Abstract

Retroviral Mediated Transfer of the Human Multidrug Resistance Gene (MDR-1) into Hematopoietic Stem Cells during Autologous Transplantation after Intensive Chemotherapy for Breast Cancer

Patients with metastatic breast cancer will receive 4-5 cycles of induction chemotherapy on one of the ongoing Medicine Branch protocols. Patients achieving at least a partial response, and who do not have evidence of bone marrow involvement, will undergo PBSC and bone marrow harvest when hematologic recovery has occurred. Patients who have not achieved a PR, but who are responding to therapy, may be treated with additional cycles of therapy in an attempt to achieve a PR. Such patients will be eligible for transplant if a PR is obtained. 70% of the bone marrow and PBSC will be cryopreserved. The CD34+ subpopulation from the remaining 30% of the bone marrow and PBSC harvest will be obtained using an anti-CD34+ antibody and immunoabsorption column. The bone marrow and peripheral blood CD34 cells will be transduced with a retroviral vector expressing the human MDR-1 cDNA. Patients with positive bone scans or histologic evidence of bone marrow involvement will be excluded from the gene transfer component of the protocol. The MDR-1 transduced CD34 cells will be reinfused along with the non-transduced bone marrow and PBSC into patients following high dose ICE chemotherapy. Serial peripheral blood and bone marrow samples will be obtained to study hematopoietic reconstitution with MDR-1 transduced cells. Patients with residual or progressive disease after ABMT will be treated with taxol or vinblastine. In these relapsed patients, peripheral blood and bone marrow samples will be obtained to study whether chemotherapy amplifies the proportion of hematopoietic cells containing the MDR-1 provirus. We will monitor the nadir blood counts of each patient receiving salvage chemotherapy for evidence of myeloprotection and correlate this data with changes in the mean proviral copy number. Sites of relapsed tumor will be biopsied to test for the presence of the MDR-1 provirus.