

## 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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### ABSTRACT

**Background:** We retrospectively investigated concordance between three programmed death-ligand 1 (PD-L1) scoring methods and clinical outcomes in RATIONALE-302 (NCT03430843), 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.

**Materials (Patients) and Methods:** Enrolled patients with evaluable PD-L1 expression by tumor area positivity (TAP) score (visual estimation of positive tumor cells [TCs] and tumor-associated immune cells [ICs]; VENTANA PD-L1 [SP263]) were categorized at 10% cutoff. Stained slides were rescored post hoc using both combined positive score (CPS; positive TCs and ICs) at cutoff 10 and TC (positive TCs only) score at 1% cutoff. Concordance at these thresholds and overall survival (OS) for PD-L1 subgroups were 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 (overall percentage agreement ([OPA]; 90% [95% 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. TAP score and CPS at these cutoffs exhibited substantial concordance. Results indicate that the quicker, 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**

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