PRODUCT INFORMATION

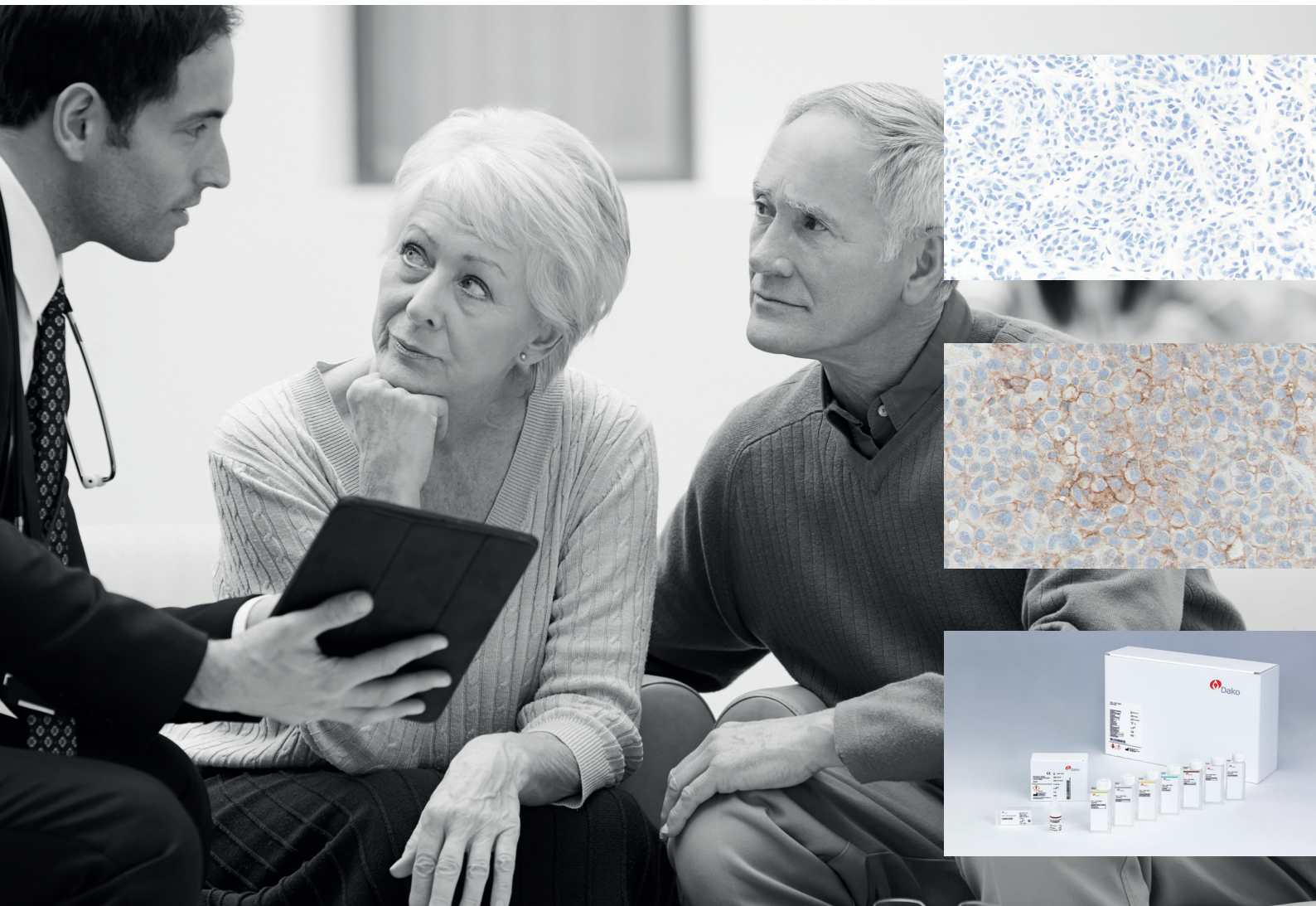
pharmDx | PD-L1 IHC 28-8 pharmDx

Dako

Agilent Pathology Solutions

Results you can trust

The first and only CE-IVD marked PD-L1 test for expression in melanoma in patients for whom OPDIVO® (nivolumab) and YERVOY® (ipilimumab) combination treatment is being considered[1]



Agilent Technologies

Confidence in PD-L1 test results

PD-L1 expression as detected by PD-L1 IHC 28-8 pharmDx in melanoma may be used as an aid in the assessment of patients for whom OPDIVO (nivolumab) and YERVOY (ipilimumab) combination treatment is being considered[1].

- The only FDA-approved and CE-IVD marked PD-L1 test with results linked to a clinical outcome in melanoma
- The only PD-L1 test validated across two tumor types: non-squamous NSCLC and melanoma[1]
- Demonstrated clinical results in the phase 3 CheckMate 067 clinical trial[2]
- Reliability. PD-L1 IHC 28-8 pharmDx kit meets all acceptance criteria for analytical performance[1]
- Confidence in scoring with a comprehensive PD-L1 Interpretation Manual
- Plug-and-play quality controlled all-inclusive kit, optimized for the Autostainer Link 48

Intended Use

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) and melanoma tissues using EnVision FLEX visualization system on Autostainer Link 48. 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).

PD-L1 expression as detected by PD-L1 IHC 28-8 pharmDx in melanoma may be used as an aid in the assessment of patients for whom OPDIVO (nivolumab) and YERVOY (ipilimumab) combination treatment is being considered.

Demonstrated clinical results with PD-L1 IHC 28-8 pharmDx[1,2]

- The CheckMate 067 study was a three armed study of OPDIVO (nivolumab) monotherapy or OPDIVO in combination with YERVOY (ipilimumab) versus YERVOY monotherapy
- Progression-free survival (PFS) was evaluated across PD-L1 subgroups
- In patients with low PD-L1 expression levels, combination of OPDIVO (nivolumab) and YERVOY (ipilimumab) demonstrated improved PFS relative to OPDIVO (nivolumab) treatment

PFS values at PD-L1 expression level ≥ 5% and < 5%

Treatment	PD-L1 expression level	N of events/ N of patients	Median PFS in month (95% CI)	HR vs. ipilimumab (95% CI)	HR vs. nivolumab monotherapy (95% CI])
nivolumab + ipilimumab	≥ 5%	28/68	13.96 (9.72, NR)	0.39 (0.25, 0.62)	0.96 (0.58, 1.58)
	< 5%	103/210	11.24 (7.98, NR)	0.42 (0.32, 0.54)	0.70 (0.54, 0.91)
nivolumab	**≥ 5%**	**33/80**	**14.00 (9.07, NR)**	**0.41 (0.26, 0.63)**	-
	< 5%	**122/208**	**5.32 (2.83, 7.06)**	**0.59 (0.47, 0.75)**	-
ipilimumab	≥ 5%	53/75	3.94 (2.79, 4.21)	-	-
	< 5%	154/202	2.83 (2.76, 3.09)	-	-

PFS values at PD-L1 expression level ≥ 1% and < 1%

Treatment	PD-L1 expression level	N of events/ N of patients	Median PFS in month (95% CI)	HR vs. ipilimumab (95% CI)	HR vs. nivolumab monotherapy (95% CI])
nivolumab + ipilimumab	≥ 1%	72/155	12.35 (8.51, NR)	0.44 (0.32, 0.58)	0.95 (0.69, 1.31)
	< 1%	59/123	11.17 (6.93, NR)	0.38 (0.27, 0.53)	0.56 (0.40, 0.79)
nivolumab	**≥ 1%**	**79/171**	**12.39 (8.11, NR)**	**0.46 (0.34, 0.61)**	-
	< 1%	**76/117**	**2.83 (2.76, 5.13)**	**0.67 (0.49, 0.92)**	-
ipilimumab	≥ 1%	122/164	3.91 (2.83, 4.17)	-	-
	< 1%	85/113	2.79 (2.66, 2.96)	-	-

Abbreviations: CI = confidence interval, NR = not reached, PFS = progression-free survival

HR = Hazard ratio for treatment effect based on Cox proportional hazard model with treatment, PD-L1 status, and treatment by PD-L1 status interaction

Summary of Progression-free Survival by PD-L1 Level and Treatment Group - All Randomized Subjects with Melanoma - CA209067

PD-L1 IHC 28-8 pharmDx testing is simple to incorporate at time of melanoma diagnosis

Benefits of PD-L1 testing at diagnosis of melanoma:

- Sample is readily available
- Results available to treating physician for patient dialogue
- Early testing enables laboratory efficiency

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

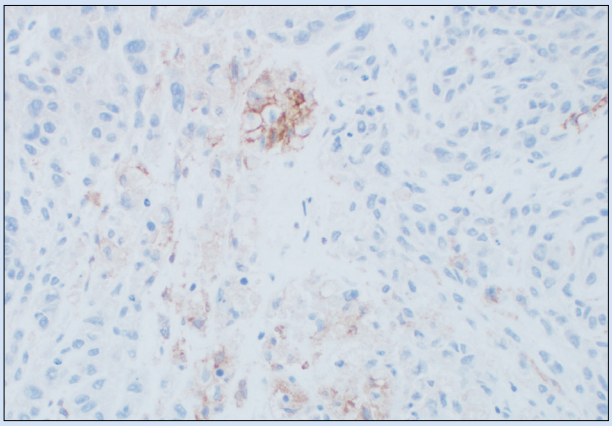
- Integrate PD-L1 IHC 28-8 pharmDx without changing staining lab workflow
- Ready-to-use reagents and control slides optimized for Autostainer Link 48
- Pre-programmed, validated protocol

Providing high quality staining results you can trust

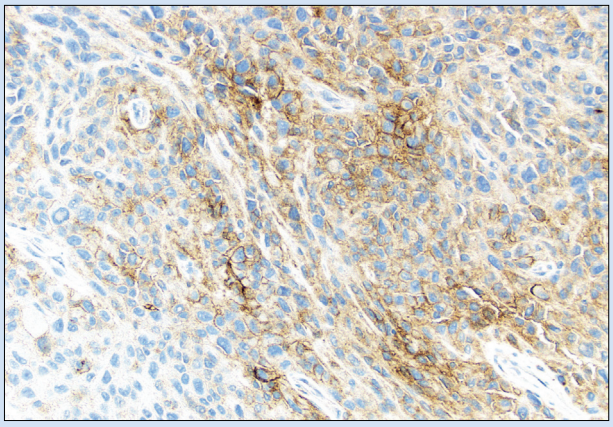
PD-L1 protein expression is defined as the percentage of tumor cells exhibiting positive membrane staining at any intensity

Examples of Melanoma Stains

PD-L1 IHC 28-8 pharmDx result report to treating physician



PD-L1 expression < 5%



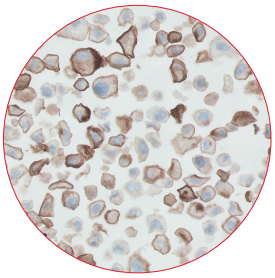
PD-L1 expression ≥ 5%

PD-L1 IHC 28-8 pharmDx includes a comprehensive Interpretation Manual for PD-L1 results you can trust

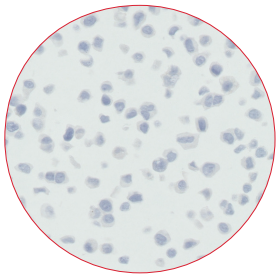
See Dako Interpretation Manual for complete interpretation of PD-L1 IHC 28-8 pharmDx staining results.

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

Robust performance with PD-L1 IHC 28-8 pharmDx[1,2]

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

Selected analytical validation parameters	Results for melanoma
Analytical Specificity	• Primary antibody: rabbit monoclonal, clone 28-8 • Detects PD-L1 on the plasma membranes of tumor cells, the staining of which can be completely abolished by PD-L1 gene knock-out • Detection in normal tissues is restricted to immune cells and infrequently the cells of epithelial origin • Clone 28-8 exhibits no cross reactivity to PD-L2
Sensitivity	• Broad dynamic range of PD-L1 expression (0-100% tumor cells positive, 0-3 staining intensity) exhibited in study of 104 unique cases of melanoma archival FFPE specimens • In BMS clinical study CheckMate CA209067 of patients with melanoma, 26.5% of patients had PD-L1 ≥5% tumour cell membrane expression
Repeatability	• Repeatability testing of inter-instrument, inter-operator, inter-day, inter-lot and intra-run performance • ≥ 90% overall agreement for ≥ 1% expression level and > 88,8% overall agreement for ≥ 5% expression level • 95% confidence intervals ranged from 83.2 to 99.4% in ≥1% and 77,6 to 96,4 in ≥5% for ANA, APA, and OA*
External Reproducibility	• Reproducibility testing of day-to-day, site-to-site and observer-to-observer performance in a blinded study in three certified clinical labs • ≥ 90% overall agreement for ≥ 1% and ≥5% expression level • 95% confidence intervals ranged from 88.1 to 100% for ANA, APA, and OA*

*Average Negative Agreement, Average Positive Agreement, Overall Agreement

Confidence in PD-L1 IHC testing with validated Dako pharmDx kits

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

All-inclusive kit with a proprietary rabbit linker is only available in PD-L1 IHC 28-8 pharmDx, validated for 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
- PD-L1 IHC 28-8 pharmDx Anti-Rabbit LINKER
- Visualization Reagent-HRP
- DAB+ Substrate Buffer
- DAB+ Chromogen
- DAB Enhancer
- Control Slides

PD-L1 IHC 28-8 pharmDx Kit, SK005

Order information

PD-L1 IHC 28-8 pharmDx Kit	Reagents required but not included in kit
SK005	EnVision FLEX Wash Buffer, 20x, Code K8007 EnVision FLEX Hematoxylin, Code K8008 EnVision FLEX Target Retrieval Solution, Low pH, 50x, Code K8005

Choose the validated PD-L1 IHC 28-8 pharmDx for melanoma PD-L1 testing[1,2]

The first and only CE-IVD marked test for use in the assessment of patients for whom OPDIVO (nivolumab) and YERVOY (ipilimumab) combination treatment is being considered

- All-inclusive kit with unique Rabbit Linker only available in PD-L1 IHC 28-8 pharmDx
- Clinically validated PD-L1 IHC 28-8 pharmDx results on the Autostainer Link 48
- High-quality results, meeting all acceptance criteria for robust analytical performance
- Fits within your lab's routine IHC workflow without modifying existing laboratory processes
- Comprehensive Interpretation Manual for melanoma

Trusted Answers. Together.

References

1. PD-L1 IHC 28-8 pharmDx Instructions For Use
2. Clinical Trial: Checkmate 067, CA209067

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