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

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**METHODS**

Tumor specific variants are identified using next generation sequencing of tumors and normal samples and immune relevant mutations are called using a machine learning algorithm factoring 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 Vaccinia Virus Ankara). Following curative intent treatment, HNSCC patients in complete remission were randomized to an immediate vaccine arm to receive weekly doses of TG4050 for 6 weeks followed by a maintenance period of one dose every 3 weeks for up to 26 doses or to a delayed vaccination arm where the same vaccination regimen is initiated at relapse. OC patients received the vaccine upon onset of signs of relapse. PBMC were collected at Baseline and after 6 doses of vaccine. Primary endpoint was vaccine safety and secondary endpoints included feasibility and immunogenicity.

**STUDY POPULATION**

- **Ovarian cancer patients**
  - Key Inclusion Criteria:
    - TMB \(\geq 9/mt\)
    - Complete response after 6–12 months, or after completion of adequate therapy
    - Complete response after 3 months after completion of adjuvant therapy
    - Duration of complete response \(\geq 6\) months
    - EOC-Performance status \(\leq 1\)
  - Key Exclusion Criteria:
    - Smaller lesions than \(>15\) mm
    - Autoimmune diseases
    - Tumor biopsies
    - ELISPOTs

- **Head and Neck (HNSCC) and Ovarian cancer (OG)**
  - Key Inclusion Criteria:
    - TMB \(>9/mt\)
    - Complete response at least 6 months after surgery or at completion of adequate therapy
    - EOC-Performance status \(\leq 1\)
  - Key Exclusion Criteria:
    - Smaller lesions than \(>15\) mm
    - Autoimmune diseases
    - Tumor biopsies
    - ELISPOTs

**RESULTS**

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 of the 16 randomized patients have experienced relapse. The average follow-up time (prior to relapse) is 9.2 months in both arms.

**SAFETY**

- **Adverse events**
  - No significant difference in immunogenicity of vaccine targets across the range of patient TMB. Immuno-gene therapy of target is defined as the presence of immune-reactive T cell prior or after vaccination.

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**ADAPTIVE T-CELL RESPONSES BY EX Vivo ELISPOTs**

There was no significant difference in immunogenicity of vaccine targets across the range of patient TMB. Immuno-gene therapy of target is defined as the presence of immune-reactive T cell prior or after vaccination. All tested patients developed a polyepitopic T-cell response against vaccine targets (3-19 responses) as assessed by ex vivo ELISPOTs. A mean number of 9 targets per patient was observed. 80% of responses were de novo immuno-reactive T cells and 20% were preexisting responses amplified by the vaccine.