

**A Phase I/II Study of a Prime-Boost Schedule of Human
GM-CSF Gene Transduced Irradiated Prostate Allogeneic Cancer Vaccine
(Allogeneic Prostate GVAX™) in Hormone-Refractory Prostate Cancer**

Non-technical Abstract

Prostate cancer is the most common form of adult male cancer in the U.S., eclipsing lung cancer in incidence. In 1996, a new case of prostate cancer was diagnosed on average every three minutes in the U.S., with a new death from metastatic disease occurring every fifteen minutes. To date, radical prostatectomy and radiation therapy are currently recognized curative treatments of clinically localized prostate cancer. However, no curative systemic therapy exists for metastatic disease. A significant unmet medical need for more effective therapy still exists for advanced prostate cancer.

The proposed study is a phase II open-label, outpatient, multicenter clinical trial. We propose to enroll forty patients with progressive hormone refractory prostate who have received no prior chemotherapy, biologic or gene therapy. Patients will receive a priming vaccination of 5×10^8 Allogeneic Prostate GVAX™ cells and boost vaccinations of 1×10^9 every two weeks for six months (total boost dose of 1.2×10^9 cells). Patients will continue after vaccinations with six additional months of follow up. Patients will be observed for toxicity, changes in PSA, and tumor responses.

The proposed protocol will evaluate the safety and efficacy of vaccination with lethally irradiated allogeneic prostate cancer cells (LNCaP and PC3) transduced with the human Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF) gene. The Allogeneic Prostate Cancer Cell Line Vaccine is composed of 2 equal cell doses of allogeneic prostate cancer cell lines (LNCaP and PC-3) genetically modified to secrete GM-CSF. Each vial is prepared to deliver 2.5×10^7 cells as a direct injectable in glycerol and human serum albumin. A retroviral vector is used to efficiently introduce the gene for GM-CSF into the allogeneic prostate cancer cell lines in this proposed trial. This immunotherapy approach to treat hormone refractory prostate cancer is based on findings in previous human clinical trials, that cytokine transduced tumor vaccines can induce antitumor and immunological responses in melanoma and renal cell carcinoma, as well as PSA responses in patients with micrometastatic hormone naïve prostate cancer. A similar study of Allogeneic Prostate GVAX™ in patients with hormone-naïve prostate cancer is currently underway at several clinical sites (Johns Hopkins, Physician's Reliance Network, UCSF Mount Zion).