

APPENDIX D

NONTECHNICAL ABSTRACT OF PROTOCOL

Many patients have advanced cancer that has not responded to standard therapies. For these patients, TIL (tumor infiltrating lymphocyte) therapy offers a new treatment method which has shown some encouraging results. In this therapy, a part of the patient's cancer is removed and taken to the laboratory. In the laboratory the tumor portion is processed in a way to encourage the growth of white cells, called lymphocytes, which are found in (had infiltrated) the tumor. These tumor infiltrating lymphocytes are grown to large numbers with interleukin-2 (a lymphocyte growth factor). These TIL are given back into the patient through a blood vein. These TIL are given with compounds, interleukin-2 and in certain cases also alpha interferon, which can increase the patient's own anti-cancer immune reaction as well as the TIL cell response to the cancer cells.

TIL therapy has been shown to be effective in a fraction of patients receiving this therapy. At this time it is not known why some patients get a favorable response with TIL therapy and some patients do not. In order to further understand TIL therapy, it is important to be able to follow the TIL cells after they are given back to the patient. This way it will be possible to determine if the length of time the TIL cells live in the patient or the ability of the TIL to "home" or return to the tumor is related to the response the patient experiences. Since the TIL are from the patient, there is no way to distinguish them from the other cells of the patient. In order to tell the difference between the TIL cells from the patient's other cells, a means to mark or identify the TIL cells is necessary. In other clinical tests with TIL it has been shown that the TIL can be marked. This marking involves putting a new gene into TIL cells by a technique called retroviral-mediated gene transfer. These marked TIL can therefore be detected by modern scientific techniques and distinguished from the patient's other cells.

This study differs from other similar studies in that a second population of cells will also be infused into the patient along with the TIL. White cells obtained from blood (Peripheral Blood Lymphocytes, PBL) will be grown up in the laboratory in a manner similar to TIL cells. These cells will be marked with a second (and different) marker. These cells will then be given back along with the TIL cells. By using the second marker it will be possible to determine if TIL cells are better than PBL cells in their ability to home to the tumor.

This study also differs from other similar studies in that the TIL cells from some patients will be separated into two types of cells, CD4 and CD8. These subfractions of the TIL will be studied like the unfractionated TIL for their ability to home better than PBL cells. Additional studies will compare CD4 and CD8 TIL cells directly for their homing ability.

The addition of the markers into a portion of the cells will provide no immediate benefit for the patient. It would provide useful information about the therapy itself. This information may enable the design of better treatment plans to help future patients. The risks associated with the gene marking procedure are felt to be small. The opportunity to learn more about TIL therapy so that future patients may be helped is the reason for using gene marked cells.