PD-L1 IHC results you can trust for OPDIVO® (nivolumab) use in non-squamous NSCLC
Dako’s PD-L1 IHC 28-8 pharmDx is the only FDA-approved test for PD-L1 expression associated with enhanced survival with OPDIVO for non-squamous NSCLC

- PD-L1 IHC 28-8 pharmDx is clinically validated
- The only PD-L1 test with results from a phase 3 randomized trial based on survival
- Highly sensitive, specific, and reproducible

Experience the easy integration of PD-L1 in your IHC workflow

- Integrate PD-L1 IHC 28-8 pharmDx without changing staining lab workflow
- Ready-to-use reagents and control slides optimized for Autostainer Link 48
- Pre-programmed, validated protocol
Demonstrated clinical results with PD-L1 IHC 28-8 pharmDx

- Patients with PD-L1 expression by the predefined expression levels in the OPDIVO group were associated with enhanced survival compared to docetaxel.

\[
\begin{align*}
\geq 1\% & \quad \text{PD-L1 expression} \rightarrow 41\% \text{ Reduction in Risk of Death (HR }= 0.59) \\
& \quad 17.1 \text{ months median OS vs. 9 months for docetaxel} \\
\geq 5\% & \quad \text{PD-L1 expression} \rightarrow 57\% \text{ Reduction in Risk of Death (HR }= 0.43) \\
& \quad 18.2 \text{ months median OS vs. 8.1 months for docetaxel} \\
\geq 10\% & \quad \text{PD-L1 expression} \rightarrow 60\% \text{ Reduction in Risk of Death (HR }= 0.40) \\
& \quad 19.4 \text{ months median OS vs. 8 months for docetaxel}
\end{align*}
\]

- In patients with no PD-L1 expression (< 1%), survival with OPDIVO was similar to docetaxel.
A complementary diagnostic for PD-L1 expression in non-squamous NSCLC

- Pathologists should use Dako PD-L1 IHC 28-8 pharmDx when an oncologist prescribing OPDIVO (nivolumab) for non-squamous non-small cell lung cancer requests a PD-L1 test.
- PD-L1 testing is not required for the use of OPDIVO, but it will provide additional information for physicians and inform patient dialogue.
- PD-L1 IHC 28-8 pharmDx provides accurate, reproducible results.

Intended Use

For In Vitro Diagnostic Use


PD-L1 protein expression is defined as the percentage of tumor cells exhibiting positive membrane staining at any intensity.

PD-L1 expression as detected by PD-L1 IHC 28-8 pharmDx in non-squamous NSCLC may be associated with enhanced survival from OPDIVO (nivolumab).
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 28-8 pharmDx measures PD-L1 expression on tumor cells.
Clinically validated scoring guidelines for assessing PD-L1 expression for OPDIVO

To assess the PD-L1 expression level in patient slides stained with PD-L1 IHC 28-8 pharmDx, pathologists should determine the percentage of viable tumor cells exhibiting partial or complete linear circumferential plasma membrane staining at any staining intensity.

See Dako Interpretation Manual for complete interpretation of PD-L1 IHC 28-8 pharmDx staining results.

<table>
<thead>
<tr>
<th>Staining pattern</th>
<th>Examples of non-squamous NSCLC</th>
<th>Examples of result reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 1% of the viable tumor cells exhibit complete circumferential or partial linear plasma membrane staining at any intensity.</td>
<td><img src="image1.png" alt="Image" /></td>
<td>PD-L1 expression &lt; 1%</td>
</tr>
<tr>
<td>≥ 1% of the viable tumor cells exhibit complete circumferential or partial linear plasma membrane staining at any intensity.</td>
<td><img src="image2.png" alt="Image" /></td>
<td>PD-L1 expression ≥ 1%</td>
</tr>
<tr>
<td>≥ 5% of the viable tumor cells exhibit complete circumferential or partial linear plasma membrane staining at any intensity.</td>
<td><img src="image3.png" alt="Image" /></td>
<td>PD-L1 expression ≥ 5%</td>
</tr>
<tr>
<td>≥ 10% of the viable tumor cells exhibit complete circumferential or partial linear plasma membrane staining at any intensity.</td>
<td><img src="image4.png" alt="Image" /></td>
<td>PD-L1 expression ≥ 10%</td>
</tr>
</tbody>
</table>

Table 1: Guidelines for scoring and reporting of PD-L1 IHC 28-8 pharmDx.

PD-L1 protein expression is defined as the percentage of tumor cells exhibiting positive membrane staining at any intensity.

Control slides for enhanced confidence in results

Control slides are provided to help validate the staining run. They are not to be used as an interpretation reference.

Positive cell pellet

Negative cell pellet
Dako PD-L1 IHC 28-8 pharmDx is FDA-approved and fully validated with analytical performance having met all pre-determined acceptance criteria for sensitivity, specificity and precision.

<table>
<thead>
<tr>
<th>Selected analytical validation parameters</th>
<th>Results for non-squamous NSCLC</th>
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</thead>
<tbody>
<tr>
<td><strong>Specificity</strong></td>
<td>- Primary antibody: rabbit monoclonal, clone 28-8</td>
</tr>
<tr>
<td></td>
<td>- Detects PD-L1 on the plasma membranes of tumor cells, the staining of which can be completely abolished by PD-L1 gene knock-out</td>
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<tr>
<td></td>
<td>- Detection in normal tissues is restricted to immune cells and infrequently the cells of epithelial origin</td>
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<td></td>
<td>- Clone 28-8 exhibits no cross reactivity to PD-L2</td>
</tr>
<tr>
<td><strong>Sensitivity</strong></td>
<td>- Broad dynamic range of PD-L1 expression (0-100% tumor cells positive, 0-3 staining intensity) exhibited in study of 112 unique cases of non-squamous NSCLC archival FFPE specimens</td>
</tr>
<tr>
<td></td>
<td>- In BMS clinical study CA209057 of patients with non-squamous NSCLC, approximately 54% and 40% had PD-L1 expression levels ≥1% and ≥5%, respectively</td>
</tr>
<tr>
<td><strong>Precision - Repeatability</strong></td>
<td>- Repeatability testing of inter-instrument, inter-operator, inter-day, inter-lot and intra-run performance</td>
</tr>
<tr>
<td></td>
<td>- ≥ 99% overall agreement for ≥ 1%, ≥ 5% and ≥ 10% expression levels</td>
</tr>
<tr>
<td></td>
<td>- 95% confidence intervals ranged from 82.4 to 100% for NPA, PPA, and OA*</td>
</tr>
<tr>
<td><strong>Precision - Reproducibility</strong></td>
<td>- Reproducibility testing of day-to-day, site-to-site and observer-to-observer performance in a blinded study in three certified clinical labs</td>
</tr>
<tr>
<td></td>
<td>- ≥ 94% overall agreement for ≥ 1% and ≥ 5% expression levels</td>
</tr>
<tr>
<td></td>
<td>- 95% confidence intervals ranged from 78.5 to 100% for NPA, PPA, and OA*</td>
</tr>
</tbody>
</table>

*Negative Percent Agreement, Positive Percent Agreement, Overall Percent Agreement

**References**

PD-L1 IHC 28-8 pharmDx instructions for use.
Use the Dako PD-L1 IHC 28-8 pharmDx

The first and only FDA-approved complementary test for PD-L1 expression associated with enhanced survival with OPDIVO for non-squamous NSCLC

- The only PD-L1 test with results from a phase 3 randomized trial based on survival
- Fits within your lab’s routine IHC workflow without modifying existing laboratory processes

**Kit components**

Dako PD-L1 IHC 28-8 pharmDx is a complete kit with reagents sufficient for 50 tests (50 slides incubated with primary antibody to PD-L1 and 50 slides incubated with the corresponding negative control reagent) and 15 Control Slides for use on Autostainer Link 48.

- EnVision FLEX Target Retrieval Solution, Low pH, 50x
- Peroxidase-Blocking Reagent
- Monoclonal Rabbit Anti-PD-L1, Clone 28-8
- Negative Control Reagent
- Anti-Rabbit LINKER
- Visualization Reagent-HRP
- DAB+ Substrate Buffer
- DAB+ Chromogen
- DAB Enhancer
- Control Slides

**Order information**

<table>
<thead>
<tr>
<th>PD-L1 IHC 28-8 pharmDx Kit</th>
<th>Reagents required but not included in kit</th>
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<tbody>
<tr>
<td>SK005</td>
<td>EnVision FLEX Wash Buffer, 20x, Code K8007</td>
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<td></td>
<td>EnVision FLEX Hematoxylin, Code K8008</td>
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</tbody>
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Relentless in our commitment to fighting cancer. Together.