Non-Small Cell Lung Cancer (NSCLC)

PD-L1 BY IMMUNOHISTOCHEMISTRY

PD-1 and PD-L1

Programmed death 1 (PD-1) is an immune inhibitory receptor expressed on the surface of activated T-cells and mediates suppression of the immune system. PD-1 interacts with the immunosuppressive PD-L1 ligand which is expressed on tumor cells, inflammatory cells, and histiocytes, and inhibits T-cell activation.

PD-L1 expression is independent of EGFR mutational status. PD-L1 expression was observed in a higher percentage of patients with KRAS mutations.

PD-L1 Expression

- Tumor PD-L1 expression levels have been shown to be a predictive marker with response to several anti-PD1 antibodies.
- PD-L1 expression can be measured by immunohistochemistry and detects PD-L1 expression in formalin-fixed, paraffin-embedded NSCLC tumor tissue samples.

Clinical Studies in NSCLC

Membranous PD-L1 expression (clone 22C3) and response to anti-PD1 immunotherapy KEYTRUDA® (pembrolizumab) was evaluated in previously treated and untreated patients with metastatic NSCLC. The study results were as follows:

- 37.6% of patients expressed PD-L1 in 1%–49% of neoplastic cells (proportion score)
- 23.2% of patients expressed PD-L1 in ≥50% of neoplastic cells (proportion score)
- A PD-L1 proportion score of at least 50% was associated with a higher response rate, longer progression-free survival, and overall survival than those with scores below 50%
- PD-L1 expression is independent of EGFR mutational status
- PD-L1 expression was observed in a higher percentage of patients with KRAS mutations

The DAKO PD-L1 IHC 22C3 pharmDx™ was recently FDA approved as a companion diagnostic assay to aid in identifying advanced NSCLC patients for treatment with KEYTRUDA® (pembrolizumab).
Clinical Studies in NSCLC (cont’d)

Another study of patients with advanced non-squamous NSCLC, PD-L1 expression (Clone 28-8), and response to anti-PD1 immunotherapy nivolumab vs. chemotherapy, included the following results:

- 46% of patients were negative for PD-L1 expression (<1%; OS HR 0.9)
- 54% of patients had ≥1% expression level (OS HR 0.59)
- 40% of patients had ≥5% expression level (OS HR 0.43)
- 36% of patients had ≥10% expression level (OS HR 0.4)

PD-L1 expression was associated with improved efficacy across all endpoints (OS, PFS, duration of response) at all expression levels. The most improvement was seen in patients with PD-L1 expression ≥5% and ≥10%, but was evident at PD-L1 expression levels as low as ≥1%.

Patients with tumors that had PD-L1 expression levels ≥1% were associated with a doubling of overall median survival.

Specimen Requirement Options

- Global Only
- Tissue should be fixed in 10% neutral buffered formalin; alternative fixatives have not been validated and may give erroneous results
- A minimum of 100 cells is required

1) Fixed Paraffin Block with Corresponding H&E
2) Unstained Slides:
   - Minimum of 4 slides (include additional slide for H&E)
   - Pre-cut slides from paraffin block in 4-5 micron sections and mount on plus (+) slides

REFERENCES