

POINTS TO CONSIDER

NON TECHNICAL ABSTRACT

While patients with Hodgkin and non-Hodgkin lymphoma may be cured by chemotherapy and radiotherapy, the outlook for patients who are resistant to this treatment or who relapse is poor. Nearly half of the patients with lymphoma have the EBV virus in their tumors which may be a target for immunotherapy approaches. We have successfully used specialized immune system cells grown in the laboratory and trained to recognize and kill EBV infected cells (EBV-specific cytotoxic T-lymphocytes [EBV-CTL]) to prevent and treat another type of cancer called post transplant lymphoma that occurs after bone marrow transplant. In post transplant lymphoma, the tumor cells have 9 proteins made by EBV on their surface. However in Hodgkin and non-Hodgkin lymphoma that develops in patients with a normal immune system, the tumor cells only express 2 EBV proteins that are much harder for the immune system to recognize. In a previous study we made EBV-CTL that recognized all 9 proteins and gave them to patients with Hodgkin disease. Some patients had a partial response to this therapy but no patients had a complete response. We think there are two reasons for this. One reason is that many of the T cells reacted with proteins that were not on the tumor cells. In a current study, we are trying to find out if we can improve this treatment by growing T cells that recognize one of the viral proteins that are really expressed on Hodgkin and non-Hodgkin lymphoma cells. This protein is called LMP-2, and the special T cells are called LMP-2 specific CTLs (LMP2-CTL). To make these LMP-2-CTL, we have obtained blood from the patients and grown special type of cell called a dendritic cell (DC) and EBV infected lymphoblastoid cells (LCL). We have then transferred an adenovirus vector that carries the LMP-2a gene into the DC and the LCL. These DC and LCL are then be treated with radiation so they cannot grow and used to stimulate and expand LMP2-CTL. This stimulation trains the T cells to kill cancer cells with LMP-2 on their surface.

We now want to build on this study, because another reason why patients with Hodgkin disease were not cured by the T cell therapy alone is because there is not enough space for the T cells to grow. The tumors are also protected by inhibitory T cells which surround them. We hope that we can improve the effect of LMP-2 specific T cells that we are already using by treating patients first with a special protein called a CD45 antibody, which removed most of the patient's resident T cells, and then giving the LMP2-CTL. CD45 antibody is a special protein that will bind to the patient's blood and immune system cells and kill them. In this study the patient will first receive 4 days of treatment with CD45 antibodies followed one dose of LMP2 specific CTL. In this way we can learn if treating the patient first with the CD45 antibodies will let the CTL we give grow better and last longer.

The LMP2 CTL in this modified study will have been made in the same way and with the same adenoviral vector as in our current RAC reviewed FDA approved LMP2 CTL study.