PRODUCT INFORMATION

PD-L1 IHC 28-8 pharmDx | Urothelial Carcinoma (UC)

FDA-approved for urothelial carcinoma

Dako
Agilent Pathology Solutions

More personalized cancer results.
One test makes it possible.

Personalized medicine option for patients with metastatic urothelial carcinoma

Bladder cancer is the most common urinary system cancer and the ninth most common cancer worldwide, with approximately 430,000 new cases annually. Urothelial carcinoma is the predominant histologic type in the United States and Western Europe, accounting for approximately 90 percent of bladder cancers.[1][2] Patients with metastatic urothelial carcinoma have a dismal prognosis after first-line chemotherapy.[3] Transitional cell carcinoma (also referred to as urothelial carcinoma) can develop anywhere along the urinary tract which is lined with transitional cells from the renal pelvis to the proximal urethra.[4]

PD-L1 IHC 28-8 pharmDx: The first **fully validated** and **clinically relevant** test for OPDIVO® (nivolumab) in urothelial carcinoma

PD-L1 expression as detected by PD-L1 IHC 28-8 pharmDx in UC may be associated with enhanced response rate from OPDIVO.[5]

In study CHECKMATE-275, Objective Response Rate (ORR) based on PD-L1 expression was evaluated using PD-L1 IHC 28-8 pharmDx and is summarized below. Median time to response was 1.9 months (range; 1.6-7.2).

Efficacy Results for study CHECKMATE-275[5]

Confirmed ORR in all patients and the two PD-L1 subgroups are summarized in the table below.

Tumor PD-L1 Expression	<1%	≥1%	All Treated Subjects
Total No. of Subjects	N=146	N=124	N=270
Confirmed Objective Response Rate No. of Subjects (95% CI)	22 (9.7, 21.9)	31 (17.7, 33.6)	53 (15.1, 24.9)
Complete Response Rate No. of Subjects (% of Total in PD-L1 expression category)	1 (0.7%)	6 (4.8%)	7 (2.6%)
Partial Response Rate No. of Subjects (% of Total in PD-L1 expression category)	21 (14.4%)	25 (20.2%)	46 (17.0%)
Median Duration of Response* Months (range)	7.6 mos. (3.7+, 12.0+)	NE (1.9+, 12.0+)	10.3 (1.9+, 12.0+)

*Estimated from the Kaplan-Meier Curve

PD-L1 IHC 28-8 pharmDx Intended for In Vitro Diagnostic Use

PD-L1 IHC 28-8 pharmDx is a qualitative immunohistochemical assay using Monoclonal Rabbit Anti-PD-L1, Clone 28-8 intended for use in the detection of PD-L1 protein in formalin-fixed, paraffin embedded (FFPE) non-squamous non-small cell lung cancer (NSCLC), squamous cell carcinoma of the head and neck (SCCHN), urothelial carcinoma (UC), and melanoma tissues using EnVision FLEX visualization system on Autostainer Link 48. PD-L1 protein expression is defined as the percentage of evaluable tumor cells exhibiting partial or complete membrane staining at any intensity. Tumor PD-L1 status is defined by indication specific staining interpretation.

Tumor Indication*	Intended Use	PD-L1 Expression Clinical Cut Off
nsNSCLC	PD-L1 expression as detected by PD-L1 IHC 28-8 pharmDx in non-squamous NSCLC and SCCHN may be associated with enhanced survival from OPDIVO® (nivolumab).	≥1%, ≥5%, ≥10%
SCCHN		≥1%
UC	PD-L1 expression as detected by PD-L1 IHC 28-8 pharmDx in UC may be associated with enhanced response rate from OPDIVO®.	≥1%
Melanoma	Positive PD-L1 status as determined by PD-L1 IHC 28-8 pharmDx in melanoma is correlated with the magnitude of the treatment effect on progression-free survival from OPDIVO®.	≥1%

*For details on staining interpretation, refer to section 13 of the product insert and indication specific PD-L1 IHC 28-8 pharmDx Interpretation Manuals.

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PD-L1 IHC 28-8 pharmDx delivers clinically validated results

Frequency of Tumor PD-L1 Expression in Samples from UC - CHECKMATE-275

Tumor PD-L1 Expression	Nivolumab (N=270)
≥1% PD-L1 Expression Subjects	124 (45.9%)
<1% PD-L1 Expression Subjects	146 (54.1%)

Baseline UC Specimen Origin - CHECKMATE-275

- 27% of nivolumab treated patients had non-bladder, urothelial carcinoma
- Regardless of tumor site, 84% of all treated patients presented with visceral metastases at baseline

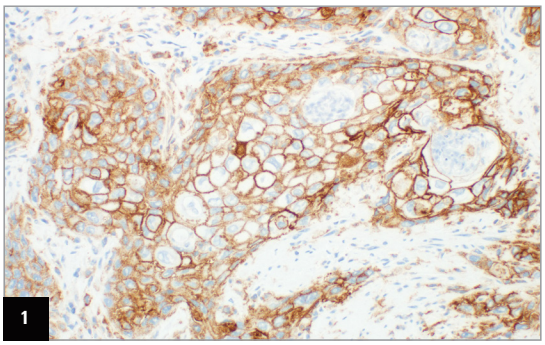
Non-bladder UC	Visceral metastases
27% (73/270)	**84%** (227/270)

PD-L1 IHC 28-8 pharmDx offers robust performance

PD-L1 IHC 28-8 pharmDx is fully validated for analytical performance, having met stringent acceptance criteria for ultimate quality results.

Selected Analytical validation parameters	Results for UC
Analytical specificity	■ Demonstrated specificity to clone 28-8 for PD-L1 detection ■ PD-L1 primary antibody displays no cross-reactivity for PD-L2 ■ Detection in normal tissues restricted to immune cells and infrequently to cells of epithelial origin
Sensitivity	■ Broad dynamic range of PD-L1 expression (0-90% of positive tumor cells, 0-3 staining intensity) exhibited in study of 138 unique cases of human urothelial carcinoma FFPE specimen stages III to IV
Repeatability	■ Demonstrated lot-to-lot repeatability ■ >91.9% overall agreement for ≥1% expression level
External reproducibility	■ ≥87.0% overall agreement for ≥1% expression level ■ Reproducibility testing of day-to-day, site-to-site and observer-to-observer in a blinded study in three certified clinical labs ■ 95% confidence intervals from 77.7%–98.2% agreement for both ANA and APA

ANA= Average Negative Agreement | APA= Average Positive Agreement | OA= Overall Agreement



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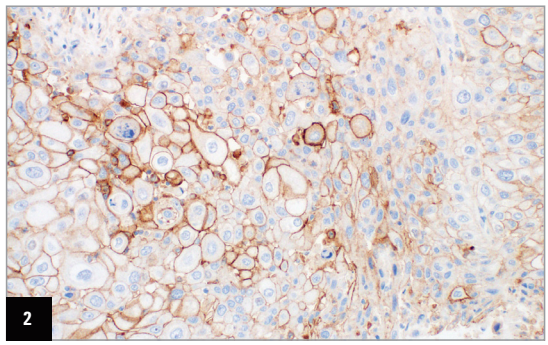

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1. Left Box: Urothelial carcinoma of the bladder stained with PD-L1.

2. Right Box: Urothelial carcinoma of the bladder stained with PD-L1.

Order information:
PD-L1 IHC 28-8 pharmDx – SK005

Include PD-L1 IHC 28-8 pharmDx in your urothelial carcinoma panel to provide more personalized cancer results for these patients.

References

(1) Ploeg M, Aben KK, Kiemeney LA. The present and future burden of urinary bladder cancer in the world. World J Urol 2009; 27:289.
(2) Torre LA, Bray F, Siegel RL, et al. Global cancer statistics, 2012. CA Cancer J Clin 2015; 65:87.
(3) Nivolumab in metastatic urothelial carcinoma after platinum therapy (CHECKMATE-275): a multicentresingle-arm, phase 2 trial Sharma, Padmanee et al. The Lancet Oncology, Volume 18, Issue 3, 312 - 322.
(4) cancer.gov
(5) PD-L1 IHC 28-8 pharmDx Instructions for Use.

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