**BACKGROUND**

INVAC-1 is an optimized DNA vaccine encoding an inactive form of human telomerase reverse transcriptase (hTERT), an “universal” tumor antigen expressed in more than 85% of human cancers with little or no expression in normal somatic cells (1,2). Telomerase activation was shown to result in cell immortalization with increased proliferative capacity, telomere length and accounts for the unlimited proliferative capacity of cancer cells. In preclinical models, INVAC-1 vaccination triggered strong and long-lasting hTERT-specific CD8+ as well as CD4+ T-cell responses and also promoted antitumor effect (3,4).

**METHODS**

**STUDY DESIGN**

A Study-in-Phase, I/II, open label classical 3+3 design, multiple dose study of single agent INVAC-1 in pts with relapsed or refractory solid tumors (NCT02030175).

**STUDY TREATMENT**

- **DOSE of INVAC-1 tested**: 100 (3 pts), 400 (3 pts), 800 µg (3 pt), extension 800 µg (11 pts)
- **Route**: Intradermal injection
- **Cycles of INVAC-1 last 28 days**: Follow up: up to one year from first dose of INVAC-1.

**STUDY POPULATION**

Twenty adult pts with histological diagnosis of adenocarcinoma or no expression in normal somatic cells (1,2). Telomerase activation is associated with maintenance of telomere homeostasis.

- **Patients had to have an adequate bone marrow, renal, liver and cardiac function.**

**SAFETY ANALYSES**

- **The primary endpoint of the study was the occurrence of Dose-Limiting Toxicities (DLTs).**
- **Full safety evaluation was also included**: (Treatment-Emergent Adverse Events (TEAE), Routine laboratory parameters, Cytokine release, Circulating auto-antibodies).

**EFFICACY AND PHARMACODYNAMICS ANALYSES**

- **Efficacy and pharmacodynamics analysis**
- **Elispot**
- **Blood and urine samples**
- **Cytokine release**
- **Circulating auto-antibodies**

**STUDY TREATMENT**

- **Elispot**, a needle-free injection system) is being evaluated instead of Electroporation.
- **The majority of pts were vaccinated with INVAC-1** following the 2nd and 3rd vaccination. In most of the pts who had a pre-existing anti-hTERT immunity, INVAC-1 vaccination increased the magnitude of the anti-hTERT CD8+ T cell response up to 59% in cases (10 pts out of 12) leading to the assumption that INVAC-1 triggered de novo anti-hTERT CD4+ T-cell response in 25% of pts.
- A majority of pts mounted the anti-hTERT CD4+ T-cell response following the 2nd and 3rd vaccination. In most of the pts who had a pre-existing anti-hTERT immunity, INVAC-1 vaccination increased the magnitude of the anti-hTERT CD4+ T cell response in 25% of pts.
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**RESULTS**

- **Antigenicity of hTERT-derived epitopes: potential synergistic effect with chemotherapy response.**

**IMMUNOLOGICAL SAFETY**

- **No DLTs were reported. No death occurred within 28 days after the last day of study treatment. 13 pts (65%) died from disease progression after these 28 days during follow up. No deaths were considered as related to study treatment.**

- **SERIOUS TEAE**
- 3 serious TEAE (acute kidney injury, RILD, and lymph node abscesses) resulted in premature discontinuation of the study treatment.

**CONCLUSIONS**

- **Intra-dermal INVAC-1 administration was safe, well tolerated and strongly immunogenic at the doses and schedule tested. No DLT or MTD was achieved.**
- Early anti-tumor activity has been observed. Although no response has been confirmed on the long term, the disease was stabilized for 60% of the pts and the median OS was higher than one year.
- INVAC-1 appeared to be capable to stimulate both CD4+ T cells and CD8+ T cells against hTERT.
- The recommended dose of INVAC-1 vaccine for phase II studies is a monthly intra-dermal injection of 800 µg. This study is still ongoing, but in 32 pts in whom an alternative intra-dermal injection device (Triposs®; a needle-free injection system) is being evaluated instead of Electroporation.
- The results obtained encourage a future evaluation of INVAC-1 in solid tumors, as well as in hematologic malignancies, either as monotherapy or in combination with various immunotherapeutic drugs. A phase II study in Chronic Lymphocytic Leukemia (CLL) pts is being initiated.

**REFERENCES**