#363634: First-in-human clinical trial of an oncolytic adenovirus armed with TNFa and IL-2 in patients with advanced melanoma receiving adoptive cell transfer of tumor-infiltrating lymphocytes.

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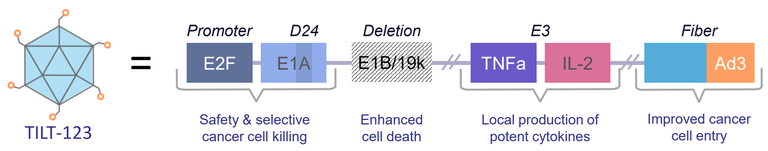
Background:

- Long-term complete remission experienced by some cancer patients after receiving immunotherapy, represent the ideal outcome to pursue for the development of therapies for oncology. Unfortunately, those responses are limited to a minority of treated patients.
- That is also the reality for adoptive cell therapy with tumor-infiltrating T lymphocytes (ACT-TILs), and adverse events resulting from preconditioning chemotherapy and postconditioning recombinant IL2 are common.
- TILT-123 is an oncolytic adenovirus (Ad5/3-E2F-D24-TNFa-IRES-IL2) designed to enable T-cell centered therapies and checkpoint inhibition against cancer.



- The open label, dose escalation trial (NCT04217473) has the main endpoint of establishing TILT-123 safety by day 36 (prior to ACT-TIL administration).
- Secondary endpoints include safety and tolerability after TIL therapy has been administered, and evaluation of antitumor responses.
- Additionally, extensive biological assays of patient aim to characterize viral transduction of tumors through the intravenous and intratumoral routes, and to elucidate the immunological impact of the drug.

Administration of TILT-123 to melanoma patients receiving adoptive cell therapy with tumor-infiltrating T cells was completed in cohorts 1-3 without DLTs

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Methods:

- Refractory or recurrent stage III/IV patients, that are eligible for ACT-TIL therapy, can potentially participate in the study.
- Patients must have > 9 mm tumor (in diameter) and at least one additional tumor (>14 mm in diameter) must be available for injections and biopsies for correlative analyses. The disease burden must be measurable, but does not need to fulfil RECIST 1.1.
- Patients receive 6 doses of TILT-123 at different visits, which occur before, during and after the ACT-TIL administration at day 36.
- Dose escalation of TILT-123 occurs in between cohorts of patients.

Future Directions for Research:

- Dose escalation of TILT-123 has proceeded to cohort four in this trial.
- Additional clinical research on the use of TILT-123 is being carried out in three other trials:
  - NCT04695327: TILT-123 as monotherapy in solid tumors.
  - NCT05271318: TILT-123 + Pembrolizumab in Ovarian Cancer.
  - NCT05222932: TILT-123 + Avelumab in HNSCC.