

## **Non-Technical Abstract**

### **A Randomized Phase I Study of Ad5CMV-p53 plus Radioactive Seed Implant vs Seed Implant Alone for PSA Relapse after External Beam Radiotherapy for Prostate Cancer**

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A rising PSA level indicates Prostate Cancer is present and may be getting worse. When the PSA goes up after a patient that has had treatment by external beam radiotherapy, it usually means the cancer is still present. These patients have four remaining possible treatment options: 1) observation with no treatment, 2) surgery to remove the body parts that make androgen, 3) surgery to remove the prostate, or 4) placing radioactive seeds in the prostate. The first two options are to relieve symptoms to make the patient more comfortable, but will not cure the cancer. Surgery to remove the prostate (prostatectomy) is associated with a high rate of patient death; 50% - 70% of patients who undergo this surgery die anyway. Placement of radioactive seeds (brachytherapy) appears to be associated with fewer side effects and about 35% of the patients survive. The rationale behind this clinical study is to make cancer cells in the prostate more sensitive to radiation by injecting adenoviral-p53 vector directly into the prostate. This strategy should enhance the effectiveness of the radiation and should subsequently reduce patient deaths.

Patients who will be eligible to participate in this trial will have documented recurrence of cancer in the prostate after external beam radiotherapy. Rising PSA levels usually identify the first sign of recurrence; this rise should be slow, with a doubling time of greater than a year. Post-external beam radiotherapy prostate biopsies must document recurrent adenocarcinoma of the prostate and there must not be any evidence that the cancer has spread outside of the prostate. The PSA at the time of failure must be less than or equal to 10 ng/ml and the prostate volume must be less than or equal to 55 cc. The plan is for three injections of adenoviral-p53 into the prostate while the 125-iodine seed radiation is active. The first intraprostatic injection would take place at the time of the seed implant and the next two injections would be spaced at two-week intervals for a total of three intraprostatic adenoviral-p53 injections. Based on prior cell culture and animal studies, it is expected that there could be significant radiosensitization by spacing the treatments in this fashion.

A total of 74 patients will be entered into the trial, with 37 randomized to treatment with adenoviral p53 plus 125-iodine seed implant versus 37 randomized to 125-iodine seed implant alone. The main end point of this study will be prostate biopsy at one year after completion of the treatment. A second biopsy will be performed at two years and PSA nadir levels will also be examined as a correlate of outcome.

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