

**PRECIS**

Prostate cancer is the most common type of cancer found in American men, other than skin cancer. The American Cancer Society estimates that there will be about 230,900 new cases of prostate cancer in the United States in the year 2004. About 29,900 men will die of this disease. Prostate cancer is the second leading cause of cancer death in men, exceeded only by lung cancer. This proposal attempts to exploit an innovative approach to prostate cancer immunotherapy that exploits a naturally occurring physiologic process in humans. It combines an unconventional suicide gene effect (direct killing without the need for a prodrug or other exogenous co-factors) with an immune enhancement effect (improved tumor antigen presentation). The expression of the murine  $\alpha(1,3)$ galactosyltransferase [ $\alpha(1,3)$ GT] gene in transfected prostate cancer cells results in the cell surface expression of  $\alpha(1,3)$ galactosyl epitopes ( $\alpha$ gal) on membrane glycoproteins and glycolipids. These epitopes are the major target of the human hyperacute rejection response that occurs when organs are transplanted from nonprimate donor species. The  $\alpha(1,3)$ GT expressed in human cells renders them susceptible to antibody (Ab) and complement-mediated cytotoxicity and results in rapid cell death. The anti-tumor effectiveness of  $\alpha(1,3)$ GT gene therapy will be tested in a Phase I and II clinical trial in men with hormone refractory prostate cancer.

**STUDY DESIGN:** This trial is organized as a sequential Phase I and Phase II trial. Men with recurrent or refractory prostate cancer who have failed hormonal therapy and may have failed one prior chemotherapy regimen and have measurable and non-measurable disease are eligible. Allogeneic human prostate cancer cells expressing the hyperacute  $\alpha$ gal antigen will be injected in an attempt to break tumor tolerance. Patients who provide informed consent will receive intradermal injections of allogeneic, lethally irradiated HAP cells expressing  $\alpha$ gal epitopes. Patients will be monitored for toxicity and for disease response. In the Phase I portion, 3 patients will be enrolled at each dose escalation level if no significant toxicity is observed. In the phase II an additional 32 patients will be enrolled to evaluate vaccine efficacy. The second stage will enroll 32 more patients at the highest vaccine dose for efficacy evaluation (35 total). Thus, the total enrollment will be 44 patients.