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)\textsuperscript{1,2}: 

**PD-L1 IHC 22C3 pharmDx**
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)\textsuperscript{1,2}
• Includes clinically validated scoring guidelines for KEYTRUDA
• PD-L1 IHC 22C3 pharmDx provides demonstrated repeatability and reproducibility\textsuperscript{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\textsuperscript{1,2}

\textbf{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)\textsuperscript{2}.

\textsuperscript{1} KEYTRUDA is a registered trademark of Merck Sharp & Dohme Corp., a subsidiary of Merck & Co., Inc.
A companion diagnostic to aid in the identification of NSCLC patients for treatment with KEYTRUDA²

The KEYNOTE-010 NSCLC clinical trial determined PD-L1 status in patients using the validated PD-L1 IHC 22C3 pharmDx assay¹.

**Proven sensitivity**

- Assessment of PD-L1 expression demonstrated staining across the dynamic range of 0–100% positive tumor cells and 0–3+ staining intensities²
- Approximately 57% of the patients with NSCLC tested with PD-L1 IHC 22C3 pharmDx were PD-L1 positive (TPS ≥ 1%) in KEYNOTE-010¹²

**Proven specificity**

- PD-L1 IHC 22C3 pharmDx includes the proprietary Mouse Monoclonal Anti-PD-L1, Clone 22C3²
- Clone 22C3 does not cross-react with human PD-L2 (Programmed Death-Ligand 2) protein²
- Clone 22C3 binds to PD-L1 on the cell membrane of tumor cells, immune cells, and cells of epithelial origin²

**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 KEYTRUDA¹²

**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

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

**PD-L1 IHC 22C3 pharmDx**

*Detects PD-L1 in NSCLC Specimens*
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 KEYTRUDA².

**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.
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

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

• 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 in patients with NSCLC screened for KEYNOTE-010

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) |

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 NCT01905667.
PD-L1 IHC 22C3 pharmDx provides demonstrated repeatability and reproducibility²

**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

Incorporate PD-L1 Testing Early

Patient presents with symptoms and/or progresses on treatment

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Clinician requests routine lung panel or additional patient testing

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Incorporate PD-L1 IHC 22C3 pharmDx in NSCLC testing panel

Non-squamous cell carcinoma

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Squamous cell carcinoma

Further testing may be requested

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PD-L1 diagnostic result now available
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**

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<thead>
<tr>
<th>Product</th>
<th>Platform</th>
<th>Code</th>
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<td>PD-L1 IHC 22C3 pharmDx</td>
<td>Autostainer Link 48</td>
<td>SK006</td>
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</tbody>
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**References**

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

- 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.