

Non-Technical Abstract - BRMP 9401

A phase I trial of B7-transfected allogeneic melanoma cell lines to induce cell-mediated immunity against tumor-associated antigens presented by HLA-A2 or HLA-A1 in patients with stage IV melanoma.

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It is possible for the body's immune system to recognize and reject some cancers. This probably occurs when blood immune cells called lymphocytes recognize an abnormal protein (called an antigen) on the tumor cell, attach to the tumor, and then either kill the tumor or call other immune cells to the site to help eliminate the cancer cells. Scientists have recently discovered that the tumors from some patients with melanoma contain distinct antigens that can be recognized by lymphocytes. However, for reasons that we still do not understand, in most patients with melanoma the immune system has somehow been paralyzed and cannot recognize or attack the tumor.

It may be possible to activate the immune system to recognize the antigens on melanoma cells. We now understand that if lymphocytes see an antigen on a tumor cell but don't receive an important second signal (which is not normally provided by the melanoma cell), the lymphocyte will be turned off. We have grown tumor cell lines in the laboratory that contain some of the melanoma antigens. We have taken a gene (a gene is the DNA that directs the production of a protein in a cell) which codes for a molecule called B7 and placed it in the melanoma tumor cell lines we have in the laboratory. We believe that the B7 will provide a necessary second signal to activate lymphocytes to recognize the melanoma tumor antigens. Once activated, the lymphocytes can recognize and kill other melanoma cells even if they do not express the B7 signal.

In order to administer treatment, we match the patient to the tumor cell lines we have in the laboratory. We do this by determining the expression of specific proteins on the surface of patient lymphocytes that we obtain prior to the study. Only patients whose lymphocytes express the proteins HLA-A1 or HLA-A2 can receive treatment on this study.

For treatment, we plan to inject a large number of cells from the tumor cell lines containing B7 under the skin. The cells are radiated so there is little chance that a tumor might grow where we inject the cells. The tumor cells are injected every two weeks for 3 doses, then once a month for 3 doses. We rotate the sites of injection, usually starting in the leg, then the arm, then the opposite arm, then the opposite leg, and so on. HLA-A1 patients receive the same dose of the same cell line each time. HLA-A2 patients will alternately receive one of three cell lines. In either group, a maximum of 6 treatments is planned.

We will treat groups of patients with each group receiving a larger number of cells. The purpose of the study is to determine how many cells we can give safely and whether an immune response develops to the cells as we predict from the laboratory studies. In the first or second group of patients, 2 injections are given (about 2 inches apart) each treatment. In the third group, 10 injections are given each time. We do not know if the B7 actually improves the immune response to the cells. Therefore, the last group will receive the same tumor cell line(s) but not containing B7. If patients do not have a good response after receiving all 6 planned injections, we may try to give the cells containing B7 in the same way as long as the patient is still in good enough condition to continue treatment on this protocol.