High-Dose Therapy and Stem Cell Transplantation

The use of high-dose therapy and stem cell transplantation for the treatment of both hematologic malignancies and solid tumors has increased dramatically over the past several years. A report from the International Bone Marrow Transplant Registry (IBMTR) and the Autologous Bone Marrow Transplant Registry (ABMTR) in 1997 described data available for more than 65,000 transplants, which represented about 40% of the allogeneic transplants performed worldwide since 1964 and approximately 50% of the autologous transplants performed in North and South America since 1989. The past several years have seen substantial changes in the field of allogeneic and autologous stem cell transplantation including improvements in graft-vs-vs-host disease prevention and treatment, increased utilization of alternative donors, and a shift from the use of bone marrow to peripheral blood stem cells, especially in patients undergoing autologous stem cell transplantation. Stem cell transplantation has become standard therapy for several malignancies. One example is the use of allogeneic bone marrow transplantation for the treatment of leukemia and certain lymphomas. Yet, despite the broad application of this therapy, as well as the substantial improvements in clinical outcomes and treatment-related mortality, the use of high-dose therapy remains controversial for the treatment of certain malignancies, most notably breast cancer and other solid tumors. This edition of Cancer Control focuses on various aspects of stem cell transplantation, including recent advances in management, as well as several controversies in the utilization of this therapy.

A major limitation of allogeneic bone marrow transplantation has been the problem of graft-vs-vs-host disease. Graft-vs-vs-host disease accounts for significant morbidity following HLA-identical sibling transplants and, in the case of a less well matched donor such as an unrelated donor, the risk of graft-vs-vs-host disease can limit the applicability of otherwise potentially curative therapies for patients with leukemia, lymphoma, or other malignancies. Strategies to maximize medical prophylaxis and treatment through nonspecific immunosuppression mechanisms have provided substantial improvements in limiting the incidence and extent of graft-vs-vs-host disease. Unfortunately, the costs of severe immunosuppression remain obvious. Stephen J. Noga, MD, PhD, and Paul V. O’Donnell, MD, PhD, present an interesting prospective on the role of graft engineering in decreasing the morbidity of graft-vs-vs-host disease while exploiting the benefits of graft-vs-tumor effects. This outstanding state-of-the-art review provides a balanced overview of the current applications of graft engineering and explores the future of this technology in improving clinical outcomes following transplantation.

With increased utilization of autologous stem cell grafts and emerging technology to select, with either positive or negative selection techniques, a relatively "pure" population of CD34+ committed progenitor cells from both bone marrow and peripheral blood, the role of contamination of the stem cell product takes on increased clinical significance. Whether contaminating tumor cells detected in the stem cell product play a role in relapse or simply reflect overall tumor burden and thus define a patient population less likely to achieve a complete response to high-dose therapy remains controversial. Unfortunately, few prospective, randomized clinical trials address the role of dose intensity in the treatment of breast cancer. Benjamin Djulbegovic, MD, and colleagues eloquently describe the process of clinical decision making and the rational use of the available medical literature for the application of high-dose therapy in the management of patients with early-stage, high-risk breast cancer. They describe a method for comparing the benefits and risks of standard-dose therapy to high-dose therapy in an attempt to define the circumstances under which high-dose chemotherapy could be used in the management of these patients. This mathematical model has broad implications for a variety of clinical situations, especially in areas where few randomized, controlled clinical trial data exist.

Increased utilization of autologous stem cell transplantation is likely due to continued advances in supportive care with concomitant decreases in treatment-related mortality. Rod Quilitz, PharmD, describes the role of several new antifungal agents in the management of the posttransplant patient. These agents have had a significant impact on decreasing early-onset fungal infections and reducing patient morbidity. This article provides an excellent overview of these important aspects of supportive care in the transplant patient population with implications for improving clinical outcomes for all patients receiving dose-intensive therapy.

In summary, the use of both allogeneic and autologous stem cell transplantation will likely continue to increase over the next several years due to improvements in technology that result in decreased toxicity and improved efficacy. The rational use of transplantation, including the appropriate patient population to be treated, will be defined as the results of carefully planned clinical trials addressing multiple aspects of the transplant process become available.

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References