STUDY EVALUATING AQUAPORIN-1 GENE THERAPY FOR THE TREATMENT OF IRRADIATION-INDUCED SALIVARY HYPOFUNCTION

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INTRODUCTION: Therapy for head and neck cancer commonly includes ionizing radiation (IR). IR irreversibly damages the salivary glands causing decrements in quality-of-life and oral health. There are no therapies to correct this disorder or its sequelae. Previously, proof-of-concept studies have demonstrated the effectiveness of adenovirus (Ad) vector gene transfer of human aquaporin-1 (hAQP1) to the parotid gland and correction of salivary hypofunction (NCT00372320). We aimed to develop and test adeno-associated virus serotype 2 (AAV2) for gene transfer of hAQP1 to correction of IR xerostomia in humans.

METHODS: Using well-established preclinical models (e.g., mice and minipigs), we tested the safety, kinetics, and effectiveness of AAV2-hAQP1 to recover IR-induced salivary hypofunction. Using this data, we developed a Phase 1 human clinical trial to test the safety of AAV2-hAQP1 and some measures of biological activity.

BACKGROUND: RADIATION XEROSTOMIA:

~50,000 cases of head and neck cancer annually
85% experience salivary complications:
- Caries, oral infections, pain, taste changes
- Functional difficulties, weight loss and malnutrition
No long-term therapies for salivary dysfunction
40% do not respond to current sialagogue medications

RESULTS: Ad-AQP1 IMPROVES SALIVA FLOW IN PATIENTS

Baum et al, PNAS. PNAS 2012 109 (47) 19403-19407.

RESULTS: AAV2-AQP1 IMPROVES SALIVA FLOW LONG-TERM IN MINIPIGS

Do you have dry mouth due to radiation therapy?

You may be eligible to participate in a new research study if:
✓ you have been treated for head and neck cancer
✓ you are cancer free

This study will test a new gene therapy drug that may increase salivary flow.

•All study-related tests and medications are provided without cost.
•Travel assistance may be provided.