SCIENTIFIC ABSTRACT

This study is a phase I clinical trial of a new form of gene therapy for head and neck cancer. Patients with recurrent head and neck cancer post external beam radiotherapy (up to 17 in number) will be recruited to receive intra-tumoral 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 image-guided transdermal injection into multiple sites of the tumor, during general anesthesia, in a fashion similar to that practiced for head and neck brachytherapy. NIS expression in the head and neck 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 ^{131}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 CRC and for up to 10 years afterwards through the Holden Comprehensive Cancer Center Clinical Follow-up Core Facility for adverse effects of the virus and the radioiodine, including thyroid function. We will also access tumor responses by imaging.

This study represents only the second clinical trial of a novel form of gene therapy through the use of NIS and radioiodine. Our collaborator Dr. John Morris at the Mayo Clinic in Rochester, Minnesota; is currently conducting a similar study directed at prostate cancer. 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 head and neck cancer and potentially for numerous other tumor types.