Safety and Immunogenicity of TG4050: a personalized cancer vaccine in head and neck carcinoma


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BACKGROUND

Immunotherapy had limited impact on Head and Neck cancer care (HNSCC) so far and while current treatments achieve significant rates of initial success through surgery and adjuvant chemotherapy/radiotherapy, patients remain at high risk of relapse in both limbs. While tumor antigen reactive T cells are associated with a better outcome and a higher response rate to immune checkpoint inhibition, it has been shown that priming of adaptive response against tumor antigens is impaired in HNSCC. Immune stimulation using a vaccine is a promising strategy to a clinically meaningful improvement. Herein we report phase 1 data of TG4050, a vaccine engineered to carry a patient tailored antigen payload, in patients with HNSCC (NCT04183166).

METHODS

Tumor specific variants are identified using next generation sequencing of tumor and normal samples and immune relevant mutations are called using a machine learning algorithm factored in parameters known to affect immunogenicity including MHC binding, level of expression, prevalence across clones, antigen processing. DNA sequences of the mutations of interest, up to 30 per patient, are cloned in a viral vector (Modified Vaccina Virus Ankara). Following a curative intent treatment, HNSCC patients in complete remission were randomized to an immediate vaccination arm to receive weekly doses of TG4050 for 6 weeks followed by a maintenance period of one month every 3 weeks for a total of 20 doses or 6 weeks or a delayed vaccination arm where the same vaccination regimen is initiated at relapse. PBMC were collected at Baseline and after T doses of vaccine. Primary endpoint was vaccine safety and secondary endpoints included feasibility and immunogenicity.

STUDY POPULATION

Key Inclusion Criteria
- Newly diagnosed stage IV or advanced recurrent solid tumor carriage of cancer, hypopharynx, tongue and oropharynx targets eligible for gross total resection.
- Complete response 3 months after completion of adjuvant therapy.
- ECOG Performance status ≤ 1.

Key Exclusion Criteria
- HLA class I or II antigens HLA-A or HLA-B antigens.
- Previous or concurrent malignancy.
- Prior exposure to cancer immunotherapy including anti-cancer vaccines, any non-specifically targeted T cell or regulatory process such as anti-CTLA-4 or anti-PD-1 or anti-PD-L1 antibodies.
- Graft-versus-host disease with organ complications.

RESULTS

None of the 16 evaluable patients randomized to the arm A (early vaccination arm) has experienced relapse. In the arm B (scheduled to receive the vaccine at relapse only) 2 out of the 16 randomized patients have experienced relapse. The median follow-up time (prior to relapse) is 10.4 months in both arms.

Adverse events were generally mild and included fatigue, rash, fever, and chills, nausea and vomiting, myalgia, dyspepsia, and headache. NEC Laboratories Europe GmbH, Heidelberg, Germany

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REFERENCES

1. Vaccination was well tolerated and no relapse was observed in the vaccinated arm after a median of 10.4 months of follow-up.
2. All patients developed a polypeptidic response regardless of HLA and TME immune features against a mean of 10 targets.
3. NGS data confirmed low TMB in these patients. Regardless, sufficient candidate antigens were identified to design a vaccine. Identification of immunogenic mutations was unaffected by TMB.
4. Robust manufacturing conditions; 86% of eligible patients were provided with vaccine in due time.

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