OmniSeq Advance

OmniSeq

PATIENT	SPECIMEN	CLIENT
Name: **DOB:** **Sex:** **MRN:** **Order ID:** **| Test ID:** **Report Date:** **Diagnosis:** C34.90, Malignant neoplasm of unsp part of unsp bronchus or lung, Stage IV	**Facility:** **ID:** **Source:** Hip Mass, Left **Collection Date:** **Received Date:**	**Provider:** **Location:**

THERAPY CONSIDERATIONS FOR NON-SMALL CELL LUNG CANCER

	Markers Identified	Therapies in Non-Small Cell Lung Cancer	Therapies in Other Tumor Types
Level 1	**PD-L1 (IHC_22C3) 5% TPS**	pembrolizumab[1,2]	None
Level 1	**TMB 13.0/Mb (High)**	pembrolizumab[3]	None
Level 2	**TMB 13.0/Mb (High)**	ipilimumab + nivolumab[4]	atezolizumab[5], ipilimumab[6], ipilimumab + tremelimumab[7]

Clinical Trial Markers Identified

	Immunotherapy	Targeted Therapy
Level 3	**CD137 85%** **CD40 74%** **LAG3 74%** **TGFB1 92%** **TIGIT 81%** **TIM3 72%** **TMB 13.0/Mb (High)**	**CDKN2A c.97G>T (E33X)** **TP53 c.833C>G (P278R)**

FDA Evidence Levels: 1) Companion diagnostic; 2) Practice guidelines, clinically validated; 3) Clinically significant, analytically validated with clinical or mechanistic rationale (clinical trials, off-label therapies, or peer reviewed evidence). See clinical trials page 2

Negative Results for Markers with FDA Companion, Complementary or Emerging Diagnostics

Immunotherapy	Targeted Therapy		
MSI Stable	**ALK fusion** **BRAF V600** **EGFR exon 19 deletion** **EGFR exon 20 insertion**	**EGFR mutation** **HER2 (ERBB2) mutation** **KRAS mutation** **MET amp/exon 14**	**NTRK fusion** **RET fusion** **ROS1 fusion**

Targeted Therapy Markers of Unknown Significance

No targeted therapy markers of unknown significance were detected

PATHOLOGIST SUMMARY INTERPRETATION

MOLECULAR SUMMARY: This CDKN2A/TP53 mutant non-small cell lung cancer with a high mutational burden is moderately inflamed with a moderate number of CD8+ T-cells, relatively high macrophage content, and modest expression of PD-L1 by IHC (TPS=5%; 22C3 clone). RNA-seq immune profiling analysis for PD-L1 shows a moderate level of expression. This tumor shows evidence of T-cell priming with over expression of CD137, T-cell recognition with over expression of TIGIT, and T-cell trafficking with over expression of TGFB1.

LIKELIHOOD OF RESPONSE BASED ON EVIDENCE IN CURRENT LITERATURE: From an immunotherapy perspective, the expression of PD-L1 by IHC at 5% meets the requirement of first line pembrolizumab as an FDA-approved agent in this tumor type. The FDA has approved atezolizumab in combination with nab-paclitaxel and carboplatin for first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer with no EGFR or ALK genetic alterations. The high TMB status in this case meets the requirement for pembrolizumab as an FDA-approved agent for patients who have progressed on prior treatment and have no satisfactory alternative treatment options. Response to PD-1 axis inhibition in this patient is indeterminate. Recommendation is pembrolizumab or combination of ipilimumab and nivolumab or durvalumab and tremelimumab .

CDKN2A c.97G>T (E33X) at codon 33 in exon 1 (VAF = 0.363) is a truncating variant and would be considered an inactivating mutation.

TP53 c.833C>G (P278R) at codon 278 in exon 8 (VAF = 0.328) is reported in ClinVar as uncertain significance and classified as deleterious and probably damaging in Sift and Polyphen, respectively.

Additional Immunotherapy Markers

NOT matched to clinical trials

	T-Cell Priming	T-Cell Trafficking	T-Cell Recognition	Killing Cancer Cells	T-Cell Infiltration	Cancer Testis Antigens
	Percentile Rank (%)*					Positive/Negative**
Level 3	**CD27** 59% **CD28** 33% **CD40LG** 27% **CD80** 45% **CD86** 80% **GITR** 58% **GZMB** 89% **ICOS** 37% **ICOSLG** 32% **IFNG** 74% **OX-40L** 82% **OX40** 37% **TBX21** 46%	**CXCL10** 78% **CXCR6** 60% **DDX58** 30% **GATA3** 78% **IL10** 36% **IL1B** 38% **MX1** 25% **STAT1** 81% **TLR7** 53% **TLR8** 67% **TLR9** 43% **TNF** 58%	**BTLA** 32% **CTLA4** 40% **NECTIN2** 49% **PD-1** 55% **PD-L1** 60% **PD-L2** 83% **PVR** 54% **TNFRSF14** 28% **VISTA** 41%	**ADORA2A** 25% **CCL2** 60% **CCR2** 18% **CD163** 49% **CD38** 61% **CD39** 41% **CD68** 71% **CSF1R** 66% **CXCR2** 22% **IDO1** 70%	**CD2** 63% **CD20** 30% **CD3** 64% **CD4** 60% **CD8** 70% **FOXP3** 47% **KLRD1** 75% **SLAMF4** 59%	**LAGE1A** Negative **MAGEA1** Negative **MAGEA3** Negative **MAGEA4** Negative **NY-ESO-1** Negative **SSX2** Negative

**Percentile Rank = percentage (%) of the reference population with normalized reads per million (nRPM) less than the measured nRPM for that marker.*
***Cancer Testis Antigens are "Positive" if nRPM ≥20, and "Negative" if nRPM <20.*
See ABOUT section for additional information about these markers

CLINICAL TRIALS

Targeted Therapy

Trial Name	Phase	NCT ID	Location
TP53 c.833C>G (P278R)			
Study of COTI-2 as Monotherapy or Combination Therapy for the Treatment of Malignancies	1	NCT02433626	Over 200 miles Houston, TX
CDKN2A c.97G>T (E33X)			
Study of SQZ-PBMC-HPV in Patients With HPV16+ Recurrent, Locally Advanced or Metastatic Solid Tumors	1	NCT04084951	Over 200 miles Boston, MA

Immunotherapy

Trial Name	Phase	NCT ID	Location
TMB			
A Phase 1/2 Study of In Situ Vaccination With Tremelimumab and IV Durvalumab Plus PolyICLC in Subjects With Advanced, Measurable, Biopsy-accessible Cancers	1/ 2	NCT02643303	1-24 miles Buffalo, NY
A Study of Nivolumab and Ipilimumab in Untreated Patients With Stage 3 Non-small Cell Lung Cancer (NSCLC) That is Unable or Not Planned to be Removed by Surgery	3	NCT04026412	100-200 miles Youngstown, OH
My Pathway: A Study Evaluating Herceptin/Perjeta, Tarceva, Zelboraf/Cotellic, Erivedge, Alecensa, and Tecentriq Treatment Targeted Against Certain Molecular Alterations in Participants With Advanced Solid Tumors	2	NCT02091141	100-200 miles Cleveland, OH
Phase 1/2 Study Exploring the Safety, Tolerability, and Efficacy of INCAGN01876 Combined With Immune Therapies in Advanced or Metastatic Malignancies	1/ 2	NCT03126110	100-200 miles Pittsburgh, PA
An Adaptive Study to Match Patients With Solid Tumors to Various	1	NCT03335540	100-200 miles

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CLINICAL TRIALS

Immunotherapy

Trial Name	Phase	NCT ID	Location
Immunotherapy Combinations Based Upon a Broad Biomarker Assessment			Pittsburgh, PA
LAG3			
A Study of Biomarker-Directed, Pembrolizumab (MK-3475) Based Combination Therapy for Advanced Non-Small Cell Lung Cancer (MK-3475-495/KEYNOTE-495)	2	NCT03516981	100-200 miles Pittsburgh, PA
An Adaptive Study to Match Patients With Solid Tumors to Various Immunotherapy Combinations Based Upon a Broad Biomarker Assessment	1	NCT03335540	100-200 miles Pittsburgh, PA
TIGIT / NECTIN2 / PVR			
Substudy 1: Efficacy and Safety Study of Pembrolizumab (MK-3475) Plus Chemotherapy When Used With Investigational Agents in Treatment-naïve Participants With Advanced Non-small Cell Lung Cancer (NSCLC) (MK-3475-01A/KEYNOTE-01A)	2	NCT04165070	100-200 miles Cleveland, OH
Safety and Pharmacokinetics (PK) of Escalating Doses of MTIG7192A as a Single Agent and in Combination With Atezolizumab With and Without Chemotherapy in Locally Advanced or Metastatic Tumors	1	NCT02794571	100-200 miles Pittsburgh, PA
Study of Vibostolimab Alone and in Combination With Pembrolizumab in Advanced Solid Tumors (MK-7684-001)	1	NCT02964013	100-200 miles Pittsburgh, PA
A Safety Study of SGN-TGT in Patients With Advanced Cancer	1	NCT04254107	100-200 miles Pittsburgh, PA
An Investigational Immuno-therapy Study to Evaluate the Safety and Effectiveness of Experimental Medication BMS-986207 by Itself and in Combination With Nivolumab in Solid Cancers That Are Advanced or Have Spread	1/ 2	NCT02913313	100-200 miles Pittsburgh, PA
TIM3			
An Investigational Immunotherapy Study of BMS-986258 Alone and in Combination With Nivolumab in Participants With Solid Cancers That Are Advanced or Have Spread	1/ 2	NCT03446040	1-24 miles Buffalo, NY
Phase I-Ib/II Study of MBG453 as Single Agent and in Combination With PDR001 in Patients With Advanced Malignancies	1/ 2	NCT02608268	Over 200 miles Baltimore, MD
CD137			
A Study Of Avelumab In Combination With Other Cancer Immunotherapies In Advanced Malignancies (JAVELIN Medley)	2	NCT02554812	Over 200 miles Detroit, MI
GEN1042 Safety Trial in Subjects With Malignant Solid Tumors	1/ 2	NCT04083599	Over 200 miles Indianapolis, IN
Avelumab, Utomilumab, Anti-OX40 Antibody PF-04518600, and Radiation Therapy in Treating Patients With Advanced Malignancies	1/ 2	NCT03217747	Over 200 miles Houston, TX
CD40			
CD40 Agonistic Antibody APX005M in Combination With Nivolumab	1/ 2	NCT03123783	100-200 miles Syracuse, NY
Safety Study of SEA-CD40 in Cancer Patients	1	NCT02376699	100-200 miles Cleveland, OH
TGFB1			
M7824 in Combination With Chemotherapy in Stage IV Non-small Cell Lung Cancer (NSCLC)	1/ 2	NCT03840915	Over 200 miles Detroit, MI
M7824 With cCRT in Unresectable Stage III Non-small Cell Lung Cancer (NSCLC)	2	NCT03840902	Over 200 miles Nyack, NY
A First-in-human Study of the Safety, Pharmacokinetics, Pharmacodynamics and Anti-tumor Activity of SAR439459 Monotherapy and Combination of SAR439459 and Cemiplimab in	1	NCT03192345	Over 200 miles Boston, MA

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CLINICAL TRIALS

Immunotherapy

Trial Name	Phase	NCT ID	Location
Patients With Advanced Solid Tumors			
Chemo/RT Augmentation			
An Open-Label, Dose-Escalation/Dose-Expansion Safety Study of INCB059872 in Subjects With Advanced Malignancies	1/ 2	NCT02712905	1-24 miles Buffalo, NY
Genetic Testing in Screening Patients With Stage IB-IIIA Non-small Cell Lung Cancer That Has Been or Will Be Removed by Surgery (The ALCHEMIST Screening Trial)	Not Specified	NCT02194738	1-24 miles Buffalo, NY
Testing the Timing of Pembrolizumab Alone or With Chemotherapy as First Line Treatment and Maintenance in Non-small Cell Lung Cancer	3	NCT03793179	50-100 miles Rochester, NY
Testing the Addition of an Antibody to Standard Chemoradiation Followed by the Antibody for One Year to Standard Chemoradiation Followed by One Year of the Antibody in Patients With Unresectable Stage III Non-Small Cell Lung Cancer	3	NCT04092283	50-100 miles Rochester, NY
Maintenance Chemotherapy With or Without Local Consolidative Therapy in Treating Patients With Stage IV Non-small Cell Lung Cancer	2	NCT03137771	100-200 miles Sayre, PA

A pathologist curated list of clinical trials, sorted by nearest location, is displayed. For immunotherapy, the list can include trial-indicated selection markers, overexpressed immune markers that are targets in clinical development, TILs recruitment trials, CD8 Inflamed PD-L1 Negative, as well as chemotherapy and/or radiation therapy (RT) augmentation combination immunotherapy trials. Targeted therapy clinical trials are displayed for detected variants used to select patients for therapies in clinical development. Clinical trial information is current as of 06/18/2020. For up to date information regarding a specific trial, search www.clinicaltrials.gov by NCT ID. Email support@omniseq.com or call 1-800-781-1259 for information about additional clinical trials that may be open.

SURGICAL PATHOLOGY REVIEW SUMMARY

Submitted Pathology Report		Reviewed Pathologic Diagnosis	Lung / Malignant Epithelial / Non-small cell lung cancer, NOS		
Sample Procurement Date		Tissue	Metastatic Tumor	Tumor Nuclei	30%
Reviewed Pathologic Tissue Site	Musculoskeletal/ Soft Tissue / Soft tissues NOS				

Summary of Received Samples for Testing

Received	Sample Label	Type	Quantity	Unit	Purpose
		FFPE Block	1	Block	Testing[Controls Adequate]

PD-L1 Immunohistochemistry (IHC)

Gross Description: Received from Roswell Park Cancer Institute is one paraffin block labeled It is accompanied by a surgical pathology report with the same number and the patient's name. These are assigned our accession number and submitted for PD-L1 evaluation per usual protocol. Returned from are two stained glass microscope slides stained for PD-L1 and labeled as These slides are accompanied by an technical procedure only report for PD-L1 immunohistochemistry with the same accession number, the patient's name, and our accession number. These slides and report are submitted for interpretation by OmniSeq pathologists.

Regulatory: PD-L1 IHC 22C3 pharmDx is a qualitative IHC assay that is FDA-approved for in vitro diagnostic use. This test was performed at 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.

THERAPY CONSIDERATION REFERENCES

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3. Merck. Keytruda (pembrolizumab) [package insert]. (2020).

4. Hellmann, M. D. et al. Nivolumab plus Ipilimumab in Lung Cancer with a High Tumor Mutational Burden. N Engl J Med. 2018;378(22):2093-2104.

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8. Taube, J. M. et al. Association of PD-1, PD-1 ligands, and other features of the tumor immune microenvironment with response to anti-PD-1 therapy. Clin. Cancer Res. 20, 5064–5074 (2014).

9. Goodman, A. M. et al. Tumor Mutational Burden as an Independent Predictor of Response to Immunotherapy in Diverse Cancers. Mol. Cancer Ther. 16, 2598–2608 (2017).