

I. Scientific Abstract

This is a phase I trial to compare two different methods of immunization with plasmid DNA encoding mouse gp100 in patients with melanoma. The objective of this study is to determine the optimal means of vaccination with plasmid DNA encoding gp100 in patients with AJCC stage IIb, IIc, III and IV melanoma who are HLA-A*0201 positive. We will assess whether one type of vaccination program is more effective in generating an immune response to an otherwise poorly immunogenic melanoma differentiation antigen.

The hypothesis being tested is that delivery of plasmid DNA as a gold particle conjugate into the skin will augment the immune response to a plasmid DNA delivered as a standard intramuscular injection. Studies in animal models have shown that immunization with xenogeneic (human) differentiation antigens is an efficient means to induce immunity to self antigens found on cancer. Our own preclinical studies have almost exclusively employed the gold particle mediated transfer (PMED) system for DNA immunization. Until the current time, however, this technology was not available to us for use in clinical trials. Using more conventional intramuscular (IM) injection techniques (with needles or needle-free jet injection) DNA vaccines have not been as effective in humans as they have been in smaller mammals. For this reason, we are interested in comparing PMED with IM injection using our well-characterized mouse gp100 DNA vaccine (evaluated in protocol #03-007). A total of at least 30 patients is planned, with 15 being randomized to each means of injection. Patients' sera and peripheral blood mononuclear cells will be collected in order to measure the antibody and T cell responses induced by the vaccines. Specifically, titers of IgM and IgG antibodies against human and mouse gp100 will be measured for serological response and ELISPOT and intracellular cytokine and MHC tetramer assays for CD8+ T cells responses will be assessed.