Important advances in allogeneic hematopoietic stem cell transplantation (HSCT) over the past 20 years have substantially reduced the risk of treatment-related morbidity and mortality. However, in that same time period, the incidence of relapse has not changed significantly, despite the introduction of donor lymphocyte infusion (DLI) as a specific modality to treat relapse [1,2]. Relapse is the leading cause of death following allogeneic HSCT, and it remains the primary cause of death among patients surviving more than 2 year after allogeneic HSCT [1]. Moreover, the risk of relapse and disease progression is significantly higher following nonmyeloablative and reduced-intensity conditioning (RIC) than after myeloablative allogeneic HSCT for almost all malignant diseases for which these regimens have been employed [3-5].

Prior to the introduction of DLI, the primary approaches to the treatment of relapse were withdrawal of immune suppression, use of conventional chemotherapeutic agents, and consideration of a second allogeneic HSCT [6,7]. Initial reports demonstrated DLI was dramatically effective for relapsed chronic phase chronic myelogenous leukemia (CML), and provided optimism that there was an efficacious modality that could potentially benefit the majority of patients who experienced relapse following allogeneic HSCT. This enthusiasm was quickly dampened by the subsequent reports that DLI benefited only a minority of patients with diseases other than CML [8,9]. The optimal dose, frequency, and cell type for DLI remains to be determined [9]. Various attempts have been made to augment the potency and specificity of DLI; however, the utilization and efficacy remains essentially unchanged [10-12].

The one major advancement that has occurred over the past 20 years, relative to the problem of relapse after allogeneic HSCT, is our improved understanding of the biology that underlies the graft-versus-leukemia/tumor (GVT) effect [13,14]. Research on the biology of GVT, such as the role of killer immunoglobulin receptors, could eventually have significant clinical impact [15]. Other factors, independent of GVT, also affect relapse. These include specific disease biology, tumor microenvironment, sanctuary sites, and chemotherapy and/or...
radiotherapy resistance. How these factors interrelate to predict long-term disease control versus disease recurrence (early versus late) is uncertain and requires further study. The experience with both syngeneic and autologous HSCT demonstrated that the conditioning regimen is important for long-term disease control [16]. However, as more and more patients are undergoing allografting with reduced-intensity and nonmyeloablative conditioning regimens, disease progression and relapse will increasingly be an important cause of treatment failure. This has led to the use of strategies, such as administration of “targeted agents” and immunomodulatory agents posttransplantation to reduce the risk of relapse associated with these conditioning regimens.

It was with the recognition that relapse after allogeneic HSCT is a significant clinical problem, that there is growing understanding of the mechanisms underlying the biology of relapse, and the perception that there was a lack of coordination of efforts in the basic, translational, and clinical research on relapse, that the idea of organizing a workshop on this subject emerged. Initially starting as an informal query, it rapidly became apparent there was significant interest in this topic, and there were many individuals who were highly interested in participating in such an effort. An initial organizational meeting hosted by the National Cancer Institute (NCI) took place in San Francisco during the 2008 Annual Meeting of the American Society of Hematology. Subsequent meetings led to the formation of separate committees addressing the biology, epidemiology, prevention, monitoring, and treatment of relapse. Committee chairs recruited various members both within and, importantly, outside the transplant community with diverse expertise relative to their specific committee topic. Each committee was given the charge of reviewing and summarizing the available scientific data on their specific topic, identifying ongoing research of great interest and potential, as well as where research was felt to be deficient. The results of these efforts were presented and discussed at a workshop sponsored by the NCI occurring November 2–3, 2009, in Bethesda, MD, and included over 250 international participants. The goals of this workshop were to review the current state of the science, to present respective committee recommendations, and to have debate and discussion among all of the workshop participants with the ultimate goal of promoting a coordinated research effort to address the problem of relapse. Over the following months a summary of each committee’s findings and recommendations will be presented in the Biology of Blood and Marrow Transplantation. The purpose of these reports is multifold, including providing a scientific review on various topics related to relapse after allogeneic HSCT, but more importantly to stimulate discussion and identify and prioritize research efforts on this important clinical problem.

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REFERENCES