

### EMERGING PROTEOMIC AND SAFETY ANALYSIS OF BLOOD FROM SOLID TUMOR PATIENTS RECEIVING TILT-123 (AD5/3-E2F-D24-HTNFA-IRES-HIL2) MONOTHERAPY IN TUNIMO PHASE 1 CLINICAL TRIAL

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**Background** TILT-123 (Ad5/3-E2F-d24-hTNFa-IRES-hIL2) is an oncolytic adenovirus encoding tumor necrosis factor alpha (hTNFa) and interleukin 2 (hIL-2) designed to enhance immune cells' reactivity against cancer cells in cold tumor microenvironments. Following more than a decade of preclinical development, the virus has now reached clinical phase and multiple trials are underway in several indications in monotherapy and combination therapy settings. NCT04695327 (TUNIMO) is an open-label phase 1 multicenter trial evaluating the safety of TILT-123 as a monotherapy in advanced solid cancers. Safety and correlative analysis have been performed from multiple different biological matrices from patients to provide mechanistic insights to TILT-123 therapy. This study focused on patient blood samples collected during the trial.

**Methods** First five cohorts of TUNIMO included 15 patients with various solid cancer types. Patients received multiple rounds of TILT-123 therapy, and blood was collected before and after therapy. Blood collected from the patients was analyzed for safety analysis through standard hospital protocols. Serum from the blood was extracted and analyzed with Olink Target 96 Immuno-Oncology Panel. Adverse events were assessed and collected by the study site investigators.

**Results** TILT-123 therapy was well tolerated across all dosing cohorts. Transient lymphopenia and neutropenia with quick normalization was observed in patients receiving treatment. A trending increase in lymphocytes and neutrophils was observed across the study. Regarding safety, therapy was well tolerated with no untoward changes in liver safety values, kidney function tests or electrolytes even at highest dose levels. Total of 63 therapy related adverse events (AEs) were observed in the 15 patients treated. Clinically, most frequent AEs were fever, chills, neutropenia, and fatigue. No treatment related grade 5 AEs were reported. Proteomic profiling of the serums revealed high levels of pro-inflammatory cytokines and chemokines post treatment.

**Conclusions** No significant toxicities related to TILT-123 therapy were observed clinically or in blood laboratory testing. Transient reduction in blood lymphocytes and neutrophils with quick normalization was observed after treatment. Even in this heavily pretreated patient population, proteomic analysis of serum indicated TILT-123's ability to induce pro-inflammatory changes associated with enhanced lymphocyte cytotoxicity and trafficking, providing encouraging results of activity in this group of patients with poor prognosis.

**Ethics Approval** This study was approved by the Finnish National Committee on Medical Research Ethics (TUKIJA); approval number HUS/1804/2020.

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