**BACKGROUND**

INVAC-1 is an optimized DNA vaccine encoding an inactivated form of human telomerase reverse transcriptase (hTERT) proto-oncogene, a prototype of shared tumor antigen expressed in more than 85% of human cancers. Telomerase activation is associated with maintenance of telomere length and accounts for the unlimited proliferative capacity of cancer cells.

Primary PO, safety pharmacology and toxicology studies, including biodistribution and local tolerance, showed that INVAC-1 was enzymatically inactive, immunogenically safe and well tolerated. In preclinical studies, INVAC-1 vaccination triggered strong and long-lasting hTERT-specific CD8+ as well as CD4+ Th1/Th2 responses. INVAC-1 was also able to slow tumor growth and increased survival rate by 50% in tumor-bearing mice (SanT2 model) (Thalmaier et al., 2016, Oncology).

Here, we report clinical and pharmacodynamics results of the first-in-human phase I study with INVAC-1 vaccine administered ID (either with electroporation or by Needle-free Injection System Tropis®) as a single agent in multiple solid tumors.

**METHODS**

**Study design**

- First-in-Human, Phase 1, open label classical 3+3 design, multiple dose study of single agent INVAC-1 in patients with relapsed or refractory solid tumors presenting progressive disease (MTC20206754)
- Administration ID followed by electroporation (EP) (1 patients) or NFS Tropis® (n patients)
- At least 3 sequential cycles (could be prolonged up to 6 additional cycles)

**Study population**

- 26 patients aged ≥18 years with histological diagnosis of advanced/metastatic solid tumors relapsed or refractory to standard treatment and with a life expectancy of at least 6 months and Eastern Cooperative Oncology Group (ECOG) performance status ≤ 1 were included
- Patients had to have an adequate skin status and adequate bone marrow, renal, liver and cardiac function.
- Female patients not enrolled if they were pregnant or of child-bearing potential
- Written informed consent was obtained from each patient.

**Safety**

- Primary endpoint: Dose Limiting Toxicities (DLTs)
- Secondary end-points:
  - Treatment-related Adverse Events
  - Cytokine release
  - Circulating auto-antibodies

**Pharmacodynamics**

- Objective responses
- Tumor response and duration of response
- Time to event (Progression Free Survival, Overall Survival)
- hTERT-specific CD4 and CD8 T cell responses (Enzyme Linked Immunosorbent Spot Assay (ELISpot))
- Polarity of anti-hTERT immune response (Luminex®)
- Peripheral Blood cell populations phenotyping (Flow Cytometry).

*Patient in assessment for cardiac effects of IN VAC-1, treatment setup by patient's cardiologist.*

**RESULTS**

**S A F E T Y**

INVAC-1 administration ID (either with EP or by Tropis®) was safe and well tolerated in all dose cohorts.

- Only one grade 3 Serious AE was reported - No DLT was defined
- No death was reported within 28 days after the last dose of study treatment whatever the number of cycles the patients received (up to 9 cycles)
- Most common study treatment-related AEs were fatigue and EP-related AEs.


*Anti-PD-1 (Nivolumab) enhances hTERT specific CD4 immune response*  
*Immune response to NY-ESO-1 was enhanced after INVAC-1 vaccination*

**CONCLUSIONS**

- INVAC-1 was demodulating and well tolerated up to nine cycles as a single intradermal treatment (130 µg, 400 µg and 800 µg) in patients with advanced solid tumors
- Disease stabilization was achieved in 58% of patients, up to 9 months
- INVAC-1, by triggering strong anti-hTERT TH1-polarized CD4 T cell response as well as CD8 cytokotoxic response without immune suppression induction, demonstrated robust immunogenicity in patients enrolled in this study
- Patients with OS > 1 year showed significantly higher hTERT specific immune response after prime/boost INVAC-1 vaccination compared with OS < 1 year
- Our results suggest prolonged OS for patients presenting an INVAC-1-induced hTERT immune response compared to non-responders (17.4 versus 7.0 months (3.0...))
- Preliminary data suggest that INVAC-1 could promote epitope spreading

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