PRODUCT INFORMATION

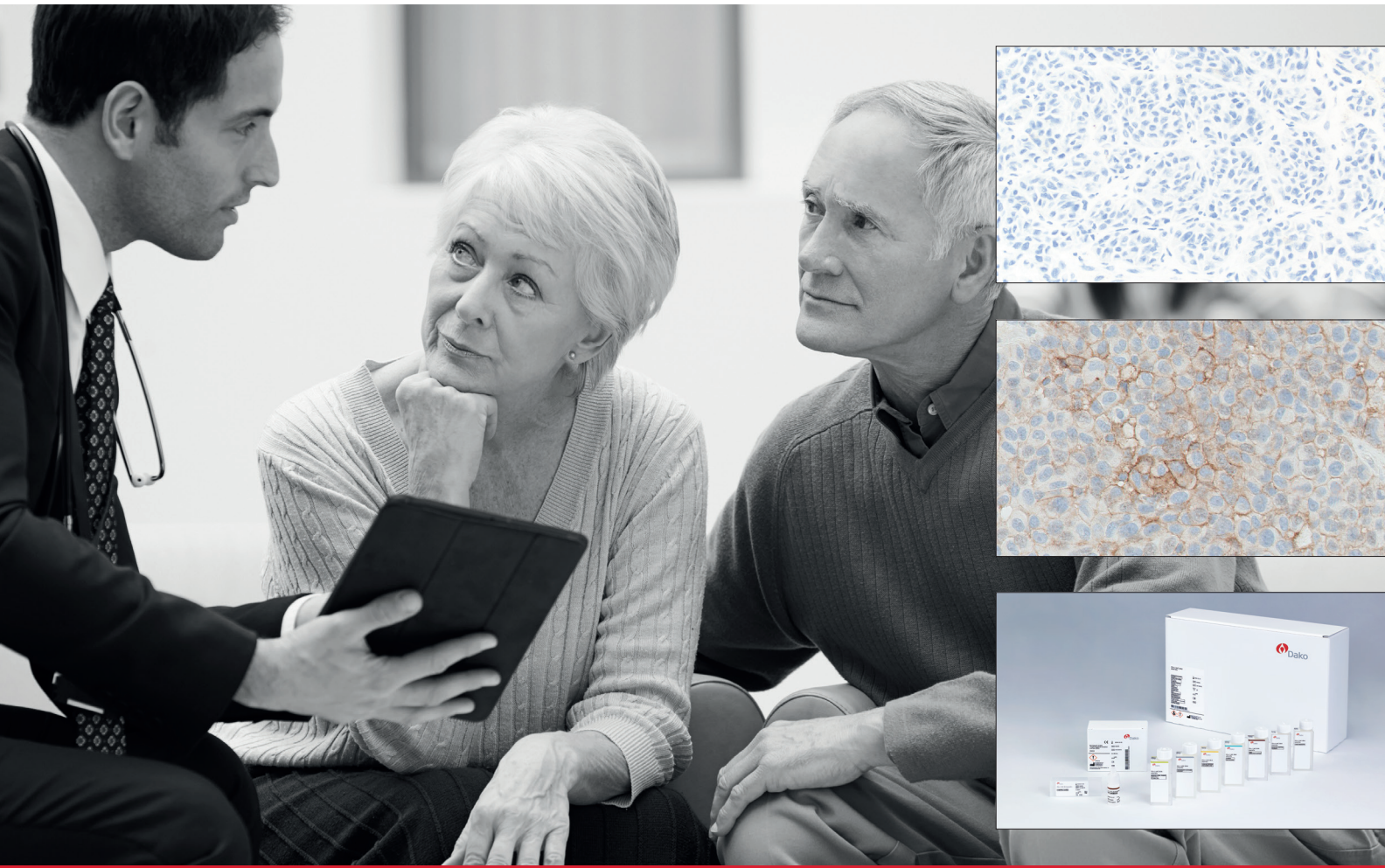
pharmDx | PD-L1 IHC 28-8 pharmDx

Dako

An **Agilent Technologies** Company

Results you can trust

The first and only FDA-approved PD-L1 test to assess the magnitude of treatment effect on progression-free survival in melanoma patients from OPDIVO®



Agilent Technologies

PD-L1 IHC 28-8 pharmDx

The only FDA-approved test with results linked to a clinical outcome in melanoma

- The only test validated across two tumor types: non-squamous NSCLC and melanoma
- Demonstrated clinical results in the phase 3 CheckMate-067 clinical trial
- The magnitude of the treatment effect on progression-free survival from OPDIVO is correlated with positive PD-L1 status as determined by PD-L1 IHC 28-8 pharmDx in melanoma

- **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 at 1% as a pre-planned retrospective analysis (secondary objective)**

PD-L1 Expression Level*	**Nivolumab Median PFS** (95% CI)	**Ipilimumab Median PFS** (95% CI)	Hazard Ratio (95% CI)[a]
≥ 1%	12.39 (8.11, NR)	3.91 (2.83, 4.17)	0.46 (0.35, 0.62)
< 1%	2.83 (2.76, 5.13)	2.79 (2.66, 2.96)	0.65 (0.48, 0.89)
	Nivolumab + Ipilimumab Median PFS (95% CI)	**Ipilimumab Median PFS** (95% CI)	Hazard Ratio (95% CI)[a]
≥ 1%	12.35 (8.51, NR)	3.91 (2.83, 4.17)	0.44 (0.33, 0.60)
< 1%	11.17 (6.93, NR)	2.79 (2.66, 2.96)	0.36 (0.26, 0.51)

* PD-L1 Expression level utilizing SK005

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

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

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

Confidence in PD-L1 test results

- Clinically relevant PD-L1 results linked to a clinical outcome in melanoma
- Reliability. PD-L1 IHC 28-8 pharmDx kit meets all acceptance criteria for analytical performance
- Confidence in scoring with a comprehensive PD-L1 Interpretation Manual
- Plug-and-play quality controlled all-inclusive kit, optimized for the Autostainer Link 48

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

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 clinician for patient dialogue
- Early testing enables laboratory efficiency

PD-L1 testing is not required for the use of OPDIVO, but it will provide additional information for physicians and should be considered in the context of all available clinical information.

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 tissue 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.

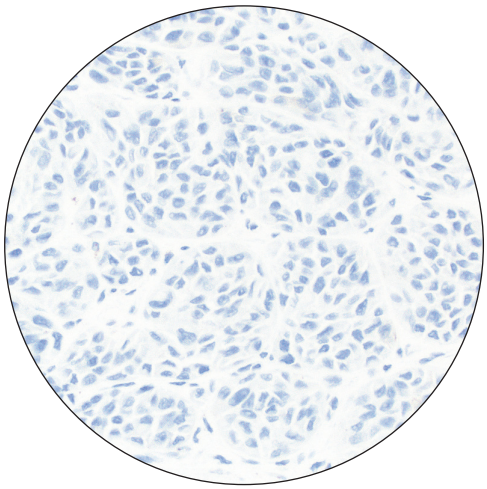
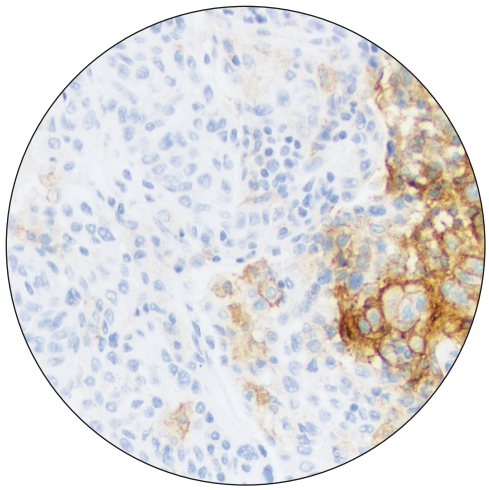
PD-L1 expression as detected by PD-L1 IHC 28-8 pharmDx in non-squamous NSCLC may be associated with enhanced survival from OPDIVO® (nivolumab).

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.

Results you can trust

Providing high quality staining results

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

Examples of Melanoma Stains		
PD-L1 IHC 28-8 pharmDx result report to treating physician	PD-L1 expression < 1%: NEGATIVE	PD-L1 expression ≥ 1%: POSITIVE

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

Robust performance with PD-L1 IHC 28-8 pharmDx

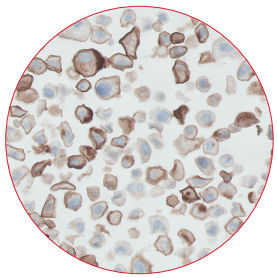
PD-L1 IHC 28-8 pharmDx is FDA-approved and fully validated with analytical performance having met all pre-determined acceptance criteria for sensitivity, specificity and reproducibility.

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 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, approximately 58% had PD-L1 expression levels ≥1%
Repeatability	■ Repeatability testing of inter-instrument, inter-operator, inter-day, inter-lot and intra-run performance ■ ≥ 90% overall agreement for ≥ 1% expression level ■ 95% confidence intervals ranged from 83.2 to 99.4% for ANA, APA, and OA*
External Reproducibility	■ Reproducibility testing 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% expression level ■ 95% confidence intervals ranged from 88.1 to 100% for ANA, APA, and OA*

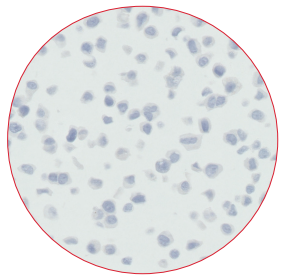
*Average Negative Agreement, Average Positive Agreement, and Overall Agreement

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

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 Rabbit LINKER
- Visualization Reagent-HRP
- DAB+ Substrate Buffer
- DAB+ Chromogen
- DAB Enhancer
- Control Slides

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

References

PD-L1 IHC 28-8 pharmDx instructions for use.

Choose the validated PD-L1 IHC 28-8 pharmDx for melanoma PD-L1 testing

The first and only FDA-approved PD-L1 test for use in the assessment of the magnitude of treatment effect on progression-free survival in melanoma patients from OPDIVO

- 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
- Comprehensive Interpretation Manual for melanoma

Relentless in our commitment to fighting cancer. Together.

Dako

An **Agilent Technologies** Company

www.dako.com

Represented in more than 100 countries

Australia +61 2 9922 0700
Austria +43 1 408 43 34 0
Belgium +32 (0) 16 38 72 20
Brazil +55 11 50708300
Canada +1 905 335 3256
China +86 21 3612 7091
Denmark +45 44 85 97 56
Finland +358 9 348 73 950
France +33 1 64 53 61 44
Germany +49 40 69 69 470
Ireland +353 1 479 0568
Italy +39 02 58 078 1
Japan +81 3 5232 9970
Korea +82 2 402 6775
The Netherlands +31 20 42 11 100
Norway +47 23 14 05 40
Poland +48 58 661 1879
Spain +34 93 344 57 77
Sweden +46 8 556 20 600
Switzerland +41 41 760 11 66
United Kingdom +44 (0)1 353 66 99 11
United States of America +1 805 566 6655

29110 2016/JAN19