STEM CELL TRANSPLANTATION FOR METASTATIC AND HIGH-RISK NONMETASTATIC BREAST CANCER: A NOVEL TREATMENT APPROACH

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CHAPTER OVERVIEW

Even after decades of investigation, the role of high-dose chemotherapy (HDC) with autologous hematopoietic stem cell transplantation (AHST) in the treatment of breast cancer remains controversial. In preclinical and clinical studies of breast cancer in the 1980s and 1990s, dose escalation of alkylating agents—such as cyclophosphamide, carboplatin, cisplatin, etoposide, carmustine, and thiotepa—resulted in increased tumor response rates. However, the pace of investigation of HDC with AHST slowed substantially beginning in 1999 because of strong negative perceptions about AHST that arose after the report of medical research fraud in a study by Bezwoda and publication of negative results of randomized clinical trials at the 1999 annual meeting of the American Society of Clinical Oncology. Even though the number of AHST procedures performed for breast cancer has dropped precipitously over the past 6 years, more than 22 phase III clinical trials of HDC with AHST have been conducted and reported to date. The results are conflicting; some results are positive and others are negative. The safety and tolerability of HDC with AHST for breast cancer have improved greatly over the last decade. Improved preparative regimens and advances in supportive care have reduced toxicity, enhanced recovery, and markedly reduced morbidity and mortality. Many regimens can safely be administered on an outpatient basis. Clinical trials of novel uses of stem cell transplantation—e.g., autologous stem cell transplantation in patients who receive targeted therapy directed against bone metastases and circulating tumor cells; allogeneic transplants for enhancement of graft-versus-tumor effects; and use of mesenchymal stem cells as gene delivery systems—are currently being conducted or are being planned at M. D. Anderson Cancer Center. The field of stem cell transplantation continues to be a viable area of research aimed at developing innovative therapies for advanced breast cancer.

INTRODUCTION

In preclinical and clinical studies of breast cancer, dose escalation of alkylating agents—such as cyclophosphamide, carboplatin, cisplatin, etoposide, carmustine, and thiotepa—has resulted in increased tumor response rates. On the basis of these studies, high-dose chemotherapy (HDC) with