

**Phase I/II Study of Metastatic Melanoma Using Lymphodepleting Conditioning
Followed by Infusion of CD8 Enriched Tumor Infiltrating Lymphocytes Genetically
Engineered to Express IL-12**

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Non-Technical Abstract:

This study will be performed in patients who have metastatic melanoma. Tumor infiltrating lymphocytes (TIL) generated from the patient's tumor will be transduced with IL-12 genes. We grow the IL-12 TIL in the laboratory, and then infuse them into patients. IL-12 has been shown to stimulate the immune system, and TIL expressing IL-12 will deliver IL-2 to the tumor environment. We have shown in mice that T cells transduced with the IL-12 genes do cause tumors to shrink.

The primary objectives of this study are to determine the side effects of this treatment and to determine whether the patient's tumor decreases in size after treatment on this study as described below. The secondary objective of this study is to determine the survival of the infused cells in the patient's body. This study will be conducted in two phases. The first phase will determine a dose which can be given safely to patients. The second phase will evaluate if the treatment can shrink tumors in patients. Up to 77 patients may participate in this experimental study.

Initially patients will have a biopsy of their tumor so that TIL can be isolated from the tumor. The TIL will be grown in the laboratory. During the procedure to grow the cells in the laboratory, IL-12 genes will be put into the cells using a process called "retroviral transduction". The retrovirus is made from a virus that has been inactivated or changed in a way that prevents it from reproducing and causing any type of illness. It serves only as a vehicle to deliver the genes into the cells.

Once the cells are grown in the laboratory and the gene inserted, patients will be given chemotherapy, (cyclophosphamide and fludarabine) for five days to suppress the immune system. One to four days after the chemotherapy, patients will be given the cells into a vein (IV) over 20-30 minutes. Patients will be given appropriate medications to treat the side effects of this treatment regimen and to prevent infection secondary to the immune suppression caused by the chemotherapy.

Patients will return to NIH after four to six weeks to have their tumor(s) evaluated. If the patient's tumor shrinks, they will continue to return to the NIH to have their tumors evaluated. If patients have a partial response to treatment or stable disease that subsequently progresses, they may be re-treated. If there is no response, patients will be taken off this study.