blood® Editorial

Introduction to a How I Treat series on management of high-risk patients following allogeneic transplant

To improve the therapeutic success of allogeneic hematopoietic cell transplantation (allo-HCT), the management of high-risk patients is essential. High risk means high likelihood for development of graft-versus-host disease (GVHD), for relapse of the underlying malignancy, and for severe infectious complications. The following How I Treat series describes state-of-the art and major recent developments in the management of prevention of relapse with cellular therapies or maintenance-based approaches and GVHD prophylaxis.

- Alexander Biederstädt and Katayoun Rezvani, "How I treat high-risk acute myeloid leukemia using preemptive adoptive cellular immunotherapy"
- Zachariah DeFilipp and Yi-Bin Chen, "How I treat with maintenance therapy after allogeneic HCT"
- Joseph Rimando, Shannon R. McCurdy, and Leo Luznik, "How I treat GVHD in high-risk patients: posttransplant cyclophosphamide and beyond"

Relapse of high-risk leukemia after allo-HCT remains a major clinical challenge. The article on the use of preemptive T-cell/natural killer cell transfer highlights cellular therapies that can be used to prevent or treat relapse. Response rates of relapsed acute myeloid leukemia and acute lymphoblastic leukemia to donor lymphocyte infusions (DLIs) are low, and the role of preemptive DLI on detection of measurable residual disease (MRD) is unclear due to the lack of prospective randomized studies. Biederstädt and Rezvani discuss the challenges of MRD-triggered DLI treatment after allo-HCT. They outline novel approaches of post-allo-HCT cellular therapies, including the role of chimeric antigen receptor–redirected cellular therapy and T-cell receptor gene therapy. In addition, a practical structure for the decision-making process whether to use preemptive cellular therapy or not for patients with high-risk leukemia is provided.

Besides cellular therapy-based approaches, drug-based maintenance therapy after allo-HCT has shown encouraging results in certain types of high-risk leukemias, which is the topic of the article by DeFilipp and Chen. The authors discuss risk factors that impact their decision to initiate maintenance therapy after allo-HCT including the biology of the leukemia, the patient's MRD status before and after allo-HCT, and the intensity of the conditioning regimen. This information may guide the decision on the use of maintenance therapy for more selective treatment of patients at high risk of relapse while sparing other patients. The article connects common case scenarios with the currently available therapeutic agents including FLT3 inhibitors, isocitrate dehydrogenase 1 and 2 inhibitors, BCL-2 inhibitors, BCR-ABL1 tyrosine kinase inhibitors, and hypomethylating agents in the context of published data and ongoing studies.

Severe acute GVHD and related infectious complications are still major causes of death in high-risk patients. Luznik and colleagues debate the emergence of new GVHD risk factors including novel immunotherapies before and after allo-HCT, the need for early cessation of immunosuppression, use of maintenance therapies in the post allo-HCT setting, and older recipient age. They provide strategies to cope with such high-risk for GVHD constellations using posttransplantation cyclophosphamide (PTCy) and other GVHD prophylaxis approaches that can be added to the calcineurin inhibitor–plus–antimetabolite strategy that is widely used for GVHD prevention. The success of PTCy and side effects of this strategy are discussed. The authors use illustrative cases to connect PTCy-based approaches for GVHD prophylaxis and discuss combination approaches with abatacept and JAK inhibitors.

This How I Treat series highlights insights into novel therapeutic strategies for patients at high risk for relapse, GVHD, and viral reactivation after allo-HCT. A major goal of this series is to provide the treating physician with an overview of novel therapeutic targets that are either already approved or in clinical testing to offer optimal clinical care for high-risk patients undergoing allo-HCT.

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