USE OF THE 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

Francisco Ponce*, Stephanie Hund, Lindsay Peltz, Chris La Placa, Monika Vilardo, Brittany Watts, Siena Tabuena-Frolli, Grant Toland, Alex Posch, Jay Milo, Karina Kulangara, Angeliki Apostolaki. Agilent Technologies, Carpinteria, CA, USA

Background The Combined Positive Score (CPS) algorithm includes tumor and immune cells for determination of Programmed Death-Ligand 1 (PD-L1) protein expression in tumor tissues and has been analytically and clinically validated for use with PD-L1 IHC 22C3 pharmDX across multiple indications and cutoffs. PD-L1 IHC pharmDX is a qualitative immunohistochemical assay using anti-PD-L1, Clone 22C3 to detect PD-L1 in formalin-fixed, paraffin-embedded (FFPE) tumor tissues using Autostainer Link 48. PD-L1 IHC 22C3 pharmDX is FDA-approved as an aid in identifying patients for treatment with KEYTRUDA® for six tumor indications at clinically validated CPS diagnostic cutoffs: gastric or gastroesophageal junction (GC/GEJ) adenocarcinoma (CPS ≥ 1), cervical cancer (CPS ≥ 1), urothelial carcinoma (CPS ≥ 10), head and neck squamous cell carcinoma (HNSCC) (CPS ≥ 1), esophageal squamous cell carcinoma (ESCC) (CPS ≥ 10), and triple-negative breast cancer (TNBC) (CPS ≥ 10).

Methods Precision of PD-L1 IHC 22C3 pharmDX using CPS was assessed for all six indications at the corresponding clinically validated diagnostic cutoffs and at additional exploratory cutoffs under normal, day-to-day testing conditions. Precision testing included Combined Precision (inter-instrument/operator/run (day)), Intra-Run Repeatability, and Observer (inter-/intra-) Scoring Reproducibility studies. FFPE specimens were stained with PD-L1 IHC 22C3 pharmDX and scored using CPS as described in the package insert. Four CPS cutoffs were evaluated: CPS ≥ 1 (GC/GEJ), urothelial carcinoma, ESCC, cervical cancer, HNSCC, TNBC), CPS ≥ 10 (GC/GEJ), urothelial carcinoma, ESCC, TNBC), CPS ≥ 20 (HNSCC), and CPS ≥ 50 (HNSCC). Data were analyzed using negative percent agreement (NPA), positive percent agreement (PPA), and overall agreement (OA) with two-sided 95% percentile bootstrap confidence intervals (CIs) based on PD-L1 binary status at the applicable cutoff(s). For each study, data from each CPS cut-off-indication pair were individually analyzed. Meta-analyses were also performed by pooling data from all indications per (i) study and cutoff, and (ii) per study for all tested cutoffs. Results Nearly all agreement analyses (142/144) for each CPS cutoff-indication pair showed NPA/PPA/OA point estimates (PE) ≥ 90% and CI lower bounds (CILB) ≥ 85%. Meta-analyses showed PE ≥ 90% for NPA/PPA/OA and CILB ≥ 85% per study and cutoff, and per study for all tested cutoffs. Discordant comparisons accounted for <5% of total comparisons performed for each study type.

Conclusions CPS used with PD-L1 IHC 22C3 pharmDX provides precise evaluation of PD-L1 expression across multiple tumor indications and cutoffs under normal, day-to-day testing conditions.

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References
1. CPS = (# PD-L1 staining cells (tumor cells, lymphocytes, macrophages))/(Total # viable tumor cells)×100
3. ESCC was analytically validated as a subtype of esophageal cancer [2].

Ethics Approval N/A
Consent N/A

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Abstracts

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