

Section 2. Non-Technical Abstract

At present, there is a paucity of treatment for head and neck cancer, and no reproducibly effective treatment for unresectable or recurrent/refractory head and neck cancer. Cytokines given as proteins have been investigated as a treatment, but the short *in vivo* half-life of the recombinant protein requires multiple administrations, and the resultant high systemic doses exhibit deleterious side-effects. It is anticipated that local, intratumoral expression of cytokine proteins will initiate generation of a tumor-specific immune response without the side effects associated with high dose systemic administration of the recombinant proteins. The objectives of the clinical program are two-fold; (1) to conduct safety studies in human patients with a new combination cytokine gene therapy for the treatment of squamous cell carcinoma of the head and neck (SCCHN) and (2) to monitor tumor responses, or effects on disease progression, which can be attributed to treatment. The genes selected for use in the trial encode for the human interferon alpha (hIFN- α) and human interleukin-12 (hIL-12) proteins. After the genes are injected into the tumors, these proteins will be produced locally by the tumor cells. In animal studies conducted by our laboratory, this combination of hIFN- α and hIL-12 proteins results in the induction of clinically significant tumor shrinkage and survival in animals.

This Phase IIa protocol is designed to test the safety, tolerability, and clinical efficacy of the formulated hIFN- α /hIL-12 plasmid treatment in patients with SCCHN. Specifically, the trial is designed in two parts. In the first part, (Phase I), safety and tolerability of three escalating doses will be evaluated. In the second part, (Phase II), the maximum safe dose identified in the Phase I portion of the study will be evaluated using a Gehan design, efficacy variables include tumor size, tumor response and presence (or absence) of development of progressive disease.

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