CARIS LIFE SCIENCES

Patient

Name:
Date of Birth:
Sex:
Case Number: TN23- **Diagnosis:** Adenocarcinoma, NOS

Specimen Information

Primary Tumor Site: Lung, NOS
Specimen Site: Lung, NOS
Specimen ID:
Specimen Collected:
Test Report Date:

Ordered By

Results with Therapy Associations

BIOMARKER	METHOD	ANALYTE	RESULT	THERAPY ASSOCIATION		BIOMARKER LEVEL*
ALK	**IHC**	**Protein**	**Positive | 3+, 90%**	**BENEFIT**	**alectinib, ceritinib, crizotinib, lorlatinib**	**Level 1**
					brigatinib	**Level 2**
PD-L1 (22c3)	**IHC**	**Protein**	**Positive, TPS: 100%**	**BENEFIT**	**cemiplimab, pembrolizumab**	**Level 1**
PD-L1 (28-8)	**IHC**	**Protein**	**Positive | 3+, 100%**	**BENEFIT**	**nivolumab/ipilimumab combination**	**Level 1**
PD-L1 (SP142)	**IHC**	**Protein**	**Positive, IC: 70% Positive, TC: 3+, 100%**	**BENEFIT**	**atezolizumab (metastatic)**	**Level 1**
PD-L1 (SP263)	**IHC**	**Protein**	**Positive, TC: 3+, 100%**	**BENEFIT**	**atezolizumab (adjuvant), cemiplimab**	**Level 1**
BRAF	Seq	DNA-Tumor	Mutation Not Detected	LACK OF BENEFIT	dabrafenib and trametinib combination therapy, vemurafenib	Level 2
EGFR	Seq	DNA-Tumor	Mutation Not Detected	LACK OF BENEFIT	erlotinib, gefitinib	Level 2
KRAS	Seq	DNA-Tumor	Mutation Not Detected	LACK OF BENEFIT	adagrasib, sotorasib	Level 2
RET	Seq	RNA-Tumor	Fusion Not Detected	LACK OF BENEFIT	pralsetinib, selpercatinib	Level 2
ROS1	Seq	RNA-Tumor	Fusion Not Detected	LACK OF BENEFIT	entrectinib	Level 2

* Biomarker reporting classification: Level 1 – Companion diagnostic (CDx); Level 2 – Strong evidence of clinical significance or is endorsed by standard clinical guidelines; Level 3 – Potential clinical significance. Bolded benefit therapies, if present, highlight the most clinically significant findings.

Important Note

This patient has a positive ALK result by IHC, however rearrangement could not be confirmed by RNA fusion analysis. The observed expression of ALK protein is either due to low transcript levels that did not meet our threshold for reporting or the result of an alternative mechanism of oncogenic activation (PMID: 31366041, 26444240). ALK IHC (D5F3) is an FDA-approved companion diagnostic for ALK tyrosine kinase inhibitors (TKIs) and can be utilized as a stand-alone test.

The choice of ALK inhibitor treatment should be made with consideration of the patient's line of therapy and central nervous system (CNS) involvement. Alectinib, brigatinib, and lorlatinib are considered NCCN-preferred agents for the first-line setting. For patients with CNS involvement, alectinib, brigatinib, ceritinib, and lorlatinib have intracranial efficacy. Optimal sequencing of ALK-targeted therapy is an active area of investigation. Please see NCCN guidelines (NSCLC and CNS) and clinicaltrials.gov for more information.

MI GPSai was performed on this case. Please see *Page 4* for results.

Results continued on the next page. >

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Cancer-Type Relevant Biomarkers

Biomarker	Method	Analyte	Result
MSI	Seq	DNA-Tumor	Stable
NTRK1/2/3	Seq	RNA-Tumor	Fusion Not Detected
Tumor Mutational Burden	Seq	DNA-Tumor	Low, 2 mut/Mb
ALK	Seq	DNA-Tumor	Mutation Not Detected
		RNA-Tumor	Fusion Not Detected
BRAF	Seq	RNA-Tumor	Fusion Not Detected
ERBB2 (Her2/Neu)	Seq	DNA-Tumor	Mutation Not Detected
FGFR3	Seq	RNA-Tumor	Fusion Not Detected
KEAP1	Seq	DNA-Tumor	Mutation Not Detected
	CNA-Seq	DNA-Tumor	Deletion Not Detected
KRAS	CNA-Seq	DNA-Tumor	Amplification Not Detected
MET	Seq	DNA-Tumor	Mutation Not Detected
	CNA-Seq	DNA-Tumor	Amplification Not Detected
	Seq	RNA-Tumor	Variant Transcript Not Detected

Biomarker	Method	Analyte	Result
MTAP	CNA-Seq	DNA-Tumor	Deletion Not Detected
NFE2L2	Seq	DNA-Tumor	Mutation Not Detected
	CNA-Seq	DNA-Tumor	Deletion Not Detected
NRG1	Seq	RNA-Tumor	Fusion Not Detected
PTEN	IHC	Protein	Positive | 3+, 100%
	CNA-Seq	DNA-Tumor	Deletion Not Detected
RB1	Seq	DNA-Tumor	Mutation Not Detected
	CNA-Seq	DNA-Tumor	Deletion Not Detected
RET	Seq	DNA-Tumor	Mutation Not Detected
STK11	Seq	DNA-Tumor	Mutation Not Detected
	CNA-Seq	DNA-Tumor	Deletion Not Detected
TP53	Seq	DNA-Tumor	Mutation Not Detected
	CNA-Seq	DNA-Tumor	Deletion Not Detected

Genomic Signatures

Biomarker	Method	Analyte	Result
Microsatellite Instability (MSI)	Seq	DNA-Tumor	Stable
Tumor Mutational Burden (TMB)	Seq	DNA-Tumor	
Genomic Loss of Heterozygosity (LOH)	Seq	DNA-Tumor	Low - 9% of tested genomic segments exhibited LOH (assay threshold is ≥ 16%)

PATIENT: **TN23-** **PHYSICIAN:**

Genes Tested with Pathogenic or Likely Pathogenic Alterations

Gene	Method	Analyte	Variant Interpretation	Protein Alteration	Exon	DNA Alteration	Variant Frequency %
CTNNB1	Seq	DNA-Tumor	Likely Pathogenic Variant	p.V22 _S37del	3	c.63 _111 delinsA	40

Unclassified alterations for DNA and RNA sequencing can be found in the MI Portal.
Formal nucleotide nomenclature and gene reference sequences can be found in the Appendix of this report.
Variants of Uncertain Significance can be found in the MI Portal.

Human Leukocyte Antigen (HLA) Genotype Results

The impact of HLA genotypes on drug response and prognosis is an active area of research. These results can help direct patients to clinical trials recruiting for specific genotypes. Please see www.clinicaltrials.gov for more information.

Gene	Method	Analyte	Genotype
MHC CLASS I			
HLA-A	Seq	DNA-Tumor	A*02:01, A*30:02
HLA-B	Seq	DNA-Tumor	B*15:01, B*44:02
HLA-C	Seq	DNA-Tumor	C*03:03, C*05:01

HLA genotypes with only one allele are either homozygous or have loss-of-heterozygosity at that position.

Immunohistochemistry Results

Biomarker	Result	Biomarker	Result
ALK	Positive | 3+, 90%	PD-L1 (SP142)	Positive, IC: 70% Positive, TC: 3+, 100%
PD-L1 (22c3)	Positive, TPS: 100%	PD-L1 (SP263)	Positive, TC: 3+, 100%
PD-L1 (28-8)	Positive | 3+, 100%	PTEN	Positive | 3+, 100%

Genes Tested with Indeterminate Results by Tumor DNA Sequencing

COL2A1	CYSLTR2	EED	KIF1B	PLCB4	PRDM6	PRKD1	PTPRD	RASA1	REST	SMARCA2	WRN
CUL3	DACH1	JAK2	NPM1								

Genes in this table were ruled indeterminate due to low coverage for some or all exons.

The results in this report were curated to represent biomarkers most relevant for the submitted cancer type. These include results important for therapeutic decision-making, as well as notable alterations in other biomarkers known to be involved in oncogenesis. Additional results, including genes with normal findings, additional variants of uncertain significance and unclassified alterations can be found in the MI Portal at **miportal.carismolecularintelligence.com.** If you do not have an MI Portal account, or need assistance accessing it, please contact Caris Customer Support at (888) 979-8669.

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The MI GPSai™ (MI Genomic Prevalence/Probability Score - Artificial Intelligence) is a cancer-type similarity assessment which compares the molecular features of a patient's tumor with other tumors in the Caris database.

Cancer Category	Probability Estimate
Endometrioid Ovarian Cancer	91 %
Cervix/Uterine Carcinoma	7 %
Adrenal Cortical Carcinoma	0 %
Bladder/Urinary Tract	0 %
Bowel	0 %
Breast	0 %
CNS/Brain	0 %
Esophagus/Stomach	0 %
Germ Cell Tumor	0 %
Hematological	0 %
Hepatocellular Carcinoma	0 %
Kidney	0 %
Melanoma	0 %
Mesothelioma	0 %
Neuroendocrine Neoplasm	0 %
Non-Small Cell Lung Carcinoma	0 %
Orogenital Squamous Cell Carcinoma	0 %
Other	0 %
Pancreatobiliary	0 %
Peripheral Nervous System	0 %
Prostate Adenocarcinoma	0 %
Salivary Gland Tumor	0 %
Sex Cord Stromal Tumor	0 %
Soft Tissue/Bone	0 %
Thymic Carcinoma	0 %
Thyroid	0 %

Methods

MI GPSai™ uses machine learning trained on large molecular datasets available in the Caris database. MI GPSai is statistically powered to generate a probability estimate (%) representing the similarity of a tumor's molecular signature to different cancer types in the Caris database. Samples that do not generate a score that meets statistical confidence level thresholds will not receive a MI GPSai result.

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Notes of Significance

SEE APPENDIX FOR DETAILS

Clinical Trials Connector ™ opportunities based on biomarker expression: 681 Targeted Therapy Trials. See page 6 for details.

Specimen Information

Specimen ID:

Specimen Collected:

Specimen Received:

Testing Initiated:

Gross Description: 1 (A) Paraffin Block - Client ID

Dissection Information: Molecular testing of this specimen was performed after harvesting of targeted tissues with an approved manual microdissection technique. Candidate slides were examined under a microscope and areas containing tumor cells (and separately normal cells, when necessary for testing) were circled. A laboratory technician harvested targeted tissues for extraction from the marked areas using a dissection microscope.

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Clinical Trials Connector™

For a complete list of open, enrolling clinical trials visit MI Portal to access the **Clinical Trials Connector**. This personalized, real-time web-based service provides additional clinical trial information and enhanced searching capabilities, including, but not limited to:

- Location: filter by geographic area
- Biomarker(s): identify specific biomarkers associated with open clinical trials to choose from
- Drug(s): search for specific therapies
- Trial Sponsor: locate trials based on the organization supporting the trial(s)

The Clinical Trials Connector lists agents that are matched to available clinical trials according to biomarker status. In some instances, older-generation agents may still be relevant in the context of new combination strategies and, therefore, will still appear on this report.

Visit www.CarisMolecularIntelligence.com to view all matched trials. Therapeutic agents listed below may or may not be currently FDA approved for the tumor type tested.

TARGETED THERAPY CLINICAL TRIALS (681)				
Drug Class	**Biomarker**	**Method**	**Analyte**	**Investigational Agent(s)**
ALK inhibitors (51)	ALK	IHC	Protein	alectinib, brigatinib, crizotinib, ensartinib, lorlatinib, repotrectinib
Immunomodulatory agents (627)	PD-L1	IHC	Protein	INBRX-105, M7824, MGD019, atezolizumab, avelumab, camrelizumab, cemiplimab, cetrelimab, dostarlimab, durvalumab, ipilimumab, nivolumab, pembrolizumab, retifanlimab, sintilimab, spartalizumab, tislelizumab, toripalimab, tremelimumab
Wnt pathway inhibitors (3)	CTNNB1	NGS	DNA-Tumor	CGX1321, ETC-1922159, tegavivint

( ) = represents the total number of clinical trials identified by the Clinical Trials Connector for the provided drug class or table.

The Clinical Trials Connector may include trials that enroll patients with additional screening of molecular alterations. In some instances, only specific gene variants may be eligible.

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Disclaimer

Decisions on patient care and treatment must be based on the independent medical judgment of the treating physician, taking into consideration all available information concerning the patient's condition, prescribing information for any therapeutic, and in accordance with the applicable standard of care. Drug associations provided in this report do not guarantee that any particular agent will be effective for the treatment of any patient or for any particular condition. Caris Life Sciences® expressly disclaims and makes no representation or warranty whatsoever relating, directly or indirectly, to the performance of services, including any information provided and/or conclusions drawn from therapies that are included or omitted from this report. Whether or not a particular patient will benefit from a selected therapy is based on many factors and can vary significantly. The selection of therapy, if any, resides solely in the discretion of the treating physician and the tests should not be considered a companion diagnostic.

Caris MPI, Inc. d/b/a Caris Life Sciences is certified under the Clinical Laboratory Improvement Amendments (CLIA) as qualified to perform high complexity clinical laboratory testing, including all Caris molecular profiling assays. Individual assays that are available through Caris molecular profiling include both Laboratory Developed Tests (LDT) and U.S. Food and Drug Administration (FDA) approved or cleared tests. In addition, certain tests have been CE-marked as a general IVD under the In Vitro Diagnostic Directive (IVDD) 98/79/EC. Offered LDTs were developed and their performance characteristics determined by Caris. Certain tests have not been cleared or approved by the FDA. Caris LDTs are used for clinical purposes. They are not investigational or for research. Caris' CLIA certification number is located at the bottom of each page of this report.

The information presented in the Clinical Trials Connector™ section of this report, if applicable, is compiled from sources believed to be reliable and current. However, the accuracy and completeness of the information provided herein cannot be guaranteed. The clinical trials information present in the biomarker description was compiled from www.clinicaltrials.gov. The contents are to be used only as a guide, and health care providers should employ their best comprehensive judgment in interpreting this information for a particular patient. Specific eligibility criteria for each clinical trial should be reviewed as additional inclusion criteria may apply.

All materials, documents, data, data software, information and/or inventions supplied to customers by or on behalf of Caris or created by either party relating to the services shall be and remain the sole and exclusive property of Caris. Customer shall not use or disclose the information provided by Caris through the services or related reports except in connection with the treatment of the patient for whom the services were ordered and shall not use such property for, or disseminate such property to, any third parties without expressed written consent from Caris. Customer shall deliver all such property to Caris immediately upon demand or upon Caris ceasing to provide the services. The technical and professional component of all testing was performed at the laboratory location displayed in the footer unless otherwise notated in the report.

Caris molecular testing is subject to Caris' intellectual property. Patent www.CarisLifeSciences.com/ip.

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Mutational Analysis by Next-Generation Sequencing (NGS)

TUMOR MUTATIONAL BURDEN	
Mutations / Megabase	Result
2	Low

TMB

Tumor Mutational Burden (TMB) is defined as the number of somatic non-synonymous mutations per million bases of sequenced DNA in a tumor sample. Tumors with high TMB may increase the number of neoantigens which is hypothesized to increase T-cell reactivity and potential for response to immune checkpoint inhibitors. TMB analysis was performed based on next generation sequencing analysis of genomic DNA isolated from a tumor sample.

MICROSATELLITE INSTABILITY ANALYSIS	
Test	Result
MSI	Stable

MSI

Microsatellite instability (MSI) status is a measure of the number of somatic mutations within short, repeated sequences of DNA (microsatellites). MSI-High status can indicate that the tumor has a defect in mismatch repair (MMR) abrogating the ability to correct mistakes during DNA replication. Tumors with MSI-high status may increase the number of neoantigens which is hypothesized to increase T-cell reactivity and potential for response to immune checkpoint inhibitors. Tumor-only microsatellite instability status by NGS (MSI-NGS) is measured by the direct analysis of known microsatellite regions sequenced in the CMI NGS panel.

GENOMIC LOSS OF HETEROZYGOSITY	
Test	Result
Genomic Loss of Heterozygosity (LOH)	Low - 9% of tested genomic segments exhibited LOH (assay threshold is ≥ 16%)

LOH

To calculate genomic loss-of-heterozygosity (LOH), the 22 autosomal chromosomes are split into 552 segments and the LOH of single nucleotide polymorphisms (SNPs) within each segment is calculated. Caris WES data consist of approximately 250k SNPs spread across the genome. SNP alleles with frequencies skewed towards 0 or 100% indicate LOH (heterozygous SNP alleles have a frequency of 50%). The final call of genomic LOH is based on the percentage of all 552 segments with observed LOH.

Additional Next-Generation Sequencing results continued on the next page. >

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Mutational Analysis by Next-Generation Sequencing (NGS)

Gene	Analyte	Variant Interpretation	Protein Alteration	Exon	DNA Alteration	Variant Frequency %	Transcript ID
CTNNB1	DNA-Tumor	Likely Pathogenic Variant	p.V22 _S37del	3	c.63 _111 delinsA	40	NM_001904.3

Interpretation: An inframe deletion mutation was found in CTNNB1. This mutation deletes several amino acids that have been found to be frequently mutated in cancer, therefore, is likely pathogenic.

CTNNB1 or cadherin-associated protein, beta 1, encodes for β-catenin, a central mediator of the Wnt signaling pathway which regulates cell growth, migration, differentiation and apoptosis. Mutations in CTNNB1 (often occurring in exon 3) prevent the breakdown of β-catenin, which allows the protein to accumulate resulting in persistent transactivation of target genes, including c-myc and cyclin-D1. Somatic CTNNB1 mutations occur in 1-4% of colorectal cancers, 2-3% of melanomas, 25-38% of endometrioid ovarian cancers, 84-87% of sporadic desmoid tumors, as well as the pediatric cancers, hepatoblastoma, medulloblastoma and Wilms' tumors.

Additional Next-Generation Sequencing results continued on the next page. >

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Mutational Analysis by Next-Generation Sequencing (NGS)

GENES TESTED WITH INDETERMINATE* RESULTS BY TUMOR DNA SEQUENCING					
COL2A1	DACH1	KIF1B	PRDM6	RASA1	WRN
CUL3	EED	NPM1	PRKD1	REST	
CYSLTR2	JAK2	PLCB4	PTPRD	SMARCA2	

*** Genes in this table were ruled indeterminate due to low coverage for some or all exons.**

For a complete list of genes tested, visit www.CarisMolecularIntelligence.com/profilemenu.

NGS Methods

Direct sequence analysis was performed on genomic DNA isolated from a micro-dissected tumor sample using Illumina NovaSeq 6000 sequencers. A hybrid pull-down panel of baits was used to enrich more than 700 clinically relevant genes along with > 20,000 other genes. Sequence data is analyzed using a customized bioinformatics pipeline to detect sequencing variants, copy number alterations (amplifications and deletions) indels and HLA genotypes. In addition, genomic signatures for tumor mutational burden (TMB), microsatellite instability (MSI), genomic loss-of-heterozygosity (LOH) or HRD-Genomic Scar Score (HRD-GSS), and homologous recombination deficiency (HRD) are reported when applicable. For a complete list of what is covered by the assay, and genes with partial coverage, please contact Caris Customer Support. HLA results are not available in New York State.

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Copy Number Alterations by Next-Generation Sequencing (NGS)

CNA Methods

The copy number alteration (CNA) of each exon is determined by a calculation using the average sequencing depth of the sample along with the sequencing depth of each exon and comparing this calculated result to a pre-calibrated value. A complete list of genes for reporting copy number alterations, including amplifications and deletions, is available upon request.

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Gene Fusion and Transcript Variant Detection by RNA Sequencing

Whole Transcriptome Sequencing (WTS) Methods

Gene fusion and variant transcript detection were performed on RNA isolated from a tumor sample using next generation sequencing. The assay also detects fusions occurring at known and novel breakpoints within genes. The genes included in this report represent the subset of genes associated with cancer. The complete list of unclassified alterations is available by request.

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Protein Expression by Immunohistochemistry (IHC)

Biomarker	Patient Tumor			Thresholds
	Staining Intensity (0, 1+, 2+, 3+)	Percent of cells	Result	Conditions for a Positive Result:
ALK	3 +	90	Positive	Intensity ≥3+ and ≥1% of cells stained
PTEN	3 +	100	Positive	Intensity ≥1+ and ≥1% of cells stained

PD-L1 TUMOR CELL STAINING				
Biomarker	Patient Tumor			Thresholds
	Staining Intensity (0, 1+, 2+, 3+)	Percent of cells	Result	Conditions for a Positive Result:
PD-L1 (28-8)	3 +	100%	Positive	Intensity ≥1+ and ≥1% of cells stained
PD-L1 (SP142)	3 +	100%	Positive	Intensity ≥1+ and ≥50% of cells stained
PD-L1 (SP263)	3 +	100%	Positive	Intensity ≥1+ and ≥1% of cells stained

PD-L1 (28-8): Scoring was based on percentage of viable tumor cells showing partial or complete membrane staining at any intensity.
PD-L1 (SP142): TC scoring was based on the presence of discernible PD-L1 membrane staining of any intensity in ≥ 50% of viable tumor cells.
PD-L1 (SP263): Scoring was based on percentage of viable tumor cells showing partial or complete membrane staining at any intensity.

PD-L1 TUMOR PROPORTION SCORE (TPS)			
Biomarker	Result	TPS	Threshold
PD-L1 (22c3)	Positive	100%	TPS ≥1 %

PD-L1 22c3: Scoring was based on the percentage of viable tumor cells showing partial or complete membrane staining. There are three categories of PD-L1 expression defined by the PD-L1 22c3 IHC pharmDx NSCLC interpretation guide: TPS < 1% (negative), TPS ≥ 1% and TPS ≥ 50%.

PD-L1 IMMUNE CELL (IC) SCORE			
Biomarker	Result	IC	Threshold
PD-L1 (SP142)	Positive	70%	≥10%

PD-L1 (SP142): IC scoring was based on discernible PD-L1 staining of any intensity in tumor-infiltrating immune cells covering ≥ 10% of tumor area occupied by tumor cells, associated intratumoral or contiguous peritumoral stroma.

Clones used: PD-L1 (SP263), PD-L1 (SP142), PD-L1 (22c3), PTEN (6H2.1), ALK (D5F3), PD-L1 (28-8).

Electronic Signature

Additional IHC results continued on the next page. >

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Protein Expression by Immunohistochemistry (IHC)

IHC Methods

The Laboratory Developed Tests (LDT) immunohistochemistry (IHC) assays were developed and their performance characteristics determined by Caris Life Sciences. These tests have not been cleared or approved by the US Food and Drug Administration. The FDA has determined that such clearance or approval is not currently necessary. Interpretations of all immunohistochemistry (IHC) assays were performed manually by a board certified pathologist using a microscope and/or digital whole slide image(s).

The following IHC assays were performed using FDA-approved companion diagnostic or FDA-cleared tests consistent with the manufacturer's instructions: ALK (VENTANA ALK (D5F3) CDx Assay, Ventana), ER (CONFIRM anti-Estrogen Receptor (ER) (SP1), Ventana), FOLR1 (VENTANA FOLR1-2.1 RxDx, Ventana), CLDN18 (43-14A, Ventana), PR (CONFIRM anti-Progesterone Receptor (PR) (1E2), Ventana), HER2/neu (PATHWAY anti-HER-2/neu (4B5), Ventana), Ki-67 (MIB-1 pharmaDx, Dako), PD-L1 22c3 (pharmDx, Dako), PD-L1 SP142 (VENTANA, non-small cell lung cancer), PD-L1 28-8 (pharmDx, Dako, gastric / GEJ, non-small cell lung cancer), PD-L1 SP263 (Ventana, non-small cell lung cancer), and Mismatch Repair (MMR) proteins (MLH1, MSH2, MSH6, and PMS2; VENTANA MMR RxDx Panel, Ventana).

HER2 results and interpretation follow the ASCO/CAP scoring criteria.

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References

#	Drug	Biomarker	Reference
1	alectinib	ALK	Camidge, D.R., A.T. Shaw, et al. (2019). "Updated Efficacy and Safety Data and Impact of the EML4-ALK Fusion Variant on the Efficacy of Alectinib in Untreated ALK-Positive Advanced Non-Small Cell Lung Cancer in the Global Phase III ALEX Study." J Thorac Oncol 14(7): 1233-1243. View Citation Online
2	alectinib	ALK	Gadgeel, S., D.R. Camidge, et al. (2018). "Alectinib versus crizotinib in treatment-naive anaplastic lymphoma kinase-positive (ALK+) non-small-cell lung cancer: CNS efficacy results from the ALEX study." Ann Oncol 29 (11): 2214-2222. View Citation Online
3	alectinib, brigatinib, ceritinib, crizotinib, lorlatinib	ALK	Lindeman, N.I., Y. Yatabe, et al. (2018). "Updated Molecular Testing Guideline for the Selection of Lung Cancer Patients for Treatment With Targeted Tyrosine Kinase Inhibitors Guideline From the College of American Pathologists, the International Association for the Study of Lung Cancer, and the Association for Molecular Pathology." J Thorac Oncol 13(3): 323-358. View Citation Online
4	alectinib, brigatinib, crizotinib	ALK	van der Wekken, A. J., H.J.M Groen, et al. (2017). "Dichotomous ALK IHC is a better predictor for ALK inhibition outcome than traditional ALK FISH in advanced Non-small cell lung cancer." Clin Cancer Res 23(15): 4251-4258. View Citation Online
5	entrectinib	ROS1	Desai AV, Brodeur GM, Foster J, et al. Phase I study of entrectinib (RXDX-101), a TRK, ROS1, and ALK inhibitor, in children, adolescents, and young adults with recurrent or refractory solid tumors. J Clin Oncol. 2018;36 (suppl;abstr 10536). doi: 10.1200/JCO.2018.36.15_suppl.10536. View Citation Online
6	entrectinib	ROS1	Demetri, G.D., R.D., Doebele, et al. (2018). "Efficacy and safety of entrectinib in patients with NTRK fusion-positive tumors: pooled analysis of STARTRK-2, STARTRK-1 and ALKA-372-001. Presented at: 2018 ESMO Congress; October 19-23, 2018; Munich, Germany. Abstract LBA17. View Citation Online
7	brigatinib, crizotinib	ALK	National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer Version 1.2020
8	brigatinib, crizotinib	ALK	Thorne-Nuzzo, T., P. Towne, et al. (2017). "A Sensitive ALK Immunohistochemistry Companion Diagnostic Test Identifies Patients Eligible for Treatment with Crizotinib." J Thorac Oncol 12(5): 804-813 View Citation Online
9	brigatinib	ALK	Camidge, D.R., S. Popat, et al. (2018). "Brigatinib versus Crizotinib in ALK-Positive Non-Small-Cell Lung Cancer." N Engl J Med 379(21): 2027-2039. View Citation Online
10	brigatinib	ALK	Lin, J.L., G.J. Riely, et al. (2018). "Brigatinib in Patients with Alectinib-refractory ALK-positive NSCLC." J Thorac Onc 13(10): 1530-1538. View Citation Online
11	ceritinib, lorlatinib	ALK	Soria, J.C., de Castro G., et al. (2017). "First-line ceritinib versus platinum-based chemotherapy in advanced ALK-rearranged non-small-cell lung cancer (ASCEND-4): a randomised, open-label, phase 3 study." Lancet 389: 917-929. View Citation Online
12	ceritinib, lorlatinib	ALK	Solomon, B. J., A. T. Shaw, et al. (2018). "Lorlatinib in patients with ALK-positive non-small cell lung cancer: results from a global phase 2 study." Lancet Oncol 19:1654-1667. View Citation Online
13	ceritinib, lorlatinib	ALK	Shaw, A.T., E. Felip, et al. (2017). "Ceritinib versus chemotherapy in patients with ALK-rearranged non-small-cell lung cancer previously given chemotherapy and crizotinib (ASCEND-5): a randomised, controlled, open-label, phase 3 trial." Lancet Oncol 18 (7):874-886. View Citation Online
14	nivolumab/ipilimumab combination	PD-L1 (28-8)	Hellmann, M.D., S.S. Ramalingam, et al., (2019). "Nivolumab plus Ipilimumab in Advanced Non-Small-Cell Lung Cancer." N Engl J Med 381:2020-31. View Citation Online
15	pralsetinib, selpercatinib	RET	National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Non-Small Cell Lung Cancer Version 6.2020 View Citation Online
16	selpercatinib	RET	Drilon, A., V. Subbiah, et al. (2020). "Efficacy of Selpercanib in RET Fusion-Positive Non-Small-Cell Lung Cancer." N Engl J Med. 383 (9): 813-824. View Citation Online

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References

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