71 HIGH SCORING PRECISION DEMONSTRATED IN MULTIPLE TUMOR INDICATIONS STAINED WITH PD-L1 IHC 22C3 PHARMDX USED IN CONJUNCTION WITH COMBINED POSITIVE SCORE

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Background PD-L1 22C3 IHC pharmDx (SK006) is a qualitative immunohistochemical (IHC) assay using anti-PD-L1, Clone 22C3 to detect PD-L1 in formalin-fixed, paraffin-embedded (FFPE) tumor tissues using the Autostainer Link 48. PD-L1 expression is determined by Combined Positive Score (CPS), which is the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100.[1] SK006 has been analytically validated using CPS across multiple tumor indications and diagnostic cutoffs and is used as an aid in identifying patients for treatment with KEYTRUDA®. A previous publication presents the analytical performance of the following indications: gastric or gastroesophageal junction (GC/GEJ) adenocarcinoma (CPS $\geq$ 1), cervical cancer (CPS $\geq$ 1), head and neck squamous cell carcinoma (HNSCC) (CPS $\geq$ 1), esophageal cancer (EC/ESCC) (CPS $\geq$ 10), and triple-negative breast cancer (TNBC) (CPS $\geq$ 10).[2] This study evaluated the analytical performance of the SK006 assay for an additional five individual tumor indications (ovarian carcinoma (OC), prostate cancer (PC), colorectal carcinoma (CRC), renal cell carcinoma (RCC), biliary tract adeno cancer (BTAC)) and a group of 11 rare tumor indications in a basket trial (BT).[3] Two CPS cutoffs were evaluated: CPS $\geq$ 1 (OC, PC, CRC, RCC, BTAC and BT [3]) and CPS $\geq$ 10 (OC, CRC and BTAC).

Methods Combined precision measured inter-instrument, -operator, -day and -lot variation. Intra-run measured repeatability and Inter/Intra-Observer measured scoring reproducibility. Negative percent agreement (NPA), positive percent agreement (PPA), and overall agreement (OA) with two-sided 95% bootstrap confidence intervals (CIs) were used for data analysis, based on the PD-L1 binary status at the evaluated cutoffs. Each tumor indication and cutoff pair was analyzed individually for Combined Precision, and Intra-Run and Inter/Intra Observer reproducibility. Meta-analysis was also performed on pooled data from all indications per study and cutoff.

Results Analyses for each indication/cutoff pair showed NPA, PPA, OA point estimates (PE) of $\geq$89.6% and CI lower bounds (CILB) of $\geq$81.8%. Meta-analyses for all indications and cutoffs showed NPA, PPA, OA PE of $\geq$92.5% and CILB of $\geq$89.3%. Table 1 summarizes the PD-L1 binary status results for all indications and the pooled meta-analysis.

Conclusions PD-L1 IHC 22C3 pharmDx used in conjunction with CPS provides high precision for evaluating PD-L1 expression across multiple tumor indications and cutoffs under standard, day-to-day laboratory testing conditions.

Abstract 71 Table 1 PD-L1 binary status results for all indications and results of meta-analysis pooled data

Table 1: PD-L1 binary status results for all indications and results of meta-analysis pooled data.

Cutoff	Study	Indication	NPA[1]	PPA[1]	OA[1]
1	Combined Precision	Basket Trial	97.4% (93.5%, 100%)	97.4% (93.5%, 100%)	97.4% (94.8%, 99.3%)
		BTAC	98.0% (94.1%, 100%)	100% (92.1%, 100%)	98.9% (96.8%, 100%)
		CRC	98.3% (94.8%, 100%)	96.4% (91.2%, 100%)	97.4% (94.0%, 100%)
		OC	98.2% (94.7%, 100%)	100% (93.6%, 100%)	99.1% (97.3%, 100%)
		PC	96.0% (90.1%, 100%)	90.9% (81.8%, 100%)	94.0% (89.2%, 98.8%)
		RCC	95.4% (90.9%, 100%)	97.6% (92.8%, 100%)	96.2% (92.5%, 99.0%)
	Intra-Run	Basket Trial	100% (92.8%, 100%)	98.5% (95.7%, 100%)	99.1% (97.5%, 100%)
		BTAC	100% (95.4%, 100%)	100% (95.4%, 100%)	100% (97.6%, 100%)
		CRC	100% (96.0%, 100%)	100% (96.3%, 100%)	100% (98.0%, 100%)
		OC	100% (96.1%, 100%)	100% (96.1%, 100%)	100% (98.0%, 100%)
		PC	97.3% (93.3%, 100%)	96.9% (92.3%, 100%)	97.1% (94.2%, 99.2%)
		RCC	98.8% (96.4%, 100%)	100% (96.1%, 100%)	99.4% (98.3%, 100%)
	Inter-Observer	Basket Trial	99.6% (98.8%, 100%)	95.6% (91.9%, 98.4%)	97.6% (95.8%, 99.2%)
		BTAC	99.5% (98.5%, 100%)	98.6% (96%, 100%)	99.0% (97.4%, 100%)
		CRC	95.4% (90.9%, 99.3%)	99.6% (98.9%, 100%)	97.5% (95.3%, 99.4%)
		OC	100% (98.5%, 100%)	97.1% (93.2%, 100%)	98.5% (96.5%, 100%)
		PC	95.0% (90.9%, 98.3%)	93.9% (90.2%, 97.3%)	94.4% (91.6%, 96.8%)
		RCC	96.0% (91.7%, 99.6%)	94.6% (90.9%, 97.9%)	95.3% (92.5%, 97.7%)
	Intra-Observer	Basket Trial	98.8% (97.5%, 100%)	98.3% (96.7%, 99.5%)	98.6% (97.6%, 99.4%)
		BTAC	99.5% (98.5%, 100%)	100% (98.2%, 100%)	99.7% (99.3%, 100%)
		CRC	97.8% (95.6%, 99.3%)	98.9% (97.7%, 100%)	98.4% (97.0%, 99.6%)
		OC	100% (98.6%, 100%)	99.2% (98.1%, 100%)	99.6% (99.0%, 100%)
		PC	97.1% (94.5%, 99.2%)	95.6% (93.0%, 97.9%)	96.2% (94.4%, 97.9%)
		RCC	97.8% (96.2%, 99.2%)	97.2% (94.9%, 99.0%)	97.5% (96.0%, 98.9%)
10	Combined Precision	BTAC	100% (92.9%, 100%)	100% (92.1%, 100%)	100% (96.1%, 100%)
		CRC	100% (94.8%, 100%)	100% (92.5%, 100%)	100% (96.8%, 100%)
		OC	96.8% (92.0%, 100%)	94.1% (88.2%, 100%)	95.6% (92.1%, 99.1%)
	Intra-Run	BTAC	97.1% (91.4%, 100%)	100% (95.9%, 100%)	98.7% (96.2%, 100%)
		CRC	99.1% (97.3%, 100%)	100% (95.6%, 100%)	99.4% (98.4%, 100%)
		OC	100% (96.4%, 100%)	97.6% (92.9%, 100%)	98.9% (96.8%, 100%)
	Inter-Observer	BTAC	96.1% (92.2%, 99.0%)	96.8% (93.3%, 99.5%)	96.5% (93.9%, 98.6%)
		CRC	91.3% (85.4%, 96.5%)	89.5% (84.0%, 94.4%)	90.4% (86.4%, 94.0%)
		OC	91.2% (85.9%, 95.9%)	93.7% (88.8%, 97.5%)	92.1% (88.4%, 95.5%)
	Intra-Observer	BTAC	98.5% (96.0%, 100%)	96.5% (93.9%, 98.7%)	97.4% (95.6%, 99.0%)
		CRC	94.8% (92.0%, 97.4%)	95.0% (92.3%, 97.4%)	94.9% (92.8%, 96.8%)
		OC	97.1% (95.0%, 98.8%)	94.2% (91.0%, 97.2%)	95.9% (93.9%, 97.7%)
1 (Meta-analysis)	Combined Precision	Basket Trial, BTAC, CRC, OC, PC, RCC	97.2% (95.5%, 98.6%)	97.4% (95.5%, 99.0%)	97.3% (96.1%, 98.3%)
	Intra-Run	Basket Trial, BTAC, CRC, OC, PC, RCC	99.3% (98.5%, 100%)	99.4% (98.6%, 100%)	99.3% (98.8%, 99.7%)
	Inter-Observer	Basket Trial, BTAC, CRC, OC, PC, RCC	97.5% (96.1%, 98.7%)	96.5% (95.1%, 97.7%)	97.0% (96.0%, 97.8%)
	Intra-Observer	Basket Trial, BTAC, CRC, OC, PC, RCC	98.5% (97.8%, 99.1%)	98.1% (97.4%, 98.8%)	98.3% (97.7%, 98.8%)
10 (Meta-analysis)	Combined Precision	BTAC, CRC, OC	98.9% (97.2%, 100%)	97.9% (95.1%, 100%)	98.4% (96.9%, 99.6%)
	Intra-Run	BTAC, CRC, OC	98.9% (97.2%, 100%)	99.2% (97.6%, 100%)	99.0% (97.8%, 100%)
	Inter-Observer	BTAC, CRC, OC	92.4% (89.3%, 95.3%)	93.0% (90.1%, 95.6%)	92.7% (90.6%, 94.6%)
	Intra-Observer	BTAC, CRC, OC	96.6% (95.2%, 97.9%)	95.2% (93.5%, 96.8%)	96.0% (94.8%, 97.1%)

1. Percent agreement (lower-bound, upper-bound)

REFERENCES

[1] $CPS = \frac{\#\ PD\text{-}L1\ staining\ cells\ (tumor\ cells,\ lymphocytes,\ macrophages)}{Total\ \#\ viable\ tumor\ cells} \times 100$

[2] Ponce F, Hund S, Peltz L, *et al* 60 Use of Combined Positive Score (CPS) with the companion diagnostic PD-L1 IHC 22C3 pharmDx provides precise evaluation of PD-L1 expression across multiple tumor indications and cutoffs. *Journal for ImmunoTherapy of Cancer 2021;9: 10.1136/jitc-2021-SITC2021.060*

[3] Basket trial consists of 11 rare tumor indications: anal canal squamous cell carcinoma, biliary adenocarcinoma, cervical squamous cell carcinoma, endometrial carcinoma, mesothelioma, neuroendocrine carcinoma, salivary gland squamous cell carcinoma, Salivary gland adenocarcinoma, small cell lung carcinoma, thyroid adenocarcinoma, vulvar squamous cell carcinoma.

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