PATIENT

DIAGNOSIS C34.11, Malignant neoplasm of upper lobe, right bronchus or lung; Unknown
NAME
DOB SEX Male
MRN
ORDER ID
REPORT DATE

SPECIMEN

FACILITY
ID
SOURCE Lung, Right Upper Lobe
COLLECTION DATE
RECEIVED DATE

CLIENT

ORDERING PROVIDER

ORDERING PROVIDER NPI
PROVIDER FACILITY

ORDERING FACILITY

OmniSeq Clinical Support

For questions or to discuss results:
1-800-781-1259
support@omniseq.com

OmniSeq INSIGHT ℠ interrogates 523 genes by next generation sequencing for mutations, select copy number alterations, and fusions/splice variants including genes associated with homologous recombination repair deficiency (HRR/HRD), microsatellite instability (MSI) and tumor mutational burden (TMB), expression of 64 immune genes, and PD-L1 by immunohistochemistry (IHC).

See last page of report for all tested markers

MARKER FINDINGS

See MARKER DETAILS for additional information

Genomic Variants (Positive)

KRAS G12C

See APPENDIX for variants of unknown significance (VUS) and limitations regarding detection of copy number alterations and fusions/splice variants

Signatures

Tumor Mutational Burden (TMB): 0.7 mut/Mb (Not High)

Microsatellite Instability (MSI): MS-Stable

Immune Markers

PD-L1 IHC (22C3): Tumor Proportion Score 10% (Positive)

Immunotherapy Targets by RNA Sequencing with Clinical Trials: ADORA2A, BTLA, CD137, CD27, CD39, CD4, CSF1R, LAG3, NECTIN2, TIGIT, TIM3, TLR8

Note: PD-L1 is measured by immunohistochemistry (IHC) and RNA-expression profiling using next generation sequencing. See APPENDIX for additional details.

PERTINENT NEGATIVE GENOMIC VARIANTS

FDA or NCCN guideline indicated variants for this tumor type tested but NOT detected

ALK fusion	EGFR exon 19 ins	MET gain
BRAF V600E	EGFR exon 20 ins	NTRK1/2/3 fusion
EGFR (L858R, S768I, L861Q, Codon 719)	HER2 (ERBB2) gain	RET fusion
EGFR T790M	HER2 (ERBB2) mut	ROS1 fusion
EGFR exon 19 del	MET exon 14 skip	

THERAPY CONSIDERATIONS SUMMARY

Number of unique therapies and clinical trials identified for this patient

Clinical benefit in patient's tumor type	Resistance/ decreased response	Clinical benefit in other tumor types	Clinical trials
6	5	0	29

COMMENTS

Pathologist

No pathologist comments.

Testing

Copy losses could not be accurately detected due to insufficient tumor purity.

Potential Germline Variants

Consider genetic counseling if an inherited cancer syndrome is suspected

No potential germline variants were identified in this patient's tumor.

THERAPY CONSIDERATIONS

CLINICALLY SIGNIFICANT MARKERS indicate clinical benefit or resistance/decreased response for therapy in this patient's tumor type based on FDA approval or professional guidelines. MARKERS WITH POTENTIAL CLINICAL SIGNIFICANCE indicate possible clinical benefit based on emerging evidence in this patient's tumor type, including therapies with FDA priority, breakthrough, accelerated, or fast track designation, FDA approval in other tumor types, or as therapy selection criteria or drug targets in clinical trials. *See THERAPY DETAILS for additional information about Marker Clinical Significance.*

CLINICALLY SIGNIFICANT MARKERS

Clinical Benefit in this Patient's Tumor Type

			Sources
Negative: ALK fusion, EGFR	atezolizumab + bevacizumab + carboplatin + paclitaxel, atezolizumab + carboplatin + nab-paclitaxel, ipilimumab + nivolumab + platinum doublet therapy, pembrolizumab + pemetrexed + platinum chemotherapy	First line	FDA (Approved), NCCN
PD-L1 IHC (22C3) Positive	pembrolizumab	First line	FDA (Approved), NCCN
	pembrolizumab	Subsequent line	FDA (Approved), NCCN
KRAS G12C	sotorasib	Subsequent line	FDA (Approved)

Resistance/Decreased Response in this Patient's Tumor Type

			Sources
KRAS G12C	afatinib, dacomitinib, erlotinib, gefitinib, osimertinib	Per NCCN, mutations in KRAS have been associated with reduced responsiveness to EGFR TKI therapy.	NCCN

MARKERS WITH POTENTIAL CLINICAL SIGNIFICANCE

Emerging Clinical Benefit in this Patient's Tumor Type

No marker-directed targeted therapies or immunotherapies with sufficient emerging evidence of clinical benefit in this patient's tumor type were identified.

Clinical Benefit in Other Tumor Types

No marker-directed targeted therapies or immunotherapies with sufficient evidence of clinical benefit in other tumor types were identified.

Clinical Trial Markers for this Patient

ADORA2A (RNA-Seq) High	BTLA (RNA-Seq) High	CD137 (RNA-Seq) High	CD27 (RNA-Seq) High	CD39 (RNA-Seq) High
1 clinical trial	*1 clinical trial*	*2 clinical trials*	*1 clinical trial*	*1 clinical trial*
CD4 (RNA-Seq) High	CSF1R (RNA-Seq) High	KRAS G12C	LAG3 (RNA-Seq) High	NECTIN2 (RNA-Seq) High
1 clinical trial	*1 clinical trial*	*11 clinical trials*	*3 clinical trials*	*1 clinical trial*

PD-L1 IHC (22C3) Positive	TIGIT (RNA-Seq) High	TIM3 (RNA-Seq) High	TLR8 (RNA-Seq) High
3 clinical trials	*1 clinical trial*	*2 clinical trials*	*2 clinical trials*

Genomic Variants with No Matched Therapies

No approved therapies or clinical trials identified for this patient

No clinically significant or potentially clinically significant genomic variants without matched therapies or clinical trials were identified.

MARKER DETAILS

MARKER DETAILS provide additional information about genomic variants and immune markers identified by next generation sequencing (NGS), including mutations (substitutions, insertions, deletions, indels) identified by sequencing full coding exonic regions and intron/exon junctions, copy number alterations (gains and losses), and fusions/splice variants, as well as tumor mutational burden (TMB), microsatellite instability (MSI), and immune gene expression profiling.

Mutations

Gene	Alteration	Location	VAF	ClinVar	Transcript ID	Type	Pathway
KRAS	c.34G>T p.G12C	exon 2	3.7%	Pathogenic /Likely pathogenic	NM_004985.3	Substitution - Missense	MAP kinase signaling

KRAS, KRAS proto-oncogene, GTPase, is a member of the small GTPase superfamily that when bound to GTP interacts with signaling molecules that regulate cell activities such as proliferation, differentiation, apoptosis and cell migration (PMID: 23622131). Additionally, KRAS is a key regulator of the MAPK, PI3K/AKT/mTOR pathways (PMID: 23622131 ; PMID: 31649840). KRAS G12C is a hotspot mutation that lies within a GTP-binding region of the Kras protein (UniProt.org). G12C results in decreased Kras GTPase activity and activation of downstream signaling in cell culture and mouse models (PMID: 26037647 PMID: 16051643 , PMID: 23455880).

Copy Number Alterations

No clinically significant or potentially clinically significant copy loss or gain alterations were identified for this patient.

Fusions/Splice Variants

No clinically significant or potentially clinically significant fusion or splice variants were identified for this patient.

Tumor Mutational Burden (TMB)

The Tumor Mutational Burden (TMB) for this specimen is 0.7 mut/Mb (Not High)

Tumor mutational burden (TMB) measures the number of non-germline synonymous and non-synonymous mutations per megabase of DNA. TMB is considered a surrogate for neoantigen load and immunogenicity in cancer.

Microsatellite Instability (MSI)

This specimen is microsatellite stable (MS-Stable)

Microsatellite Instability (MSI) is measured by analyzing 130 potential targeted microsatellites for evidence of instability. MSI is a condition of genetic hypermutability that generates excessive amounts of short insertion/deletion mutations in the genome.

Immune Gene Expression

Immune gene expression by RNA sequencing is measured relative to a reference population as either the % of the reference population with normalized reads per million (nRPM) less than the nRPM for that marker (% Rank), or as an absolute value indicating a positive or negative result (nRPM reads).

Low (< 25)
Moderate (25-74)
High (≥ 75)

Positive (≥ 20)
Negative (< 20)

T-cell priming

Interaction of stimulatory receptors and ligands required to prime T-cells and infiltrate the tumor

Marker	% Rank
CD137	97
CD27	85
CD28	70
CD40	63
CD40LG	89
CD80	87
CD86	65
GITR	53
GZMB	97
ICOS	80
ICOSLG	20
IFNG	93
OX-40L	58
OX40	68
TBX21	87

T-cell trafficking

Cytokines/chemokines released in the stroma and vessels that drive movement of T-cells to the tumor

Marker	% Rank
CXCL10	90
CXCR6	97
DDX58	90
GATA3	41
IL10	77
IL1B	53
MX1	53
STAT1	92
TGFB1	93
TLR7	69
TLR8	79
TLR9	90
TNF	78

T-cell infiltration

Expression of immune activation within the tumor microenvironment

Marker	% Rank
CD2	95
CD20	91
CD3	94
CD4	94
CD8	93
FOXP3	84
KLRD1	88
SLAMF4	98

T-cell recognition

Interaction of checkpoint receptors and ligands that inhibit T-cells to initiate cancer cell death

Marker	% Rank
BTLA	82
CTLA4	51
LAG3	82
NECTIN2	78
PD-1	85
PD-L1	82
PD-L2	78
PVR	11
TIGIT	96
TIM3	78
TNFRSF14	30
VISTA	53

Killing cancer cells

Inhibit activated T-cells from killing cancer cells

Marker	% Rank
ADORA2A	87
CCL2	83
CCR2	89
CD163	96
CD38	99
CD39	79
CD68	83
CSF1R	89
CXCR2	68
IDO1	81

Cancer testis antigens

Immunogenic tumor antigens

Marker	Result
LAGE1A	negative
MAGEA1	negative
MAGEA3	negative
MAGEA4	negative
NY-ESO-1	negative
SSX2	negative

Immunotherapy Targets by RNA Sequencing with Clinical Trials

Genes associated with immunomodulatory agents, adoptive cell therapies, vaccines, oncolytic viruses and targeted antibodies

ADORA2A (RNA-Seq) High	ADORA2A, adenosine A2a receptor, is a G-protein coupled receptor that binds adenosine to regulate a number of physiological functions and is expressed by a variety of cells, including dendritic cells, T-cells and NK-cells (PMID: 23856527). ADORA2A in the tumor microenvironment evades immune surveillance by inhibiting T-cell receptor function (PMID: 23856527, PMID: 25377469) and therapeutic blockade may restore the anti-tumor response (PMID: 28174424).
BTLA (RNA-Seq) High	BTLA, B and T lymphocyte attenuator, is a member of the immunoglobulin superfamily and inhibitory receptor belonging to the CD28 family (PMID: 31774112; PMID: 27717503). Additionally, BTLA expression on T-cells aids in the negative regulation of T-cells, leads to decreased T-lymphocytes and has been associated with dampening immune responses, mediating immune memory, and pro-survival effects (PMID: 31774112; PMID: 27717503; PMID: 21220749).
CD137 (RNA-Seq) High	TNFRSF9 (CD137), TNF Receptor Superfamily Member 9, is a costimulatory receptor expressed on activated T-cells (PMID: 22406983). Additionally, TNFRSF9 promotes cellular proliferation, survival, cytokine production and plays a role in the differentiation of effector memory CTLs (PMID: 22406983; PMID: 12384425).
CD27 (RNA-Seq) High	CD27, CD27 molecule, encodes for a member of the tumor necrosis factor (TNF) receptor family, is located on NK cells, CD4+ and CD8+ T cells (PMID: 15886117). Additionally, upon ligation to CD70, CD27 activates NF-kB and promotes cell survival, enhances T and B-cells proliferative signals and increases effector functions (PMID: 15886117; PMID: 23264908).
CD39 (RNA-Seq) High	ENTPD1 (CD39), ectonucleoside triphosphate diphosphohydrolase 1, is expressed by B-cells, innate cells, regulatory T-cells as well as activated CD4 and CD8 T-cells (PMID: 30006565). Additionally, CD39 converts ATP to adenosine to regulate cellular homeostasis and functions as an immune checkpoint inhibitor and is a marker for exhausted T-cells in patients with chronic viral infections (PMID: 29914571; PMID: 30006565).
CD4 (RNA-Seq) High	CD4, CD4 molecule, is a glycoprotein that recognizes MHC class II peptides on antigen-presenting cells and is expressed on NK cells, macrophages, eosinophils, neutrophils, and CD8+ T cells (PMID: 16951326). Additionally, CD4 regulates activation of T-lymphocytes leading to proliferation and differentiation of effector T-cells, and plays a key role in adaptive immune response (PMID: 22474485; PMID: 8057386).
CSF1R (RNA-Seq) High	CSF1R, macrophage colony-stimulating factor 1 receptor, is a tyrosine kinase and receptor for CSF1 and IL34, which upon ligand binding activates PI3K-AKT-mTOR, RAS-RAF-MEK-ERK and STAT signaling pathways (PMID: 22186992).
LAG3 (RNA-Seq) High	LAG3, lymphocyte activation gene 3 protein, is expressed on activated T-cells and NK-cells and binds MHC class II molecules to inhibit the immune response (PMID: 28258692).
NECTIN2 (RNA-Seq) High	NECTIN 2 (CD112), Nectin cell adhesion molecule 2, is a single pass type I membrane glycoprotein that binds to CD28 family member TIGIT (PMID: 29855615). Additionally, NECTIN2 co-stimulates T-cells when bound to CD226, and also inhibits T-cell response through the co-inhibitory receptor TIGIT (PMID: 26755705).
TIGIT (RNA-Seq) High	TIGIT, T cell immunoglobulin and ITIM domain, is a T cell and NK cell specific gene that encodes a protein containing an immunoglobulin variable (IgV) domain, a transmembrane domain and an immunoreceptor tyrosine-based inhibitory motif (ITIM) (PMID: 19011627). Additionally, TIGIT is a co-inhibitory receptor that limits anti-tumor and other CD8+ T-cell dependent chronic immune responses by inducing IL-10 production by dendritic cells (PMID: 25465800; PMID: 19011627).
TIM3 (RNA-Seq) High	HAVCR2 (TIM3), hepatitis A virus cellular receptor 2, is a member of the T-cell immunoglobulin and mucin domain (Tim) family and expressed on differentiated Th1 cells (PMID: 24825777). Additionally, HAVCR2 has possible role in dampening the immune response and in contributing to a tumor's ability to acquire resistance to the immune checkpoint blockade (PMID: 31733828).
TLR8 (RNA-Seq) High	TLR8, toll like receptor 8, is part of a family of receptors in innate immunity that play an important role in the initiation of host defense and recognizes single stranded RNA and self RNA from dead or dying cells (PMID: 23520111; PMID: 17932028).

THERAPY DETAILS & CLINICAL TRIALS

THERAPY DETAILS provide select evidence of marker clinical significance for therapeutic response. CLINICAL TRIALS are matched for tested marker results, patient demographics, tumor histology and location within 200 miles of the patient/provider. Clinical trials are prioritized by proximity to the patient /provider and later trial phase. This is not a comprehensive list of all published efficacy data and clinical trials. Information is current as of as described in the OmniSeq Knowledgebase®. For up to date information regarding available clinical trials, please see www.clinicaltrials.gov

Marker Clinical Significance

IA FDA-approved or professional guideline-indicated therapies in the tested tumor type

IB Well-powered clinical studies with expert consensus in the tested tumor type

IIC FDA-approved therapies for other tumor types or clinical trial inclusion criteria for the tested tumor type

IID Plausible therapeutic significance with some evidence in the tested tumor type

KRAS G12C

sotorasib

FDA APPROVED: FDA approved for KRAS G12C-mutated locally advanced or metastatic NSCLC after at least one prior systemic therapy.

CLINICAL SIGNIFICANCE (IA): The FDA approval for sotorasib was supported by data from the single-arm, open-label, phase-I/II trial CodeBreaK 100 (NCT03600883; PMIDs: 32540954 and 33547148). CodeBreaK 100 demonstrated that subsequent-line sotorasib had an ORR of 30% (CR, 2% (2/124); PR, 28% (35/124)) in patients with locally advanced or metastatic NSCLC with KRAS G12C. The co-primary endpoint was median DOR (10 mo.).

NCT03600883	A Phase 1/2, Study Evaluating the Safety, Tolerability, PK, and Efficacy of AMG 510 in Subjects With Solid Tumors With a Specific KRAS Mutation (CodeBreaK 100)	Phase 1 /Phase 2	Indianapolis, IN
NCT04185883	Sotorasib Activity in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation (CodeBreak 101)	Phase 1	Indianapolis, IN

afatinib

NCCN UNCERTAIN BENEFIT: Per NCCN, mutations in KRAS have been associated with reduced responsiveness to EGFR TKI therapy.

CLINICAL SIGNIFICANCE (IA): In a preclinical study, a lung adenocarcinoma patient-derived xenograft (PDX) model was sensitive to treatment with Gilotrif (afatinib), demonstrating inhibition of tumor growth (PMID: 29925635).

dacomitinib

NCCN UNCERTAIN BENEFIT: Per NCCN, mutations in KRAS have been associated with reduced responsiveness to EGFR TKI therapy.

CLINICAL SIGNIFICANCE (IA): Marker is in an FDA approval or professional guideline.

erlotinib

NCCN UNCERTAIN BENEFIT: Per NCCN, mutations in KRAS have been associated with reduced responsiveness to EGFR TKI therapy.

CLINICAL SIGNIFICANCE (IA): In a Phase II trial (BATTLE-2), Tarceva (erlotinib) treatment resulted in comparable 8-week disease control rate in KRAS wild-type (36%, 5/14) and KRAS mutated (20%, 1/5) patients with advanced non-small cell lung carcinoma (PMID: 27480147; NCT01248247).

gefitinib

NCCN UNCERTAIN BENEFIT: Per NCCN, mutations in KRAS have been associated with reduced responsiveness to EGFR TKI therapy.

CLINICAL SIGNIFICANCE (IA): In a clinical study, KRAS codon 12 or 13 mutations were correlated with a lack of response to Iressa (gefitinib) in patients with lung adenocarcinoma (PMID: 15696205).

osimertinib

NCCN UNCERTAIN BENEFIT: Per NCCN, mutations in KRAS have been associated with reduced responsiveness to EGFR TKI therapy.

CLINICAL SIGNIFICANCE (IA): Marker is in an FDA approval or professional guideline.

MRTX849

MRTX849 MRTX849 covalently binds to and stabilizes GDP-bound KRAS G12C, therefore prevents KRAS downstream signaling, resulting in tumor growth inhibition (PMID: 31658955).

CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.

NCT04685135	Phase 3 Study of MRTX849 vs Docetaxel in Patients With Advanced Non-Small Cell Lung Cancer With KRAS G12C Mutation	Phase 3	Arlington Heights, IL
NCT03785249	Phase 1/2 Study of MRTX849 in Patients With Cancer Having a KRAS G12C Mutation KRYSTAL-1	Phase 1 /Phase 2	Niles, IL

(anti-PD-1 antibody or anti-PD-L1 antibody) + sotorasib	ANTI-PD-1 ANTIBODY Limited information is currently available on this drug. ANTI-PD-L1 ANTIBODY Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT03600883	A Phase 1/2, Study Evaluating the Safety, Tolerability, PK, and Efficacy of AMG 510 in Subjects With Solid Tumors With a Specific KRAS Mutation (CodeBreaK 100)	Phase 1 /Phase 2	Indianapolis, IN
sotorasib + midazolam	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT03600883	A Phase 1/2, Study Evaluating the Safety, Tolerability, PK, and Efficacy of AMG 510 in Subjects With Solid Tumors With a Specific KRAS Mutation (CodeBreaK 100)	Phase 1 /Phase 2	Indianapolis, IN
MRTX849 + TNO155	TNO155 TNO155 is an inhibitor of PTPN11 (SHP2), which potentially blocks SHP2 signaling, thereby inhibiting activation of the MAPK pathway and subsequent cell growth (NCI Drug Dictionary). MRTX849 MRTX849 covalently binds to and stabilizes GDP-bound KRAS G12C, therefore prevents KRAS downstream signaling, resulting in tumor growth inhibition (PMID: 31658955). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04330664	Phase 1/2 Study in Patients With Cancer Having a KRAS G12C Mutation KRYSTAL 2	Phase 1 /Phase 2	Saint Louis, MO
VS-6766	VS-6766 Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04620330	A Study of VS-6766 v. VS-6766 + Defactinib in Recurrent G12V or Other KRAS-Mutant Non-Small Cell Lung Cancer	Phase 2	Saint Louis, MO
VS-6766 + defactinib	VS-6766 Limited information is currently available on this drug. DEFACTINIB Defactinib (VS-6063) inhibits FAK, resulting in decreased downstream signaling, and potentially leading to reduced tumor cell proliferation and survival (PMID: 31739184). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04620330	A Study of VS-6766 v. VS-6766 + Defactinib in Recurrent G12V or Other KRAS-Mutant Non-Small Cell Lung Cancer	Phase 2	Saint Louis, MO
GRT-C903 + GRT-R904 + ipilimumab + nivolumab	GRT-C903 GRT-C903 is a neoantigen cancer vaccine, which activates cytotoxic T-lymphocyte to kill cancer cells (NCI Drug Dictionary). GRT-R904 GRT-R904 is a neoantigen cancer vaccine, which activates cytotoxic T-lymphocyte to kill cancer cells (NCI Drug Dictionary). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT03953235	A Study of a Personalized Cancer Vaccine Targeting Shared Neoantigens	Phase 1 /Phase 2	Chicago, IL
RMC-4630 + cobimetinib	RMC-4630 RMC-4630 is an inhibitor of SHP2 (PTPN11) that prevents MAPK signaling and cell growth (PMID: 31727671). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT03989115	Dose-Escalation/Expansion of RMC-4630 and Cobimetinib in Relapsed/Refractory Solid Tumors and RMC-4630 and Osimertinib in EGFR Positive Locally Advanced/Metastatic NSCLC	Phase 1 /Phase 2	Chicago, IL
D-1553; D-1553 + standard of care	D-1553 Limited information is currently available on D-1553, a putative KRAS G12C inhibitor (Mar 2021). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04585035	Study to Evaluate D-1553 in Subjects With Solid Tumors	Phase 1 /Phase 2	Louisville, KY

pembrolizumab + MRTX849	MRTX849 MRTX849 covalently binds to and stabilizes GDP-bound KRAS G12C, therefore prevents KRAS downstream signaling, resulting in tumor growth inhibition (PMID: 31658955). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04613596	Phase 2 Trial of MRTX849 Plus Pembrolizumab for NSCLC With KRAS G12C Mutation KRYSTAL-7	Phase 2	Goshen, IN
	NCT03785249	Phase 1/2 Study of MRTX849 in Patients With Cancer Having a KRAS G12C Mutation KRYSTAL-1	Phase 1 /Phase 2	Niles, IL
MRTX849 + afatinib; MRTX849 + cetuximab	MRTX849 MRTX849 covalently binds to and stabilizes GDP-bound KRAS G12C, therefore prevents KRAS downstream signaling, resulting in tumor growth inhibition (PMID: 31658955). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT03785249	Phase 1/2 Study of MRTX849 in Patients With Cancer Having a KRAS G12C Mutation KRYSTAL-1	Phase 1 /Phase 2	Niles, IL
HER2 inhibitor + sotorasib	HER2 INHIBITOR Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04185883	Sotorasib Activity in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation (CodeBreak 101)	Phase 1	Indianapolis, IN
MAPK inhibitor + sotorasib	MAPK INHIBITOR Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04185883	Sotorasib Activity in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation (CodeBreak 101)	Phase 1	Indianapolis, IN
PD1 inhibitor + sotorasib	PD1 INHIBITOR Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04185883	Sotorasib Activity in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation (CodeBreak 101)	Phase 1	Indianapolis, IN
SHP2 Inhibitor + sotorasib	SHP2 INHIBITOR Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04185883	Sotorasib Activity in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation (CodeBreak 101)	Phase 1	Indianapolis, IN
anti-PD-L1 antibody + sotorasib	ANTI-PD-L1 ANTIBODY Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04185883	Sotorasib Activity in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation (CodeBreak 101)	Phase 1	Indianapolis, IN
cyclin-dependent kinase inhibitor + sotorasib	CYCLIN-DEPENDENT KINASE INHIBITOR Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04185883	Sotorasib Activity in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation (CodeBreak 101)	Phase 1	Indianapolis, IN
mTOR inhibitor + sotorasib	MTOR INHIBITOR Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04185883	Sotorasib Activity in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation (CodeBreak 101)	Phase 1	Indianapolis, IN
sotorasib + chemotherapy	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04185883	Sotorasib Activity in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation (CodeBreak 101)	Phase 1	Indianapolis, IN

GDC-6036; GDC-6036 + bevacizumab; GDC-6036 + erlotinib; atezolizumab + GDC-6036	GDC-6036 Limited information is currently available on GDC-6036 (Nov 2020). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria. NCT04449874 — A Study to Evaluate the Safety, Pharmacokinetics, and Activity of GDC-6036 Alone or in Combination in Participants With Advanced or Metastatic Solid Tumors With a KRAS G12C Mutation	Phase 1	Chicago, IL

PD-L1 IHC (22C3) Positive

pembrolizumab	FDA APPROVED, NCCN RECOMMENDED: FDA approved for the first-line treatment of NSCLC expressing PD-L1 (Tumor Proportion Score, TPS ≥1%), with no EGFR or ALK genomic tumor aberrations, and stage III when not a candidate for surgical resection or definitive chemoradiation, or metastatic. Per NCCN, for TPS <50%, consider for patients with poor PS or other contraindications to combination chemotherapy (Category 2B, Useful in certain circumstances). CLINICAL SIGNIFICANCE (IA): In a Phase III trial (KEYNOTE-042) that supported FDA approval, treatment with Keytruda (pembrolizumab) resulted in significantly improved overall survival compared to chemotherapy in all three TPS populations (50% or greater, HR=0·69, p=0·0003; 20% or greater, HR=0·77, p=0·0020, and 1% or greater, HR=0·81, p=0·0018) of untreated advanced non-small cell lung cancer patients with no sensitizing EGFR mutations or ALK rearrangement (PMID: 30955977; NCT02220894).		
pembrolizumab	FDA APPROVED, NCCN RECOMMENDED: FDA approved for metastatic NSCLC that expresses PD-L1 (TPS >=1%), with disease progression on or after platinum-containing chemotherapy. Recommended by NCCN as Category 1 /Preferred intervention. CLINICAL SIGNIFICANCE (IA): In a Phase II/III trial (KEYNOTE-010) that supported FDA approval, treatment with Keytruda (pembrolizumab) resulted in improved overall survival (10.4 months at 2mg/kg, 12.7 months at 10mg/kg, vs 8.5 months) compared to chemotherapy in previously treated non-small cell lung cancer patients with CD274 (PD-L1) expression in over 1% of tumor cells (PMID: 26712084, PMID: 27026676, PMID: 27718847; NCT01905657).		
pembrolizumab + carboplatin + pemetrexed	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria. NCT03793179 — Testing the Timing of Pembrolizumab Alone or With Chemotherapy as First Line Treatment and Maintenance in Non-small Cell Lung Cancer	Phase 3	Mattoon, IL
domvanalimab + etrumadenant + zimberelimab	ZIMBERELIMAB Zimberelimab (GLS-010) is a monoclonal antibody that targets PD-1 (PDCD1) and inhibits binding of the PD-L1 (CD274) ligand, potentially resulting in enhanced anti-tumor immune response (PMID: 28679395). ETRUMADENANT AB928 (etrumadenant) is an antagonist of the adenosine receptors A2aR and A2bR, which may relieve adenosine-mediated immune suppression and lead to enhanced anti-tumor activity in combination with other agents (European Journal of Cancer, Vol 92, S14-S15, PMID: 30569245). DOMVANALIMAB Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria. NCT04791839 — Safety and Efficacy of Zimberelimab (AB122) in Combination With Domvanalimab (AB154) and Etrumadenant (AB928) in Patients With Previously Treated Non-Small Cell Lung Cancer	Phase 2	Saint Louis, MO

Negative: ALK fusion, EGFR

atezolizumab + bevacizumab + carboplatin + paclitaxel	FDA APPROVED, NCCN RECOMMENDED: FDA approved for the first line treatment of metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations. NCCN recommended as Category 1/Other recommended intervention. CLINICAL SIGNIFICANCE (IA): In a Phase III trial (IMpower150) that supported FDA approval, Tecentriq (atezolizumab) in combination with bevacizumab, paclitaxel, and carboplatin resulted in significantly improved median progression-free survival (8.3 vs 6.8 months, HR=0.62, p<0.001) and median overall survival (19.2 vs 14.7 months, HR=0.78, p=0.02) compared to control in patients with metastatic nonsquamous non-small cell lung cancer, regardless of PD-L1 expression and EGFR or ALK mutation status (PMID: 29863955; NCT02366143).		

atezolizumab + carboplatin + nab-paclitaxel	FDA APPROVED, NCCN RECOMMENDED: FDA approved for the first line treatment of metastatic non-squamous NSCLC with no EGFR or ALK genomic tumor aberrations. NCCN recommended as Category 2A/Other recommended intervention. CLINICAL SIGNIFICANCE (IA): In a Phase III trial (IMpower130) that supported FDA approval, Tecentriq (atezolizumab) in combination with carboplatin and nab-paclitaxel resulted in significantly improved median overall survival (18.6 vs 13.9 months, HR=0.79, p=0.033) and median progression-free survival (7.0 vs 5.5 months, HR=0.64, p<0.0001) compared to chemotherapy in patients with stage IV non-squamous non-small-cell lung cancer harboring no ALK or EGFR mutations (PMID: 31122901; NCT02367781).
ipilimumab + nivolumab + platinum doublet therapy	FDA APPROVED, NCCN RECOMMENDED: FDA approved for metastatic or recurrent NSCLC with no EGFR or ALK genomic tumor aberrations as first-line treatment. NCCN recommended as Category 1/Other recommended intervention. CLINICAL SIGNIFICANCE (IA): In a Phase III trial (CheckMate 9LA) that supported FDA approval, Yervoy (ipilimumab) and Opdivo (nivolumab) combined with 2 cycles of platinum-containing chemotherapy significantly prolonged overall survival (15.6 vs 10.9 mo, HR=0.69, p=0.0006) compared to chemotherapy in patients with treatment-naive, advanced or metastatic non-small cell lung cancer without known EGFR or ALK alterations (J Clin Oncol 38: 2020 (suppl; abstr 9501); NCT03215706).
pembrolizumab + pemetrexed + platinum chemotherapy	FDA APPROVED, NCCN RECOMMENDED: FDA approved as first-line treatment of metastatic nonsquamous NSCLC, with no EGFR or ALK genomic tumor aberrations. NCCN recommended as Category 1/Preferred intervention. CLINICAL SIGNIFICANCE (IA): In a Phase III trial (KEYNOTE-189) that supported FDA approval, Keytruda (pembrolizumab) in combination with Alimta (pemetrexed), and a platinum therapy (cisplatin or carboplatin), resulted in improved overall survival rate at 12 months (69.2% vs 49.4%, HR=0.49, p<0.001) and median progression-free survival (8.8 vs 4.9 months, HR=0.52, p<0.001) compared to placebo in previously untreated metastatic nonsquamous non-small-cell lung cancer patients without EGFR or ALK mutations (PMID: 29658856; NCT02578680).

CD4 (RNA-Seq) High

ipilimumab + nivolumab	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT02408861	Nivolumab and Ipilimumab in Treating Patients With HIV Associated Relapsed or Refractory Classical Hodgkin Lymphoma or Solid Tumors That Are Metastatic or Cannot Be Removed by Surgery	Phase 1	Saint Louis, MO

NECTIN2 (RNA-Seq) High

BMS-986207 + COM701 + nivolumab	BMS-986207 BMS-986207 is a human monoclonal antibody against T-cell immunoreceptor with Ig and ITIM domains (TIGIT), which removes the immune checkpoint blockade by preventing the interaction of TIGIT with its ligands, NECTIN2 (CD112) and PVR (CD155) (NCI Drug Dictionary). COM701 COM701 is an antibody directed against PVRIG, which interferes with binding to its ligand PVRL2, potentially resulting in increased anti-tumor immune response (J Clin Oncol 35, 2017 (suppl; abstr 3074), PMID: 32345592). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04570839	COM701 in Combination With BMS-986207 and Nivolumab in Subjects With Advanced Solid Tumors.	Phase 1 /Phase 2	Chicago, IL

PD-L1 IHC (22C3) Positive + TIGIT (RNA-Seq) High

atezolizumab + tiragolumab	TIRAGOLUMAB Tiragolumab (MTIG7192A) is an anti-human TIGIT (T cell immunoreceptor with Ig ITIM domain) antibody that potentially has anti-tumor activities through modulating the immune response to tumors (PMID: 29991503, PMID: 32576590). CLINICAL SIGNIFICANCE (IIC): Marker is drug target. In a phase 2 prospective, randomized trial in non-small cell lung carcinoma, atezolizumab + tiragolumab had an objective response rate (ORR) of 31.3%, median progression free survival (PFS) of 5.4 months compared to atezolizumab + placebo with an ORR of 16.2%, and PFS of 3.6 months in patients who were chemotherapy-naive, ECOG Performance Status of 0 or 1, and locally advanced or metastatic disease with life expectancy greater than 12 weeks (DOI: 10.1200/JCO.2020.38.15_suppl.9503; NCT03563716).			
	NCT04513925	A Study of Atezolizumab and Tiragolumab Compared With Durvalumab in Participants With Locally Advanced, Unresectable Stage III Non-Small Cell Lung Cancer (NSCLC)	Phase 3	Peoria, IL

TIM3 (RNA-Seq) High

cobolimab + dostarlimab

COBOLIMAB TSR-022 (Cobolimab) is monoclonal antibody that targets T-cell immunoglobulin and mucin domain-3 protein (TIM-3, HAVCR2), potentially resulting in enhanced anti-tumor immune response (NCI Drug Dictionary).
CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.

NCT02817633	A Study of TSR-022 in Participants With Advanced Solid Tumors (AMBER)	Phase 1	Chicago, IL

BMS-986258

BMS-986258 BMS-986258 (ONO-7807) is monoclonal antibody that targets T-cell immunoglobulin and mucin domain-3 protein (TIM-3, HAVCR2), potentially resulting in enhanced anti-tumor immune response (NCI Thesaurus).
CLINICAL SIGNIFICANCE: Marker is drug target.

NCT03446040	An Investigational Immunotherapy Study of BMS-986258 Alone and in Combination With Nivolumab in Participants With Solid Cancers That Are Advanced or Have Spread	Phase 1 /Phase 2	Cincinnati, OH

cobolimab

COBOLIMAB TSR-022 (Cobolimab) is monoclonal antibody that targets T-cell immunoglobulin and mucin domain-3 protein (TIM-3, HAVCR2), potentially resulting in enhanced anti-tumor immune response (NCI Drug Dictionary).
CLINICAL SIGNIFICANCE: Marker is drug target.

NCT02817633	A Study of TSR-022 in Participants With Advanced Solid Tumors (AMBER)	Phase 1	Chicago, IL

CD137 (RNA-Seq) High

GEN1046

GEN1046 GEN1046 is a bispecific antibody that binds to and simultaneously targets PD-L1 and TNFRSF9 (4-1BB), potentially resulting in the activation of T-lymphocytes, leading to increased anti-tumor immune response and decreased tumor growth (J. Immunotherapy Cancer, 6, 115 (2018), Abs nr: P647).
CLINICAL SIGNIFICANCE (IID): Marker is drug target. In a phase 1/2a prospective sequential assignment trial in malignant solid tumor, GEN1046 demonstrated a DCR of 65.6% among patients with metastatic or unresectable disease stage and ECOG performance of 0 or 1 (URL: https://www.onclive.com/view/next-generation-bispecific-antibody-shows-early-clinical-activity-in-advanced-solid-tumors; NCT03917381).
In a phase 1/2a prospective sequential assignment trial in non-small cell lung carcinoma, GEN1046 demonstrated a PR of 16.7% and SD of 33.3% among patients with metastatic or unresectable disease stage and ECOG performance of 0 or 1 (URL: https://www.onclive.com/view/next-generation-bispecific-antibody-shows-early-clinical-activity-in-advanced-solid-tumors; NCT03917381).

NCT03917381	GEN1046 Safety Trial in Patients With Malignant Solid Tumors	Phase 1 /Phase 2	Saint Louis, MO

CTX-471

CTX-471 CTX-471 is an agonistic antibody that binds to CD137 (4-1BB), which potentially activates immune cells resulting in reduced tumor growth (PMID: 32161196).
CLINICAL SIGNIFICANCE: Marker is drug target.

NCT03881488	Study of CTX-471 in Patients Post PD-1/PD-L1 Inhibitors in Metastatic or Locally Advanced Malignancies	Phase 1	Saint Louis, MO

LAG3 (RNA-Seq) High

fianlimab

FIANLIMAB REGN3767 (Fianlimab) is a monoclonal antibody that targets LAG3, potentially resulting in increased anti-tumor immune response (PMID: 31395688).
CLINICAL SIGNIFICANCE (IID): Marker is drug target. In a phase 1 prospective, non-randomized, parallel assignment trial in solid tumors, fianlimab (REGN3767) had a stable disease (SD) of 40.1% in patients who have progressed on prior therapy(ies), not been previously treated with a PD-1/PD-L1 inhibitor, and have ECOG performance status of 0 or 1 (DOI: 10.1200/JCO.2019.37.15_suppl.2508; NCT03005782).

NCT03005782	Study of REGN3767 (Anti-LAG-3) With or Without REGN2810 (Anti-PD1) in Advanced Cancers	Phase 1	Saint Louis, MO

relatlimab	RELATLIMAB Relatlimab (BMS-986016) is a monoclonal antibody that targets LAG3 and inhibits binding of MHC II molecules to increase cytokine production by T-cells and prevent tumor growth (Journal of Clinical Oncology 35, no. 15_suppl (9520-9520). CLINICAL SIGNIFICANCE: Marker is drug target.		
	NCT01968109 An Investigational Immuno-therapy Study to Assess the Safety, Tolerability and Effectiveness of Anti-LAG-3 With and Without Anti-PD-1 in the Treatment of Solid Tumors	Phase 1 /Phase 2	Saint Louis, MO
MGD013	MGD013 MGD013 is an engineered antibody protein that targets both PDCD1 (PD-1) and LAG3 resulting in enhanced T-cell mediated anti-tumor immune response (Cancer Res (76) (14 Supplement) 3217). CLINICAL SIGNIFICANCE: Marker is drug target.		
	NCT03219268 A Study of MGD013 in Patients With Unresectable or Metastatic Neoplasms	Phase 1	Chicago, IL

ADORA2A (RNA-Seq) High + CD39 (RNA-Seq) High

TTX-030	TTX-030 TTX-030 is a monoclonal antibody that binds to and inhibits soluble and membrane-bound ENTPD1 (CD39), resulting in decreased ATP hydrolysis, which potentially leads to activation of T-lymphocytes and anti-tumor immune response (AACR; Cancer Res 2019;79(13 Suppl):Abstract nr 5012). CLINICAL SIGNIFICANCE: Marker is drug target.		
	NCT03884556 TTX-030 Single Agent and in Combination With Immunotherapy or Chemotherapy for Patients With Advanced Cancers	Phase 1	Chicago, IL

BTLA (RNA-Seq) High

JS004	JS004 JS004 is a monoclonal antibody that binds to B- and T-lymphocyte attenuator (BTLA) and activates T-cells, thereby potentially resulting in the proliferation of antigen specific T-lymphocytes and activation of tumor cell specific immune response (NCI Drug Dictionary). CLINICAL SIGNIFICANCE: Marker is drug target.		
	NCT04137900 Safety, Tolerability and Pharmacokinetics of a Monoclonal Antibody Specific to B-and T-Lymphocyte Attenuator (BTLA) as Monotherapy and in Combination With an Anti-PD1 Monoclonal Antibody for Injection in Subjects With Advanced Malignancies	Phase 1	Saint Louis, MO

CD27 (RNA-Seq) High

CDX-527	CDX-527 CDX-527 is a tetravalent human antibody targeting both CD27 and PD-L1 (CD274), which may lead to enhanced immune activation (AACR Annual Meeting 2019, Abstract 2392, PMID: 32451681). CLINICAL SIGNIFICANCE: Marker is drug target.		
	NCT04440943 A Study of the PD-L1xCD27 Bispecific Antibody CDX-527 in Patients With Advanced Malignancies	Phase 1	Chicago, IL

CSF1R (RNA-Seq) High

Q702	Q702 Q702 selectively inhibits Axl, Mertk, and Csf1r, which may relieve immunosuppression in the tumor microenvironment and increase infiltration of immune cells into tumors, potentially leading to tumor regression (AACR; Cancer Res 2020;80(16 Suppl):Abstract nr 4974) CLINICAL SIGNIFICANCE: Marker is drug target.		
	NCT04648254 Oral Axl/Mer/CSF1R Selective Tyrosine Kinase Inhibitor in Patients With Advanced Solid Tumor	Phase 1	Chicago, IL

TLR8 (RNA-Seq) High

DN1508052	DN1508052 DN1508052 acts as an agonist of TLR8, potentially resulting in activation of NFkappaB signaling and increased anti-tumor immune response (NCI Drug Dictionary). CLINICAL SIGNIFICANCE: Marker is drug target.		
	NCT03934359 A Study to Evaluate the Safety, Tolerability of DN1508052-01 in Advanced Solid Tumors	Phase 1	Saint Louis, MO

SGN-CD228A	SGN-CD228A SGN-CD228A is an antibody-drug conjugate comprising a CD228 monoclonal antibody linked to eight molecules of the anti-microtubule compound MMAE, which delivers the cytotoxic agent to CD228-expressing tumor cells, potentially resulting in delayed tumor growth (Cancer Res 2019;79(13 Suppl):Abstract nr 2688). CLINICAL SIGNIFICANCE: Marker is drug target.		
	NCT04042480 A Study of SGN-CD228A in Advanced Solid Tumors	Phase 1	Chicago, IL

TISSUE Specimen Review Summary

Specimen Details

Submitted Pathology Report ID		Histologic evaluation/Clinical Impression	Lung / Malignant Epithelial / Adenocarcinoma				
Sample Collection Date		Tumor Origin	Primary	Tumor Nuclei	35%	#Neoplastic Cells per slide	400-999
Organ/Tissue Site	Thorax / Lung right upper lobe of, NOS						

Samples Received for Testing

Received Date	PD-L1 Report Date	Sample Label	Type	Quantity	Purpose
			Unstained FFPE Slide	14	Testing [controls adequate]

PD-L1 Immunohistochemistry

Gross Description: Received from Accupath Diagnostic Laboratories are a control slide and stained slides labeled . These are accompanied by a surgical pathology report and a technical-only procedure report for PD-L1(22C3) immunohistochemistry with patient's name and accession number. These are submitted for interpretation by OmniSeq pathologists.

Regulatory: PD-L1 IHC 22C3 pharmDx is a qualitative IHC assay that is FDA-approved companion assay for in vitro diagnostic use. This test was performed at Accupath Diagnostic Laboratories, Inc., 5005 S. 40th Street, Suite 1100, Phoenix, AZ 85040 under the direction of , Medical Director, (CLIA #03D2054956), and interpreted by OmniSeq, Inc. The results of this assay are not intended to be used as the sole means for clinical diagnosis or patient management decisions. The OmniSeq Laboratory is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) and by the New York State Clinical Laboratory Evaluation Program to perform high complexity clinical laboratory testing.

APPENDIX Variants of Unknown Significance (VUS)

Genomic variants of unknown significance (VUS) are not well characterized in the scientific literature as of the date of this report.

BMPR1A V240I	CUX1 F623L	INSR D946E	PLCG2 E565D	TMPRSS2 G8R

APPENDIX About OmniSeq INSIGHT

INTENDED USE

OmniSeq INSIGHT is a next generation sequencing-based in vitro diagnostic device for the detection of genomic variants, signatures, and immune gene expression in formalin-fixed paraffin-embedded (FFPE) tumor tissue. DNA is sequenced to detect small variants in the full exonic coding region of 523 genes (single and multinucleotide substitutions, insertions, deletions and indels), including genes leading to homologous recombination repair defects (HRR/HRD), copy number alterations in 59 genes (gains and losses), as well as analysis of microsatellite instability (MSI) and tumor mutational burden (TMB) genomic signatures. RNA is sequenced to detect fusions and splice variants in 55 genes, in addition to mRNA expression in 64 immune genes. The resultant information, along with PD-L1 protein expression by immunohistochemistry (IHC), is intended for use by qualified health care professionals in accordance with professional guidelines in oncology for management of patients with solid neoplasms, and is not conclusive or prescriptive for use of any specific therapeutic product. *(See last page of report for a complete list of markers included in OmniSeq INSIGHT.)*

TEST PRINCIPLE

OmniSeq INSIGHT is performed exclusively as a laboratory service using DNA and RNA co-extracted from FFPE tumor tissue. The assay employs a single nucleic acid extraction method from routine FFPE biopsy or surgical resection specimens; 40 - 100 ng of DNA and 20 - 100 ng RNA undergo library construction and hybridization-based capture of all coding exons from 523 cancer-related genes and select regions from 55 commonly rearranged genes. Hybrid capture-selected libraries are sequenced to high uniform depth (targeting >150X median coverage with >90% of exons at coverage >50X). The sequence data are analyzed to detect genomic variants and signatures. Amplicon-based targeted next generation RNA-sequencing for digital gene expression is used to assess mRNA expression in 64 immune genes, and immunohistochemistry (IHC) is used to measure PD-L1 protein expression (SP142 or 22C3 antibodies) based on the tumor type tested.

Small Variants

DNA-sequencing of the full exonic coding region for 523 genes is performed to detect single nucleotide variants (SNV), multinucleotide variants (MNV), insertions, deletions and indels. Detected small variants are not reportable if present in the gnomAD database (https://gnomad.broadinstitute.org/) at a prevalence of 1% or greater, are benign or likely benign in the ClinVar database (https://www.ncbi.nlm.nih.gov/clinvar/), synonymous, or intronic (outside of splice sites greater than 2 base pairs). Select variants with FDA or guideline indicated therapies are considered detected at a minimum of 2% variant allele frequency (VAF). These variants are considered "Indeterminate" when testing for the variant position was performed but did not meet minimum coverage criteria for reporting the variant as a pertinent negative finding, or, when evidence of a sequence mutation is observed in an area of low coverage, but results do not meet acceptance criteria for reporting as a positive finding. All other variants are considered detected at a minimum of 5% VAF.

Copy Number Alterations

DNA-sequencing is performed to detect and report gene copy number alterations (CNA), including gain (amplification) in 59 genes, and loss (deletion) in 4 genes. For accurate detection and reporting of copy gain, specimens must have at least 30% tumor purity. A fold change (FC) ≥3.2 is considered a copy "gain" and a FC=2.2-<3.2 as copy "gain indeterminate." A 2.2x FC is equivalent to 10 copies in a tumor at 30% tumor purity. Copy gain is fully validated for *CCND1, CCNE1, CDK4, CDK6, EGFR, ERBB2, FGFR1, FGFR2, KIT, KRAS, MET, MDM2, MYC* and *PIK3CA* genes. Copy gain in other genes are also reported, and these results may be confirmed by additional testing at the discretion of the ordering clinician. For accurate detection and reporting of copy loss, specimens must have at least 50% tumor purity. A FC ≤0.5 is considered as copy "loss" and a FC >0.5-0.7 as copy "loss-indeterminate". A 0.5x FC is equivalent to 0 copies (somatic homozygous deletion) in a tumor at 50% tumor purity. Copy loss is fully validated and reported for *ATM, BRCA1, BRCA2,* and *PTEN* genes.

Fusions and Splice Variants

RNA-sequencing of 55 commonly rearranged genes is performed for fusion analysis and 2 genes for splice variants. Fusion calling uses unique gene fusion reads to score variants, with a minimum number of unique candidate reads required for detection, Fusions are fully validated for *ALK, FGFR3, NTRK1, NTRK3, RET,* and *ROS1*. Fusions in other genes are also reported, and these results may be confirmed by additional testing at the discretion of the ordering clinician. Fusion donor and acceptor genes are annotated as GeneA-GeneB fusion for reporting. Splice variant calling is performed for *EGFR* and *MET* to identify reads in these genes that span candidate splice junctions. Only splice variants that do not match a database of non-tumor junctions from normal FFPE samples and that align with MET exon 14 and EGFR exons 2-7 are reported as skipping mutations.

Tumor Mutational Burden (TMB)

Tumor mutational burden (TMB) is determined using the small variant DNA-sequencing output from 523 genes, excluding HLA, and dynamically adjusted per sample based on sequencing depth. Non-germline synonymous and nonsynonymous variants >5% VAF are included in the TMB score after application of filters. The TMB is calculated as follows: TMB = (Eligible Variants / Effective panel size). The resulting TMB result is reported as mutations per megabase units (mut /Mb) and interpreted as "High" (≥10 mut/Mb) or "Not High" (<10 mut /Mb). This cutoff was determined in non-small cell lung cancer (NSCLC) patients. Tumor-specific cutoffs have not been established in other tumor types.

Microsatellite Instability (MSI)

Microsatellite instability (MSI) status is determined by analyzing microsatellite sites for evidence of instability. There are 130 potential sites assessed for MSI, however, the total number of assessed sites varies between samples. To ensure MSI calling quality, a sample must have a minimum of 40 assessable sites and each site must have a minimum of 60 reads spanning the site. The proportion of unstable MSI sites to total evaluable MSI sites is reported as a sample-level microsatellite score. The score is then evaluated against a pre-defined threshold to determine whether the sample is reported as MSI-High (≥20% MSI unstable sites) or MS-Stable (<20% MSI unstable sites).

APPENDIX About OmniSeq INSIGHT

PD-L1 Immunohistochemistry (IHC)

PD-L1 by immunohistochemistry (IHC) is measured based on the tumor type tested. The Dako PD-L1 IHC 22C3 FDA approved assay follows scoring guidelines for reporting combined positive score (CPS) in cervical cancer, esophageal squamous cell carcinoma, gastric/gastroesophageal junction adenocarcinoma, urothelial carcinoma, and head and neck squamous cell carcinoma. The Dako PD-L1 IHC 22C3 FDA approved assay is also used to report PD-L1 protein expression scored as the percentage of viable tumor cells showing % membrane staining at any intensity as a tumor proportion score (% TPS) for non-small cell lung cancer. The Dako PD-L1 IHC 22C3 assay is also used to report % TPS for non-indicated tumor types or tumors of unknown origin. The VENTANA PD-L1 IHC SP142 FDA approved assay is used to measure PD-L1 status based on proportion of tumor area occupied by PD-L1 expressing tumor-infiltrating immune cells (% IC) of any intensity. Scoring guidelines are followed for reporting % IC stained in urothelial carcinoma and triple negative breast cancer. The VENTANA PD-L1 IHC SP142 assay is also used to report % IC in non-indicated breast tumor types or tumors of unknown origin. See https://www.fda.gov/media/119249/download for interpretation details.

Immune Gene Expression

Amplicon-based targeted next generation sequencing (NGS) for digital gene expression detection (RNA-Seq) is used to interrogate 50 T-cell receptor signaling (TCRS) genes including PD-L1, and 8 tumor infiltrating lymphocytes (TILs) genes including CD8, that have functions across the cycle of immunity, and 6 cancer testis antigen (CT antigens) genes frequently expressed in various types of cancer making them promising candidate targets for cancer immunotherapy, including cancer vaccination and adoptive T-cell transfer with chimeric T-cell receptors. Interpretation of TCRS and TILs gene expression by RNA-Seq: each gene is compared to a reference population derived from 735 unique tumors, normalized to a value between 1 and 100, and scored as the percentile relative rank (% Rank). TCRS and TILS gene expression ranks ≥75 are considered "highly expressed" and may have immunotherapy targets in clinical trials. CT antigen genes are interpreted as "Positive" for markers with normalized reads per million (nRPM) ≥20, and "Negative" for markers with nRPM <20.

MARKER CLINICAL SIGNIFICANCE

The criteria used to classify the clinical significance of reported genomic variants relative to the tested tumor type is reported in accordance with recommendations described in *Li MM, et al., Standards and Guidelines for the Interpretation and Reporting of Sequence Variants in Cancer: A Joint Consensus Recommendation of the Association for Molecular Pathology, American Society of Clinical Oncology, and College of American Pathologists. J Mol Diagnostics. 2017;19(1):4-23.* While this guidance was developed specifically for genomic variants, OmniSeq INSIGHT extends interpretation and application of this classification to all reported markers.

Tier I: Variants/Markers with strong clinical significance

- Level A: FDA-approved or professional guideline-indicated therapies for the tested tumor type
- Level B: Well-powered clinical studies with consensus from experts in the field for therapies in the tumor type tested

Tier II: Variants/Markers with potential clinical significance

- Level C: FDA-approved therapies for other tumor types or clinical trial inclusion criteria for the tested tumor type.
- Level D: Plausible therapeutic significance with some evidence in the tested tumor type.

Note: OmniSeq INSIGHT does not report genomic variants/markers as potentially clinically significant based on evidence from non-human studies.

Tier III: Variants of unknown clinical significance (VUS)

Variants not observed at a significant allele frequency in general or specific subpopulation databases, or pan-cancer or tumor-specific variant databases. No convincing published evidence of cancer association.

Potential Germline Variants

OmniSeq INSIGHT identifies only those variants in the germline that, when present, may be associated with increased susceptibility to cancer. OmniSeq INSIGHT results do not distinguish between somatic and germline variants as only tumor tissue is tested. Genetic counseling may be appropriate if an inherited syndrome associated with a reported possible germline variant is suspected.

PRIORITIZATION OF THERAPY CONSIDERATIONS

Genomic variants and immune markers from OmniSeq INSIGHT are matched to therapies based on the tested patient's tumor type, FDA regulatory approval status, National Comprehensive Cancer Center (NCCN) professional guideline indications, published emerging efficacy data to support unmet clinical need, including FDA breakthrough and fast track designations (see https://www.fda.gov/patients/learn-about-drug-and-device-approvals/fast-track-breakthrough-therapy-accelerated-approval-priority-review), potential expanded access /compassionate use (https://www.fda.gov/news-events/public-health-focus/expanded-access), and other peer-reviewed human clinical studies as described in the OmniSeq Knowledgebase® on the report date. Therapy Considerations are prioritized as follows: markers associated with clinical benefit or resistance/decreased response in the patient's tumor type, prioritized by approval status and variant clinical significance (if applicable); markers associated with clinical benefit in other tumor types (ordered alphabetically by marker and ranked by variant clinical significance, if applicable); and markers associated with clinical trials (ordered by proximity to the patient and later trial phase). Genomic variants with potential clinical significance but no therapy considerations identified on the report date, are also provided.

PERFORMANCE CHARACTERISTICS

Performance characteristics were established using DNA and RNA derived from a wide range of FFPE tissue specimens harboring variants with both strong and potential clinical significance, including resections, needle core biopsies and cell blocks from fine needle aspirations. For genomic profiling, each performance study included representative variant types

APPENDIX About OmniSeq INSIGHT

from each alteration class (substitutions, insertions, and deletions, copy number alterations, and fusions/splice variants), in various genomic contexts across a broad selection of genes, in addition to analysis of TMB and MSI genomic signatures. The detection of genomic variants by OmniSeq INSIGHT was compared to results of other validated next generation sequencing assays to assess concordance with orthogonal methods. For immune gene expression, sequencing analytical validation studies were performed to confirm standard measurements including accuracy, sensitivity and specificity. Additional studies addressed variability in nucleic acid input amounts, genomic DNA contamination of RNA, batch size and linearity of detection across all genes within a wide distribution of signal on the overall immune response signature.

Table 1. OmniSeq INSIGHT Performance Characteristics

NGS	Passing Criteria	Genes/Loci	Marker	Positive Percent Agreement (PPA)	Negative Percent Agreement (NPA)
DNA-Seq	Tier I hotspots: ≥ 2% VAF Non-hotspots: ≥ 5% VAF	523	Substitutions	99%	>99%
			Insertions	96%	>99%
			Deletions	99%	>99%
	≥ 2 2x fold change; 30% tumor purity	59	Copy gain*	99%	99%
	≤ 0.7x fold change; 50% tumor purity	4	Copy loss*	77%	97%
	≥ 20% tumor purity	521	TMB ≥ 10 mut/Mb	85%	88%
		130	MSI	88%	>99%
RNA-Seq		55	Fusions	92%	>99%
		2	Splice variants	89%	>99%
	≥ 20 reads	64	Immune gene expression	Not applicable	

Includes indeterminate findings

LIMITATIONS OF PROCEDURE

1. OmniSeq INSIGHT is not conclusive or prescriptive for use of any specific therapeutic product.
2. OmniSeq INSIGHT has been validated using genomic DNA and RNA from formalin fixed paraffin-embedded tumor samples.
3. OmniSeq INSIGHT is designed to report somatic variants and is not intended to report germline variants.
4. Clinical validity performance of this test for predicting treatment effect of any specific therapeutic product has not been established.
5. The assay has been validated using samples with a minimum of 20% tumor purity in the tissue area to be extracted.
6. For the detection of copy number alterations (CNA), tumor purity above 30% yields consistent detection of fold change (FC) ≥2.2 for gain, and tumor purity above 50% yields consistent detection of FC ≤0.7 for loss.
7. Concordance with other validated methods for the detection of copy number alterations (CNA), fusions and splice variants has been demonstrated for copy gain genes *CCND1, CCNE1, CDK4, CDK6, EGFR, ERBB2, FGFR1, FGFR2, KIT, KRAS, MET, MDM2, MYC,* and *PIK3CA,* copy loss genes *ATM, BRCA1, BRCA2,* and *PTEN,* fusion genes *ALK, FGFR3, NTRK1, NTRK3, RET,* and *ROS1,* and splice variant genes *EGFR* and *MET.* If clinically indicated, copy alterations and fusions identified in other genes tested by OmniSeq INSIGHT should be confirmed by additional testing.
8. The MSI-High/MS-Stable designation by the OmniSeq INSIGHT test is based on genome-wide analysis of 130 potential microsatellite loci. The threshold for MSI-High/MS-Stable was determined by analytical concordance to a validated comparator NGS assay using colorectal, uterine and other cancer FFPE tissues. Samples with ≥20% MSI unstable sites are consider MSI-High, while samples with <20% unstable sites are considered MS-Stable. The clinical validity of the qualitative MSI designation has not been established.
9. TMB is reported as mutations per megabase (mut/Mb). TMB may differ across specimens (e.g., primary versus metastatic, tumor content) and targeted panels. The TMB calculation will increase or decrease depending on:
   - Size and region used to calculate TMB
   - Percentage of tumor in the sample
   - Germline variant filtering method
   - Read depth and other bioinformatic test specifications
10. Performance of OmniSeq INSIGHT has not been established for the detection of insertions and deletions larger than 25 base pairs.
11. A negative result does not rule out the presence of a mutation below the limits of detection of the assay.
12. The variant allele frequency (VAF) associated with each alteration is for informational use only and should not be used to make any quantitative clinical assessment.

DISCLAIMER

The selection of any, all or none of the matched therapies reported by OmniSeq INSIGHT resides solely with the treating physician. Associated therapies may or may not be suitable for administration to a specific patient. OmniSeq, Inc., does not promise or guarantee that a specific therapeutic product will be effective in the treatment of the tested patient's disease, nor that a drug with potential lack of benefit will not provide clinical benefit to the tested patient. Decisions about patient care and treatment must be based on the independent medical judgment of the treating physician, accounting for all information concerning the patient's condition, such as patient and family history, physical examinations, information from other diagnostic tests, and patient preferences, in accordance with the community standard of care. A treating physician's decisions should not be solely based on the OmniSeq INSIGHT test, or the information contained in this report.

OmniSeq INSIGHT was developed, and its performance characteristics determined by OmniSeq, Inc. in Buffalo, NY. OmniSeq® is certified under the Clinical Laboratory Improvement Amendments of 1988 (CLIA-88) and by the New York State Clinical Laboratory Evaluation Program as qualified to perform high complexity clinical laboratory testing, including all components of OmniSeq INSIGHT. OmniSeq's CLIA certification number is located at the bottom of each report, and all registered marks are the property of OmniSeq, Inc. The genomic and immune NGS components of OmniSeq INSIGHT are laboratory developed tests and do not currently require clearance or approval by the U.S. Food and Drug Administration (FDA). The FDA has approved the PD-L1 IHC components of OmniSeq INSIGHT for in vitro diagnostic use. OmniSeq INSIGHT is for clinical purposes and should not be regarded as investigational or for research.

APPENDIX All Markers Assayed by OmniSeq INSIGHT

DNA-Sequencing of 523 genes (full coding exonic regions) for the detection of substitutions, indels, MSI and TMB

ABL1	BLM	CRLF2	ERCC4	FLI1	HIST1H3I	KDR	MRE11A	PAX3	PTCH1	SDHD	TCF7L2
ABL2	BMPR1A	CSF1R	ERCC5	FLT1	HIST1H3J	KEAP1	MSH2	PAX5	PTEN	SETBP1	TERC
ACVR1	BRAF	CSF3R	ERG	FLT3	HIST2H3A	KEL	MSH3	PAX7	PTPN11	SETD2	TERT
ACVR1B	BRCA1	CSNK1A1	ERRFI1	FLT4	HIST2H3C	KIF5B	MSH6	PAX8	PTPRD	SF3B1	TET1
AKT1	BRCA2	CTCF	ESR1	FOXA1	HIST2H3D	KIT	MST1	PBRM1	PTPRS	SH2B3	TET2
AKT2	BRD4	CTLA4	ETS1	FOXL2	HIST3H3	KLF4	MST1R	PDCD1	PTPRT	SH2D1A	TFE3
AKT3	BRIP1	CTNNA1	ETV1	FOXO1	HLA-A	KLHL6	MTOR	PDCD1LG2	QKI	SHQ1	TFRC
ALK	BTG1	CTNNB1	ETV4	FOXP1	HLA-B	KMT2A	MUTYH	PDGFRA	RAB35	SLIT2	TGFBR1
ALOX12B	BTK	CUL3	ETV5	FRS2	HLA-C	KMT2B	MYB	PDGFRB	RAC1	SLX4	TGFBR2
AMER1	C11orf30	CUX1	ETV6	FUBP1	HNF1A	KMT2C	MYC	PDK1	RAD21	SMAD2	TMEM127
ANKRD11	CALR	CXCR4	EWSR1	FYN	HNRNPK	KMT2D	MYCL	PDPK1	RAD50	SMAD3	TMPRSS2
ANKRD26	CARD11	CYLD	EZH2	GABRA6	HOXB13	KRAS	MYCN	PGR	RAD51	SMAD4	TNFAIP3
APC	CASP8	DAXX	FAM175A	GATA1	HRAS	LAMP1	MYD88	PHF6	RAD51B	SMARCA4	TNFRSF14
AR	CBFB	DCUN1D1	FAM46C	GATA2	HSD3B1	LATS1	MYOD1	PHOX2B	RAD51C	SMARCB1	TOP1
ARAF	CBL	DDR2	FANCA	GATA3	HSP90AA1	LATS2	NAB2	PIK3C2B	RAD51D	SMARCD1	TOP2A
ARFRP1	CCND1	DDX41	FANCC	GATA4	ICOSLG	LMO1	NBN	PIK3C2G	RAD52	SMC1A	TP53
ARID1A	CCND2	DHX15	FANCD2	GATA6	ID3	LRP1B	NCOA3	PIK3C3	RAD54L	SMC3	TP63
ARID1B	CCND3	DICER1	FANCE	GEN1	IDH1	LYN	NCOR1	PIK3CA	RAF1	SMO	TRAF2
ARID2	CCNE1	DIS3	FANCF	GID4	IDH2	LZTR1	NEGR1	PIK3CB	RANBP2	SNCAIP	TRAF7
ARID5B	CD274	DNAJB1	FANCG	GLI1	IFNGR1	MAGI2	NF1	PIK3CD	RARA	SOCS1	TSC1
ASXL1	CD276	DNMT1	FANCI	GNA11	IGF1	MALT1	NF2	PIK3CG	RASA1	SOX10	TSC2
ASXL2	CD74	DNMT3A	FANCL	GNA13	IGF1R	MAP2K1	NFE2L2	PIK3R1	RB1	SOX17	TSHR
ATM	CD79A	DNMT3B	FAS	GNAQ	IGF2	MAP2K2	NFKBIA	PIK3R2	RBM10	SOX2	U2AF1
ATR	CD79B	DOT1L	FAT1	GNAS	IKBKE	MAP2K4	NKX2-1	PIK3R3	RECQL4	SOX9	VEGFA
ATRX	CDC73	E2F3	FBXW7	GPR124	IKZF1	MAP3K1	NKX3-1	PIM1	REL	SPEN	VHL
AURKA	CDH1	EED	FGF1	GPS2	IL10	MAP3K13	NOTCH1	PLCG2	RET	SPOP	VTCN1
AURKB	CDK12	EGFL7	FGF10	GREM1	IL7R	MAP3K14	NOTCH2	PLK2	RFWD2	SPTA1	WISP3
AXIN1	CDK4	EGFR	FGF14	GRIN2A	INHA	MAP3K4	NOTCH3	PMAIP1	RHEB	SRC	WT1
AXIN2	CDK6	EIF1AX	FGF19	GRM3	INHBA	MAPK1	NOTCH4	PMS1	RHOA	SRSF2	XIAP
AXL	CDK8	EIF4A2	FGF2	GSK3B	INPP4A	MAPK3	NPM1	PMS2	RICTOR	STAG1	XPO1
B2M	CDKN1A	EIF4E	FGF23	H3F3A	INPP4B	MAX	NRAS	PNRC1	RIT1	STAG2	XRCC2
BAP1	CDKN1B	EML4	FGF3	H3F3B	INSR	MCL1	NRG1	POLD1	RNF43	STAT3	YAP1
BARD1	CDKN2A	EP300	FGF4	H3F3C	IRF2	MDC1	NSD1	POLE	ROS1	STAT4	YES1
BBC3	CDKN2B	EPCAM	FGF5	HGF	IRF4	MDM2	NTRK1	PPARG	RPS6KA4	STAT5A	ZBTB2
BCL10	CDKN2C	EPHA3	FGF6	HIST1H1C	IRS1	MDM4	NTRK2	PPM1D	RPS6KB1	STAT5B	ZBTB7A
BCL2	CEBPA	EPHA5	FGF7	HIST1H2BD	IRS2	MED12	NTRK3	PPP2R1A	RPS6KB2	STK11	ZFHX3
BCL2L1	CENPA	EPHA7	FGF8	HIST1H3A	JAK1	MEF2B	NUP93	PPP2R2A	RPTOR	STK40	ZNF217
BCL2L11	CHD2	EPHB1	FGF9	HIST1H3B	JAK2	MEN1	NUTM1	PPP6C	RUNX1	SUFU	ZNF703
BCL2L2	CHD4	ERBB2	FGFR1	HIST1H3C	JAK3	MET	PAK1	PRDM1	RUNX1T1	SUZ12	ZRSR2
BCL6	CHEK1	ERBB3	FGFR2	HIST1H3D	JUN	MGA	PAK3	PREX2	RYBP	SYK	
BCOR	CHEK2	ERBB4	FGFR3	HIST1H3E	KAT6A	MITF	PAK7	PRKAR1A	SDHA	TAF1	
BCORL1	CIC	ERCC1	FGFR4	HIST1H3F	KDM5A	MLH1	PALB2	PRKCI	SDHAF2	TBX3	
BCR	CREBBP	ERCC2	FH	HIST1H3G	KDM5C	MLLT3	PARK2	PRKDC	SDHB	TCEB1	
BIRC3	CRKL	ERCC3	FLCN	HIST1H3H	KDM6A	MPL	PARP1	PRSS8	SDHC	TCF3	

DNA-Sequencing of 59 genes for the detection of copy gain and copy loss in ATM, BRCA1, BRCA2, and PTEN

AKT2	BRCA1	CDK4	ERBB2	FGF1	FGF23	FGF7	FGFR3	LAMP1	MYCL	PDGFRB	RET
ALK	BRCA2	CDK6	ERBB3	FGF10	FGF3	FGF8	FGFR4	MDM2	MYCN	PIK3CA	RICTOR
AR	CCND1	CHEK1	ERCC1	FGF14	FGF4	FGF9	JAK2	MDM4	NRAS	PIK3CB	RPS6KB1
ATM	CCND3	CHEK2	ERCC2	FGF19	FGF5	FGFR1	KIT	MET	NRG1	PTEN	TFRC
BRAF	CCNE1	EGFR	ESR1	FGF2	FGF6	FGFR2	KRAS	MYC	PDGFRA	RAF1	

RNA-Sequencing of 55 genes for the detection of fusions and skipping mutations (splice variants) in MET and EGFR

ABL1	BCL2	CSF1R	ESR1	EWSR1	FLI1	KIF5B	MSH2	NRG1	PAX7	RAF1
AKT3	BRAF	EGFR	ETS1	FGFR1	FLT1	KIT	MYC	NTRK1	PDGFRA	RET
ALK	BRCA1	EML4	ETV1	FGFR2	FLT3	KMT2A	NOTCH1	NTRK2	PDGFRB	ROS1
AR	BRCA2	ERBB2	ETV4	FGFR3	JAK2	MET	NOTCH2	NTRK3	PIK3CA	RPS6KB1
AXL	CDK4	ERG	ETV5	FGFR4	KDR	MLLT3	NOTCH3	PAX3	PPARG	TMPRSS2

RNA-sequencing of 64 immune genes

ADORA2A	CD2	CD4	CSF1R	FOXP3	IDO1	MS4A1	TGFB1	TNFSF4	TLR8	MAGEA1
BTLA	CD244	CD40	CTLA4	GATA3	IFNG	MX1	TNF	CXCR2	TLR9	MAGEA4
C10orf54	CD27	CD40LG	CXCL10	GZMB	IL10	PDCD1	TNFRSF14	NECTIN2	CTAG1B	CD3
CCL2	CD274	CD68	CXCR6	HAVCR2	IL1B	PDCD1LG2	TNFRSF18	PVR	CTAG2	CD8
CCR2	CD28	CD80	DDX58	ICOS	KLRD1	STAT1	TNFRSF4	TIGIT	SSX2	
CD163	CD38	CD86	ENTPD1	ICOSLG	LAG3	TBX21	TNFRSF9	TLR7	MAGEA3	

Immunohistochemistry for expression of PD-L1

PD-L1 IHC (22C3), PD-L1 IHC (SP142)