improvement in clinical efficacy (40% objective response rate [ORR], 5.26 month median progression-free survival [PFS], and 15.2 month median OS) than other subgroups (table 1). In addition to immune-related genes in the microenvironment, DEG analysis also revealed that tumor-related genes were highly expressed in non-responders, such as intrinsic genes related to angiogenesis (VEGFA [P=0.07], KDR [P=0.07]), the mTOR pathway (MTOR [P=0.015]), and DNA damage repair (REV3L [P=0.007]). MTOR and REV3L were associated with shorter PFS (P=0.02; P=0.003) and OS (P=0.03; P =0.008), respectively.

Conclusions By using GEP, T-cell and MHC I GS were identified as potentially predictive biomarkers of response to tislelizumab monotherapy in PD-L1+ UC in this retrospective analysis. By combining these two GS scores, patients with optimal efficacy responses could be identified. Conversely, high expression of tumor intrinsic genes related to angiogenesis and the mTOR pathway may indicate resistance and suggest potential future drug combinations for these patients. Both findings warrant further validation in a phase 3 study (NCT03967977).

Acknowledgements Editorial assistance was provided by Stephan Lindsey, PhD, and Elizabeth Hermans, PhD (OPEN Health Medical Communications, Chicago. IL), and funded by the study sponsor.

Trial Registration CTR20170071

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0078

79 TUMOR-IMMUNE SIGNATURES ASSOCIATED WITH RESPONSE OR RESISTANCE TO TISLELIZUMAB (ANTI-PD-1) IN ESOPHAGEAL SQUAMOUS CELL CARCINOMA (ESCC)

[1]Jianming Xu, [2]Nong Xu, [3]Yuxian Bai, [4]Chia-Chi Lin, [5]Michael Millward, [6]Jingwen Shi, [6]Yun Zhang, [6]Xiaopeng Ma, [6]Zhirong Shen, [6]Ruiqi Huang, [6]Wei Huang, [7]Lin Shen*. *[1]The Fifth Medical Center, General Hospit, Beijing, China; [2]The First Affiliated Hospital, College o, Hangzhou, China; [3]Harbin Medical University Cancer Hospita, Harbin, China; [4]National Taiwan University Hospital, Taipei, Taiwan, Province of China; [5]Linear Clinical Research Limited, Western Australia, Australia; [6]BeiGene (Beijing) Co., Ltd., Beijing, China; [7]Peking University Cancer Hospital, Beijing, China*

Background Tislelizumab, an anti-PD-1 monoclonal antibody, showed promising clinical outcomes for patients with ESCC. Here, the tumor and immune microenvironment is investigated using gene expression profiles (GEP) and gene signatures associated with clinical efficacy in patients with ESCC receiving tislelizumab either as monotherapy (NCT02407990, NCT04068519) or in combination with chemotherapy (5-fluorouracil plus cisplatin; NCT03469557).

Methods Baseline tumor samples were subjected to GEP using a 1392-gene HTG EdgeSeq panel. Signature scores were calculated using the Gene Set Variation Analysis package with publicly available gene signatures. Differential gene signature (DEG) analysis was performed between responders and non-responders using the Wilcoxon rank-sum test. Associations between gene signatures and survival were evaluated using the Cox proportional hazards model.

Results In GEP-evaluable patients receiving monotherapy (n=43), DEG analysis showed toll-like receptor (TLR) signature scores, driven by TLR8, TLR6, TIRAP, and TLR4, were positively correlated with response and survival, while Treg scores, driven by FOXP3, EBI3, TNFRSF18, and BATF, showed a negative correlation. After combining TLR-high and Treg-low scores (as defined by median cutoff), the prediction of clinical efficacy was further improved (table 1). In addition to Treg scores, non-responders (NR) to tislelizumab monotherapy could be further clustered into four subgroups (NR1, NR2, NR3, and NR4), each exhibiting distinct resistance signatures. Despite a high level of immune infiltration, NR1 expressed a higher exhaustion signature (CD96, CTLA4, TIGIT, HAVCR2, etc.) versus responders (P=0.01). Both NR2 and NR3 demonstrated a trend of enhanced cell-cycle signatures versus responders (P=0.07 and P=0.08, respectively), accompanied by a lower NK signature (KIR2DS4, KIR.panL, CD56) in NR2 and a lack of immune infiltration in NR3. In the NR4 subgroup, a trend toward higher TH17 (P<0.01) and IL-17F signatures ($Log_2FC=0.56$, P=0.10) versus responders was observed. GEP-evaluable patients (n=12) receiving tislelizumab in combination with chemotherapy had an objective response rate of 58% (n=7), with a different gene signature pattern than those observed in patients receiving monotherapy. Responders to combination therapy showed higher DNA repair expression versus NR (P=0.07), while angiogenesis signatures were significantly higher in NR vs responders (P=0.01). Consistent with this, NR exhibited higher expression of VEGFC at a single gene level ($Log_2FC=2.46$, P <0.01).

Abstract 79 Table 1 Tumor-immune signatures associated with clinical efficacy of tislelizumab in patients with ESCC

Tislelizumab monotherapy	GEP-evaluable	Single TLR signature		Single Treg signature		Combined signature	
Subgroup	n=43	TLR-high (n=21)	TLR-low* (n=22)	Treg-high (n=21)	Treg-low* (n=22)	TLR-high and Treg-low (n=10)	Others* (n=33)
ORR, n (%)	6 (14.0)	5 (23.8)	1 (4.5)	1 (4.8)	5 (22.7)	4 (40.0)	2 (6.1)
DCR, n (%)	15 (34.9)	11 (52.4)	4 (18.2)	4 (19.0)	11 (50.0)	8 (80.0)	7 (21.2)
Median PFS, mo (95% CI)	2.09 (2.00-4.17)	2.50 (2.04-8.02)	2.00 (1.64-2.63)	2.04 (1.87-2.63)	2.50 (2.00-8.02)	6.31 (2.50-NR)	2.00 (1.87-2.27)
Hazard ratio (95% CI)	NA	0.51 (0.27-0.99)		1.74 (0.89-3.4)		0.40 (0.18-0.89)	
Median OS, mo (95% CI)	4.76 (3.65-8.44)	7.92 (4.14-NR)	3.98 (2.00-8.08)	6.31 (2.63-10.25)	4.76 (2.50-12.95)	8.51 (4.14-NR)	4.44 (2.63-8.44)
Hazard ratio (95% CI)	NA	0.52 (0.26-1.04)		1.14 (0.58-2.28)		0.56 (0.24-1.29)	

*Subgroups were used as reference for hazard ratio analysis.
Abbreviation: CI, confidence interval; DCR, disease control rate; GEP, gene expression profiling; NA, not applicable; NR, not reached; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; TLR, toll-like receptor.

Conclusions While higher TLR signaling was associated with clinical benefit of tislelizumab monotherapy, elevated Treg, exhaustion, cell cycle, and TH17 signatures may indicate resistance. Signatures predictive for combination therapy may vary. Both immune- and tumor-related features may be considered for validation in phase 3 studies (NCT03430843, NCT03783442).

Acknowledgements Editorial assistance was provided by Stephan Lindsey, PhD, and Elizabeth Hermans, PhD (OPEN Health Medical Communications, Chicago. IL), and funded by the study sponsor.

Trial Registration NCT02407990, NCT04068519, NCT03469557

http://dx.doi.org/10.1136/jitc-2020-SITC2020.0079

80 EVALUATION OF THE TRUSIGHT ONCOLOGY 500 ASSAY FOR ROUTINE CLINICAL TESTING OF TUMOR MUTATIONAL BURDEN (TMB) AND CLINICAL UTILITY FOR PREDICTING RESPONSE TO PEMBROLIZUMAB

Bo Wei*, John Kang, Miho Kibukawa, Gladys Arreaza, Maureen Maguire, Lei Chen, Ping Qiu, Lixin Lang, Deepti Aurora-Garg, Razvan Cristescu, Diane Levitan. *Merck and Co., Inc., Kenilworth, NJ, USA*

Background Various biomarkers have been investigated for their ability to identify patients more likely to respond to