

BRIEF RESEARCH SUMMARY

(To be written in terms which nonscientists can easily understand)

Lymphoma is a frequent complication of AIDS. It usually occurs late in the course of the disease but occasionally it can be its first manifestation. Conventional chemotherapy is somewhat less effective to treat lymphoma in HIV patients than in uninfected individuals. Autologous (self) bone marrow transplants (BMT) and allogeneic (donor) BMT have been successfully used in patients with lymphoma that fail first line therapy and/or have high risk for relapse. Some autologous and allogeneic BMT's have been attempted for the treatment of HIV associated lymphoma. The results were in general disappointing but the experience was accumulated during the era of single drug HIV treatment.

Several new developments in HIV and transplantation biology have led to a renewed interest in this modality of treatment: 1) the availability of multidrug treatment for HIV and the possibility to induce a dramatic fall in the load of HIV virus in the blood, 2) the ability to collect autologous (self) stem cells for transplantation that are virtually free of virus, 3) the ability to use allogeneic stem cells from compatible donors that lead to rapid recovery of marrow and immune function after transplantation 4) the possibility to introduce genes into stem cells prior to transplantation that confer HIV resistance and, 5) the ability to identify donors that may be immune to HIV infection.

Our protocol will use autologous BMT (for patients without donors) and allogeneic BMT for those with compatible donors to treat HIV associated lymphoma. At the time of transplantation we will transduce portion of the stem cells (either autologous or allogeneic). This involves introducing an artificial gene into the cells that may provide protection against HIV infection. The method for introducing the gene is called retroviral gene transfer. This method has been widely used in other FDA approved protocols to "genetically mark" cells before transplantation. To mark the cells a defective virus has been designed carrying the gene of interest. The virus can infect cells and endow them with new genes but is unable to replicate further and infect other cells or other people. Also the virus has been stripped of its pathogenic genes and is thus unable to cause disease. A small risk exists that the virus can insert the new genetic material near or within an important gene and cause a cell to proliferate out of control. The statistical chance of this happening at random is exceedingly small. Hundreds of patients have been treated under gene marking protocols without any direct effect attributable to the gene marking. The follow up is now long enough to provide a fair degree of confidence that if insertion near a vital gene if it happens must be quite rare.

The goal of this study is to learn whether, in combination with aggressive anti-HIV therapy, autologous and allogeneic BMT can improve on the overall and disease free survival of patients with high risk and relapsed HIV associated lymphoma. Also we expect to determine whether autologous and allogeneic cells can be marked with anti-HIV genes and whether these genes can induce HIV resistance upon the cells that carry them. Finally, we may be able to determine whether HIV re-infection after transplant is blocked if an allogeneic donor happens to carry the gene that confers natural resistance to HIV infection.