PATIENT

DIAGNOSIS C34.90, Malignant neoplasm of unsp part of unsp bronchus or lung; Stage IV
NAME
DOB SE
MRN
ORDER ID
REPORT DATE

SPECIMEN

FACILITY
ID
SOURCE
COLLECTION DATE
RECEIVED DATE

CLIENT

ORDERING PROVIDER
ORDERING PROVIDER
PROVIDER FACILITY

ORDERING FACILIT

OmniSeq Clinical Support

For questions or to discuss results:
1-800-781-1259
OMS-Support@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 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)

SNV /Indel	**EGFR E746_A750del (exon 19 del)** TP53 R175G
Fusion	No positive findings
Copy Gain	AKT2 gain **ERBB2 gain**
Copy Loss	No positive findings

See APPENDIX for variants of unknown significance (VUS)

Signatures

Tumor Mutational Burden (TMB): 10.1 mut/Mb (High)

Microsatellite Instability (MSI): MS-Stable

Immune Markers

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

Immune Gene Expression by RNA Sequencing in Clinical Trials:
BTLA, CTLA4, NY-ESO-1, TGFB1, TLR9, VISTA

HLA CLass I:

A*24:02, 11:01	B*46:01, 40:10	C*01:02, 04:03

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

ALK G1202R	EGFR exon 19 ins	MET gain
ALK fusion	EGFR exon 20 ins	NTRK1/2/3 fusion
BRAF V600E	HER2 (ERBB2) mut	RET fusion
EGFR (L858R, S768I, L861Q, Codon 719)	KRAS mut	ROS1 fusion
EGFR T790M	MET exon 14 skip	

COMMENTS

Pathologist
No pathologist comments.

Testing
All testing was completed.

Potential Germline Variants
Consider genetic counseling if an inherited cancer syndrome is suspected
TP53 R175G

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 APPENDIX: Genomic Variant Clinical Significance Classification)*

CLINICALLY SIGNIFICANT MARKERS

Clinical Benefit in this Patient's Tumor Type			Sources
EGFR E746_A750del	afatinib, dacomitinib, erlotinib + ramucirumab, gefitinib, osimertinib	First line	FDA (Approved), NCCN
	erlotinib	Metastatic	FDA (Approved), NCCN
	afatinib + cetuximab	Subsequent line	NCCN
TMB (High)	pembrolizumab	Subsequent line, and no satisfactory alternative therapy	FDA (Approved)
Resistance/Decreased Response in this Patient's Tumor Type			**Sources**
ERBB2 gain	afatinib, dacomitinib, erlotinib, gefitinib, osimertinib	Per NCCN, resistance to EGFR TKIs can be mediated by ERBB2 amplification.	NCCN

MARKERS WITH POTENTIAL CLINICAL SIGNIFICANCE

Emerging Clinical Benefit in this Patient's Tumor Type			Sources
EGFR E746_A750del	patritumab deruxtecan	Metastatic	FDA (Breakthrough Therapy)
	osimertinib + quaratusugene ozeplasmid	Subsequent line	FDA (Fast Track)
Clinical Benefit in Other Tumor Types			
ERBB2 gain	ado-trastuzumab emtansine	Breast Carcinoma, Malignant Salivary Gland Neoplasm	
	lapatinib + capecitabine, margetuximab + chemotherapy, neratinib + capecitabine, pertuzumab + trastuzumab +/- (paclitaxel or docetaxel), pertuzumab/trastuzumab /hyaluronidase, trastuzumab + tucatinib + capecitabine, trastuzumab +/- chemotherapy, trastuzumab/hyaluronidase	Breast Carcinoma	

	pembrolizumab + trastuzumab + fluoropyrimidine + platinum chemotherapy, trastuzumab + chemotherapy	Adenocarcinoma of the Gastroesophageal Junction, Esophageal Adenocarcinoma, Gastric Adenocarcinoma
	fam-trastuzumab deruxtecan	Adenocarcinoma of the Gastroesophageal Junction, Breast Carcinoma, Colorectal Carcinoma, Esophageal Adenocarcinoma, Gastric Adenocarcinoma, Malignant Salivary Gland Neoplasm
	pertuzumab + trastuzumab	Biliary Tract Carcinoma, Colorectal Carcinoma, Malignant Salivary Gland Neoplasm
	lapatinib + trastuzumab	Breast Carcinoma, Colorectal Carcinoma
	trastuzumab + carboplatin + paclitaxel	Endometrial Serous Adenocarcinoma
	trastuzumab +/- docetaxel	Malignant Salivary Gland Neoplasm
TMB (High)	ipilimumab + nivolumab	Bone Osteosarcoma, Chondrosarcoma, Chordoma, Ewing Sarcoma of Bone
	nivolumab	Diffuse Glioma

Clinical Trial Markers for this Patient

AKT2 gain *2 clinical trials*	BTLA (RNA-Seq) High *1 clinical trial*	CTLA4 (RNA-Seq) High *3 clinical trials*	EGFR E746_A750del *30 clinical trials*	ERBB2 gain *14 clinical trials*
MS-Stable *1 clinical trial*	NY-ESO-1 (RNA-Seq) positive *2 clinical trials*	PD-L1 IHC (22C3) Negative *1 clinical trial*	TGFB1 (RNA-Seq) High *2 clinical trials*	TLR9 (RNA-Seq) High *1 clinical trial*
TMB (High) *4 clinical trials*	VISTA (RNA-Seq) High *1 clinical trial*			

Genomic Variants with No Matched Therapies

No approved therapies or clinical trials identified for this patient

TP53 R175G

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), and immune gene expression profiling. Sequencing for mutations includes full coding exonic regions and intron/exon junctions.

Mutations

Gene	Alteration	Location	VAF	ClinVar	Transcript ID	Type	Pathway
EGFR	c.2235_2249del p.E746_A750del	exon 19	56.8%	drug response	NM_005228.3	Deletion - In frame	Receptor tyrosine kinase /growth factor signaling

EGFR (HER1), epidermal growth factor receptor, is a tyrosine kinase receptor oncogene, which activates RAS/RAF/MEK and PI3K/AKT/mTOR pathways. Additionally, EGFR activation induces cell growth and proliferation, and EGFR inhibition leads to proliferation arrest and apoptosis (PMID: 24312144 ; PMID: 24651011). Germline mutations in EGFR may be associated with increased susceptibility to certain cancers (PMID: 24736080 , PMID: 30225213). EGFR E746_A750del results in the deletion of five amino acids in the protein kinase domain of the Egfr protein from amino acids 746 to 750 (UniProt.org). E746_A750del results in increased Egfr kinase activity, activation of p44/42 MAPK and AKT in cell culture, promotes tumor growth in xenograft models (PMID: 16373402 , PMID: 16912195), and is transforming in cell culture (PMID: 29533785).

Gene	Alteration	Location	VAF	ClinVar	Transcript ID	Type	Pathway
TP53	c.523C>G p.R175G	exon 5	67.7%	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 R175G is a hotspot mutation that lies within the DNA-binding domain of the Tp53 protein (PMID: 22713868). R175G results in decreased Tp53 transactivation activity in cell culture (PMID: 28369373), and therefore, is predicted to result in a loss of Tp53 protein function.

Copy Number Alterations

Gene	Alteration	Location	Fold Change /Copy Number	Transcript ID	Pathway
AKT2	gain	chr19	13.437/51.7	NM_001626.4	PI3K/AKT1/MTOR

AKT2, RAC-beta serine/threonine-protein kinase, is highly expressed in muscle and adipocytes and contributes to insulin-mediated regulation of glucose homeostasis (PMID: 21620960). In addition AKT2 regulates a number of cell functions, including proliferation, survival, growth, angiogenesis, and metabolism through PI3K signaling (PMID: 28557977).

Gene	Alteration	Location	Fold Change /Copy Number	Transcript ID	Pathway
ERBB2	gain	chr17	17.241/67.0	NM_004448.2	Receptor tyrosine kinase/growth factor signaling

ERBB2 (HER2), erb-b2 receptor tyrosine kinase 2, is an EGFR receptor tyrosine kinase family and an oncogene through heterodimerization with other EGFR family members (PMID: 29209536). Additionally, ERBB2 activates PI3K-AKT-mTOR and RAS-RAF-MEK-ERK pathways, therefore regulating growth and transformation (PMID: 17471238).

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 10.1 mut/Mb (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	59
CD27	76
CD28	72
CD40	33
CD40LG	76
CD80	61
CD86	35
GITR	37
GZMB	90
ICOS	73
ICOSLG	21
IFNG	67
OX-40L	46
OX40	53
TBX21	96

T-cell trafficking

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

Marker	% Rank
CXCL10	33
CXCR6	50
DDX58	28
GATA3	43
IL10	35
IL1B	48
MX1	37
STAT1	21
TGFB1	83
TLR7	49
TLR8	66
TLR9	80
TNF	48

T-cell infiltration

Expression of immune activation within the tumor microenvironment

Marker	% Rank
CD2	72
CD20	93
CD3	71
CD4	36
CD8	48
FOXP3	63
KLRD1	91
SLAMF4	89

T-cell recognition

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

Marker	% Rank
BTLA	94
CTLA4	81
LAG3	35
NECTIN2	8
PD-1	69
PD-L1	40
PD-L2	31
PVR	4
TIGIT	72
TIM3	46
TNFRSF14	41
VISTA	79

Killing cancer cells

Inhibit activated T-cells from killing cancer cells

Marker	% Rank
ADORA2A	46
CCL2	56
CCR2	71
CD163	22
CD38	60
CD39	22
CD68	60
CSF1R	13
CXCR2	97
IDO1	36

Cancer testis antigens

Immunogenic tumor antigens

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

Immunotherapy Targets by RNA Sequencing with Clinical Trials *Genes associated with immunomodulatory agents, adoptive cell therapies, vaccines, oncolytic viruses and targeted antibodies*	
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).
CTLA4 (RNA-Seq) High	CTLA4 (CD152), cytotoxic T-lymphocyte-associated protein 4, is a negative regulator of T-cell activation that is constitutively expressed on Tregs and upregulated upon T-cell receptor (TCR) signaling to compete with the co-stimulatory molecule, CD28, for binding to CD80 and CD86 (PMID: 27249753; PMID: 30565239, PMID: 28102259). Additionally, immune checkpoint inhibitor blockade of CTLA4 is an important component of anti-tumor immunotherapies (PMID: 23748107; PMID: 26325034).
NY-ESO-1 (RNA-Seq) positive	CTAG1B (NY-ESO-1), cancer/testis antigen 1B, encodes for a cancer testis antigen that is normally expressed on male germ cells and may play a role in the regulation of gene expression (PMID: 15715909 ; PMID: 22936067).
TGFB1 (RNA-Seq) High	TGFB1, transforming growth factor beta 1, is a secreted cytokine that regulates cell growth, proliferation, differentiation, and apoptosis (PMID: 3861940). Additionally, TGFB induces the epithelial mesenchymal transition (EMT) and of myofibroblast differentiation which is important for normal tissue repair (PMID: 30696809).
TLR9 (RNA-Seq) High	TLR9, toll like receptor 9, is part of a family of receptors in innate immunity that play an important role in the initiation of host defense. Additionally, TLR9 recognizes CpG motifs that exist in both viral and bacterial DNA, along with stimulation of immune cells to confer defense against pathogens (PMID: 17932028; PMID: 31054156).
VISTA (RNA-Seq) High	VSIR (VISTA; C10orf54), V-set immunoregulatory receptor, is a member of the B7-family that shares homology with PD-L1 and PD-L2 (PMID: 30382166). Additionally, VSIR is an immune checkpoint blockade that suppresses T-cell activation when expressed as a ligand on APCs or a receptor on T-cells (PMID: 31781843).

Human Leukocyte Antigen (HLA) Class I Genotype		
A*24:02, 11:01	B*46:01, 40:10	C*01:02, 04:03

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 12/21/2022 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

EGFR E746_A750del

afatinib	FDA APPROVED, NCCN RECOMMENDED: FDA approved for first-line treatment of metastatic NSCLC with non-resistant EGFR mutations. NCCN recommended as Category 1/Other recommended intervention (for L858R/exon 19 del) or Category 2A/Preferred intervention (for other sensitizing mutations). CLINICAL SIGNIFICANCE (IA): The FDA approval for afatinib was supported by data from the open-label, randomized, phase-III trial LUX-Lung 3 (NCT00949650). LUX-Lung 3 demonstrated that first-line afatinib (n = 170), compared with pemetrexed and cisplatin (n = 115), improved median PFS (HR = 0.28; 13.7 mo. vs. 5.6 mo.) and median OS (HR = 0.55; 33.3 mo. vs. 21.1 mo.) in patients with metastatic NSCLC with EGFR exon 19 deletion.
dacomitinib	FDA APPROVED, NCCN RECOMMENDED: FDA approved for the first-line treatment of metastatic NSCLC with EGFR exon 19 deletion or exon 21 L858R substitution mutations. NCCN recommended as Category 1/Other recommended intervention. CLINICAL SIGNIFICANCE (IA): In a Phase III trial (ARCHER 1050) that supported FDA approval, treatment with Vizimpro (dacomitinib) as first-line therapy in patients with non-small cell lung cancer harboring an EGFR exon 19 deletion or EGFR L858R resulted in an improved median progression-free survival (mPFS) of 14.7 months compared to 9.2 months with Iressa (gefitinib), with a mPFS of 12.3 months with dacomitnib vs. 9.8 months with Iressa (gefitinib) among patients with EGFR exon 19 deletions (PMID: 28958502; NCT01777421).
erlotinib + ramucirumab	FDA APPROVED, NCCN RECOMMENDED: FDA approved for the first-line treatment of metastatic NSCLC with EGFR exon 19 deletions or exon 21 (L858R) substitution mutations. NCCN recommended as Category 2A/Other recommended intervention. CLINICAL SIGNIFICANCE (IA): In a Phase III trial (RELAY), Cyramza (ramucirumab) in combination with Tarceva (erlotinib) demonstrated improved progression-free survival compared to Tarceva (erlotinib) plus placebo (19.4 vs 12.4 months, HR=0.59, p<0.0001) in patients with advanced non-small cell lung cancer harboring EGFR exon 19 deletion mutations or L858R (PMID: 31591063; NCT02411448).
gefitinib	FDA APPROVED, NCCN RECOMMENDED: FDA approved for the first-line treatment of metastatic NSCLC with EGFR exon 19 deletions or exon 21 (L858R) substitution mutations. NCCN recommended as Category 1/Other recommended intervention. CLINICAL SIGNIFICANCE (IA): The FDA approval for gefitinib was supported by two trials: IPASS Study 1 and IPASS Study 2 (NCT00322452; PMID: 19692680). Data from the single-arm, open-label phase-III trial IPASS Study 1 demonstrated that first-line gefitinib had an ORR of 50% (n = 106; CR, 0.9%; PR, 49%) in patients with metastatic NSCLC with EGFR Exon 19 Deletion or EGFR L858R. The secondary endpoint was median DOR (6.0 mo.). Data from the open-label, randomized, phase-III trial IPASS Study 2 demonstrated that first-line gefitinib, compared with carboplatin + paclitaxel, improved median PFS (HR = 0.54; 10.9 mo. vs. 7.4 mo.) and had a better ORR (67% (n = 88) vs. 41% (n = 98)) in patients with metastatic Lung Adenocarcinoma with EGFR Exon 19 Deletion or EGFR L858R.
osimertinib	FDA APPROVED, NCCN RECOMMENDED: FDA approved for the first-line treatment of metastatic NSCLC with EGFR exon 19 deletion or exon 21 L858R mutations. NCCN recommended as Category 1/Preferred intervention. CLINICAL SIGNIFICANCE (IA): In a Phase III (FLAURA) trial that supported FDA approval, treatment with Tagrisso (osimertinib) resulted in a longer median progression-free survival compared to treatment with either Tarceva (erlotinib) or Iressa (gefitinib) (18.9 mo vs 10.2 mo) in previously untreated non-small cell lung cancer patients harboring either EGFR L858R or EGFR exon 19 deletion (PMID: 29151359; NCT02296125).

erlotinib	FDA APPROVED, NCCN RECOMMENDED: FDA approved for metastatic NSCLC with EGFR exon 19 deletions or exon 21 (L858R) substitution mutations receiving first-line, maintenance, or second or greater line treatment after progression following at least one prior chemotherapy regimen. NCCN recommended as first line therapy (Category 1/Other recommended intervention). CLINICAL SIGNIFICANCE (IA): The FDA approval for erlotinib was supported by data from the open-label, phase-III trial EURTAC (ML20650; PMID: 22285168). EURTAC demonstrated that first-line erlotinib, compared with (carboplatin or cisplatin) + (docetaxel or gemcitabine), improved median PFS (HR = 0.34; p < 0.001; 10.4 mo. vs. 5.2 mo.; no. of events, 83% (71/86) vs. 72% (63/88)) in patients with metastatic NSCLC with EGFR Exon 19 Deletion or EGFR L858R. Secondary endpoints were OS (HR = 0.93) and ORR (65% vs. 16%).
afatinib + cetuximab	NCCN RECOMMENDED: Per NCCN, may be considered after progression on on EGFR TKIs. CLINICAL SIGNIFICANCE (IA): In a Phase Ib trial, Gilotrif (afatinib) and Erbitux (cetuximab) combination treatment in EGFR-mutant non-small cell lung cancer patients (62% exon 19 del 48/126), 33% L858R (41/126)) with erlotinib or gefitinib resistance resulted in an overall response rate of 29% (37/126; all partial responses), stable disease in 41% (52/126), median duration of response of 5.7 mo for all patients and 9.8 mo for patients without EGFR T790M, and a median progression-free survival of 4.7 mo (PMID: 25074459; NCT01090011).
patritumab deruxtecan	PATRITUMAB DERUXTECAN Patritumab deruxtecan (U3-1402) is an antibody-drug conjugate (ADC) comprised of an ERBB3 (HER3) antibody and Exatecan, which once internalized may result in apoptotic cell death (Journal of Thoracic Oncology, 12;11S2, 2017, PMID: 31395690, PMID: 31661465, PMID: 31471314). CLINICAL SIGNIFICANCE (IIC): FDA Breakthrough Therapy. Marker is in clinical trial inclusion criteria. NCT05338970 — HERTHENA-Lung02: A Study of Patritumab Deruxtecan Versus Platinum-based Chemotherapy in Metastatic or Locally Advanced EGFRm NSCLC After Failure of EGFR TKI Therapy — Phase 3 — La Jolla, CA NCT03260491 — U3-1402 in Metastatic or Unresectable Non-Small Cell Lung Cancer — Phase 1 — Duarte, CA
osimertinib + quaratusugene ozeplasmid	QUARATUSUGENE OZEPLASMID Quaratusugene Ozeplasmid is a complex of liposomal nanoparticles with a plasmid expression cassette encoding the human FUS1 protein, which may lead to induction of tumor cell apoptosis and suppression of tumor cell proliferation (PMID: 15486560). CLINICAL SIGNIFICANCE (IIC): FDA Fast Track. Marker is in clinical trial inclusion criteria. NCT04486833 — Quaratusugene Ozeplasmid (Reqorsa) and Osimertinib in Patients With Advanced Lung Cancer Who Progressed on Osimertinib — Phase 1 /Phase 2 — Los Angeles, CA
osimertinib + stereotactic body radiation therapy	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria. NCT03833154 — Durvalumab vs Placebo With Stereotactic Body Radiation Therapy in Early Stage Unresected Non-small Cell Lung Cancer (NSCLC) Patients / Osimertinib Following SBRT in Patients With Early Stage Unresected NSCLC Harboring an EGFR Mutation — Phase 3 — San Diego, CA
alvocidib + lazertinib	LAZERTINIB Lazertinib (YH25448) is an irreversible protein kinase inhibitor with selective activity against mutant EGFR, which may lead to growth inhibition of EGFR-mutant tumor cells and reduced toxicity (PMID: 30670498, PMID: 32599977). ALVOCIDIB Alvocidib (flavopiridol) is an inhibitor of CDK1, CDK2, CDK4, CDK6, CDK7, and CDK9, which may induce cell cycle arrest and apoptosis in cancer cells (PMID: 12165651, PMID: 8674031, PMID: 24470357). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria. NCT05388669 — A Study of Lazertinib With Subcutaneous Amivantamab Compared With Intravenous Amivantamab in Participants With Epidermal Growth Factor Receptor (EGFR)-Mutated Advanced or Metastatic Non-small Cell Lung Cancer — Phase 3 — La Jolla, CA

amivantamab + lazertinib + recombinant human hyaluronidase	LAZERTINIB Lazertinib (YH25448) is an irreversible protein kinase inhibitor with selective activity against mutant EGFR, which may lead to growth inhibition of EGFR-mutant tumor cells and reduced toxicity (PMID: 30670498, PMID: 32599977). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05388669	A Study of Lazertinib With Subcutaneous Amivantamab Compared With Intravenous Amivantamab in Participants With Epidermal Growth Factor Receptor (EGFR)-Mutated Advanced or Metastatic Non-small Cell Lung Cancer	Phase 3 — La Jolla, CA
	NCT04606381	A Study of Amivantamab Subcutaneous (SC) Administration for the Treatment of Advanced Solid Malignancies	Phase 1 — West Hollywood, CA
osimertinib + savolitinib	SAVOLITINIB Savolitinib (AZD6094) is a selective MET inhibitor, which inhibits MET kinase activity, resulting in decreased downstream signaling, and may inhibit growth of MET-expressing tumors (PMID: 25248999, PMID: 32027846, PMID: 30952639). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05261399	Savolitinib Plus Osimertinib Versus Platinum-based Doublet Chemotherapy in Participants With Non-Small Cell Lung Cancer Who Have Progressed on Osimertinib Treatment	Phase 3 — La Jolla, CA
	NCT03944772	Phase 2 Platform Study in Patients With Advanced Non-Small Lung Cancer Who Progressed on First-Line Osimertinib Therapy (ORCHARD)	Phase 2 — La Jolla, CA
	NCT03778229	Osimertinib Plus Savolitinib in EGFRm+/MET+ NSCLC Following Prior Osimertinib	Phase 2 — La Jolla, CA
amivantamab + carboplatin + pemetrexed	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT04988295	A Study of Amivantamab and Lazertinib in Combination With Platinum-Based Chemotherapy Compared With Platinum-Based Chemotherapy in Patients With Epidermal Growth Factor Receptor (EGFR)-Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer After Osimertinib Failure	Phase 3 — Orange, CA
amivantamab + lazertinib + carboplatin + pemetrexed	LAZERTINIB Lazertinib (YH25448) is an irreversible protein kinase inhibitor with selective activity against mutant EGFR, which may lead to growth inhibition of EGFR-mutant tumor cells and reduced toxicity (PMID: 30670498, PMID: 32599977). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT04988295	A Study of Amivantamab and Lazertinib in Combination With Platinum-Based Chemotherapy Compared With Platinum-Based Chemotherapy in Patients With Epidermal Growth Factor Receptor (EGFR)-Mutated Locally Advanced or Metastatic Non-Small Cell Lung Cancer After Osimertinib Failure	Phase 3 — Orange, CA
	NCT05498428	A Study of Amivantamab in Participants With Advanced or Metastatic Solid Tumors Including Epidermal Growth Factor Receptor (EGFR)-Mutated Non-Small Cell Lung Cancer	Phase 2 — Orange, CA
	NCT04077463	A Study of Lazertinib as Monotherapy or in Combination With Amivantamab in Participants With Advanced Non-small Cell Lung Cancer	Phase 1 — Orange, CA
abemaciclib + osimertinib	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT04545710	Osimertinib and Abemaciclib in EGFR Mutant Non-Small Cell Lung Cancer After Osimertinib Resistance	Phase 2 — La Jolla, CA

alectinib + osimertinib; durvalumab + carboplatin + pemetrexed; gefitinib + osimertinib; necitumumab + osimertinib; osimertinib + pemetrexed + (carboplatin or cisplatin); osimertinib + selpercatinib	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT03944772	Phase 2 Platform Study in Patients With Advanced Non-Small Lung Cancer Who Progressed on First-Line Osimertinib Therapy (ORCHARD)	Phase 2	La Jolla, CA
datopotamab deruxtecan + osimertinib	DATOPOTAMAB DERUXTECAN Datopotamab Deruxtecan (DS-1062a) is an antibody-drug conjugate comprising an antibody that targets TROP2 linked to the topoisomerase I inhibitor DXd, which may induce apoptosis and inhibit tumor growth (PMID: 34413126). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT03944772	Phase 2 Platform Study in Patients With Advanced Non-Small Lung Cancer Who Progressed on First-Line Osimertinib Therapy (ORCHARD)	Phase 2	La Jolla, CA
osimertinib + selumetinib	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria. In a Phase Ib trial (TATTON), Tagrisso (osimertinib) and Selumetinib (AZD6244) combination therapy resulted in partial response in 42% (15/36) and stable disease in 39% (14/36) of patients with EGFR-mutant non-small cell lung cancer in the dose-finding arm, and partial response in 34% (16/47) and stable disease in 23% (11/47) of patients in the dose expansion arm (AACR Annual Meeting 2019, Abstract CT034).			
	NCT03944772	Phase 2 Platform Study in Patients With Advanced Non-Small Lung Cancer Who Progressed on First-Line Osimertinib Therapy (ORCHARD)	Phase 2	La Jolla, CA
sunvozertinib	SUNVOZERTINIB Sunvozertinib (DZD9008) is an irreversible EGFR inhibitor that preferentially inhibits mutant EGFR and ERBB2 (HER2), which may lead to growth inhibition of tumor cells with EGFR activation (AACR Annual Meeting 2019, Abstract 3081, PMID: 35404393). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT03974022	Assessing an Oral EGFR Inhibitor, DZD9008 in Patients Who Have Advanced Non-small Cell Lung Cancer With EGFR or HER2 Mutation (WU-KONG1)	Phase 1 /Phase 2	La Jolla, CA
EMB-01 + osimertinib	EMB-01 EMB-01 is a bispecific antibody against EGFR and MET, which prevents tumor cell proliferation (NCI Drug Dictionary). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05498389	EMB-01 in Combination With Osimertinib in Patients With EGFR Mutant Lung Cancer	Phase 1 /Phase 2	Orange, CA
ERAS-007 + osimertinib	ERAS-007 ERAS-007 (ASN007) is a small molecule that inhibits ERK1/2, which may result in decreased tumor cell proliferation and reduced tumor growth (PMID: 34337566). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04959981	A Study of Anti-Cancer Therapies Targeting the MAPK Pathway in Patients With Advanced NSCLC	Phase 1 /Phase 2	Orange, CA

amivantamab + lazertinib	LAZERTINIB Lazertinib (YH25448) is an irreversible protein kinase inhibitor with selective activity against mutant EGFR, which may lead to growth inhibition of EGFR-mutant tumor cells and reduced toxicity (PMID: 30670498, PMID: 32599977). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05498428	A Study of Amivantamab in Participants With Advanced or Metastatic Solid Tumors Including Epidermal Growth Factor Receptor (EGFR)-Mutated Non-Small Cell Lung Cancer	Phase 2	Orange, CA
	NCT02609776	Study of Amivantamab, a Human Bispecific EGFR and cMet Antibody, in Participants With Advanced Non-Small Cell Lung Cancer	Phase 1	La Jolla, CA
	NCT04077463	A Study of Lazertinib as Monotherapy or in Combination With Amivantamab in Participants With Advanced Non-small Cell Lung Cancer	Phase 1	Orange, CA
	NCT04606381	A Study of Amivantamab Subcutaneous (SC) Administration for the Treatment of Advanced Solid Malignancies	Phase 1	West Hollywood, CA
poziotinib	POZIOTINIB Poziotinib (HM781-36B) is a pan-ErbB inhibitor that inhibits EGFR, ERBB2 (HER2) and ERBB4 (HER4), thereby reducing proliferation of tumor cells that overexpress these receptors (PMID: 21306821, PMID: 31588020). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT03318939	Phase 2 Study of Poziotinib in Patients With NSCLC Having EGFR or HER2 Exon 20 Insertion Mutation	Phase 2	Long Beach, CA
ONC-392	ONC-392 ONC-392 is a pH-sensitive monoclonal antibody that targets CTLA4 (CD152), potentially resulting in antitumor activity (Journal for ImmunoTherapy of Cancer 2022;10). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04140526	Safety, PK and Efficacy of ONC-392 in Monotherapy and in Combination of Anti-PD-1 in Advanced Solid Tumors and NSCLC	Phase 1 /Phase 2	Downey, CA
AFM24	AFM24 AFM24 is a bispecific antibody that targets EGFR and CD16A, which may result in an anti-tumor immune response against tumor cells expressing Egfr (Cancer Res 2022;82(12_Suppl):Abstract nr CT149, PMID: 34325617). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04259450	Study to Assess AFM24 in Advanced Solid Cancers	Phase 1 /Phase 2	Los Angeles, CA
necitumumab + osimertinib + trastuzumab	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04285671	Necitumumab and Trastuzumab in Combination With Osimertinib for the Treatment of Refractory Epidermal Growth Factor Receptor (EGFR)-Mutated Stage IV Non-small Cell Lung Cancer	Phase 1 /Phase 2	Los Angeles, CA
HBI-2376	HBI-2376 HBI-2376 inhibits SHP2, potentially leading to decreased tumor cell proliferation and inhibition of tumor growth (Cancer Res 2022;82(12_Suppl):Abstract nr 1041). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05163028	A Dose Escalation Study of SHP2 Inhibitor in Patients With Solid Tumors Harboring KRAS of EGFR Mutations	Phase 1	Encinitas, CA
lazertinib	LAZERTINIB Lazertinib (YH25448) is an irreversible protein kinase inhibitor with selective activity against mutant EGFR, which may lead to growth inhibition of EGFR-mutant tumor cells and reduced toxicity (PMID: 30670498, PMID: 32599977). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria. In a Phase I/II trial, Lazertinib (YH25448) demonstrated safety and preliminary efficacy, resulted in objective response in 54% (69/127, 3 complete response, 66 partial response) and disease control in 87% (110/127) of patients with advanced non-small cell lung cancer harboring EGFR exon 19 deletion or L858R, with a median duration of response of 15.2 months and median progression-free survival of 9.5 months (PMID: 31587882; NCT03046992).			
	NCT04077463	A Study of Lazertinib as Monotherapy or in Combination With Amivantamab in Participants With Advanced Non-small Cell Lung Cancer	Phase 1	Orange, CA

BAY2927088	BAY2927088 BAY2927088 is a mutant-selective ERBB2 (HER2) and EGFR inhibitor with activity against EGFR and ERBB2 (HER2) exon 20 insertions, which decreases downstream signaling potentially resulting in reduced tumor growth (NCI Drug Dictionary). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05099172	First in Human Study of BAY2927088 in Participants Who Have Advanced Non-small Cell Lung Cancer (NSCLC) With Mutations in the Genes of Epidermal Growth Factor Receptor (EGFR) and/or Human Epidermal Growth Factor Receptor 2 (HER2)	Phase 1 Duarte, CA
BBP-398	BBP-398 Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT04528836	First-in-Human Study of the SHP2 Inhibitor BBP-398 in Patients With Advanced Solid Tumors	Phase 1 Duarte, CA
NX-019	NX-019 Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05514496	A Study of NX-019 in Patients With Advanced, Epidermal Growth Factor Receptor (EGFR) Mutant Cancer	Phase 1 Duarte, CA
osimertinib + telisotuzumab vedotin	TELISOTUZUMAB VEDOTIN Telisotuzumab vedotin (ABBV-399) is an antibody-drug conjugate comprising a MET-targeted antibody linked to MMAE, which delivers the cytotoxic agent to MET expressing tumor cells, resulting in cell death (PMID: 27573171, PMID: 32127466). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT02099058	A Study Evaluating the Safety, Pharmacokinetics (PK), and Preliminary Efficacy of ABBV-399 in Participants With Advanced Solid Tumors	Phase 1 Duarte, CA
osimertinib + triptolide analog	TRIPTOLIDE ANALOG Minnelide is a water-soluble prodrug of the naturally derived diterpene triepoxide, triptolide, which induces apoptosis and inhibits cell proliferation, leading to reduced tumor growth (PMID: 28192510, PMID: 32733649). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05166616	Minnelide and Osimertinib for the Treatment of Advanced EGFR Mutated Non-Small Cell Lung Cancer	Phase 1 Duarte, CA
alflutinib	ALFLUTINIB Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05364073	Study of Furmonertinib in Patients With Advanced or Metastatic Non-Small Cell Lung Cancer With Activating EGFR or HER2 Mutations	Phase 1 Glendale, CA
ZZ06	ZZ06 Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT04412616	ZZ06 in Adult Patients With Advanced EGFR Positive Solid Tumor Malignancies	Phase 1 Los Angeles, CA
carotuximab + osimertinib	CAROTUXIMAB Carotuximab (TRC105) is a monoclonal antibody that binds to endoglin (CD105), a TGF beta-1 accessory receptor highly expressed on tumor vessel endothelial cells, blocking signaling essential for angiogenesis and potentially decreasing proliferation of tumor cells (PMID: 28465443). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT05401110	Study of Osimertinib With Carotuximab in Advanced, EGFR-mutated Non-Small Cell Lung Cancer	Phase 1 Los Angeles, CA
ERBB2 gain			
afatinib	NCCN UNCERTAIN BENEFIT: Per NCCN, resistance to EGFR TKIs can be mediated by ERBB2 amplification. CLINICAL SIGNIFICANCE (IA): Marker is in an FDA approval or professional guideline.		

dacomitinib	NCCN UNCERTAIN BENEFIT: Per NCCN, resistance to EGFR TKIs can be mediated by ERBB2 amplification. CLINICAL SIGNIFICANCE (IA): In a Phase II trial, Vizimpro (dacomitinib) treatment resulted in an overall response rate of 0% (0/4) in patients with lung adenocarcinoma harboring ERBB2 (HER2) amplification (PMID: 25899785; NCT00818441).
erlotinib	NCCN UNCERTAIN BENEFIT: Per NCCN, resistance to EGFR TKIs can be mediated by ERBB2 amplification. CLINICAL SIGNIFICANCE (IA): The NCCN guideline for resistance to erlotinib was supported by a clinical sequencing study (PMID: 29530932). Data from the study demonstrated that erlotinib had a shorter TTP (HR = 2.4; p = 0.018; 6 mo. vs 11 mo.) in patients with metastatic NSCLC with ERBB2 Amplification. Secondary endpoint was OS (no diff.).
gefitinib	NCCN UNCERTAIN BENEFIT: Per NCCN, resistance to EGFR TKIs can be mediated by ERBB2 amplification. CLINICAL SIGNIFICANCE (IA): In a preclinical study, a lung squamous cell carcinoma cell line with ERBB2 (HER2) amplification demonstrated resistance to treatment with Iressa (gefitinib) in culture (PMID: 26545934).
osimertinib	NCCN UNCERTAIN BENEFIT: Per NCCN, resistance to EGFR TKIs can be mediated by ERBB2 amplification. CLINICAL SIGNIFICANCE (IA): The NCCN guideline for resistance to ositerimb was supported by a clinical sequencing study (PMID: 29530932). Data from the study demonstrated that osimertinib had a shorter TTP (HR = 2.4; p = 0.018; 6 mo. vs 11 mo.) in patients with metastatic NSCLC with ERBB2 Amplification. Secondary endpoint was OS (no diff.).
pembrolizumab + trastuzumab + fluoropyrimidine + platinum chemotherapy	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.
pertuzumab + trastuzumab +/- (paclitaxel or docetaxel)	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.
trastuzumab + chemotherapy	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.
ado-trastuzumab emtansine	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. In a Phase II (MATCH) trial, Kadcyla (trastuzumab emtansine) treatment resulted in partial response in 8.1% (3/37) and stable disease in 43% (16/37) of patients with ERBB2 (HER2) amplified non-breast, non-gastric advanced solid tumors, with a 6-month progression-free survival rate of 24.8% (J Clin Oncol 36, 2018 (suppl; abstr 100); NCT02465060). In a Phase II trial, Kadcyla (ado-trastuzumab emtansine) treatment in lung cancer patients harboring ERBB2 (HER2) activating mutations and/or ERBB2 (HER2) amplification resulted in a RECIST overall response rate of 51% (25/49) and a median progression-free survival of 5 months, with a RECIST response rate of 55% (6/11) for patients with ERBB2 (HER2) amplification (PMID: 32213539; NCT02675829).
pertuzumab/trastuzumab /hyaluronidase	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.
trastuzumab +/- chemotherapy	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.
trastuzumab /hyaluronidase	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.

fam-trastuzumab deruxtecan	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. Marker is in clinical trial inclusion criteria.			
	NCT04686305	Phase Ib Study of the Safety of T-DXd and Durvalumab With Chemotherapy in Advanced or Metastatic HER2+ Non-squamous NSCLC	Phase 1	Orange, CA
lapatinib + capecitabine	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.			
margetuximab + chemotherapy	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.			
neratinib + capecitabine	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.			
trastuzumab + tucatinib + capecitabine	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.			
lapatinib + trastuzumab	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.			
pertuzumab + trastuzumab	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. In a Phase II trial (MyPathway), Herceptin (trastuzumab) and Perjeta (pertuzumab) combination treatment resulted in objective response in 13% (2/16, all partial response) and stable disease lasting over 120 days in 13% (2/16) of patients with non-small cell lung cancer harboring ERBB2 (HER2) amplification or overexpression (PMID: 29320312; NCT02091141).			
trastuzumab + carboplatin + paclitaxel	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.			
trastuzumab +/- docetaxel	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.			
DF1001; DF1001 + nab-paclitaxel; DF1001 + nivolumab	DF1001 DF1001 is a natural killer (NK) cell engager therapy consisting of a trispecific antibody that targets ERBB2 and NK receptors, potentially resulting in increased anti-tumor immune response (PMID: 32054397, PMID: 32934330). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04143711	Study of DF1001 in Patients With Advanced Solid Tumors	Phase 1 /Phase 2	San Diego, CA
evorpacept + zanidatamab	EVORPACEPT Evorpacept (ALX148) is a chimeric protein consisting of the Fc region of immunoglobulin fused to the CD47 SIRPa-binding domain, that blocks the ability of CD47 to bind SIRPa on macrophages thereby promoting phagocytosis of tumor cells (PMID: 28286286), and may also stimulate cytotoxic T-cells (PMID: 29873856). ZANIDATAMAB Zanidatamab (ZW25) is a bispecific antibody targeting ERBB2 (HER2), which induces anti-tumor immune response against Erbb2 (Her2)-expressing tumors (Ann Oncol 2017, Vol 28, Suppl 5, Abstract # 255P, PMID: 32054397). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05027139	A Study of Zanidatamab (ZW25) With Evorpacept (ALX148) in Patients With Advanced HER2-expressing Cancer	Phase 1 /Phase 2	La Jolla, CA

trastuzumab + tucatinib	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04579380	Basket Study of Tucatinib and Trastuzumab in Solid Tumors With HER2 Alterations	Phase 2	La Jolla, CA
MRG002	MRG002 MRG002 consists of a humanized anti-ERBB2 (HER2) IgG1 antibody in conjugation with a cytotoxic agent monomethyl auristatin E (MMAE), which may have antitumor activity against ERBB2 (HER2)-positive tumors (Journal of Clinical Oncology 38, no. 15_suppl, Abstract TPS1101). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04492488	A Study of MRG002 in Patients With HER2-Positive Advanced Solid Tumors and Locally Advanced or Metastatic Gastric /Gastroesophageal Junction (GEJ) Cancer	Phase 1 /Phase 2	Orange, CA
DB-1303	DB-1303 DB-1303 is an antibody-drug conjugate (ADC) comprised of a biosimilar to the ERBB2 (HER2)-targeted antibody Herceptin (trastuzumab) conjugated to the topoisomerase I inhibitor P1003, which potentially leads to growth inhibition of ERBB2 (HER2)-expressing tumor cells and tumor regression (European Journal of Cancer 174 (2022): S91). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT05150691	A Study of DB-1303 in Advanced/Metastatic Solid Tumors	Phase 1 /Phase 2	Whittier, CA
atezolizumab + pertuzumab/trastuzumab /hyaluronidase; trastuzumab /hyaluronidase + tucatinib	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	Los Angeles, CA
BPX-603 + rimiducid	BPX-603 BPX-603 are autologous T lymphocytes engineered to express a chimeric antigen receptor (CAR) for ERBB2 (HER2) and a dual-switch consisting of chemical inducer of dimerization (CID)-inducible co-activation domain (MyD88/CD40) and an inducible caspase 9 safety switch (CaspaCIDe), which may lead to activation of anti-tumor immune responses in the tumor microenvironment (NCI Drug Dictionary). RIMIDUCID Rimiducid is a tacrolimus analogue drug that contains an analogue of FKBP12, which allows homodimerization of genetically engineered receptors containing an FKBP12 binding domain, thereby, inducing apoptosis when necessary (NCI Drug Dictionary). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04650451	Safety and Activity Study of HER2-Targeted Dual Switch CAR-T Cells (BPX-603) in Subjects With HER2-Positive Solid Tumors	Phase 1	La Jolla, CA
durvalumab + fam-trastuzumab deruxtecan + carboplatin; durvalumab + fam-trastuzumab deruxtecan + cisplatin; durvalumab + fam-trastuzumab deruxtecan + pemetrexed	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04686305	Phase Ib Study of the Safety of T-DXd and Durvalumab With Chemotherapy in Advanced or Metastatic HER2+ Non-squamous NSCLC	Phase 1	Orange, CA
MT-5111	MT-5111 MT-5111 is an Erbb2 (Her2) antibody in conjugation with a ribosome-targeting toxin, which may demonstrate cytotoxicity against Erbb2 (Her2)-positive tumor cells (Cancer Res 2018;78(13 Suppl):Abstract nr 5769). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04029922	Study of MT-5111 in HER2-positive Solid Tumors	Phase 1	Los Alamitos, CA
CT-0508	CT-0508 CT-0508 consists of adenovirus-transduced macrophages expressing an anti-Erbb2 (Her2) chimeric antigen receptor (CAR), which may activate the tumor microenvironment and stimulate anti-tumor immune response (Cancer Immunol Res 2020;8(3 Suppl):Abstract nr B65). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04660929	CAR-macrophages for the Treatment of HER2 Overexpressing Solid Tumors	Phase 1	Duarte, CA

ZW49	ZW49 ZW49 is an antibody-drug conjugate (ADC) comprising a bispecific ERBB2 (HER2) antibody linked to auristatin, which delivers the cytotoxic agent to ERBB2 (HER2)-expressing cells, potentially resulting in cell growth inhibition and tumor regression (Cancer Res 2019;79(4 Suppl):Abstract nr P6-17-13). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT03821233	A Dose Finding Study of ZW49 in Patients With HER2-Positive Cancers	Phase 1 Duarte, CA
autologous anti-HER2-CAR-4-1BB-CD3zeta-CD19t+-expressing Tcm-enriched T-lymphocytes	AUTOLOGOUS ANTI-HER2-CAR-4-1BB-CD3ZETA-CD19T+-EXPRESSING TCM-ENRICHED T-LYMPHOCYTES Limited information is currently available on this drug. CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT03696030	HER2-CAR T Cells in Treating Patients With Recurrent Brain or Leptomeningeal Metastases	Phase 1 Duarte, CA
ceralasertib + trastuzumab	CERALASERTIB Ceralasertib (AZD6738) is an inhibitor of ATR, which may enhance the sensitivity of chemotherapeutic agents, potentially resulting in tumor regression (PMID: 26517239, PMID: 31836456). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT04704661	Testing the Combination of Two Anti-cancer Drugs, DS-8201a and AZD6738, for The Treatment of Patients With Advanced Solid Tumors Expressing the HER2 Protein or Gene, The DASH Trial	Phase 1 Los Angeles, CA
BI 1810631	BI 1810631 BI 1810631 is an ERBB2 (HER2) selective inhibitor with potential anti-tumor activity (J of Clin Oncol 40, no. 16_suppl (June 01, 2022) TPS9143). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.		
	NCT04886804	A Study to Test Different Doses of BI 1810631 in People With Different Types of Advanced Cancer (Solid Tumours With Changes in the HER2 Gene)	Phase 1 Los Angeles, CA

TMB (High)

pembrolizumab	FDA APPROVED: FDA approved for unresectable or metastatic tumor mutational burden-high (TMB-H, >=10 muts /Mb) solid tumors with progression following prior treatment and with no satisfactory alternative treatment options. CLINICAL SIGNIFICANCE (IA): In a retrospective analysis of a Phase II trial (KEYNOTE-158) that supported FDA approval, Keytruda (pembrolizumab) treatment resulted in superior objective response rate (28.3% vs 6.5%) in adult and pediatric patients with TMB high (TMB >= 10 mut/Mb, n=120) advanced solid tumors compared to patients with TMB low (TMB < 10 mut/Mb, n=635) tumors (Ann Oncol, 30 (Suppl 5), Oct 2019, v477-v478; NCT02628067).		
	NCT02628067	Study of Pembrolizumab (MK-3475) in Participants With Advanced Solid Tumors (MK-3475-158/KEYNOTE-158)	Phase 2 Los Angeles, CA
nivolumab	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. In a Phase III trial (CheckMate 026), patients with stage IV or recurrent non-small cell lung cancer with high tumor mutational burden (TMB) demonstrated a response rate of 48% (n=47) following treatment with Opdivo (nivolumab) compared to a response rate of 28% (n=60) in patients treated with chemotherapy, and a median progression-free survival of 9.7 months vs. 5.8 months with chemotherapy treatment (PMID: 28636851; NCT02041533).		
ipilimumab + nivolumab	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. Marker is in clinical trial inclusion criteria. In a Phase III (CheckMate 227) trial, Opdivo (nivolumab) and Yervoy (ipilimumab) combination treatment resulted in prolonged progression-free survival (7.2 vs 5.5 months, HR=0.58, p<0.001) and higher objective response rate (45.3% vs 26.9%) compared to chemotherapy in non-small cell lung cancer patients with a high tumor mutational burden (PMID: 29658845; NCT02477826).		
	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 Los Angeles, CA

atezolizumab	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria. In a meta-analysis, treatment with immune checkpoint inhibitors including Tecentriq (atezolizumab), Opdivo (nivolumab), Yervoy (ipilimumab), and Keytruda (pembrolizumab) resulted in improved progression-free survival (HR=0.41, p<0.001) and overall survival (HR=0.26, p=0.009) in non-small cell lung cancer patients with high TMB compared to patients with low TMB (PMID: 31290993).			
	NCT04589845	Tumor-Agnostic Precision Immuno-Oncology and Somatic Targeting Rational for You (TAPISTRY) Platform Study	Phase 2	Newport Beach, CA
AKT2 gain				
paxalisib	PAXALISIB Paxalisib (GDC-0084) is a dual pan-PI3K and mTOR inhibitor, which prevents cell proliferation and potentially inhibits tumor growth (PMID: 22619466, PMID: 32269051, PMID: 31937616). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT03994796	Genetic Testing in Guiding Treatment for Patients With Brain Metastases	Phase 2	San Diego, CA
RMC-5552	RMC-5552 RMC-5552 selectively inhibits mTORC1, resulting in decreased downstream signaling and potentially leading to reduced growth and increased apoptosis in tumor cells (European Journal of Cancer 138 (2020): S1-S62). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04774952	Dose Escalation of RMC-5552 Monotherapy in Relapsed /Refractory Solid Tumors	Phase 1	Irvine, CA
CTLA4 (RNA-Seq) High				
ONC-392	ONC-392 ONC-392 is a pH-sensitive monoclonal antibody that targets CTLA4 (CD152), potentially resulting in antitumor activity (Journal for ImmunoTherapy of Cancer 2022;10). CLINICAL SIGNIFICANCE (IIC): Marker is drug target.			
	NCT04140526	Safety, PK and Efficacy of ONC-392 in Monotherapy and in Combination of Anti-PD-1 in Advanced Solid Tumors and NSCLC	Phase 1 /Phase 2	Downey, CA
XTX101	XTX101 XTX101 is an anti-CTLA4 antibody engineered for tumor microenvironment-specific activity, which may lead to proliferation of CD8+ T lymphocytes, activation of T lymphocyte function, and tumor regression (Journal for ImmunoTherapy of Cancer 2020;8) CLINICAL SIGNIFICANCE: Marker is drug target.			
	NCT04896697	XTX101 Monotherapy and XTX101 and Pembrolizumab Combination Therapy in Patients With Advanced Solid Tumors	Phase 1 /Phase 2	Encinitas, CA
botensilimab	BOTENSILIMAB AGEN1181 is an antibody that targets CTLA4, potentially resulting in increased anti-tumor immune response (NCI Drug Dictionary). CLINICAL SIGNIFICANCE: Marker is drug target.			
	NCT03860272	Fc-Engineered Anti-CTLA-4 Monoclonal Antibody in Advanced Cancer	Phase 1	Duarte, CA
MS-Stable + TMB (High)				
etigilimab + nivolumab	ETIGILIMAB Etigilimab (OMP-313M32) 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 (AACR, Vol 58, April 2017, Abstract #599, PMID: 31874056). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04761198	A Study of Etigilimab and Nivolumab in Subjects With Locally Advanced or Metastatic Tumors.	Phase 1 /Phase 2	Los Angeles, CA

NY-ESO-1 (RNA-Seq) positive

ASP0739	ASP0739 ASP0739 are human artificial adjuvant vector cells loaded with the CD1d ligand alpha-galactosylceramide and modified to express the tumor associated antigen NY-ESO-1 (CTAG1B), which potentially induce activation of immune cells, and cytotoxic T-cell mediated response against tumor cells expressing NY-ESO-1 (NCI Thesaurus). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04939701	Study of ASP0739 Alone and With Pembrolizumab in Advanced Solid Tumors With NY-ESO-1 Expression Participants	Phase 1 /Phase 2	Duarte, CA
LV-NY-ESO-1 TCR/sr39TK PBSC + NY-ESO-1 TCR retroviral vector-transduced autologous PBMCs + plerixafor + aldesleukin + filgrastim + busulfan + fludarabine	LV-NY-ESO-1 TCR/SR39TK PBSC LV-NYESO TCR/sr39TK PBSC are peripheral blood stem cells that have been engineered to express a NY-ESO-1-specific T-cell receptor and the sr39TK cell suicide gene, which may enhance anti-tumor immune response (PMID: 30409823) NY-ESO-1 TCR RETROVIRAL VECTOR-TRANSDUCED AUTOLOGOUS PBMCS RV-NY-ESO TCR PBMC are peripheral blood mononuclear cells that have been engineered to express an NY-ESO-1-specific T-cell receptor, which may result in enhanced anti-tumor immunity (PMID: 25038231, PMID: 30409823). PLERIXAFOR Mozobil (plerixafor) inhibits CXCR4 and CXCL12-mediated cell signaling to influence tumor metastasis (PMID: 19641136, PMID: 16815309). CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT03240861	Genetically Engineered PBMC and PBSC Expressing NY-ESO-1 TCR After a Myeloablative Conditioning Regimen to Treat Patients With Advanced Cancer	Phase 1	Los Angeles, CA

PD-L1 IHC (22C3) Negative

ipilimumab + nivolumab + pembrolizumab + carboplatin + nab-paclitaxel + paclitaxel + pemetrexed; ipilimumab + nivolumab + pembrolizumab + carboplatin + nab-paclitaxel + paclitaxel + pemetrexed + stereotactic body radiation therapy	CLINICAL SIGNIFICANCE (IIC): Marker is in clinical trial inclusion criteria.			
	NCT04929041	Testing the Addition of Radiation Therapy to the Usual Treatment (Immunotherapy With or Without Chemotherapy) for Stage IV Non-Small Cell Lung Cancer Patients Who Are PD-L1 Negative	Phase 2 /Phase 3	Upland, CA

BTLA (RNA-Seq) High

icatolimab	ICATOLIMAB Icatolimab (JS004) is a humanized monoclonal antibody that binds to B- and T-lymphocyte attenuator (BTLA) and activates T-cells, thereby potentially resulting in the activation of antitumor immune response (J Clin Oncol 40, no. 16_suppl (June 01, 2022) 2643). 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	Los Angeles, CA

TGFB1 (RNA-Seq) High

SRK-181	SRK-181 SRK-181 is TGFbeta1 (TGFB1) antibody, which potentially enhances anti-tumor immune response (PMID: 32213632). CLINICAL SIGNIFICANCE: Marker is drug target.			
	NCT04291079	SRK-181 Alone or in Combination With Anti-PD-(L)1 Antibody Therapy in Patients With Locally Advanced or Metastatic Solid Tumors (DRAGON)	Phase 1	Fullerton, CA

STP707	STP707 STP707 is a siRNA-based polypeptide nanoparticle consisting of siRNAs that target TGF-beta 1 and COX-2, leading to decreased TGF-beta 1 and COX-2 signaling, potentially resulting in enhanced antitumor immune response and decreased tumor growth (NCI Drug Dictionary). CLINICAL SIGNIFICANCE: Marker is drug target.			
	NCT05037149	Ph. 1, Evaluation of Safety, Tolerability, PK, Anti-tumor Activity of STP707 IV in Subjects With Solid Tumors	Phase 1	Los Angeles, CA
TLR9 (RNA-Seq) High				
TAC-001	TAC-001 Limited information is currently available on this drug. CLINICAL SIGNIFICANCE: Marker is drug target.			
	NCT05399654	A Dose Escalation and Expansion Study of TAC-001 in Patients With Select Advanced or Metastatic Solid Tumors	Phase 1 /Phase 2	Los Angeles, CA
VISTA (RNA-Seq) High				
HMBD-002	HMBD-002 HMBD-002 is an antibody that targets and VISTA (VSIR), potentially resulting in relief of immunosuppression and reduced tumor growth (J Clin Oncol 39:15_suppl, e14569). CLINICAL SIGNIFICANCE: Marker is drug target.			
	NCT05082610	A Study of HMBD-002, a Monoclonal Antibody Targeting VISTA, as Monotherapy and Combined With Pembrolizumab	Phase 1	Los Angeles, CA

TISSUE Specimen Review Summary

Specimen Details

Submitted Pathology Report ID		Histologic evaluation/ Clinical Impression	Lung / Malignant Epithelial / Non-small cell lung cancer, NOS				
Sample Collection Date		Tumor Origin	Metastatic	Tumor Nuclei	50%	#Neoplastic Cells per slide	1000-1999
Organ/Tissue Site	Hematopietic / Lymph node NOS					Necrosis	0%

Samples Received for Testing

Received Date	PD-L1 Report Date	Sample Label	Type	Quantity	Purpose

PD-L1 Immunohistochemistry

Gross Description: Received from Accupath Diagnostic Laboratories are a control slide and stained slides labele . 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 Sassan Rostami, MD, 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 Indeterminate Findings with Potential Clinical Significance

Single nucleotide variants, short variants, indels, and copy number alterations associated with off-label therapies or clinical trials that could not be confirmed as positive or negative.

No indeterminate variants with potential clinical significance 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.

AMER1 A29T	APC S1126R	AR P449L	BAP1 P293L	BRCA1 G890R
C11orf30 P347A	EP300 D530H	EP300 G515A	EP300 G518A	GPR124 R1180G
HIST1H1C A171V	IRS1 R1220C	KDM5A K1382E	MDC1 R1299Q	MLH1 R389Q
PGR R623S	RANBP2 V1936M	SF3B1 G915D	SHQ1 S473L	YAP1 T428I

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, HLA Class I genotypes, 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). 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 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 tissue; 40 - 100 ng of DNA and 30 - 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. For more details about the performance characteristics please see the Validation Summary at:

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 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 AR, CCND1, CCNE1, CDK4, CDK6, EGFR, ERBB2, FGFR1, FGFR2, KIT, KRAS, MET, MDM2, MYC, MYCN, PDGFRA, and PIK3CA, fusion genes ALK, FGFR2, FGFR3, NRG1, 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: 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. 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.
13. 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.

DISCLAIMER

The selection of any, all or none of the matched therapies reported by OmniSeq INSIGHT resides solely with the treating physician and should not be solely based on the OmniSeq INSIGHT report. 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.

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; 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 component 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://www.omniseq.com/omniseq-insight/About OmniSeq INSIGHT

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)