Clinical Trial Completed

1518 T-CELL INDUCING ONCOLYTIC VIRUS (IGRELIMOGENE LITADENOREPVEC; TILT-123) SHOWS SAFETY, ANTI-TUMOR ACTIVITY AND INDUCTION OF IMMUNE RESPONSES IN ADVANCED SOLID TUMOR PATIENTS (FULL REPORT ON TUNIMO)

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Background Oncolytic viruses selectively replicate in and lyse cancer cells, while simultaneously stimulating immune responses towards the tumor. Igrelimogene litadenorepvec (Ad5/3-E2F-d24-hTNF-IRES-hIL2; TILT-123), is an oncolytic adenovirus encoding for interleukin-2 and tumor necrosis factor alpha, designed for recruiting, propagating and stimulating T-cells for re-invigoration of the tumor microenvironment.

Methods TUNIMO (NCT04695327) is a single-armed open-label phase 1 clinical trial designed to assess the safety of TILT-123 monotherapy in patients with advanced solid tumors which are refractory to standard therapy. The trial followed a 3+3 dose-escalation design where patients received a dose of TILT-123 intravenously, followed by at least five planned intratumoral and/or intravenous injections. The primary endpoint was safety by day 85, assessed by adverse events, vital signs, laboratory values and electrocardiogram. Secondary endpoints included evaluation of tumor responses, neutralizing antibodies, analysis of biopsies, virus persistence in blood and shedding. Enrollment was completed on Aug 31st 2023.

Results 20 patients were enrolled, with a median age of 58 (33–72) years. The most prevalent cancer types were sarcomas (35%), melanoma (15%) and ovarian cancer (10%). Patients were heavily pretreated, receiving a median of 4.5 (range 0–16) lines of systemic therapy prior to trial entry. Patients received at least 3 doses of TILT-123 and dose-limiting toxicities were not observed. The most frequent grade 1–3 AEs (>10% of patients) were chills, fatigue, and pyrexia. By Aug 31st, 9 patients had been evaluated on d78 for response with RECIST 1.1, iRECIST or PET-based criteria. The overall disease control rate by PET was 6/9 (66%), including 4/9 (44%) stable metabolic disease and 2/9 (22%) minor or partial metabolic response. 2/9 (22%) patients showed disease control by RECIST1.1, including 1/9 (11%) partial response. Virus was detected in biopsies of injected and non-injected lesions. High virus amounts were seen in blood at one hour, with lower levels at 16 hours, and virus could still be detected several weeks later. Shedding into urine/saliva was negligible. Most patients had undetectable baseline neutralizing antibodies towards the chimeric 5/3 capsid, but titers increased after treatment. Biological data supporting T-cell infiltration into the tumor, was generated. Analysis of the serum proteome and cellular compartments revealed systemic immune activation following intratumoral and intravenous delivery.

Conclusions Treatment with TILT-123 was safe and demonstrated signs of anti-tumor activity across different cancer types in highly pre-treated patients. Good tolerability of TILT-123 facilitates combination therapies, and several such trials are under way (NCT04217473, NCT05271318, NCT05222932).

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Ethics Approval TUNIMO (TILT-T115): This study was approved by the Finnish National Committee on Medical Research Ethics (TUKIJA); approval number HUS/1804/2020

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