TG4001 (Tipapikogene sovacivec) and avelumab for recurrent/metastatic (R/M) Human Papilloma Virus (HPV)-16+ cancers: clinical efficacy and immunogenicity

**IMPACT OF DISEASE/PATIENT CHARACTERISTICS**

**IMMUNE DATA**

- **LUNG METASTASES**
  - ORR for PD-L1<15% vs ≥15%: 16.7% vs 9.5% in the R/M cohort
  - Pathogenesis of PD-L1- and PD-L1+ tumors: pivotal role of PD-1 and PD-L1 in tumor escape
  - PD-L1 expression and expression of immune-related genes in tumors

- **CONCLUSIONS**
  - The combination of TG4001 and avelumab demonstrates a clinically relevant tumor activity in patients with HPV-16 positive cancers having received multiple previous lines of treatment
  - Presence of liver metastases has a profound impact on outcome in terms of ORR and PFS. In patients without liver metastases an ORR of 34.8% and median PFS of 5.6 months is achieved
  - The treatment is associated with changes in tumor microenvironment such as increase in immune infiltrates and expression of genes associated with activation of the immune system. Increased expression of PD-L1 may be the basis of a synergy between TG4001 and avelumab
  - These results warrant further confirmation in a larger, randomized clinical study

**POOLED SUMMARY EFFICACY ANALYSIS**

**SUMMARY OF TREATMENT RELATED ADVERSE EVENTS (AEs)**

- **GRAFT VS HOST DISEASE (GvHD)**
  - **General disorders and administration site conditions**
    - **Viral infection**
      - **CMV**
        - **Neutropenia**
          - **Creatinine increased**
          - **Potassium increased**
          - **Pyrexia**
          - **Gastrointestinal disorders**
            - **Diarrhoea**
            - **Rectal bleeding**

**IMMUNE RESPONSE ASSESSMENT**

- **Lymphocytes**
  - **CD3+ and CD8+ T-cells**
  - **CD4+ T-cells**
  - **CD8+ T-cells**

**EVALUATION OF TUMOR SIZE IN PATIENTS WITHOUT LIVER METASTASES**

- **EVALUATION OF TUMOR SIZE IN PATIENTS WITH LIVER METASTASES**

**INDIVIDUAL LONGITUDINAL CHANGE**

- **NEW PRIMARY TUMOR**
  - **Change in infiltrated CD3+ cells (cell/mm²)**
  - **Percentage of PD-L1+ cells**

**ESTABLISHED PRIMARY TUMOR**

- **Change in infiltrated CD8+ cells (cell/mm²)**

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**Study design and treatments**

- Multicenter, open label, single arm study evaluating the combination of TG4001 and avelumab in patients with recurrent/metastatic HPV-16 positive, oropharyngeal squamous cell carcinoma of the head and neck (ESCHiNE), anal, cervical, vulvar or vaginal cancer.
- TG4001 was administered at a dose of 5×10^7 pfu SC weekly for 6 weeks, every 2 weeks up to M8, and every 12 weeks thereafter. Avelumab was given IV at 10 mg/kg every 2 weeks starting one week after the first vaccine dose.
- PK/MC and tissue samples were collected longitudinally prior to and during the treatment period (Day 43).
- Study endpoints and assessments:
  - Safety of the combination of TG4001 and avelumab.
  - Efficacy and tumor response as assessed by RECIST 1.1.
  - Immune parameters: priming of specific T cell responses against HPV E6 and E7 antigens, expression of immune related genes in the tumor, and changes in PD-L1 expression on tumor cells (2023).

**POOLED EFFICACY PARAMETERS**

- **PD-L1 (≥ 4 patients)**
  - **Total Response**
    - **NCT03459439**
  - **ORR**
    - **R/M patients**
      - **NCT03459439**

**ADVERSE EVENTS (AE)**

- **Grade 3/4 AEs**
  - **Hepatobiliary disorders**
  - **Gastrointestinal disorders**
  - **Metastatic or recurrent/recurrent HPV-16+ cancer including oropharyngeal SCC, anal, cervical, vulvar or vaginal cancer**
  - **HPV positive detected in central laboratory by in vitro PGP with HPV-16 specific probes and intact of negative results by sequencing.
  - **Prior to the two prior lines of treatment for the management of metastatic or recurrent disease**

**POOLED SAFETY PROFILE**

- **Most Commonly reported grade 3/4 AEs by population**

**TRAIAS of grade 3/4**

- **Clinical Laboratory Abnormalities**
  - **Anemia**
  - **Aspartate aminotransferase increased**
  - **Chloride increased**
  - **Creatinine increased**
  - **Creatinine decreased**

**EVALUATION OF TUMOR SIZE**

- **Evolution of tumor size in patients with liver metastases**
- **Evolution of tumor size in patients without liver metastases**

**METASTASES DISTRIBUTION**

- **Number of CT lines for R/M disease**
- **Number of organs involved**

**PATIENT DEMOGRAPHICS AND BASELINE CHARACTERISTICS**

- **Patients without liver metastases (n=22)**
- **Patients with liver metastases (n=26)**

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