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Editorial

Introduction to a How I Treat series on major complications after allogeneic stem cell transplantation

The therapeutic success of allogeneic hematopoietic cell transplantation (allo-HCT) is mainly hindered by cytomegalovirus (CMV) reactivation, steroid-refractory acute graft-versus-host disease (GVHD), and relapse of acute leukemia. The following articles in this "How I Treat" series describe state-of-the art and major novel developments in the prophylaxis and therapy of CMV reactivation, treatment strategies for steroid-refractory GVHD, and approaches to manage leukemia relapse after allo-HCT:

- Hermann Einsele, Per Ljungman, and Michael Boeckh, "How I treat CMV reactivation after allogeneic hematopoietic stem cell transplantation"
- Paul J. Martin, "How I treat steroid-refractory acute graft-versus-host disease"
- Alexandros Spyridonidis, "How I treat measurable (minimal) residual disease in acute leukemia after allogeneic hematopoietic cell transplantation"

CMV reactivation remains one of the most common and life-threatening infectious complications after allo-HCT. Einsele et al describe the antiviral prophylaxis to prevent viral replication, which was shown to be beneficial for seropositive patients following allo-HCT. They discuss the novel mode of action of letermovir and its lower toxicity profile with respect to myelotoxicity or nephrotoxicity, which allow for its use in the relatively fragile allo-HCT patients. Also, the phase 3 trial testing prophylaxis with letermovir is discussed, reporting reduced mortality and rates of clinically significant CMV infection. The authors point out that preemptive antiviral treatment, triggered by early detection of CMV reactivation, before clinical manifestations is an important component of CMV management to avoid CMV pneumonia, gastroenteritis, or retinitis. CMV-specific T-cell reconstitution and vaccination strategies against CMV are also debated.

The article on acute steroid-refractory GVHD highlights biological mechanisms that could be responsible for the failure to respond to glucocorticoids, including the involvement of myeloid cells and granulocyte macrophage–colony-stimulating factor–producing T cells, transition of T cells from a T helper 1 (Th1) to a Th17 phenotype, endothelial damage, and impaired epithelial regeneration. Major principles for the clinical management of steroid-refractory GVHD are described, including use of the lowest effective dose of glucocorticoids, prophylactic medications, follow-up endoscopy, and avoidance of excessive immunosuppression with multiple agents given concurrently. Martin discusses novel therapy approaches such as lithium to promote intestinal epithelial repair as well as the results of the REACH1 trial. Prognostic biomarkers predicting nonrelapse mortality in patients with acute GVHD are highlighted.

Spyridonidis debates the clinical management of minimal residual disease (MRD) after allo-HCT performed for acute leukemia, and provides recommendations on how to best implement MRD testing and MRD-directed therapy after allo-HCT. MRD measurements of disease-specific mutational burden, Wilms tumor 1, or classical and lineage-specific chimerism monitoring are discussed with respect to their predictive value and illustrated by case studies. MRD-guided interventions that boost the graft-versus-leukemia effect such as donor lymphocyte infusions and pharmacological therapy are reported.

This "How I Treat" series highlights insights into novel therapeutic strategies for common medical problems after allo-HCT. A major goal of this series is to provide the treating physician with an overview of standard and novel therapeutic strategies that have reached clinical testing.

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