Phase 1 studies of personalized neoantigen vaccine TG4050 in ovarian carcinoma (OvC) and head and neck squamous cell carcinoma (HNSCC)

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Head and Neck (HNSCC) and Ovarian cancer (OvC) are two indications for which immunotherapy had limited impact so far. Current treatments achieve high rates of initial success through surgery and adjuvant chemotherapy, but patients remain at high risk of relapse in both indications. Immune modulating vaccine is a promising strategy to a clinically meaningful improvement. In this report we present the interim analysis of data of TG4050, a vaccine engineered to carry a patient tailored autologous payload, in patients with HNSCC (NCT0389524) or OvC (NCT04183166).

STUDY POPULATION

Ovarian cancer patients

Key Entry Criteria

- Single HLA class I × 2 (High) positive (HLA-A*02:01, HLA-A*03:01, HLA-A*04:01, HLA-A*11:01, HLA-A*24:02, HLA-A*26:01, HLA-B*07:02, HLA-B*13:02, HLA-B*14:01, HLA-B*15:03, HLA-B*27:02, HLA-B*40:01, HLA-B*40:02, HLA-B*40:06, HLA-B*44:04, HLA-B*48:01, HLA-B*58:02)
- Complete response or stable disease at least 6 months after disease control
- Tumor progression and dermatological testing

Key Exclusion Criteria

- Patients with a prior history of malignant cancer, any antibodies targeting 1 or more regulatory proteins such as PD1, PD-L1, and/or CTLA-4
- Clinical evidence of ongoing contamination

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Identification of neoantigens

Number of candidate epitopes correlated with overall nonsynonymous mutations. Identification of epitopes for design of the personalized vaccine was feasible in most patients across different HLA genotypes.

IMMUNE RESPONSES BY EX VIVO ELISPOTS

Patients were treated at onset of asymptomatic relapse based on CA-125 increase or radiologic relapse. Vaccine period extended until a maximum of 20 TG4050 administrations (~1 year) or disease progression according to RECIST 1.1 whenever first occurred.

In the OvC trial, 5 patients initiated treatment. One patient with elevated CA-125 at treatment start showed normalization after 9 weeks which has been maintained for 9 months. The remaining patients had evidence of radiologic relapse at treatment start. Among them, one had stable disease for 11.5 months and the others progressed either at first or second tumor evaluation.

TIME FEATURES AND CLINICAL FOLLOW-UP IN HUMAN HEAD AND NECK CANCER

A time of randomization per clinical/radiological and molecular criteria (patient informed ciDNA), Exploration of tumor TME through deconvolution of RNAseq data reveals a challenging population with high prevalence of predictive PD-L1 expression and relatively poor immune infiltrates.

TIME FEATURES AND CLINICAL FOLLOW-UP IN OVARIAN CANCER

None of the 15 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 15 randomized patients have experienced relapse.

ADAPTIVE T-CELL RESPONSES BY EX VIVO ELISPOTS

There was no significant difference in immunogenicity of vaccine targets across the range of patient TMB. Immunogenicity of target is defined as the presence of immunoreactive T cell prior or after vaccination.

SAFETY

All tested patients developed a polyepitopic T-cell response against vaccine antigens (3-19 responses) as assessed by ELISPOT ELISA. A mean number of 9 targets per patient was observed. 80% of responses were de novo immunoreactive T cells and 20% were preexisting responses amplified by the vaccine.

KEY MESSAGES

- NGS data confirmed low TMB in these patient populations. Regardless, sufficient candidate antigens were identified to design a vaccine.
- Performance to identify immunogenic mutations was unaffected by TMB.
- Robust manufacturing conditions; 86% of eligible patients were provided with vaccine in due time
- All patients developed a polyepitopic response regardless of HL and TME immune features
- Vaccination was well tolerated and associated with encouraging preliminary signs of anti-tumor efficacy

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