679 NT-I7 FOR THE TREATMENT OF LOCALLY RECURRENT SQUAMOUS CELL CARCINOMA OF HEAD AND NECK UNDERGOING SALVAGE SURGERY: A CLINICAL TRIAL IN PROGRESS

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Background The current standard of care for recurrent/metastatic squamous cell carcinoma of head and neck (SCCHN) includes immune checkpoint inhibitors, which have demonstrated survival benefit. However, overall response rate remains around 10-15% and almost 40% of patients do not benefit from the therapy. We have identified low baseline absolute lymphocyte count (ALC) as a predictive biomarker associated with a lower likelihood of response to immune checkpoint inhibitors.[1]Patients with higher ALC tend to respond better to immune checkpoint inhibitors, but a majority of patients tend to have low baseline ALC from previous radiation.[2] The cytokine interleukin-7 (IL-7) promotes the proliferation and survival of naïve and memory T-cells, without inducing proliferation of immunosuppressive regulatory T-cells. Administration of IL-7 induces T-cell expansion without evidence of hyperinflammation or acute cytokine storm in murine preclinical models; however, this approach was limited by the short half-life of IL-7. NT-I7 (efineptakin alfa) is a fusion product of IL-7 with a human Fc domain and a longer half-life. NT-I7 has demonstrated an excellent safety profile and the ability to significantly and persistently expand peripheral ALC [SFM1] in phase 1/2 studies. This is a window of opportunity study of a single dose of NT-I7 in patients with locally recurrent squamous cell carcinoma of head and neck undergoing salvage surgery (NCT04588038).

Methods Patients with recurrent SCCHN (SCC of oral cavity, oropharynx, hypopharynx and larynx) undergoing curative intent salvage surgery are eligible. Patients will receive a single intramuscular injection of NT-I7 up to 2 weeks prior to planned surgery, after pre-treatment core biopsies are collected. Surgical specimens will be collected at the time of surgery for analysis of tumor infiltrating lymphocytes[HL1] and immune cell subsets. Peripheral blood will be collected pre-treatment, at the time of surgery and post-operatively (36 days after surgery). The primary objective is to establish the safety and feasibility of administering a pre-operative dose of NT-I7 in this population. Secondary[ALB2] objectives are (1) to determine changes in ALC in peripheral blood, (2) to examine changes in tumor infiltrating lymphocytes (TILs) [SFM3] , (3) to evaluate changes in immune subsets in peripheral blood after a single injection of NT-I7 and (4) to assess exploratory biomarkers for pharmacodynamic (PD) activity in peripheral blood and/or tumor tissue[SFM4] . Baseline biopsy and surgical specimens will be compared to describe and compare TILs. The study plans to enroll 10 patients and is currently on-going.

Trial Registration NCT04588038

Ethics Approval This study was approved by the University of California San Francisco IRB (#20-31673).

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