

**Fig 1. In vivo TIL persistence in patients with durable TIL benefit VS patients with no durable TIL benefit. Linear mixed model fit by REML. t-tests use Satterthwaite's method.**

**Abstract 280 Figure 1** In vivo TIL persistence in patients with durable TIL benefit VS patients with no durable TIL benefit

time. Combined with single cell RNA sequencing & TCR sequencing, functional features of neoantigen-specific T cells in both baseline and progressive disease (PD) tumors were analyzed.

**Results** Our data show that the presence of neoantigen-specific TIL is associated with durable TIL benefit ( $p=0.031$ ). We also identified tumor antigen-specific TCR clonotypes for 3 TIL-treated patients and followed these cells longitudinally in PBMCs. We found that although neoantigen-specific T cells had a dramatic increase after TIL infusion, patients with durable TIL benefit had a longer TIL persistence ( $p=0.048$ , figure 1). RNA sequencing on baseline tumors showed that in patients with no durable TIL benefit, genes contributing to extracellular matrix formation were highly expressed, preventing infused TILs from migrating into tumor sites.<sup>4</sup> In 2 TIL-treated patients, we found that neoantigens which were recognized by infused TILs were missing in PD tumors. In one patient, further investigation of TRM cells from both baseline and PD tumors showed that although T cells in the PD tumor can recognize PD tumor antigens, the T cells highly expressed PD-1, CTLA-4, Lag3 and TIGIT (figure 2), indicating an inability to control tumor progression. Enumeration of

immunocyte compositions using CIBERSORT showed that higher M1/M2 ratios were found in patients with durable TIL benefit.

**Conclusions** In summary, higher expression of tumor antigens, longer TIL persistence and more M1 macrophages are associated with durable TIL benefit, while lack of tumor antigens, expression of immune checkpoint molecules, and upregulated formation of extracellular matrix may cause TIL resistance. Therefore, both tumor intrinsic factors and extrinsic factors contribute to TIL resistance in lung cancer patients.

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**Trial Registration** NCT03215810

**Ethics Approval** The study was approved by Chesapeake IRB, approval number Pro00021984.

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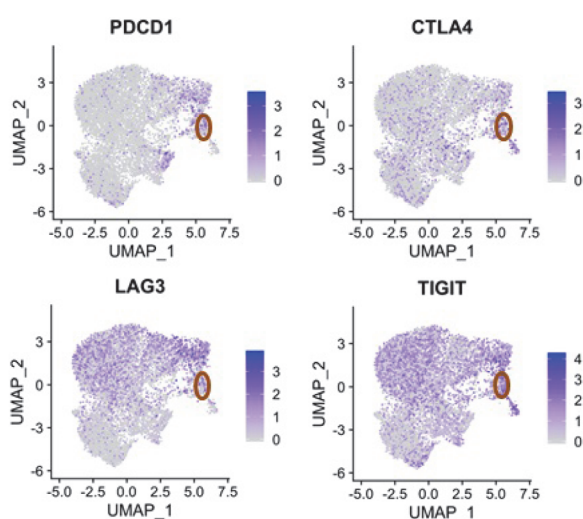
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## JAVELIN MEDLEY VEGF: PHASE 2 STUDY OF AVELUMAB + AXITINIB IN PATIENTS WITH PREVIOUSLY TREATED NON-SMALL CELL LUNG CANCER (NSCLC) OR TREATMENT NAIVE, CISPLATIN-INELIGIBLE UROTHELIAL CANCER (UC)

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**Background** Avelumab, a human anti-PD-L1 monoclonal antibody, has shown a manageable safety profile and antitumor activity in multiple tumor types, including platinum-resistant metastatic or recurrent NSCLC,<sup>1</sup> and is approved

**Abstract 280 Figure 2** PD tumor neoantigen specific T cells (red circled) express immune checkpoint molecules



for patients with locally advanced or metastatic UC who have progressed after  $\geq 1$  previous line of platinum-based chemotherapy<sup>2,3</sup> and as maintenance treatment for those who have not progressed with platinum-based chemotherapy.<sup>4</sup> JAVELIN Medley VEGF (NCT03472560) evaluated the efficacy and safety of avelumab + axitinib, a potent inhibitor of VEGFR 1, 2, and 3, in patients with advanced or metastatic NSCLC or UC.

**Methods** Eligible patients with NSCLC had received  $\geq 1$  prior platinum-containing therapy and  $\leq 2$  prior lines of systemic therapy for locally advanced or metastatic disease; patients with UC were treatment naïve in the locally advanced or metastatic setting and ineligible for cisplatin-containing chemotherapy. Patients were immune checkpoint inhibitor naïve and received avelumab 800 mg intravenously every 2 weeks + axitinib 5 mg orally twice daily. The primary endpoint was confirmed objective response (OR) per investigator assessment (RECIST 1.1). Secondary endpoints included progression-free survival (PFS) and safety. PD-L1 expression was assessed in baseline tumor samples (Ventana SP263 assay). Data have not undergone standard quality checks and are subject to change due to COVID-19-related healthcare burden.

**Results** A total of 41 patients with NSCLC and 20 with UC received avelumab + axitinib. The confirmed OR rate was 31.7% (95% CI, 18.1–48.1) in the NSCLC cohort and 10% (95% CI, 1.2–31.7) in the UC cohort (all partial responses); 16 patients (39.0%) and 5 (25.0%) had stable disease, respectively. Responses were observed regardless of PD-L1 expression status. Median PFS was 5.5 months (95% CI, 2.5–7.0) in the NSCLC cohort and 2.3 months (95% CI, 1.8–5.6) in the UC cohort. Grade  $\geq 3$  treatment-related adverse events (TRAEs) occurred in 24 patients (58.5%) in the NSCLC cohort; the most common was hypertension (n=7 [17.1%]). Grade  $\geq 3$  TRAEs occurred in 9 patients (45.0%) in the UC cohort; the most common were amylase increased, asthenia, decreased appetite, and palmar-plantar erythrodysesthesia syndrome (n=2 [10%] each). One patient in each cohort experienced a TRAE that led to death (gastric perforation and urinary bladder hemorrhage).

**Conclusions** Avelumab + axitinib showed antitumor activity and a manageable safety profile in patients with advanced or metastatic NSCLC or UC consistent with findings from studies of each drug alone and in combination.

**Trial Registration** NCT03472560

**Ethics Approval** The study was approved by each site's independent ethics committee.

**Consent** N/A

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## PAN-TUMOR ANALYSIS OF THE ASSOCIATION BETWEEN PD-L1 COMBINED POSITIVE SCORE AND RESPONSE TO PEMBROLIZUMAB MONOTHERAPY

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**Background** PD-L1 is expressed on both tumor and immune cells; however, the mechanism by which PD-L1 modulates the adaptive immune response on tumor versus immune cells may differ. Additionally, the prevalence of PD-L1 expression and the partitioning between tumor and immune compartments varies by tumor type. While PD-L1 expression on tumor or immune cells can be scored separately, the PD-L1 combined positive score (CPS) captures both tumor and immune cell expression in one aggregate score. We performed a retrospective, exploratory analysis of the effectiveness of CPS as an enrichment biomarker across several studies of pembrolizumab monotherapy in patients with multiple tumor types.

**Methods** PD-L1 expression was assessed using PD-L1 IHC 22C3 pharmDx. Expression was measured using CPS (defined as the number of PD-L1–staining cells [tumor cells, lymphocytes, macrophages] divided by the total number of tumor cells, multiplied by 100) in tumor samples from single-arm (KEYNOTE-052 [UC], KEYNOTE-059 cohort 1 [G/GEJ], KEYNOTE-086 [TNBC], KEYNOTE-158 [cervical; SCLC], KEYNOTE-180 [EC], KEYNOTE-224 [HCC], KEYNOTE-427 [RCC]) and randomized (KEYNOTE-040 [HNSCC], KEYNOTE-045 [UC], KEYNOTE-061 [G/GEJ], KEYNOTE-119 [TNBC], KEYNOTE-240 [HCC]) pembrolizumab studies. Data were pooled across tumor types for pembrolizumab and for standard-of-care (in controlled studies), and then estimates of response rate, prevalence, and receiver operating characteristics (ROC) analysis were performed over various CPS cutpoints. CPS distribution by response, tumor type, and line of therapy were also assessed.

**Results** There were 3769 treated patients with available PD-L1 CPS (pembrolizumab, n=2678; standard-of-care, n=1091). The area under the ROC curve for ORR was 0.63 (95% CI, 0.61–0.66) for pembrolizumab and 0.48 (95% CI, 0.43–0.53) for standard-of-care when a positive association was evaluated between CPS and ORR (figure 1); individual cutpoints of 1, 10, 20, and 50 were examined (table 1). Figure 2 shows a boxplot of CPS distribution for response in pembrolizumab-treated patients.

**Conclusions** This retrospective, exploratory pan-tumor analysis demonstrates that CPS is an effective scoring method for measuring PD-L1 expression and can be used as a predictive biomarker to identify patients likely to respond to pembrolizumab.

**Abstract 282 Table 1** Response Rates and Sensitivity at Individual CPS Cutpoints for Pembrolizumab-Treated Patients

Population	Prevalence, %	ORR, %	Sensitivity
Overall	100	17.6	1
CPS = 0	34.8	11.1	0.22
CPS $\geq 1$	65.2	21	0.78
CPS $\geq 10$	28.6	27.7	0.45
CPS $\geq 20$	19.3	30.4	0.33
CPS $\geq 50$	10	33.1	0.19

CPS, combined positive score; ORR, objective response rate.