia or iron overload. 1. Activin II Receptor Ligand Traps Luspatercept is a leading therapeutic that traps TGF-β superfamily ligands (including GDF11 and Activin A). By sequestering these ligands, luspatercept prevents receptor binding, promoting terminal erythroid maturation and reducing IE. Clinical trials show that luspatercept significantly increases hemoglobin and reduces transfusion requirements in β-thalassemia. 2. Targeting Iron Metabolism Novel agents modulate iron metabolism to reduce iron overload and improve erythropoiesis. Ferroportin inhibitors (e.g., VIT-2763) aim to block iron export from cells. Other strategies aim to enhance hepcidin activity or inhibit erythroferrone (ERFE) (4). 3. Gene Therapy and Gene Editing Emerging approaches include gene-based strategies to correct globin imbalance or regulate erythropoiesis, with potential to reduce IE. 4. Combination and MicroRNA-Targeting Approaches indicates that combining Tmprss6-ASO with EPO or Tfr2 haploinsufficiency yields superior outcomes in Hb and splenomegaly reduction, compared with single therapies. Additionally, targeting dysregulated microRNAs may provide supplementary therapeutic avenues (5). **Conclusion:** IE remains a central feature of β-thalassemia, driven by iron dysregulation, oxidative stress, and impaired erythroid maturation via TGF-β signaling. Luspatercept and other activin receptor ligand traps have demonstrated clinical benefit. Emerging combinations that couple iron-restriction strategies with erythropoietic stimulation show promise for enhanced efficacy. Ongoing research is essential to optimize regimens, identify responders, and translate preclinical findings into durable clinical solutions.

https://doi.org/10.1016/j.htct.2025.106200

Abstract 024

STEM CELL MOBILIZATION: AUTOLOGOUS AND ALLOGENEIC

Gülsüm Akgün Çağlıyan

Pamukkale University Faculty Of Medicine, Türkiye