Updated clinical results of BT-001, an oncolytic virus expressing an anti-CTLA4 mAb, administered in combination with pembrolizumab in patients with advanced solid tumors.

C. Lebbe[1], R. Bahleda[2], E. Ezine[1], B. Baroudjian[1], M. Sakkal[2], E. Rowinski[3], A. Vinceneux[3], S. Champiat[4], K. Bidet Huang[5], N. Stojkowitz[5], H. Makhloufi[5], A. Sadoun[5], A. Ropenga[6], M. Semmrich[6], A. McAllister[6], M. Chisamore[7], P. Cassier[3]

[1] Université Paris Cite ,AP-HP Dermato-oncology and CIC , Cancer institute APHP.nord Paris cité, INSERM U1342 - Equipe 1 - CNRS EMR8000, Saint Louis Hospital, Paris, France, [2]Drug Development Department (DITEP), Gustave Roussy Cancer Campus, Villejuif, Cedex, France, [3]Medical Oncology Department, Centre Léon Bérard, Lyon, France, [4]Department of Investigational Cancer Therapeutics, The University of Texas MD Anderson Cancer Center, Houston, TX, USA, [5]Transgene SA, Illkirch-Graffenstaden, France, [6]BioInvent International AB, Lund, Sweden, [7]Merck & Co., Inc., Rahway, NJ, USA.

Background

BT-001 is an oncolytic vaccinia virus with selective tumor cell replication encoding GM-CSF and an anti-CTLA-4 mAb. We previously reported (ESMO 2024, Abstract #3190)24 patients (pts) with advanced solid tumors treated with intratumoral (IT) injections of BT-001 alone (n=18) or at the dose of 10^7 pfu/mL in combination with IV pembrolizumab (n=6), we showed that 2 of 6 pts in the combination part had partial response (PR). Herein, we report the updated data of the combination part with 7 additional pts treated with BT-001 at the dose of 10^8 pfu/mL.

Methods

Patients with advanced, pretreated select tumor types (sarcoma, mel, TNBC, NSCLC) were eligible. BT-001 was given IT Q3W at the dose of 10^7 pfu/mL (n=6) or 10^8 pfu/mL (n=7) in combination with pembrolizumab 200 mg IV Q3W until disease progression. Tumor response was assessed using iRECIST. Anti-CTLA-4 mAb expression and biodistribution were monitored in blood and injected lesions. Translational analyses were performed in blood and tumor biopsies to characterize the tumor-specific and systemic immune effects.

Results

A total of 13 pts (8F, 5M, median age = 54 y) with melanoma (n=9), all previously exposed to immune checkpoint inhibitors (ICI), leiomyosarcoma (n=3), and breast cancer (n=1) were enrolled. As of Apr 21, 2025 (median follow-up = 4.6 months), patients received a median number of 6 BT-001 injections and pembrolizumab infusions (ranges 2-25 and 2-23, respectively). One dose-limiting toxicity was observed at 10^8pfu/ml (grade 3 pyrexia). Most common treatment-related AEs (TRAEs) were pyrexia (9/13 pts), chills and pruritis, (4/13, each), erythema, nausea, and eosinophilia (3/13, each). Three grade 3 TRAEs were reported in 2 pts (2 pyrexias and one lymphopenia). Best overall response was PR in 2 of the 13 pts, 1 pt with PD(L)-1 resistant melanoma and 1 pt with heavily pretreated but ICI naïve leiomyosarcoma and lasting 6 and 12+ months, respectively. Tumor shrinkage was observed in both injected and non-injected lesions. Translational data and updated clinical results will be presented.

Conclusions

IT BT-001 injection in combination with IV pembrolizumab was well tolerated and showed encouraging and sustained anti-tumor activity in some patients with advanced refractory tumors. BT-001 could be an effective option to improve the response to ICI.