

**PART 2: NON-TECHNICAL ABSTRACT**

Melanoma is a disease of the skin in which cancer cells are found in the cells that color the skin, called melanocytes. Melanoma is associated with exposure to the sun, and is 40 times as prevalent in whites than blacks. It is far more serious than other types of skin cancer, accounting for three quarters of all deaths from skin cancer despite representing only 5% of all skin cancer cases. Because chemotherapy has relatively little impact on the natural history of metastatic melanoma, researchers are looking to other therapies as possible approaches to melanoma.

This proposed clinical investigation uses a vaccine to stimulate the patient's immune system into destroying cancerous cells. (The word *vaccine* as used here may be different from the conventional meaning of the word. Whereas prophylactic vaccines have been administered to prevent the onset of disease, the term *vaccine* as used here refers to a therapeutic treatment designed to bolster the anti-tumor cell immune response in patients with pre-existing diseases. The use of these tumor vaccines is also known as immunotherapy.) This particular experimental vaccine is referred to as Modified Dendritic Cells.

In this study, autologous (derived from the patient's own body) peripheral blood mononuclear cells (PBMCs) are obtained from the patient by leukapheresis, a procedure similar to giving blood. The PBMCs are processed to extract dendritic cells (DCs), potent stimulators of T lymphocytes, which play a central role in starting the body's immune response. The DCs, after being cultured using autologous plasma and the cytokines rhGM-CSF and rhIL-4, are infected (or transduced) with two adenovirus vectors which separately encode two human melanoma tumor proteins: gp100 and MART-1. These proteins act as markers on cancer cells by enabling the body's T lymphocytes to recognize the cancerous cells. Both adenoviral vectors encoding either MART-1 or gp100 have been used previously in human clinical trials and have proved to be safe and well-tolerated. To determine if the patient is able to evoke an immune response, a Hepatitis B core peptide will be pulsed onto a portion of the DCs and added to the combination of DCs transduced with adenoviral vectors encoding gp100 and MART-1 proteins.

The gp100 and MART-1 proteins are delivered to the DCs using an adenoviral vector, which works as a vehicle to carry the genes encoding the proteins into the DCs. The adenovirus, a common virus that can infect human airways resulting in a cold, has been altered so that it cannot reproduce and cause illness. An earlier version of this adenoviral vector has been used previously in human clinical trials and has proved to be safe and well-tolerated.

Additionally, a subset of patients also will receive low dose recombinant human Interleukin-2 in an attempt to enhance the immune response and maximize the effects of the administered product. Interleukin-2 has been approved by the Food and Drug Administration as a treatment for metastatic melanoma and renal cell carcinoma.

Once the final product is delivered to the body, it is believed the Modified Dendritic Cells will stimulate the immune system to seek out and attack cancerous cells. The safety and ability of DCs transduced with an adenovirus vector encoding the melanoma-associated proteins gp100 and MART-1 to elicit an immune response has been confirmed in pre-clinical animal and cell culture studies conducted by the sponsor, Genzyme Molecular Oncology.