

Scientific Abstract

This study is a phase I clinical trial of a new form of gene therapy for prostate cancer. Patients with recurrent prostate cancer post external beam radiotherapy (up to 17 in number) will be recruited to receive intra-prostatic administration of a replication deficient adenovirus (Ad5-CMV-NIS) in order to monitor for adverse effects and to determine the maximally tolerated dose (MTD). This virus will induce expression of the human sodium iodide symporter (NIS) driven by the cytomegalovirus immediate early promoter. The delivery method will involve transperineal injection into multiple sites, during general anesthesia, in a fashion similar to that practiced for prostate brachytherapy. NIS expression in the prostate cancer cells will result in uptake and trapping of iodine, similar to that seen in the normal thyroid and deposits of metastatic thyroid cancer. This uptake will be quantitated 3 days after virus injection by administration of tracer amounts of ^{123}I and gamma camera imaging at multiple time points and radioiodine dosimetry will be determined from these results. On the next day a therapeutic dose of ^{131}I will be administered to the patient using doses identical to those used to treat metastatic thyroid cancer. Uptake in the normal thyroid will be blocked by prior administration of L-T3 to the patients to reduce TSH mediated NIS expression within the gland. Patients will be carefully monitored in the GCRC and for up to 10 years afterwards through the Mayo Foundation Clinical Follow-up Core Facility for adverse effects of the virus and the radioiodine, including thyroid function. We will also assess tumor responses by imaging and PSA measurements.

This study represents the first clinical trial of a novel form of gene therapy through the use of NIS and radioiodine. This form of radiotherapy which is the most effective form of radiotherapy available to the clinician, is currently effective only for thyroid cancer. Our studies, if successful, will open this avenue for use of radioiodine for prostate cancer and potentially for numerous other tumor types.