Concordance Among Three Programmed Death-Ligand 1 (PD-L1) Scoring Methods and Their Association With Clinical Outcomes of Tislelizumab (TIS) Monotherapy in Esophageal Squamous Cell Carcinoma (ESCC)

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Background:

Multiple scoring methods and cutoffs have been developed to evaluate tumor PD-L1 expression status in patients with ESCC, and PD-L1 expression level has been associated with the degree of response to anti-programmed cell death protein 1 (PD-1)/PD-L1 therapy. Here, we retrospectively investigated concordance between three PD-L1 scoring methods and their association with clinical outcomes in RATIONALE-302, a phase 3 study of the anti-PD-1 antibody TIS vs investigator-chosen chemotherapy (ICC) as second-line treatment for advanced unresectable/metastatic ESCC (NCT03430843).

Methods:

Patients enrolled in RATIONALE-302 with evaluable PD-L1 expression by the tumor area positivity (TAP) score (based on visual estimation of positive tumor cells [TCs] and tumor-associated immune cells [ICs]) using the VENTANA PD-L1 (SP263) assay were categorized at a 10% cutoff. Stained slides from those patients were rescored post hoc using both combined positive score (CPS; based on counting positive TCs and ICs) at cutoff 10 and TC (based on counting positive TCs only) score at a 1% cutoff, thresholds currently used in ESCC for anti-PD-(L)1 therapy. Concordance at these thresholds was investigated. Clinical efficacy (overall survival [OS]) for PD-L1 subgroups was assessed.

Results:

Of 512 pts enrolled, 364 had evaluable TAP scores (TIS, n=180; ICC, n=184), of whom 355 had evaluable post-hoc CPS and TC scores (TIS, n=175; ICC, n=180). TAP score and CPS showed high concordance in terms of overall percentage agreement (OPA; 90% [95% confidence interval (CI): 86, 93]) and Cohen's Kappa (0.79 [95% CI: 0.72, 0.85]), while

TAP and TC scores had lower concordance (OPA: 78% [95% CI: 73, 82]; Cohen's Kappa: 0.56 [95% CI: 0.47, 0.64]). OS benefit with TIS vs ICC in PD-L1 subgroups defined by TAP, CPS, and TC score cutoffs were generally similar (Table).

Conclusions:

OS subgroup analysis showed comparable treatment effect by TAP score at 10% cutoff, CPS at cutoff 10, and TC score at 1% cutoff based on SP263 staining. TAP score and CPS at these cutoffs exhibited substantial concordance. The results indicate that the less time-consuming, visually estimated TAP score and CPS may be interchangeable for clinical measurement of PD-L1 expression in patients with ESCC.

Table: OS benefit in PD-L1 subgroups by scoring method

	Median OS, months (95% CI) [event/total]		**Hazard ratio (95% CI)**
	Tislelizumab	**ICC**	
TAP ≥10%	10.0 (8.5, 15.1) [54/80]	5.1 (3.8, 8.2) [53/62]	0.52 (0.35, 0.76)
TAP <10%	7.5 (5.5, 8.9) [83/100]	5.8 (4.8, 6.9) [106/122]	0.86 (0.64, 1.14)
CPS ≥10	10.0 (8.5, 13.2) [56/80]	5.1 (3.7, 8.2) [59/65]	0.54 (0.37, 0.78)
CPS <10	7.5 (5.3, 8.7) [80/95]	5.8 (4.9, 7.4) [100/115]	0.83 (0.62, 1.12)
TC ≥1%	9.9 (7.5, 11.4) [69/94]	5.1 (3.8, 6.1) [69/77]	0.56 (0.40, 0.79)
TC <1%	7.7 (5.2, 9.8) [67/81]	6.9 (4.9, 8.6) [90/103]	0.83 (0.60, 1.14)