Randomized phase I trial of adjuvant personalized cancer vaccine TG4050 in resected locally advanced (LA) head and neck squamous cell carcinoma (HNSCC) patients (pts)

Background

Approximately one third of pts with resected LA HNSCC recur. T-cells targeting tumor specific mutations drive anti-tumor immune responses. TG4050 is a viral-based personalized cancer vaccine, encoding up to 30 tumor-specific DNA sequences bearing in-silico predicted class I and class II epitopes. We hypothesized that TG4050 prime an adaptive immune response against tumor antigens and prevent relapse in pts with resected LA HNSCC after treatment with curative intent (NCT04183166).

Method

The multicenter, open label, randomized, 2-arm Phase I trial evaluated TG4050 in LA HNSCC pts achieving complete remission following surgery and adjuvant radiotherapy +/- chemotherapy. Pts were randomized to receive (Arm A) weekly doses of TG4050 for 6 weeks followed by a maintenance period of one dose every 3 weeks for up to 20 doses or no vaccine (Arm B, vaccination at relapse in combination with SOC). Safety, efficacy and immunogenicity were evaluated. In selected pts, exploratory characterization of the T cell response was performed using tetramer staining, bulk and single-cell (sc)TCR sequencing.

Results

33 pts were randomized between January 2021 and April 2023, 17 pts to Arm A and 16 pts to Arm B. Median age was 61 years (26-79 years), tumor location was oral cavity in 24 pts (72.7%), hypopharynx and oropharynx in 4 pts (12.1%), respectively and larynx in one pt (3.0%). TG4050 was safe and well tolerated with only grade 1 or 2 treatment-related adverse events (AEs). The most frequently reported were injection site reactions. After a median follow-up of 28.5 months, all 16 pts receiving TG4050 in Arm A remained disease-free whereas 3 out of 16 pts in Arm B relapsed. Disease Free Survival (DFS) data at 24 months for all patients will be presented. Exploratory qualitative analyses of the neoantigen-specific T cell response by ELISpot were presented previously. In-depth characterization of the neoantigen-specific T cells including clonal expansion by TCR sequencing and longitudinal analysis by tetramer staining will be presented.

Conclusions

TG4050 is safe and induces immune responses in pts with resected LA HNSCC. No relapse occurred in the vaccine arm as opposed to 19% in the control arm. With the evolution of the landscape, adjuvant anti-PD1 therapy may become standard in resected LA HNSCC. TG4050 warrants further evaluation in combination with anti-PD1 therapy in phase III trials.

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