

II. Non-Technical Abstract

Non-Hodgkin's lymphoma (NHL) is a malignancy of the immune system afflicting over 55,000 Americans each year. Modern chemotherapy and radiation therapy is curative in the majority of patients with limited disease at the time of diagnosis. For the greater than 50% of patients with disseminated disease, however, the relapse rate is approximately 66%. High-dose chemotherapy with stem cell rescue is currently the most effective modality for eradicating recurrent NHL but is plagued by a high incidence of post-transplant relapse. This pilot Phase I protocol seeks to establish the safety of targeting lymphoma cells that have survived the myeloablative preparative regimen with post-transplant immunotherapy utilizing autologous immune cells rendered lymphoma-specific cell by genetic modification. Taking advantage of the high incidence of expression of a cell-surface protein designated CD20 on NHL tumor cells, a recombinant DNA molecule encoding a CD20-specific T cell receptor has been engineered that when expressed in cytolytic T lymphocytes redirects their killing function to lymphoma cells. Study subjects will have immune cells harvested and genetically modified prior to autologous transplantation. T cell clones expressing the CD20-specific receptor will be grown to high numbers outside the body then re-infused to patients following the transplant procedure. Each study subject will receive a series of three escalating cell dose infusions of their clones and the safety of this procedure monitored. Additionally, patients will be studied to determine how long these cells remain in the circulation, if they migrate to lymph nodes, and if patients mount immune responses against their genetically-modified cells. This study will provide the necessary safety data to justify larger Phase I/II protocols to determine the capacity of adoptively transferred CD20-specific T cells to prevent lymphoma relapse.