for patients with locally advanced or metastatic UC who have progressed after ≥1 previous line of platinum-based chemotherapy[2 3] and as maintenance treatment for those who have not progressed with platinum-based chemotherapy.[4] 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 ≥1 prior platinum-containing therapy and ≤2 prior lines of systemic therapy for locally advanced or metastatic disease; patients with UC were treatment naive 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 ≥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 ≥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

REFERENCES

1. Gulley JL, Rajan A, Spigel DR, *et al*. Avelumab for patients with previously treated metastatic or recurrent non-small-cell lung cancer (JAVELIN Solid Tumor): dose-expansion cohort of a multicentre, open-label, phase 1b trial. *Lancet Oncol* 2017;**18**:599–610.
2. Patel MR, Ellerton J, Infante JR, *et al*. Avelumab in metastatic urothelial carcinoma after platinum failure (JAVELIN Solid Tumor): pooled results from two expansion cohorts of an open-label, phase 1 trial. *Lancet Oncol* 2018;**19**:51–64.
3. Bavencio (avelumab) injection. [package insert] Darmstadt, Germany: Merck KGaA; 2019.
4. US Food and Drug Administration. FDA approves avelumab for urothelial carcinoma maintenance treatment. https://www.fda.gov/drugs/drug-approvals-and-databases/fda-approves-avelumab-urothelial-carcinoma-maintenance-treatment. Accessed August 19, 2020.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0281

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

Lingkang Huang, Jared Lunceford, Junshui Ma, Kenneth Emancipator*. *Merck and Co., Inc., Kenilworth, NJ, USA*

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.

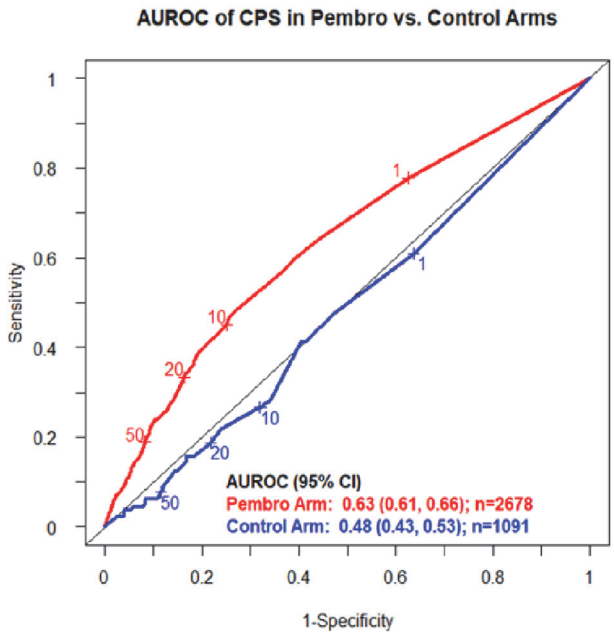
Results There were 3769 treated patients with available PD-L1 CPS (pembrolizumab, n=2678; standard-of-care, n=1091). The area under the ROC curve for ORR was 0.63 (95% CI, 0.61–0.66) for pembrolizumab and 0.48 (95% CI, 0.43–0.53) for standard-of-care when a positive association was evaluated between 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 pembrolizu-

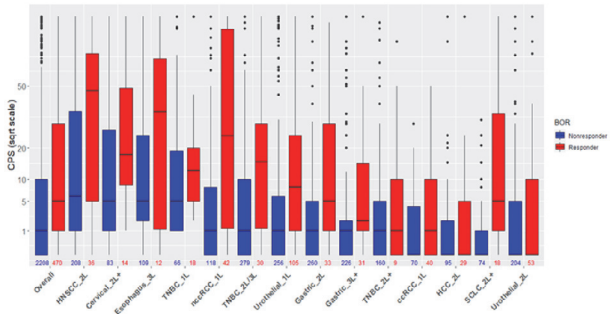
Abstract 282 Table 1 Response Rates and Sensitivity at Individual CPS Cutpoints for Pembrolizumab-Treated Patients

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

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



Abstract 282 Figure 1 ROC analysis of PD-L1 CPS for pembrolizumab versus standard-of-care therapy



Abstract 282 Figure 2 Boxplot of PD-L1 CPS distribution for responders versus nonresponders in pembrolizumab-treated patients by tumor type and line of therapy in order of descending median CPS

mab monotherapy. CPS demonstrated enrichment of response to pembrolizumab monotherapy across most, but not all, tumor types, including some tumor types for which efficacy favors pembrolizumab regardless of PD-L1 expression, and for which a companion diagnostic is therefore not needed. In the randomized studies, CPS did not show a consistent association with ORR for standard-of-care therapy.

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0282

283 SAFETY AND EFFICACY SIGNALS IN THE COMPLETE PHASE I STUDY OF LIVE BIOTHERAPEUTIC MRX0518 IN COMBINATION WITH PEMBROLIZUMAB IN PATIENTS REFRACTORY TO IMMUNE CHECKPOINT INHIBITORS (ICIS)

[1]Shubham Pant*, [1]Amishi Shah, [1]Pavlos Msaouel, [1]Matthew Campbell, [1]Shi-Ming Tu, [1]Jianjun Gao, [1]George Blumenschein, [1]Frank Mott, [1]Xiuning Le, [1]Mehmet Altan, [1]Funda Meric-Bernstam, [1]Timothy Yap, [1]Vivek Subbiah, [1]Jordi Rodon, [2]Axel Glasmacher, [2]Imke Mulder, [3]Michael Chisamore, [2]Alexander Stevenson, [1]Nizar Tannir. *[1]MD Anderson Cancer Center, Houston, TX, USA; [2]4D pharma plc, Leeds, UK; [3]Merck and Co., Inc., Wheaton, Illinois, USA*

Background MRx0518 is a novel, human gut microbiome-derived, single-strain, live biotherapeutic in clinical development for treatment of solid tumours. Preclinically, MRx0518 induced broad immunostimulatory activity and demonstrated anti-tumorigenic effects in a range of murine tumor models. MRx0518 increased CD4+ and CD8+ T cell and NK cell tumor infiltration and decreased Tregs. Activation of tumour TLR5 was observed and linked to the bacterial flagellin moiety, which was shown to strongly induce NFκB, cytokine responses and IFNγ+ CD4+ and CD8+ T cells.

Methods Heavily pre-treated patients refractory to ICIs were enrolled from March 2019 to March 2020. Patients had experienced at least SD from previous ICI (monotherapy or combination) but eventually progressed as confirmed by two radiological scans ≥4 weeks apart in the absence of rapid clinical progression and within 12 weeks of last dose of ICI. Patients were treated with 1 capsule of MRx0518 (1×10^{10} to 1×10^{11} CFU) BID and pembrolizumab (200 mg every 3 weeks) for up to 35 cycles or disease progression. Tumour response was assessed every 9 weeks per RECIST 1.1. The primary objective was to evaluate safety of the combination by monitoring toxicities in the first cycle of treatment. Secondary objectives were to evaluate efficacy via ORR, DOR, DCR and PFS.

Results In Part A, patients with mRCC (n=9) and mNSCLC (n=3) were recruited. At data cut-off (21 Aug 20), 5 patients remain on study treatment. 83% of patients were male and 17% were female. Median number of prior lines of therapy was 3. 10 patients received nivolumab previously (83%), one received avelumab (8%) and one received pembrolizumab and nivolumab (8%). 83% of patients had experienced SD as best response to prior ICI and 17% had PR as best response. Of 6 patients with available PD-L1 results, 5 had a positive CPS/TPS (≥1) and 1 negative (<1). The combination shows a positive safety profile with no treatment-related SAEs or toxicity-related drug discontinuations. No increase in irAEs has been reported.On study treatment, 2 RCC patients and 1 NSCLC patient experienced a PR, with an additional 2 RCC patients experiencing durable SD (6 and 13 months), a protocol defined DCR of 42%. Median PFS is 2.14 months at data cut-off (table 1).

Abstract 283 Table 1 Summary of RECIST v1.1 response data

	Total	RCC	NSCLC
N	12	9	3
Continuing on Study	5	4	1
ORR	(3/12) 25%	(2/9) 22%	(1/3) 33%
DCR (PR and SD at 6 months)	(5/12) 42%	(4/9) 44%	(1/3) 33%
DOR, months*		1.4+, 8.1	9.9+
Median PFS, months (95% CI)	2.14 (0.43, NE)		

* Data censored at 21 Aug 20 for patients continuing on treatment, updated data will be reported at the meeting

Conclusions This data represents first-in-class proof of concept for a live biotherapeutic in an oncology setting. The combination was tolerable and there were preliminary signals of efficacy. Part B (phase II) in NSCLC, RCC and bladder cancer is ongoing.

Trial Registration www.clinicaltrials.gov NCT03637803

Ethics Approval This study was approved by University of Texas MD Anderson's Institutional Review Board; approval ref. 2018-0290

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0283