

NON-TECHNICAL ABSTRACT

Autologous stem cell transplantation can provide a cure for up to 65% of germ cell tumor patients who relapse after initial therapy. Unfortunately, those patients who never attain a remission, who relapse within 3 months after initial therapy, or relapse after salvage chemotherapy, have only a 15% long-term survival.

In an effort to increase the tolerability of the patient's marrow to the drug etoposide administered post-transplantation, we propose to add a gene to the patient's peripheral blood stem cells at the time this is collected from the patient, and then reinfuse this back into the patient (Bone Marrow Transplantation). Survival rates can be increased if patients are given etoposide chemotherapy after transplant. This has proven difficult for a number of patients due to the effect of this drug on the bone marrow when given after a transplant.

In this study we will study the safety of exposing bone marrow cells to a retroviral vector containing the MDR-1 gene, a gene that confers resistance to chemotherapy agents, including etoposide. The bone marrow cells will be stimulated to leave the marrow and enter the blood using the drug G-CSF. These cells will be collected through a process called apheresis and used for transplantation. The cells will be exposed to the vector after four days of stimulation in order to increase gene transfer rates. In addition, the cells will be exposed to the vector in the presence of a recombinant protein CH-296, which has been shown to increase gene transfer.

As is standard for treatment of our germ cell tumor patients, two transplants will be performed. The first will use untreated cells. The second will use the gene transduced cells. Patients will receive three courses of oral etoposide after the transplant, starting when their blood counts have recovered from the second transplant.

The potential harm of the use of this "gene therapy" is believed to be very low. Animal studies and other laboratory tests have shown this type of gene therapy to be safe. However, there are some theoretical (possible) risks. It is possible that the treatment may result in a new cancer. While this has never occurred in extensive animal studies that have been performed, and it is felt to be unlikely, the possibility exists. The gene could be accidentally placed in a tumor cell that was present in the collected, peripheral blood stem cells, potentially making the tumor cells resistant to chemotherapy. This is very unlikely since germ cell tumors rarely go to the bone marrow and do not have CD34 on their surface, and should be removed during CD34 selection. Since these studies are fairly new there may be additional risks that are unknown.