Your Guide for Accurate Scoring in Head and Neck Squamous Cell Carcinoma (HNSCC) Using PD-L1 IHC 22C3 pharmDx (SK006)

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Use this quick scoring guide as a reference when evaluating HNSCC specimens for PD-L1 expression using PD-L1 IHC 22C3 pharmDx.

For more information on Combined Positive Score (CPS) calculation, review the HNSCC Interpretation Manual.

Steps for scoring

Determine specimen adequacy
Verify that the specimen has ≥ 100 viable tumor cells

Evaluate controls
Ensure that Control Cell Line Slide and lab-supplied and patient tissue controls demonstrate acceptable staining

Evaluate PD-L1 staining
Estimate the number of PD-L1 staining cells (CPS numerator) and the total number of viable tumor cells (CPS denominator)

Calculate CPS and determine PD-L1 expression level
Report numerical CPS and PD-L1 expression level: **CPS < 1, CPS ≥ 1,** or **CPS ≥ 20**

Note: PD-L1 expression level CPS ≥ 20 may be of interest to treating physician but does not determine eligibility for first-line treatment with KEYTRUDA® (pembrolizumab) as a single agent.

Definition of CPS and PD-L1 staining cells

CPS is the number of PD-L1 staining cells (tumor cells, lymphocytes, macrophages) divided by the total number of viable tumor cells, multiplied by 100.

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

Note: *CPS is reported as a whole number. Although the result of the calculation can exceed 100, the maximum score is defined as CPS 100.*

By definition, **PD-L1 staining cells** in HNSCC are:

- **Viable tumor cells** with perceptible and convincing partial or complete linear membrane staining (at any intensity) that is perceived distinct from cytoplasmic staining
- **Lymphocytes and macrophages** (mononuclear inflammatory cells, MICs) within the tumor nests and/or adjacent supporting stroma with membrane and/or cytoplasmic staining (at any intensity). MICs must be directly associated with the response against the tumor

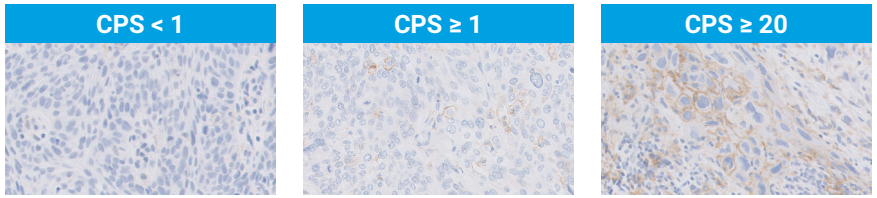

Figure 1 (left): HNSCC specimen stained with PD-L1 antibody exhibiting a CPS of 0.
Figure 2 (center): HNSCC specimen stained with PD-L1 antibody exhibiting a CPS of 6, however any numerical CPS between 4–8 could be assigned to this image.
Figure 3 (right): HNSCC specimen stained with PD-L1 antibody exhibiting a CPS of 100.

Intended Use
For in vitro diagnostic use.

PD-L1 IHC 22C3 pharmDx is a qualitative immunohistochemical assay using monoclonal mouse anti-PD-L1, Clone 22C3 intended for use in the detection of PD-L1 protein in formalin-fixed, paraffin-embedded (FFPE) head and neck squamous cell carcinoma (HNSCC) tissue using EnVision FLEX visualization system on Autostainer Link 48.

Head and Neck Squamous Cell Carcinoma (HNSCC)
PD-L1 protein expression in HNSCC is determined by using 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. The specimen should be considered to have PD-L1 expression if CPS ≥1.

PD-L1 IHC 22C3 pharmDx is indicated as an aid in identifying HNSCC patients for treatment with KEYTRUDA® (pembrolizumab). See the KEYTRUDA® product label for specific clinical circumstances guiding PD-L1 testing.

For descriptions of the intended use in other indications, please refer to the current version of the Instructions for Use (IFU) for PD-L1 IHC 22C3 pharmDx, Code SK006.

Tissue samples supplied by Asterand Bioscience.

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Tissue Elements	HNSCC CPS numerator		HNSCC CPS denominator	
	Included	**Excluded**	**Included**	**Excluded**
Tumor Cells	Convincing partial or complete linear membrane staining (at any intensity) of viable invasive tumor cells	– Non-staining tumor cells – Tumor cells with only cytoplasmic staining	All viable invasive tumor cells	Any necrotic or non-viable tumor cells
Immune Cells	Membrane and/or cytoplasmic* staining (at any intensity) of mononuclear inflammatory cells (MICs) within tumor nests and adjacent supporting stroma†: – Lymphocytes (including lymphocyte aggregates) – Macrophages‡ Only MICs directly associated with the response to the tumor are scored	– Non-staining MICs – MICs (including lymphoid aggregates) associated with ulcers or other inflammatory processes – MICs associated with carcinoma in situ – MICs associated with benign structures – Neutrophils, eosinophils, and plasma cells	Not included	All immune cells of any type
Other Cells	Not included	– Carcinoma in situ – Benign cells – Stromal cells (including fibroblasts) – Necrotic cells and/or cellular debris	Not included	– Carcinoma in situ – Benign cells – Stromal cells (including fibroblasts) – Necrotic cells and/or cellular debris

** In MICs, membrane and cytoplasmic staining are often indistinguishable due to high nuclear to cytoplasmic ratio. Therefore, membrane and/or cytoplasmic staining of MICs are included in the score; † Adjacent MICs are defined as being within the same 20× field as the tumor. However, MICs that are NOT directly associated with the response to the tumor should be excluded; ‡ Macrophages and histiocytes are considered the same cells*

Partial and complete linear membrane staining

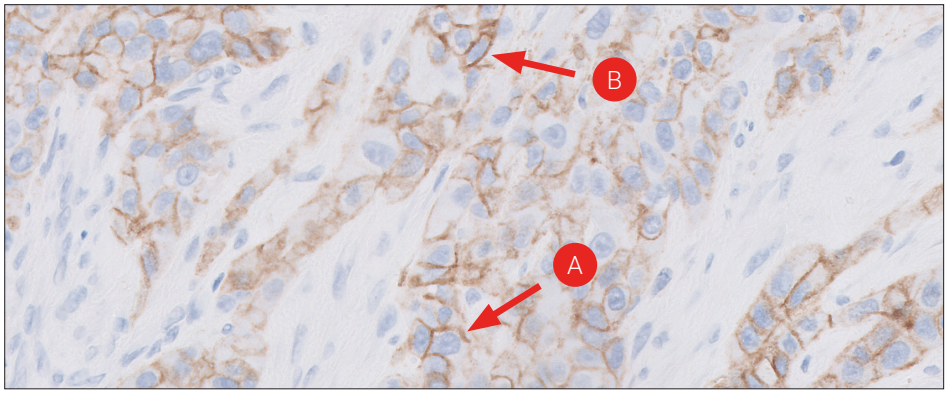

Figure 4: PD-L1 staining of partial (A) and complete (B) linear membrane staining of tumor cells (20× magnification).

Tumor-associated immune cells

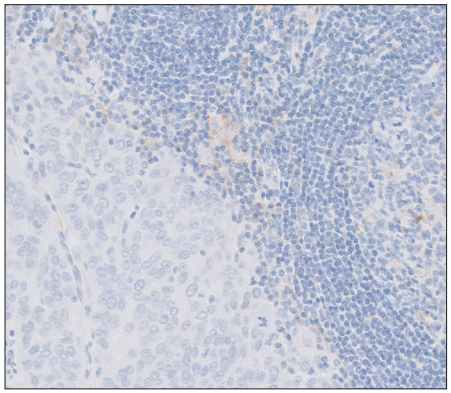

Figure 5: When positioning the edge of the tumor mass in the approximate center of a 20× field, PD-L1 staining MICs that are present within the same field should be included in the numerator (20× magnification).

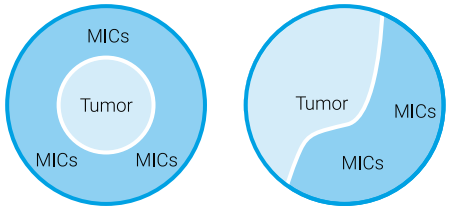

Figure 6: Simulation of a 20× microscope field showing tumor surrounded by PD-L1 staining tumor-associated MICs that should be included in the numerator.

For countries outside of the United States, see the local KEYTRUDA® (pembrolizumab) product label for approved indications and expression cutoff values to guide therapy.

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This information is subject to change without notice.

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