PATIENT

DIAGNOSIS C56.9, Malignant neoplasm of unspecified ovary; Metastatic
NAME Test
DOB SEX Female
MRN
ORDER ID P-
REPORT DATE 2025

SPECIMEN

FACILITY My Medical Center Lab
ID
SOURCE Peritoneal Biopsy
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
MedOncSupport@labcorp.com

OmniSeq® INSIGHT interrogates 523 genes by next generation sequencing for mutations, select copy number alterations, HLA Class I genotypes and fusions/splice variants, microsatellite instability, homologous recombination deficiency (HRD) status when clinically indicated, tumor mutational burden (TMB), 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)

SNV /Indel	JAK1 N11fs NF1 c.4578-43_4586del TP53 Y220C
Fusion	*No positive findings*
Copy Gain	*No positive findings*
Copy Loss	*No positive findings*

See APPENDIX for variants of unknown significance (VUS)

Signatures

Tumor Mutational Burden (TMB): 5.5 mut/Mb (Not High)
Microsatellite Instability (MSI): MS-Stable
Homologous Recombination Deficiency (HRD) Status: Positive
Genomic Instability Score (GIS): 69 (Positive)
BRCA1/2 Mutation Status: Negative

Immune Markers

PD-L1 IHC (22C3): Tumor Proportion Score <1%

HLA Class I:
A*01:01, 03:01 B*07:02, 15:24 C*03:03, 07:02

Note: PD-L1 is measured by immunohistochemistry (IHC) and RNA-expression profiling, and HLA Class I genotyping 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

BRAF V600E	HER2 (ERBB2) gain
BRCA1 loss	KRAS mut
BRCA1 mut	NTRK1/2/3 fusion
BRCA2 loss	RET fusion
BRCA2 mut	

COMMENTS

Pathologist
No pathologist comments.

Testing
All testing was completed.

Potential Germline Variants
Listed alterations may represent inherited variants and should prompt dedicated germline testing and/or genetic counseling in the appropriate clinical context. More information on germline testing can be found at www.invitae.com or at 800-436-3037.
NF1 c.4578-43_4586del

THERAPY CONSIDERATIONS

CLINICALLY SIGNIFICANT biomarkers, including genomic variants, signatures, and immune markers, indicate evidence of clinical benefit from or resistance/decreased response to therapy in this patient's tumor type based on FDA approval or professional guidelines. Biomarkers 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 markers or drug targets in clinical trials. *(See THERAPY DETAILS & CLINICAL TRIALS: Genomic Variant Clinical Significance Classification)*

CLINICALLY SIGNIFICANT

Clinical Benefit in this Patient's Tumor Type

			Sources
HRD Positive	bevacizumab + olaparib, niraparib	Maintenance (post-primary)	FDA (Approved), NCCN
	niraparib	Subsequent line	NCCN
	bevacizumab + niraparib, olaparib	Maintenance (post-primary)	NCCN

Resistance/Decreased Response in this Patient's Tumor Type

No marker-associations with strong evidence of resistance or decreased response to targeted therapies or immunotherapies in this patient's tumor type were identified.

POTENTIAL CLINICAL SIGNIFICANCE

Emerging Clinical Benefit in this Patient's Tumor Type

			Sources
TP53 Y220C	rezatapopt	Metastatic	FDA (Fast Track)

Clinical Benefit in Other Tumor Types

NF1 c.4578-43_4586del	selumetinib	Low Grade Glioma

Clinical Trial Markers for this Patient

HRD Positive	NF1 c.4578-43_4586 del	TP53 Y220C
5 clinical trials	*7 clinical trials*	*2 clinical trials*

Genomic Variants with No Matched Therapies

No approved therapies or clinical trials identified for this patient

JAK1 N11fs

MARKER DETAILS

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

Mutations

Gene	Alteration	Location	VAF	ClinVar	Transcript ID	Type	Pathway
JAK1	c.30dup p.N11fs	exon 3	49.6%	-	NM_002227.2	Insertion - Frameshift	JAK-STAT signaling

JAK1, janus kinase 1, is a non-receptor protein tyrosine kinase involved in the interferon-alpha/beta/gamma pathway, is ubiquitously expressed, and is a member of the JAK/STAT signaling pathway (PMID: 15575979). Additionally, frameshift mutations in JAK1 are associated with high mutational burden and microsatellite instability (PMID: 29121062).

Gene	Alteration	Location	VAF	ClinVar	Transcript ID	Type	Pathway
NF1	c.4578-43_4586del	exon 35	23.8%	-	NM_001042492.2	Splice Acceptor Site	Receptor tyrosine kinase /growth factor signaling

NF1, neurofibromin 1, is a tumor suppressor gene that functions to downregulate RAS by stimulating GTPase activity and converting active RAS-GTP state to the inactive RAS-GDP state decreasing cellular proliferation (PMID: 30562755 ; PMID: 28637487). Germline mutations in NF1 may be associated with increased susceptibility to neurofibromatosis type 1 (PMID: 33734413).

Gene	Alteration	Location	VAF	ClinVar	Transcript ID	Type	Pathway
TP53	c.659A>G p.Y220C	exon 6	27.4%	Pathogenic	NM_000546.5	Substitution - Missense	Cell cycle control

TP53, tumor protein p53, is a tumor suppressor and oncogene and responds to various stresses to regulate expression of target genes by inducing cell cycle arrest, senescence, DNA repair, cell metabolism and apoptosis (PMID: 30562755 ; PMID: 30577483 ; PMID: 10065147 ; PMID: 22713868 ; PMID: 29786075). Germline mutations in TP53 may be associated with increased susceptibility to Li-Fraumeni syndrome (PMID: 20301488 , PMID: 22006311). TP53 Y220C is a hotspot mutation that lies within the DNA-binding domain (PMID: 17401432). Y220C results in decreased DNA binding, reduced Tp53 transcriptional activity, leads to resistance to apoptosis and failure of G1 arrest in cell culture (PMID: 16861262 , PMID: 23630318 , PMID: 31395785).

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 5.5 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.

Homologous Recombination Deficiency (HRD)

This specimen is Homologous Recombination Deficiency (HRD) Positive

The Genomic Instability Score (GIS) for this specimen is 69 (Positive)

The tumor BRCA1/2 mutation status is Negative for a clinically significant mutation

HRD status is determined by either the presence of a causal genomic event in BRCA1 or BRCA2 or by a GIS ≥ 42. GIS is an aggregate measure of three genomic scars (loss of heterozygosity (LOH), telomeric-allelic imbalance (TAI), and large-scale state transitions (LST) associated with HRD.

Human Leukocyte Antigen (HLA) Class I Genotype

A*01:01, 03:01	B*07:02, 15:24	C*03:03, 07:02

The HLA genotype is determined by aligning the sequenced nucleic acids to an HLA-specific reference genome and is reported as HLA-A, HLA-B* and HLA-C* to the two-field, four-digit level using standard HLA nomenclature.*

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 07/29/2025 as described in the OmniSeq Knowledgebase®. For up to date information regarding available clinical trials, please see www.clinicaltrials.gov

Genomic Variant 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

HRD Positive

bevacizumab + olaparib	FDA APPROVED, NCCN RECOMMENDED: FDA approved for the maintenance treatment of advanced epithelial ovarian, fallopian tube or primary peritoneal cancer with homologous recombination deficiency (HRD) positive status (deleterious or suspected deleterious BRCA mutation, and/or genomic instability), with complete or partial response to first-line platinum-based chemotherapy. NCCN recommended as Category 1. CLINICAL SIGNIFICANCE (IA): In a Phase III (PAOLA-1) trial that supported FDA approval, addition of maintenance Lynparza (olaparib) to Avastin (bevacizumab) improved median progression-free survival compared to placebo (37.2 vs 17.7 mo, HR=0.33) in patients with advanced epithelial ovarian, fallopian tube, or primary peritoneum cancer following standard first-line therapy who were homologous-recombination deficient, as defined by deleterious or suspected deleterious BRCA mutations or genomic instability (PMID: 31851799; NCT02477644). NCT06580314 Testing Olaparib for One or Two Years, With or Without Bevacizumab, to Treat Ovarian Cancer — Phase 3 — Orlando, FL
niraparib	FDA APPROVED, NCCN RECOMMENDED: FDA approved for maintenance treatment of adults with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy, with homologous recombination deficiency (HRD)-positive status (deleterious or suspected deleterious BRCA mutation, and/or genomic instability). NCCN recommended as Category 1 for BRCA mutation with no bevacizumab during primary treatment, or Category 2A otherwise. CLINICAL SIGNIFICANCE (IA): The FDA approval for niraparib was supported by data from double-blind, placebo-controlled, phase-III trial PRIMA (NCT02655016). PRIMA demonstrated that maintenance niraparib (n = 247), compared to placebo (n = 126), improved median PFS (21.9 mo. vs. 10.4 mo., HR = 0.43; p < 0.0001) in patients with advanced epithelial ovarian, fallopian tube, or primary peritoneal cancer who are in a complete or partial response to first-line platinum-based chemotherapy and whose cancer is associated with HRD-positive status defined by either a deleterious or suspected deleterious BRCA mutation, and/or genomic instability. Secondary endpoint was median OS (71.9 mo. vs. 69.8 mo.).
niraparib	NCCN RECOMMENDED: NCCN recommended for recurrent ovarian, fallopian tube, or primary peritoneal cancer with homologous recombination deficiency (HRD) (either a deleterious or suspected deleterious BRCA mutation, or genomic instability), after three or more prior chemotherapy regimens with progression >6 months after response to the last platinum-based chemotherapy (Category 3/Other recommended intervention). CLINICAL SIGNIFICANCE (IA): In a Phase II trial (QUADRA), Zejula (niraparib) demonstrated efficacy in patients with ovarian, fallopian tube, and primary peritoneal cancer who have received 3 or more chemotherapies, particularly in those harboring deleterious or suspected deleterious BRCA1/2 mutations or with homologous recombination deficiency, resulted in an overall response rate of 29% (18/63) and 15% (29/189), and an overall survival of 26.0 and 19.0 months, respectively (PMID: 30948273; NCT02354586).
olaparib	NCCN RECOMMENDED: NCCN recommended for the maintenance treatment (post-primary treatment) of stage II-IV epithelial ovarian, fallopian tube or primary peritoneal cancer with homologous recombination deficiency (HRD) positive status (Category 2B). CLINICAL SIGNIFICANCE (IA): Marker is in an FDA approval or professional guideline. NCT06580314 Testing Olaparib for One or Two Years, With or Without Bevacizumab, to Treat Ovarian Cancer — Phase 3 — Orlando, FL
bevacizumab + niraparib	NCCN RECOMMENDED: NCCN recommended as maintenance therapy post-primary therapy for ovarian, fallopian tube, or primary peritoneal cancer with BRCA1/2 mutation or HR deficient status, if unable to tolerate olaparib (Category 2A). CLINICAL SIGNIFICANCE (IA): Marker is in an FDA approval or professional guideline.

atezolizumab + talazoparib	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT02693535 TAPUR: Testing the Use of Food and Drug Administration (FDA) Approved Drugs That Target a Specific Abnormality in a Tumor Gene in People With Advanced Stage Cancer	Phase 2	Gainesville, FL
ISM3091; ISM3091 + olaparib	ISM3091 ISM3091 inhibits USP1, which potentially results in decreased tumor cell proliferation and reduced tumor growth (Cancer Res (2023) 83 (7_Supplement): 502).		
	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05932862 A Phase 1 Study of XL309 (ISM3091) Alone and in Combination in Patients With Advanced Solid Tumors	Phase 1	Orlando, FL
MOMA-313; MOMA-313 + olaparib	MOMA-313 MOMA-313 inhibits the helicase domain of DNA polymerase theta (POLQ), which may prevent the repair of DNA double-strand breaks, resulting in decreased tumor growth (Cancer Res (2025) 85 (8_Supplement_1): 1749).		
	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT06545942 Study of Orally Administered MOMA-313 in Participants With Advanced or Metastatic Solid Tumors	Phase 1	Lake Mary, FL
pidnarulex	PIDNARULEX CX-5461 is an RNA polymerase I (Pol I) inhibitor that inhibits rRNA synthesis, resulting in growth arrest and apoptosis in cancer cells (PMID: 26472108, PMID: 32719798).		
	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT04890613 Study of CX-5461 in Patients With Solid Tumours and BRCA1/2, PALB2 or Homologous Recombination Deficiency (HRD) Mutation	Phase 1	Tampa, FL
NF1 c.4578-43_4586del			
selumetinib	EXPANDED ACCESS This therapy may be available through the FDA Expanded Access program (*See* https://www.fda.gov/news-events/public-health-focus/expanded-access)		
	CLINICAL SIGNIFICANCE (IIC): FDA approved in other tumor types.		
DCC-3084	DCC-3084 DCC-3084 is a switch control inhibitor targeting class 1, 2, and 3 BRAF mutations, fusions, and BRAF/CRAF heterodimers, which potentially inhibits Mapk signaling, proliferation, and tumor growth (Cancer Res (2023) 83 (7_Supplement): 4045).		
	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT06287463 Study of DCC-3084 in Participants With Advanced Malignancies Driven by the Mitogen-Activated Protein Kinase (MAPK) Pathway	Phase 1 /Phase 2	Orlando, FL
avutometinib + defactinib	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05512208 A Phase 2 Study of Avutometinib (VS-6766) Plus Defactinib	Phase 2	Orlando, FL
olaparib + selumetinib	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05564377 Targeted Therapy Directed by Genetic Testing in Treating Patients With Locally Advanced or Advanced Solid Tumors, The ComboMATCH Screening Trial	Phase 2	Gainesville, FL
JZP815	JZP815 JZP815 is a pan-Raf inhibitor, which potentially inhibits Mapk signaling and tumor growth (Cancer Res 2022; 82(12_Suppl):Abstract nr 2677).		
	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05557045 A Study of JZP815 Oral Capsules in Adult Participants With Advanced or Metastatic Solid Tumors Harboring Mitogen Activated Protein Kinase (MAPK) Pathway Alterations to Investigate the Safety, Dosing, and Antitumor Activity of JZP815	Phase 1	Orlando, FL

KQB198	KQB198 Limited information is currently available on KQB198 (Jul 2024). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT06507306	A Study to Investigate the Safety and Efficacy of KQB198 as Monotherapy and in Combination in Participants With Advanced Solid Malignancies	Phase 1	Orlando, FL
NST-628	NST-628 NST-628 stabilizes the RAF-MEK complex, which inhibits MEK/ERK/RSK phosphorylation and reactivation of the pathway, potentially leading to tumor growth inhibition (PMID: 38588399). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT06326411	A Study to Investigate the Safety and Efficacy of NST-628 Oral Tablets in Subjects With Solid Tumors	Phase 1	Tampa, FL
RMC-4630	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.			
	NCT03634982	Dose Escalation of RMC-4630 Monotherapy in Relapsed /Refractory Solid Tumors	Phase 1	Tampa, FL
TP53 Y220C				
rezatapopt	REZATAPOPT PC14586 is a small molecule that stabilizes TP53 Y220C and reactivates TP53 function, which may lead to cell cycle arrest and growth inhibition (AACR Annual Meeting Apr 2021, Session MS.LBA01, Abstract # LB006). CLINICAL SIGNIFICANCE (IIC): FDA Fast Track. Marker is in clinical trial inclusion criteria.			
	NCT04585750	The Evaluation of PC14586 in Patients With Advanced Solid Tumors Harboring a TP53 Y220C Mutation (PYNNACLE)	Phase 1 /Phase 2	Orlando, FL
pembrolizumab + rezatapopt	REZATAPOPT PC14586 is a small molecule that stabilizes TP53 Y220C and reactivates TP53 function, which may lead to cell cycle arrest and growth inhibition (AACR Annual Meeting Apr 2021, Session MS.LBA01, Abstract # LB006). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04585750	The Evaluation of PC14586 in Patients With Advanced Solid Tumors Harboring a TP53 Y220C Mutation (PYNNACLE)	Phase 1 /Phase 2	Orlando, FL
JAB-30355	JAB-30355 JAB-30355 is a selective TP53 Y220C reactivator, which increases expression of TP53 target genes and potentially decreases tumor cell viability and inhibits growth of tumors harboring TP53 Y220C (Cancer Res (2024) 84 (6_Supplement): 5940). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT06386146	JAB-30355 in Patients With Advanced Solid Tumors Harboring TP53 Y220C Mutation	Phase 1 /Phase 2	Lake Mary, FL

TISSUE Specimen Review Summary

Specimen Details

Submitted Pathology Report ID		Histologic evaluation/ Clinical Impression	Ovary / Surface epithelial-stromal tumors / Serous tumors / Malignant / Adenocarcinoma				
Sample Collection Date		Tumor Origin	Metastatic	Tumor Nuclei	50%	#Neoplastic Cells per slide	100-199
Organ/Tissue Site	GYN / Peritoneum NOS					Necrosis	0%

Samples Received for Testing

Received Date	Sample Label	Type	Quantity	Purpose
		FFPE Block	1	Testing

PD-L1 Immunohistochemistry

Technical Information: OmniSeq has prepared a control slide and stained slides for PD-L1 IHC (22C3) which are submitted for interpretation by OmniSeq pathologists.

Indications and Regulatory: PD-L1 IHC 22C3 pharmDx is an FDA-approved companion assay for in vitro diagnostic use. Technical component was performed at OmniSeq. Results and adequate quality control were 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.

Interpretation: Results and adequate quality controls were interpreted by Kazunori Kanehira at OmniSeq, Inc., 700 Ellicott Street, Buffalo NY 14203, on x/x/2025 at 13:00 EST.
PD-L1 by IHC is measured based on the tumor type tested. The PD-L1 IHC 22C3 pharmDx FDA approved assay follows scoring guidelines for reporting either tumor proportion score (TPS) for non-small cell lung cancer or combined positive score (CPS) for other indicated tumor types with interpretation. The PD-L1 IHC 22C3 pharmDx assay is also used in non-indicated tumor types or tumors of unknown origin but no interpretation is provided. Scoring information can be found at the link https://www.accessdata.fda.gov/cdrh_docs/pdf15/P150013S020B.pdf

About the Test:
METHOD: PD-L1 IHC 22C3 pharmDx is a qualitative immunohistochemical (IHC) assay using Monoclonal Mouse Anti-PD-L1, Clone 22C3 intended for use in the detection of PD-L1 protein in formalin-fixed, paraffin-embedded (FFPE) tissues using EnVision FLEX visualization system on Autostainer Link 48.

Limitations:
Specimens with extensive necrosis or regular decalcification are not acceptable. A minimum of 100 neoplastic cells is required.

APPENDIX Indeterminate Findings with Potential Clinical Significance

Single nucleotide variants, short variants, and indels identified below our reporting thresholds.

No indeterminate variants with potential clinical significance were identified.

APPENDIX Regions with Decreased Sensitivity Due to Low Coverage

Single nucleotide variants, short variants, and indels that could not be confirmed as positive or negative.

No regions with decreased sensitivity due to low coverage were identified.

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.

AKT1 G286R	ATM R2459C	ERBB2 R226C	ERCC5 A761T	KDR G1108R
MTOR P1249S	SOX17 R125S	SPEN I1440V		

APPENDIX About OmniSeq INSIGHT®

INTENDED USE

OmniSeq INSIGHT is a next generation sequencing-based in vitro diagnostic device (IVD) Laboratory Developed Test (LDT) for the detection of genomic variants, HLA Class I genotypes, genomic signatures in formalin-fixed paraffin-embedded (FFPE) tumor tissue. DNA is sequenced to detect small variants in the full exonic coding region of 523 genes (substitutions, insertions, deletions and deletion-insertion, copy number alterations in 59 genes (gains and losses), as well as analysis of microsatellite instability (MSI) and tumor mutational burden (TMB). For clinically relevant indications, an assessment of homologous recombination deficiency (HRD) is performed using a combination of causal *BRCA1* or *BRCA2* alterations and a genomic instability score (GIS) algorithm, which is a measurement of Loss of Heterozygosity (LOH), Telomeric Allele Imbalance (TAI), and Large-scale State Transitions (LST). RNA is sequenced to detect fusions and splice variants in 55 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 for a complete list of markers.

TEST PRINCIPLE

OmniSeq INSIGHT is performed as a laboratory service using DNA and RNA co-extracted from FFPE tumor samples; DNA and 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) and the sequence data are analyzed to detect genomic variants and signatures. Immunohistochemistry (IHC) is used to measure PD-L1 protein expression (22C3 antibody) using tumor type specific scoring criteria. For more details about the performance characteristics please Performance Characteristics Summary.

MARKER CLINICAL SIGNIFICANCE

OmniSeq INSIGHT reported genomic variants and immune markers are matched to therapies and clinical trials relative to the tested tumor type as described in the OmniSeq Knowledgebase® on the report date. Therapy and clinical trial associations for genomic variants are reported as clinically significant or potentially clinically significant 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. Genomic variants with potential clinical significance but no therapy considerations as of report date are identified for the tested patient.

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 FFPE tumor samples.
3. OmniSeq INSIGHT is performed on tumor tissue and does not distinguish between somatic and germline origin of genomic 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) ≥3.2 for gain and FC=2.2-<3.2 for equivocal gain. Equivocal gain is reported when testing was performed and the results provide some, but not unambiguous evidence that the gene fold change exceeds the threshold for identifying copy gain. Additionally, tumor purity above 50% yields consistent detection of FC ≤0.5 for loss and FC >0.5-0.7 for equivocal loss. Equivocal loss is reported when testing was performed, and the results provide some, but not unambiguous evidence of a homozygous deletion.
7. Concordance with other validated methods for the detection of copy number alterations (CNA), fusions and splice variants has been demonstrated for copy number gains in genes *AR, CCND1, CCNE1, CDK4, CDK6, EGFR, ERBB2, FGFR1, FGFR2, KIT, KRAS, MET, MDM2, MYC, MYCN, PDGFRA,* and *PIK3CA,* copy number loss in genes *ATM, BRCA1, BRCA2,* and *PTEN,* fusion events involving genes *ALK, BRAF, FGFR1, FGFR2, FGFR3, FGFR4, NRG1, NTRK1, NTRK2, NTRK3, RET,* and *ROS1,* and splice variants in genes *EGFR* and *MET*. If clinically indicated, copy alterations, fusions, and splice variants 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 considered 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: i) Size and region used to calculate TMB, ii) Percentage of tumor in the sample, iii) Germline variant filtering method, and iv) Read depth and other bioinformatic test specifications.
10. HRD positive status is determined by either the presence of a clinically significant alteration in *BRCA1* or *BRCA2* or by a GIS ≥ 42. GIS is an aggregate measure of the three genomic scars including (LOH, TAI, and LST) associated with HRD. This assay has not been validated to report large rearrangements in *BRCA1* and *BRCA2*. Specimens with low tumor content (<30%) are more likely to fail GIS testing.
11. Performance of OmniSeq INSIGHT has not been established for the detection of insertions and deletions larger than 25 base pairs.
12. A negative result does not rule out the presence of a mutation below the limits of detection of the assay.
13. 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.
14. The assay does not genotype HLA class II molecules, HLA class I genes HLA-E, HLA-F, or HLA-G, nor provide HLA class I resolution greater than four-digits, copy number, somatic, or loss of heterozygosity (LOH) calls.
15. OmniSeq INSIGHT is not validated for use in samples with extensive necrosis nor regular decalcification.

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 drug may be effective in the treatment of the tested patient's disease, nor that a drug with potential lack of benefit may 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 (NYS CLEP) 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 NGS components of OmniSeq INSIGHT are laboratory developed tests (LDT) that have not been cleared or approved 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.

Additional information available here:

https://oncology.labcorp.com/sites/default/files/INSIGHT_websiteABOUT.pdf

APPENDIX All Markers Assayed by OmniSeq INSIGHT

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

ABL1	BCR	COP1	ERBB3	FGFR4	H3C15	KDM5C	MLLT3	PARP1	PRKN	SDHC	TCF7L2
ABL2	BIRC3	CREBBP	ERBB4	FH	H3C2	KDM6A	MPL	PAX3	PRSS8	SDHD	TENT5C
ABRAXAS1	BLM	CRKL	ERCC1	FLCN	H3C3	KDR	MRE11	PAX5	PTCH1	SETBP1	TERC
ACVR1	BMPR1A	CRLF2	ERCC2	FLI1	H3C4	KEAP1	MSH2	PAX7	PTEN	SETD2	TERT
ACVR1B	BRAF	CSF1R	ERCC3	FLT1	H3C6	KEL	MSH3	PAX8	PTPN11	SF3B1	TET1
ADGRA2	BRCA1	CSF3R	ERCC4	FLT3	H3C7	KIF5B	MSH6	PBRM1	PTPRD	SH2B3	TET2
AKT1	BRCA2	CSNK1A1	ERCC5	FLT4	H3C8	KIT	MST1	PDCD1	PTPRS	SH2D1A	TFE3
AKT2	BRD4	CTCF	ERG	FOXA1	HGF	KLF4	MST1R	PDCD1LG2	PTPRT	SHQ1	TFRC
AKT3	BRIP1	CTLA4	ERRFI1	FOXL2	HLA-A	KLHL6	MTOR	PDGFRA	QKI	SLIT2	TGFBR1
ALK	BTG1	CTNNA1	ESR1	FOXO1	HLA-B	KMT2A	MUTYH	PDGFRB	RAB35	SLX4	TGFBR2
ALOX12B	BTK	CTNNB1	ETS1	FOXP1	HLA-C	KMT2B	MYB	PDK1	RAC1	SMAD2	TMEM127
AMER1	CALR	CUL3	ETV1	FRS2	HNF1A	KMT2C	MYC	PDPK1	RAD21	SMAD3	TMPRSS2
ANKRD11	CARD11	CUX1	ETV4	FUBP1	HNRNPK	KMT2D	MYCL	PGR	RAD50	SMAD4	TNFAIP3
ANKRD26	CASP8	CXCR4	ETV5	FYN	HOXB13	KRAS	MYCN	PHF6	RAD51	SMARCA4	TNFRSF14
APC	CBFB	CYLD	ETV6	GABRA6	HRAS	LAMP1	MYD88	PHOX2B	RAD51B	SMARCB1	TOP1
AR	CBL	DAXX	EWSR1	GATA1	HSD3B1	LATS1	MYOD1	PIK3C2B	RAD51C	SMARCD1	TOP2A
ARAF	CCN6	DCUN1D1	EZH2	GATA2	HSP90AA1	LATS2	NAB2	PIK3C2G	RAD51D	SMC1A	TP53
ARFRP1	CCND1	DDR2	FANCA	GATA3	ICOSLG	LMO1	NBN	PIK3C3	RAD52	SMC3	TP63
ARID1A	CCND2	DDX41	FANCC	GATA4	ID3	LRP1B	NCOA3	PIK3CA	RAD54L	SMO	TRAF2
ARID1B	CCND3	DHX15	FANCD2	GATA6	IDH1	LYN	NCOR1	PIK3CB	RAF1	SNCAIP	TRAF7
ARID2	CCNE1	DICER1	FANCE	GEN1	IDH2	LZTR1	NEGR1	PIK3CD	RANBP2	SOCS1	TSC1
ARID5B	CD274	DIS3	FANCF	GID4	IFNGR1	MAGI2	NF1	PIK3CG	RARA	SOX10	TSC2
ASXL1	CD276	DNAJB1	FANCG	GLI1	IGF1	MALT1	NF2	PIK3R1	RASA1	SOX17	TSHR
ASXL2	CD74	DNMT1	FANCI	GNA11	IGF1R	MAP2K1	NFE2L2	PIK3R2	RB1	SOX2	U2AF1
ATM	CD79A	DNMT3A	FANCL	GNA13	IGF2	MAP2K2	NFKBIA	PIK3R3	RBM10	SOX9	VEGFA
ATR	CD79B	DNMT3B	FAS	GNAQ	IKBKE	MAP2K4	NKX2-1	PIM1	RECQL4	SPEN	VHL
ATRX	CDC73	DOT1L	FAT1	GNAS	IKZF1	MAP3K1	NKX3-1	PLCG2	REL	SPOP	VTCN1
AURKA	CDH1	E2F3	FBXW7	GPS2	IL10	MAP3K13	NOTCH1	PLK2	RET	SPTA1	WT1
AURKB	CDK12	EED	FGF1	GREM1	IL7R	MAP3K14	NOTCH2	PMAIP1	RHEB	SRC	XIAP
AXIN1	CDK4	EGFL7	FGF10	GRIN2A	INHA	MAP3K4	NOTCH3	PMS1	RHOA	SRSF2	XPO1
AXIN2	CDK6	EGFR	FGF14	GRM3	INHBA	MAPK1	NOTCH4	PMS2	RICTOR	STAG1	XRCC2
AXL	CDK8	EIF1AX	FGF19	GSK3B	INPP4A	MAPK3	NPM1	PNRC1	RIT1	STAG2	YAP1
B2M	CDKN1A	EIF4A2	FGF2	H1-2	INPP4B	MAX	NRAS	POLD1	RNF43	STAT3	YES1
BAP1	CDKN1B	EIF4E	FGF23	H2BC5	INSR	MCL1	NRG1	POLE	ROS1	STAT4	ZBTB2
BARD1	CDKN2A	ELOC	FGF3	H3-3A	IRF2	MDC1	NSD1	PPARG	RPS6KA4	STAT5A	ZBTB7A
BBC3	CDKN2B	EML4	FGF4	H3-3B	IRF4	MDM2	NTRK1	PPM1D	RPS6KB1	STAT5B	ZFHX3
BCL10	CDKN2C	EMSY	FGF5	H3-4	IRS1	MDM4	NTRK2	PPP2R1A	RPS6KB2	STK11	ZNF217
BCL2	CEBPA	EP300	FGF6	H3-5	IRS2	MED12	NTRK3	PPP2R2A	RPTOR	STK40	ZNF703
BCL2L1	CENPA	EPCAM	FGF7	H3C1	JAK1	MEF2B	NUP93	PPP6C	RUNX1	SUFU	ZRSR2
BCL2L11	CHD2	EPHA3	FGF8	H3C10	JAK2	MEN1	NUTM1	PRDM1	RUNX1T1	SUZ12	
BCL2L2	CHD4	EPHA5	FGF9	H3C11	JAK3	MET	PAK1	PREX2	RYBP	SYK	
BCL6	CHEK1	EPHA7	FGFR1	H3C12	JUN	MGA	PAK3	PRKAR1A	SDHA	TAF1	
BCOR	CHEK2	EPHB1	FGFR2	H3C13	KAT6A	MITF	PAK5	PRKCI	SDHAF2	TBX3	
BCORL1	CIC	ERBB2	FGFR3	H3C14	KDM5A	MLH1	PALB2	PRKDC	SDHB	TCF3	

DNA-Sequencing of 59 genes for the detection of copy gain and 4 genes for copy loss (ATM, BRCA1, BRCA2, 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 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
VSIR	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)