Fully intravenous delivery regimen of oncolytic adenovirus coding for TNFa and IL-2 (TILT-123) in patients with advanced solid cancers.

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Background

The need for intratumoral administration has been a limiting factor for development and use of oncolytic virus based immunotherapy. Igrelimogene litadenorepvec (Ad5/3-E2F-d24-hTNF-IRES-hIL2; TILT-123) is a chimeric oncolytic adenovirus, with fiber knob from serotype 3, and dual selectivity devices, facilitating systemic delivery via intravenous injection.

Methods

A fully intravenous delivery regimen of TILT-123 was studied in 6 patients with advanced solid cancers (NCT04695327). The cancer types included three rectal carcinomas, gastric intestinal type carcinoma, pancreatic ductal adenocarcinoma, and liposarcoma. TILT-123 was administered twice daily (each injection $1x10^{12}$ viral particles) on days 1, 3, 8, 10, 22, 43 and 64. The split dose regimen was used to increase bioavailability through effects on hepatic Kupffer cells. The primary endpoint was safety by adverse events and laboratory tests. Secondary endpoints included treatment effects by RECIST1.1 and PET criteria. Correlative studies included analysis of blood and tumor biopsies for presence of virus and treatment induced immunological changes.

Results

All patients were safely treated with a completely intravenous TILT-123 regimen. The most common adverse events included chills, fever, and transiently decreased lymphocyte count (20%, 13% and 7% of all adverse events, respectively). No liver enzyme elevation was noted by ALT, AST, or ALP. No dose-limiting toxicities were seen. Lymphocytes decreased in peripheral blood, compatible with trafficking to tumors. Of patients evaluable by imaging by data cutoff (26 Apr 2024), disease control was seen in 33% of patients (1/3) with RECIST1.1 and 66% of patients (2/3) with PET-based criteria. Tumor biopsies indicated successful delivery of virus to tumors by qPCR and staining of viral proteins.

Conclusions

Fully intravenous delivery of TILT-123 was safe, resulting in tumor transduction and immunological effects in metastases. Further studies utilizing this regimen are mandated.