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)

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Abstract 023

MODULATION OF INEFFECTIVE ERYTHROPOIESIS IN THALASSEMIA

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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.

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Abstract 024

STEM CELL MOBILIZATION: AUTOLOGOUS AND ALLOGENEIC

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