383 DURABLE RESPONSES WITH INTRATUMORAL ELECTROPORATION OF PLASMID INTERLEUKIN 12 PLUS PEMBROLIZUMAB IN PATIENTS WITH ADVANCED MELANOMA PROGRESSING ON AN ANTI-PD-1 ANTIBODY: UPDATED DATA FROM KEYNOTE 695

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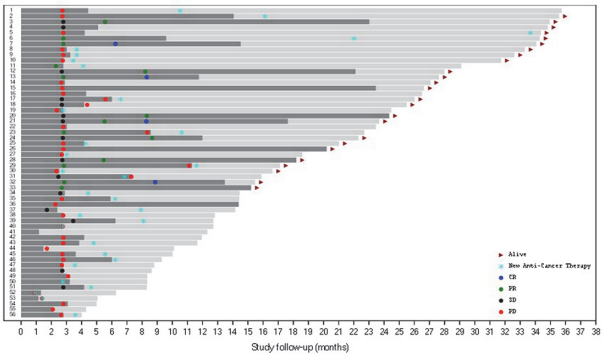
Background Electroporated plasmid interleukin-12 (pIL-12-EP; tavokinogene telseplasmid; TAVO) induces sustained intratumoral expression of IL-12, a cytokine that is integral for response to anti-PD-1 antibodies. Here, we present updated safety and response duration data from KEYNOTE 695, a Phase 2, multicenter, open-label trial of pIL-12-EP in combination with pembrolizumab in patients with stage III/IV melanoma immediately following confirmed progression on an anti-PD-1 antibody.

Methods Patients with confirmed disease progression after ≥12 weeks' treatment with an anti-PD-1 antibody alone or in combination were eligible. Patients received intratumoral pIL-12-EP on days 1, 5 and 8 every 6 weeks and pembrolizumab 200 mg every 3 weeks. Responses were assessed by the investigator at 12-week intervals using RECIST v1.1; overall survival (OS) and duration of response (DoR) assessments were conducted using the Kaplan-Meier method.

Results Of the first 56 patients treated, 50% had visceral disease (M1b-d), 80% had received 1–2 and 20% ≥3 prior lines of therapy, 27% had prior ipilimumab and 21% prior BRAF/MEK inhibitors. 61% of patients were primary refractory to anti-PD-1. 54 patients were efficacy evaluable, defined as patients who had at least one post-treatment scan. The investigator-assessed objective response rate (ORR) per RECIST was 27.8% (4 CR, 11 PR); ORR per iRECIST was 29.6%. In patients with M1b-d staging, ORR was 33.3% (n=9/27), and in those receiving prior ipilimumab, ORR was 33.3% (n=5/15). Seven patients had 100% reduction in target lesions, and regression was observed in non-injected lesions. The median DoR had not been reached. With a median follow up of 19.3 months, the median OS (95% CI) was 24.5 (14.4, NR) months (figure 1). The study is now fully enrolled. In 105 patients with safety data, there were no Grade 4/5 treatment-related adverse events (TRAEs) reported. Grade 3 TRAEs occurred in 5.7% and comprised cellulitis in two patients and arthralgia, pneumonitis, enteritis, keratoacanthoma, lichen planus and musculoskeletal chest pain in one patient each. The Grade 1/2 TRAEs in ≥10% patients were fatigue (27.6%), procedural pain (20.0%), diarrhea (17.1%), nausea (10.5%) and pruritus (10.5%). ORR by blinded independent central review has commenced and a global phase 3 trial is planned.



Abstract 383 Figure 1 Overall survival in patients treated with pIL-12-EP in combination with pembrolizumab. Dark grey bars: time on study treatment, light grey bars: end of treatment to death or censoring

Conclusions Patients with anti-PD-1 therapy refractory advanced melanoma can achieve deep, durable responses in both injected and non-injected lesions with pIL-12-EP plus pembrolizumab. Intratumoral pIL-12-EP in combination with pembrolizumab was generally well tolerated, with minimal Grade 3 and no Grade 4/5 TRAEs.

Trial Registration NCT03132675

Ethics Approval The study was approved by a central IRB and/or local institutional IRB/Ethics Committee as required for each participating institution.

Consent Written informed consent was obtained from the patients participating in the trial; the current abstract does not include information requiring additional consent

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