PRODUCT INFORMATION

pharmDx | PD-L1 IHC 22C3 pharmDx

Dako

Agilent Pathology Solutions

Leading the way in PD-L1 testing

The leaders in companion diagnostics introduce the only CE-IVD–marked test to aid in the identification of NSCLC patients for treatment with KEYTRUDA® (pembrolizumab)[1,2]:

PD-L1 IHC 22C3 pharmDx

Agilent Technologies

PD-L1 IHC 22C3 pharmDx is the right choice

- The only CE-IVD–marked companion diagnostic to aid in the identification of NSCLC patients for treatment with KEYTRUDA® (pembrolizumab)[1,2]
- Includes clinically validated scoring guidelines for KEYTRUDA
- PD-L1 IHC 22C3 pharmDx provides demonstrated repeatability and reproducibility[2]
- KEYTRUDA demonstrated superior overall survival compared to the control arm in patients with NSCLC with positive PD-L1 expression as determined by PD-L1 IHC 22C3 pharmDx[1,2]

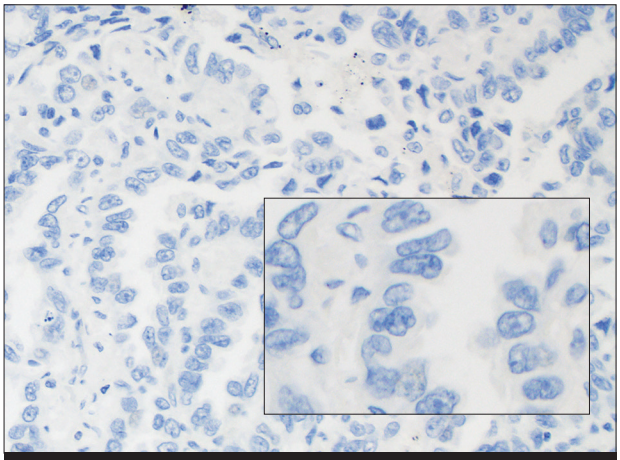


Figure 1: No expression: TPS < 1% (PD-L1 negative) (20x magnification, inset: 40x magnification).

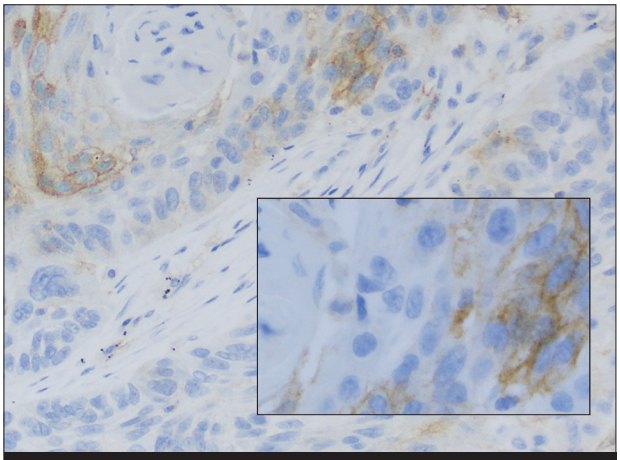


Figure 2: Low expression: TPS 1–49% (PD-L1 positive) (20x magnification, inset: 40x magnification).

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) non-small cell lung cancer (NSCLC) tissue using EnVision FLEX visualization system on Autostainer Link 48. PD-L1 protein expression is determined by using Tumor Proportion Score (TPS), which is the percentage of viable tumor cells showing partial or complete membrane staining.

PD-L1 IHC 22C3 pharmDx is indicated as an aid in identifying NSCLC patients for treatment with KEYTRUDA® (pembrolizumab)[2].

A companion diagnostic to aid in the identification of NSCLC patients for treatment with KEYTRUDA[2]

The KEYNOTE-010 NSCLC clinical trial determined PD-L1 status in patients using the validated PD-L1 IHC 22C3 pharmDx assay[1].

Proven sensitivity

- Assessment of PD-L1 expression demonstrated staining across the dynamic range of 0–100% positive tumor cells and 0–3+ staining intensities[2]
- Approximately 57% of the patients with NSCLC tested with PD-L1 IHC 22C3 pharmDx were PD-L1 positive (TPS ≥ 1%) in KEYNOTE-010[1,2]

Proven specificity

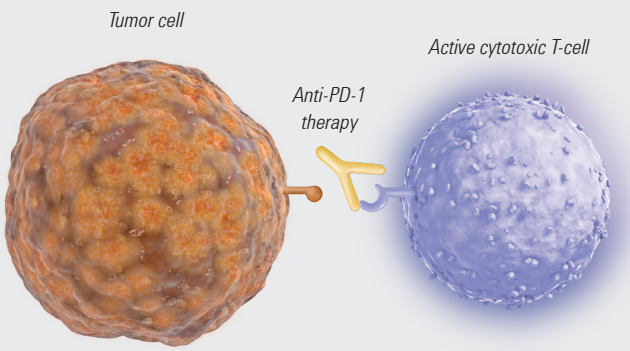
- PD-L1 IHC 22C3 pharmDx includes the proprietary Mouse Monoclonal Anti-PD-L1, Clone 22C3[2]
- Clone 22C3 does not cross-react with human PD-L2 (Programmed Death-Ligand 2) protein[2]
- Clone 22C3 binds to PD-L1 on the cell membrane of tumor cells, immune cells, and cells of epithelial origin[2]

Clinically validated and reproducible

- PD-L1 IHC 22C3 pharmDx provides reproducible results, without the extensive burden of validation that lab-developed tests require
- PD-L1 IHC 22C3 pharmDx includes validated scoring guidelines to aid in the identification of NSCLC patients for treatment with KEYTRUDA[1,2]

Automated method for operational efficiency

- PD-L1 IHC 22C3 pharmDx is a standardized IHC assay with ready-to-use components for 50 tests in one kit
- Designed for use on Autostainer Link 48
- Results can be available within one working day



PD-L1 IHC 22C3 pharmDx Detects PD-L1 in NSCLC Specimens

Figure 3: Blocking the PD-1/PD-L1 interaction helps to enable active T-cells and tumor cell death and elimination.

Clinically validated scoring guidelines to aid in the identification of NSCLC patients for treatment with KEYTRUDA® (pembrolizumab)[2]

NSCLC patient specimens should be considered positive for PD-L1 expression if the Tumor Proportion Score (TPS) is ≥ 1%. This means ≥ 1% of the viable tumor cells exhibit membrane staining at any intensity (i.e. ≥ 1+). Patients with a TPS ≥ 1% may be considered for treatment with KEYTRUDA[2].

PD-L1 staining definition

PD-L1 staining is any perceptible and convincing (≥ 1+ intensity) partial or complete cell membrane staining of viable tumor cells.

Interpretation of PD-L1 expression

Patient specimens tested with PD-L1 IHC 22C3 pharmDx are interpreted as having No Expression, Low Expression, or High Expression of PD-L1 (Figures 4, 5, and 6). The TPS, or the percentage of viable tumor cells showing partial or complete cell membrane staining, determines the PD-L1 expression status of the specimen.

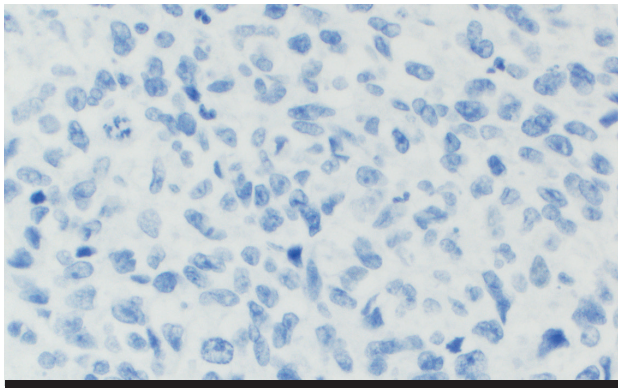


Figure 4: No expression (TPS < 1%) 40x.

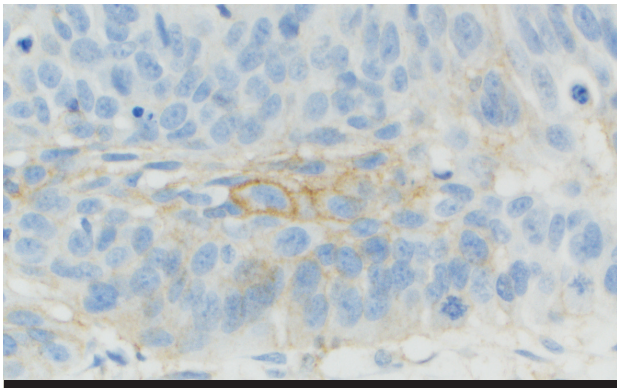


Figure 5: Low expression (TPS 1–49%) 40x.

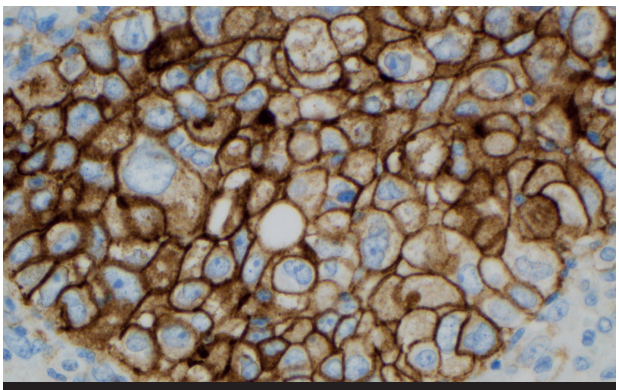


Figure 6: High expression (TPS ≥ 50%) 40x.

PD-L1 IHC 22C3 pharmDx is clinically relevant[1,2]

KEYTRUDA demonstrated superior overall survival compared to the control arm in patients with NSCLC with positive PD-L1 expression as determined by PD-L1 IHC 22C3 pharmDx[1]

NSCLC patient specimens were tested for PD-L1 expression using PD-L1 IHC 22C3 pharmDx. Efficacy of KEYTRUDA was based on the PD-L1 IHC 22C3 pharmDx TPS ≥ 1% population[1].

- The KEYNOTE-010 NSCLC clinical trial determined PD-L1 status in patients using the validated PD-L1 IHC 22C3 pharmDx assay
- Out of the study cohorts of 1,007 previously treated patients with NSCLC screened for the study, tumor tissue from 574 patients demonstrated positive PD-L1 expression by PD-L1 IHC 22C3 pharmDx on retrospective testing
- The percentage of tumor cells with PD-L1 membrane staining is called the **"Tumor Proportion Score (TPS)"**

PD-L1 prevalence[a] in patients with NSCLC[b] screened for KEYNOTE-010[c,1]

The specimen should be considered PD-L1 positive if the TPS ≥ 1%, meaning ≥ 1% of the viable tumor cells exhibit membrane staining at any intensity (i.e. ≥ 1+).

PD-L1 IHC 22C3 pharmDx expression is based on assessment of TPS.

PD-L1 Expression	No Expression TPS < 1%	Low Expression TPS 1%–49%	High Expression TPS ≥ 50%
Prevalence (n)	43.0% (433)	34.2% (344)	22.8% (230)

a. Merck & Co., data on file.
b. Patients screened for enrollment in KEYNOTE-010 NSCLC.
c. International phase 2/3 study comparing pembrolizumab with docetaxel in patients with non-small cell lung carcinoma who have experienced disease progression after platinum-containing systemic therapy. ClinicalTrials.gov number NCT01905657.

PD-L1 IHC 22C3 pharmDx provides demonstrated repeatability and reproducibility[2]

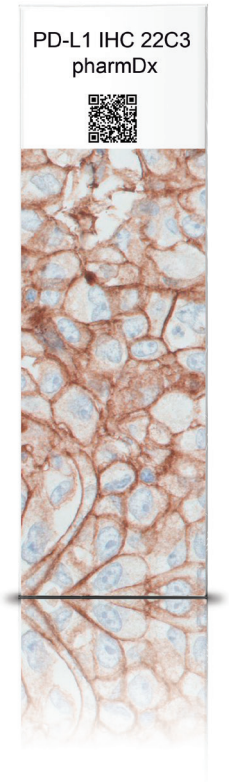
Repeatability

- The PD-L1 IHC 22C3 pharmDx assay has undergone rigorous testing to ensure reliable results
- Repeatability testing performed at Dako, including inter-instrument, inter-operator, inter-day, and intra-run, was performed using a cut-off of TPS ≥ 1% with all tests demonstrating 100% overall agreement

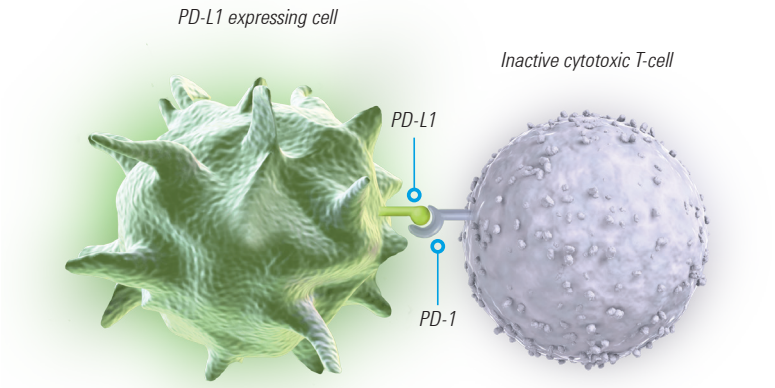
Reproducibility

- Reproducibility testing was performed at three external testing sites, including inter-site, intra-site, inter-observer, and intra-observer, using a cut-off of TPS ≥ 1% with all tests demonstrating > 85% overall agreement*

*Overall agreement is based on average negative and average positive agreements

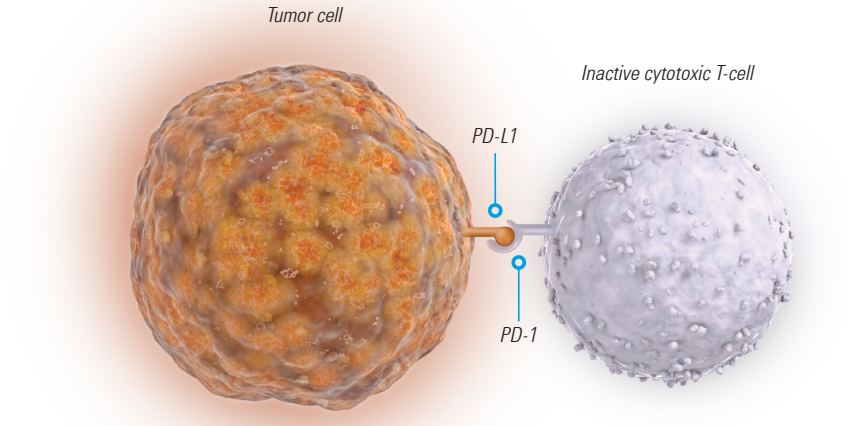


The role of the PD-1/PD-L1 pathway in cancer



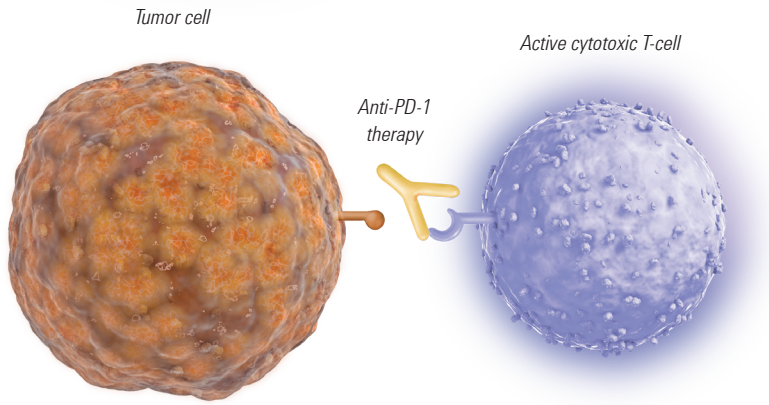
Limiting damage to healthy tissue

Inactivation of T-cells limits damage to healthy tissue.



The tumor escapes detection

Inactivation of T-cells reduces tumor cell killing.



Immuno-oncology therapies harness the immune response to fight tumors

Blocking PD-L1 enables cytotoxic T-cells to actively remove tumor cells.

PD-L1 IHC 22C3 pharmDx measures PD-L1 expression on tumor cells.

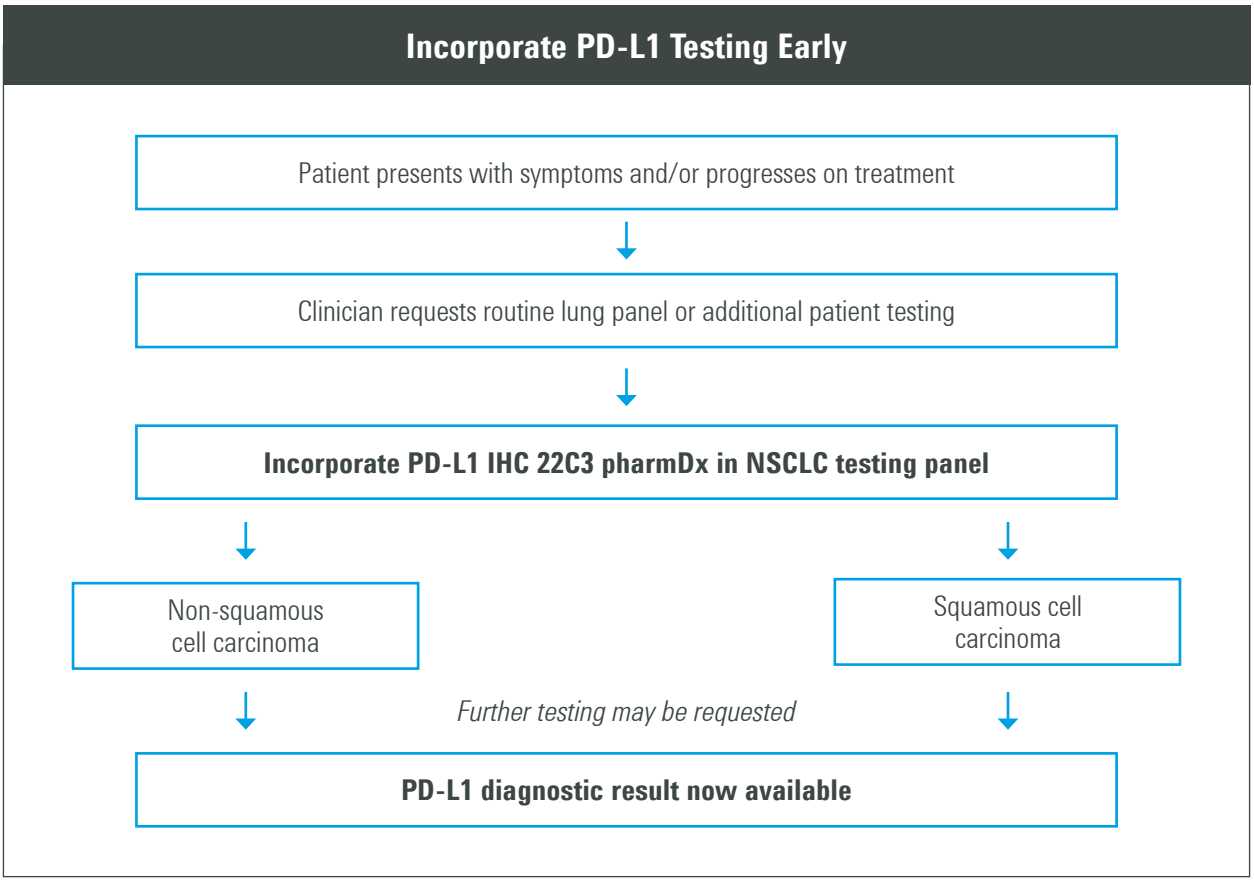
Early testing for PD-L1 expression may better inform patient management

Why test early?

- Help ensure pathologists identify PD-L1 expression early for informed patient management
- To ensure that adequate patient sample material is available
- To ensure test results can be available regardless of the patient's treatment center

Results you should expect

- Prevalence of PD-L1 expression is variable in published literature, mostly due to unvalidated and varying tests and different patient populations
- PD-L1 IHC 22C3 pharmDx was used in the KEYTRUDA® (pembrolizumab) NSCLC study[1]



PD-L1 IHC 22C3 pharmDx is the right choice

- Clinically validated assay and scoring guidelines to aid in the identification of NSCLC patients for treatment with KEYTRUDA® (pembrolizumab)[2]
- Includes all reagents necessary to perform a complete staining run
- Includes positive and negative control cell line slides to validate staining run

Figure 7: Autostainer Link 48 and PD-L1 IHC 22C3 pharmDx kit, Code No. SK006.

Order information

Product	Platform	Code
PD-L1 IHC 22C3 pharmDx	Autostainer Link 48	SK006

References

1. Herbst RS, Baas P, Kim DW, et al. Pembrolizumab versus docetaxel for previously treated, PD-L1-positive, advanced non-small-cell lung cancer (KEYNOTE-010): a randomised controlled trial. *Lancet.* 2016;387(10027):1540-1550.
2. PD-L1 IHC 22C3 pharmDx - Package Insert.

Make the right test choice to aid in the identification of NSCLC patients for treatment with KEYTRUDA® (pembrolizumab): PD-L1 IHC 22C3 pharmDx[2]

- Use the same test employed in the KEYTRUDA clinical studies
- Incorporate PD-L1 testing early
- Utilize our extensive education and training resources to incorporate PD-L1 testing in your laboratory

Trusted Answers. Together.

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