

Neuroblastoma is a form of cancer that is usually fatal without treatment. In most cases the cancer has spread in the body by the time it is diagnosed. Current approaches to treatment frequently include several chemotherapy drugs which kill normal cells in bone marrow as well as tumor cells. Because of this, a bone marrow transplant using the patient's own marrow is given to restore the normal blood cells following the intensive chemotherapy. Even with this treatment, the neuroblastoma may come back. The reason for this is unknown, but could involve the transfer of contaminating neuroblastoma cells in the bone marrow which are undetectable by routine methods.

Many studies currently employ a treatment step (purging) of the bone marrow outside of the body designed to remove contaminating tumor cells. However since the reason for reoccurrence of the tumor is not known, the potential clinical benefit of this treatment step is also unknown. Due to the difficulty of detecting very low numbers of contaminating tumor cells in the marrow, and the small number of neuroblastoma patients available for study, it has not been possible to demonstrate the clinical benefit of purging either by examining the performance of removal methods on marrows for transplant or by clinical studies of purged versus unpurged marrow transplantation.

For this reason, an alternative method, employing recombinant DNA technology, is proposed to examine safety and efficacy issues related to the use of a Neuroblastoma Bone Marrow Purging System. The proposal is to give 12 patients with advanced neuroblastoma, bone marrow which has been "marked". Following chemotherapy designed to place the patient in bone marrow "remission" (no cancer cells detected in the marrow), bone marrow will be removed under anesthesia and stored for later transfer back to the patient.

Two distinct genetic markers will be put into two separate portions of the marrow. One part will be stored immediately after marking. A second part will be treated (purged) before storing. This procedure may remove contaminating cancer cells. Following additional intensive chemotherapy, both parts will be mixed and then given back to the patient. If the cancer returns (relapse), the marrow will be examined for the presence of neuroblastoma cells containing the genetic markers. This may help determine if the returned marrow contributed to the relapse. If markers are detected, the relapse marrow will also be analyzed to determine if marked neuroblastoma cells are from the purged or unpurged portion of the returned marrow. This can be done because the two markers used can be distinguished from each other. This will provide information about the potential benefit of purging.

Close monitoring of the patients for 24 months following transplantation is expected to provide information about the safety of purging, the usefulness of gene marking for examining the contribution of the returned marrow to relapse, and the potential benefit of purging. Long term follow-up of patients (14 years) will address any concerns related to the safety of gene marking. Information obtained from this study will be used to design additional studies to statistically validate the purging system being studied as safe and effective for the removal of neuroblastoma cells from bone marrow prior to transplantation.