Investigation of PD-L1 Expression and Tislelizumab Efficacy in Gastroesophageal Adenocarcinoma Using a Novel Tumor and Immune Cell Score With VENTANA PD-L1 (SP263) Assay and Combined Positive Score (CPS)

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Background: Tumor (TC) and immune cell (IC) PD-L1 expression may be associated with anti-PD-1 efficacy in gastroesophageal adenocarcinoma (GEA) and can be assessed via cell counting using the Combined Positive Score (CPS) with the Dako 22C3 assay. However, the CPS scoring method can be challenging to utilize. A novel combined algorithm, Tumor and Immune Cell (TIC) score, was developed for the Ventana SP263 assay to assess TC and IC PD-L1 expression based on tumor area. Associations between CPS and TIC scoring methods, and potential correlations with efficacy, were investigated in patients with GEA from the tislelizumab first-in-human study (NCT02407990).

Methods: PD-L1 expression was evaluated using the Ventana SP263 and Dako 22C3 assays in 74 and 49 patients, respectively. Correlation of PD-L1 TIC scores (% tumor area covered by PD-L1+ TC/IC by SP263) and CPS (by 22C3) with clinical efficacy was assessed. Cases were considered PD-L1+ at ≥5% for TIC or ≥1 for CPS. Analytical validation of TIC was further assessed by reproducibility of results.

Results: Based on statistical analysis and other considerations, TIC ≥5% was determined as the optimal cutoff. Response, prevalence, positive predictive value, and negative predictive value for TIC ≥5% and CPS ≥1 are shown (**Table**). At a 17.4-month median follow-up, patients with TIC ≥5% or CPS ≥1 showed survival benefit. Inter-reader and -laboratory overall agreement for TIC ≥5% were 99% (95% CI, 98-100) and 96% (95% CI, 94-98), respectively.

Conclusions: At evaluated cutoffs, both SP263 TIC and 22C3 CPS assays aided in the identification of patients with GEA likely to benefit from tislelizumab. TIC is a robust, reproducible scoring method. Further clinical validation is underway for TIC ≥5% in patients with gastric and gastroesophageal junction adenocarcinoma from a phase 3 study (NCT03777657).

Scoring Method (Cut-off)	PD-L1 Status	BEP	ORR (%)	PD-L1 Prevalence (%)	Response Odds Ratio	PPV (%)	NPV (%)	PFS HR (95% CI)	OS HR (95% CI)
TIC (SP263) ≥5%	+	38	18.2	51	6.67	15.8	83.3	0.497 (0.298, 0.823)	0.529 (0.295, 0.935)
	−	36	3.2						
CPS (22C3) ≥1	+	22	20.0	45	∞*	18.2	88.9	0.880 (0.474, 1.606)	0.665 (0.339, 1.259)
	−	27	0						

*Odds ratio could not be estimated due to no responders in CPS <1.
Abbreviations: BEP, biomarker evaluable population; CI, confidence interval; CPS, combined positive score; HR, hazard ratio; NPV, negative predictive value; ORR, objective response rate; OS, overall survival; PFS, progression-free survival; PPV, positive predictive value, TIC, tumor and immune cell.