Biomarkers for Immune Checkpoint Inhibitors Point of Care Reference Tool

Immune Checkpoint Inhibitors

Drug classification	Product	Associated PD-L1 Tests
PD-1 inhibitors	Nivolumab (Opdivo®) Pembrolizumab (Keytruda®) Cemiplimab-rwlc (Libtayo®)	PD-L1 IHC 28-8 pharmDx** PD-L1 IHC 22C3 pharmDx*
PD-L1 inhibitors	Atezolizumab (Tecentriq®) Avelumab (Bavencio®) Durvalumab (Imfinzi™)	VENTANA PD-L1 (SP142) assay**
CTLA-4 inhibitor	Ipilimumab (Yervoy®)	

* Companion diagnostic: medical device that provides information that is essential for the safe and effective use of a corresponding therapeutic product, and is required for the use of the product.
** Complementary diagnostic: diagnostic that identifies a subset of patients that may respond well to a drug, but is not required for the use of the product.
PD-1: Programmed Death Receptor-1; PD-L1: Programmed Death Receptor Ligand-1; CTLA-4: Cytotoxic T-lymphocyte Antigen-4

Predictive Biomarkers for Immuno-Oncology Agents

Biomarker	Description	Testing Methods
Programmed Death Receptor Ligand-1 (PD-L1)	Protein expressed on the surface of tumor cells in response to a T-cell infiltrate and inflamed tumor microenvironment. PD-L1 positive expression can be quantified using standardized scoring systems that reflect the percentage of tumor cells tested that stain at any intensity. PD-L1 positivity, in some types of cancers, is predictive of a better outcome with immune checkpoint blockade.	IHC; NGS
Deficient Mismatch Repair (dMMR)	Deficiency in one or more of the DNA mismatch repair genes, MLH1, MSH2, MSH6, and PMS2, via inactivation or germline mutations results in microsatellite instability. MSI-H tumors may be more immunogenic and thus responsive to immune checkpoint blockade.	IHC; PCR; NGS

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Predictive Biomarkers for Immuno-Oncology Agents

Biomarker	Description	Testing Methods
Microsatellite Instability-High (MSI-H)	MSI results in different lengths of microsatellites (DNA nucleotide repeats) that are present in tumor DNA compared to normal tissue DNA from an individual. MSI-H tumors possess greater numbers of mutations that may be more immunogenic and thus responsive to immune checkpoint blockade.	PCR; IHC; NGS
Tumor mutation burden (TMB)[1]	Total number of nonsynonymous somatic mutations measured per tumor DNA megabase (Mb). Tumors with large numbers of mutations may be more immunogenic and thus responsive to immune checkpoint blockade. Threshold values indicative of a high TMB vary, but a TMB ≥ 10 mutations per Mb was predictive of a prolonged response to immune checkpoint therapy in NSCLC.[2]	Whole genome sequencing; WES; targeted panel NGS

[1]TMB as a predictive biomarker has not been incorporated into FDA-approved label indications for immune-oncology agents.
[2]Ramalingam SS, et al. Cancer Res 2018;78(suppl 13):CT078A.
WES: whole-exome sequencing; NGS: next-generation sequencing; IHC: immunohistochemistry; PCR: polymerase chain reaction

Immuno-Oncology Drug Use Indications With Biomarker Requirements (as of 11.18.2019)

Malignancy	Tumor Biomarker	Description	Product
Cervical cancer	PD-L1 CPS ≥1	First-line or subsequent treatment for patients with recurrent or metastatic cervical cancer with disease progression on or after chemotherapy.	Pembrolizumab
Colorectal Cancer (CRC)	MSI-H or dMMR tumors	Second-line or subsequent treatment of adult and pediatric patients with unresectable or metastatic MSI-H or dMMR CRC that has progressed following treatment with fluoropyrimidine, oxaliplatin, and irinotecan.	Nivolumab Nivolumab + ipilimumab Pembrolizumab
Esophageal cancer	PD-L1 CPS ≥10	Second-line or subsequent treatment of patients with recurrent locally advanced or metastatic squamous cell carcinoma of the esophagus, with disease progression after one or more prior lines of systemic therapy.	Pembrolizumab
Gastric or gastroesophageal junction (GEJ) cancer	PD-L1 CPS ≥1	Third-line or subsequent treatment of patients with recurrent locally advanced or metastatic gastric or GEJ adenocarcinoma, with disease progression on or after 2 or more prior lines of therapy including fluoropyrimidine- and platinum-containing chemotherapy and if appropriate, HER2/neu-targeted therapy.	Pembrolizumab
Head and neck squamous cell cancer (HNSCC)	PD-L1 CPS ≥1	First-line monotherapy in patients with metastatic or unresectable, recurrent HNSCC.	Pembrolizumab

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Immuno-Oncology Drug Use Indications With Biomarker Requirements (as of 11.18.2019)

Malignancy	Tumor Biomarker	Description	Product
Non-Small Cell Lung Cancer (NSCLC)	PD-L1 expression (TPS) ≥1%	• First-line monotherapy in patients with nonsquamous and squamous cell advanced NSCLC, with no EGFR or ALK genomic tumor aberrations, and is stage III where patients are not candidates for surgical resection or definitive chemoradiation, or metastatic. • Second-line or subsequent monotherapy in patients with nonsquamous and squamous cell metastatic NSCLC, with disease progression on or after platinum-containing chemotherapy. Patients with EGFR or ALK genomic tumor aberrations should have disease progression on FDA-approved therapy for these aberrations.	Pembrolizumab
Triple-negative breast cancer (TNBC)	PD-L1 expression ≥1%	First-line or subsequent treatment in combination with paclitaxel protein-bound for adult patients with unresectable locally advanced or metastatic TNBC.	Atezolizumab
Urothelial carcinoma	PD-L1 expression ≥5%	First-line or subsequent treatment of patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy.	Atezolizumab
	PD-L1 CPS ≥10	First-line or subsequent therapy for patients with locally advanced or metastatic urothelial carcinoma who are not eligible for cisplatin-containing chemotherapy.	Pembrolizumab
MSI-H cancer	MSI-H or dMMR tumors	Adult and pediatric patients with unresectable or metastatic MSI-H or dMMR solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options.	Pembrolizumab

PD-L1: Programmed Death Receptor Ligand-1; TPS: Tumor Proportion Score; CPS: Combined Positive Score; MSI-H: microsatellite instability-high; dMMR: mismatch repair deficient

Patient Assistance for Biomarker Testing

Patient Advocate Foundation (PAF)
https://www.patientadvocate.org/

https://www.patientadvocate.org/connect-with-services/copay-relief/

PAF is an organization that provides financial assistance to patients in a variety of disease types. They provide more than just co-pay assistance; they can also provide funds to help patients cover other medical costs, or other costs, including genetic testing.

Myriad
https://myriad.com/

Similar to Foundation Medicine, Myriad provides assistance for patients who have financial difficulty paying for their tests specifically.

Foundation Medicine
https://www.foundationmedicine.com/

Foundation is a testing company that has proprietary testing in both the biopsy and liquid testing types. Many of the tests are multi-assay tests. They provide assistance to access their tests specifically.

The Association of Community Cancer Centers (ACCC)
https://www.accc-cancer.org/home/learn/publications/patient-assistance-and-reimbursement-guide

Has a guide that compiles many patient assistance program.

Additional Resources:

CancerCare
https://www.cancercare.org/financial_assistance

Good Days
https://www.mygooddays.org/

Leukemia and Lymphoma Society (LLS)
https://www.lls.org/support/financial-support

National Comprehensive Cancer Network (NCCN) Virtual Reimbursement Resource Room
https://www.nccn.org/reimbursement_resource_room/default.aspx

Patient Access Network
https://panfoundation.org/index.php/en/