

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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In autologous HSCT, stem cells are collected from the patient following prior exposure to chemotherapy. The standard mobilization approach is granulocyte colony-stimulating factor (G-CSF) alone or in combination with chemotherapy, such as cyclophosphamide. While chemotherapy-based mobilization may increase CD34+ yields and contribute to disease cytoreduction, it is associated with increased infectious and hematologic complications. Plerixafor, a CXCR4 antagonist, has emerged as a highly effective adjunct in patients with poor mobilization, particularly those heavily pretreated or with impaired marrow reserve. Predictors of mobilization failure include advanced age, extensive prior therapy, and low baseline blood counts. In allogeneic HSCT, stem cells are obtained from healthy donors. G-CSF administration for 4–5 days remains the standard strategy, providing sufficient peripheral blood stem cell (PBSC) yields and enabling rapid hematopoietic recovery. Compared with bone marrow harvest, PBSC collection is less invasive and results in higher CD34+ cell counts, but is associated with an increased incidence of chronic graft-versus-host disease. Plerixafor has been investigated as an alternative or adjunct in specific donor populations with inadequate mobilization, though its use remains limited. Donor safety, tolerability of mobilization agents, and long-term health implications are major considerations in the allogeneic context. Despite distinct indications, both autologous and allogeneic mobilization share key challenges: ensuring adequate stem cell yield, minimizing toxicity, and reducing the need for multiple apheresis procedures. Recent advances have improved mobilization outcomes, yet the problem of poor mobilizers persists. Novel mobilizing agents, optimization of dosing schedules, and risk-adapted strategies are under evaluation to enhance efficiency and safety. Stem cell mobilization remains a critical determinant of HSCT success. Autologous mobilization is challenged by prior therapy and patient-related factors, whereas allogeneic mobilization prioritizes donor safety and graft quality. The incorporation of agents such as plerixafor has significantly expanded the mobilization armamentarium. Future directions include individualized mobilization protocols, novel pharmacologic combinations, and strategies aimed at improving long-term transplant outcomes.

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Abstract 025

LABORATORY EVALUATION IN MYELOMA: WHICH TESTS SHOULD BE PREFERRED DURING DIAGNOSIS AND FOLLOW-UP?

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Introduction: Multiple myeloma (MM) is a plasma cell malignancy characterized by clonal proliferation of abnormal plasma cells, production of monoclonal immunoglobulins, and organ dysfunction, often defined by the CRAB criteria (hypercalcemia, renal impairment, anemia, and bone disease). Laboratory testing is central to diagnosis, risk

assessment, and monitoring during therapy and remission. **Baseline Evaluation at Diagnosis: Hematology and Biochemistry** - CBC with differential → detection of anemia, leukopenia, or thrombocytopenia. - Biochemistry panel → creatinine, urea, calcium, albumin, LDH. - β 2-microglobulin and albumin → incorporated into the Revised International Staging System (R-ISS). - CRP may reflect disease activity (IL-6 driven). **Monoclonal Protein Studies:** - Serum protein electrophoresis (SPEP): quantifies the M-spike. - Urine protein electrophoresis (UPEP, 24 h): detects Bence Jones proteinuria. - Immunofixation (serum and urine): confirms the type of heavy and light chain. - Serum free light chain (sFLC) assay: critical for light-chain, non-secretory, and oligo-secretory myeloma. **Bone Marrow Examination** - Morphology: percentage of plasma cells. - Multiparameter flow cytometry: demonstrates clonality and immunophenotype. - Cytogenetics/FISH: identifies high-risk abnormalities (del[17p], t[4;14], t[14;16]) that influence prognosis. **Laboratory Evaluation During Follow-Up Routine Monitoring** - M-protein quantification (SPEP/UPEP): mainstay of monitoring. - Immunofixation: required to confirm complete response. - sFLC assay: sensitive tool for relapse, especially in light-chain disease. - CBC, renal function, calcium, LDH, β 2-microglobulin: routine for treatment toxicity and disease burden. **Advanced Monitoring** - Minimal Residual Disease (MRD): assessed via next-generation flow cytometry or next-generation sequencing. MRD negativity correlates with superior survival and is increasingly used as a response endpoint. - Mass spectrometry and liquid biopsy are promising future tools for detecting residual disease with high sensitivity. **Preferred Tests in Clinical Practice** - At diagnosis: a comprehensive panel including SPEP, UPEP, serum/urine immunofixation, sFLC, bone marrow studies (with cytogenetics/FISH), and advanced imaging is essential. - During follow-up: routine monitoring can be streamlined to SPEP and sFLC, supplemented by basic hematology and chemistry. UPEP is reserved for patients with baseline significant proteinuria. - In specialized centers: MRD testing should be incorporated, especially in clinical trials, to refine response evaluation. **Conclusion** Laboratory evaluation remains the cornerstone of myeloma diagnosis and long-term management. While a full diagnostic panel is indispensable at baseline, streamlined monitoring with SPEP and sFLC is sufficient in most patients during follow-up. Advanced tools such as MRD assessment and mass spectrometry are reshaping the landscape, providing unprecedented sensitivity in disease monitoring. The optimal combination of tests ensures accurate diagnosis, appropriate risk stratification, and effective treatment monitoring in multiple myeloma.

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Abstract 026

ACUTE AND CHRONIC GRAFT-VERSUS-HOST DISEASE: INSIGHTS INTO ETIOPATHOGENESIS

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