MAYO CLINIC

1-800-533-1710

MayoComplete Solid Tumor Panel

MCSTP

PATIENT NAME				ORDER NUMBER
IMPLEMENTATION, TEST T				**O020000405**
PATIENT ID X100458442	DATE OF BIRTH 05/01/1973	AGE 50 Y	SEX Female	REQUESTED BY CLIENT TESTING
COLLECTED 3/20/2024, 7:00 AM	RECEIVED 3/20/2024, 1:53 PM	REPORTED 4/5/2024, 1:24 PM		

The collected, received, and reported dates and times on the report are in the time zone of the performing location.

7028846
MCL RochesterCampus
Rochester MN 55901

CLIENT ORDER NUMBER
X100458442

CLIENT MRN
321

RESULT

Variant	AMP Tier	FDA Approved Therapies	FDA Approved Therapies (for other tumor type)	Clinical Trials
Tumor Mutational Burden LOW (0 mutations/Mb)	2D	None	None	None
Microsatellite STABLE (1.2%)	2C	None	None	Yes

PROVIDED DIAGNOSIS: LUNG ADENOCARCINOMA

INTERPRETATION

RNA testing revealed no evidence of fusions or splice/transcript variants.

Tumor Mutational Burden (TMB)/Microsatellite Instability (MSI): No high mutational burden or microsatellite instability was observed in this sample.

TMB: LOW (0 mutations/Mb)
MSI: STABLE (MSS)

Current data suggests that the efficacy of targeted therapies in patients with non-small cell lung cancer is limited to tumors with rearrangements or mutations in certain genes [PMID 23562183, PMID 27151654, PMID 27080216, PMID 27283860, PMID 25971939, PMID 25971938, PMID 24162815]. Thus, the absence of a targetable mutation or rearrangement within this tumor suggests that therapies may have limited value for this patient. However, for patients with advanced, recurrent, or metastatic non-small cell lung cancer without targetable genomic aberrations, immune checkpoint blockade may be considered in proper clinical settings [fda.gov/drugs].

ADDITIONAL INFORMATION

Sequencing coverage greater than or equal to 100X was observed in 98.0% of targeted regions.

Low coverage regions (< 100X coverage):
BIRC3 (Exon 6); CHD2 (Exon 27); DIS3 (3'UTR); EIF4E (Exon 7); GEN1 (3'UTR); H3-3A (3'UTR); IDH1 (3'UTR); IFNGR1 (3'UTR); KRAS (3'UTR); MAGI2 (Exon 11); MRE11 (3'UTR); NCOR1 (Exon 12, Exon 4); NFE2L2 (3'UTR); NPM1 (3'UTR, Exon 10); PIK3C2G (Exon 10); PIK3C3 (3'UTR, Exon 24); PIK3CA (Exon 13); PTEN (Exon 3); PTPRD (Exon 16,Exon 26); RANBP2 (Exon 11, Exon 19); RASA1 (Exon 6, Exon 7); RB1 (Exon 15); RICTOR (Exon 19); RUNX1 (Exon 3); SF3B1 (3'UTR); SH2D1A (3'UTR, Exon 4); STAG2 (Exon 21); SUZ12 (3'UTR); TET1 (5'UTR)

Evidence-based sequence variant classification was performed according to the 2017 AMP/ASCO/CAP Joint consensus recommendation [PMID 27993330] as follows: Tier 1 - Variant with strong clinical significance; Tier 2 - Variant with

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potential clinical significance; Tier 3 - Variant of unknown (uncertain) clinical significance; Tier 4 - Benign or likely benign variant. Tiers 1 and 2 variants are clinically significant mutations and rearrangements. Only Tiers 1 and 2 variants are interpreted.

A complete gene list is available online (www.mayoclinic.org; test code MCSTP)

CLINICAL TRIALS

Markers	Trial ID	Title	Locations/Contact
Microsatellite STABLE (1.2%)	NCT03947385	A Phase 1/2 Study of IDE196 in Patients With Solid Tumors Harboring GNAQ/11 Mutations or PRKC Fusions	United States: CA NC NY OH PA TN TX(IDEAYA Clinical Trials; IDEAYAClinicalTrials@ideayabio.com; +1 650 534 3616)
Microsatellite STABLE (1.2%)	NCT05572684	A Phase 1b/2 Open-Label Safety Tolerability and Efficacy Study of NC410 Plus Pembrolizumab for Participants With Advanced Unresectable and/or Metastatic Immune Checkpoint Inhibitor (ICI) Refractory Solid Tumors or ICI Naïve MSS/MSI-Low Solid Tumors	United States: AZ CO KY LA MD NJ OH TX VA WA(Associate Director Clinical Operations at NextCure Inc.; NCClin@nextcure.com; 859-468-8632)

Clinical trials associated with Tiers 1 and 2 variants that have a status of recruiting are included in the table above.

SPECIMEN

Tissue, Tumor

TISSUE ID

56123

METHOD

Microscopic examination was performed by a pathologist to identify areas of tumor for enrichment by macrodissection.

DNA and RNA were extracted from FFPE or cytology slides, and next generation sequencing using the Illumina TruSight Oncology 500 chemistry was performed. The following variant types and molecular profiles were evaluated: tumor mutation burden (TMB) status, microsatellite instability (MSI) status, sequence variants involving exonic regions and exon/intron boundaries of 515 genes, gene amplifications in 96 genes, homozygous deletion of 133 genes, biallelic inactivation of 31 tumor suppressor genes, fusions involving any of 55 genes, and transcript variants in 3 genes. For TMB calculation, the minimal coding region size considered for TMB calculation that is consistently meeting the required 50x minimal sequence coverage criteria is 1.1 Mb, but is 1.28 MB on average. All nonsynonymous and synonymous qualifying somatic SNVs and DELINSs that have a minimum VAF of 5% and 50x depth at the variant position are considered for TMB computation. Driver mutations are not included in the TMB calculation.

AMP/ASCO/CAP classifications and clinical trials and therapeutic information were powered by Qiagen Clinical Insights -

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Interpret One (QCI-11). Variant nomenclature is based on build GRCh37 (hg19). For targeted gene lists, details about gene transcripts (GenBank accession numbers), specific targeted regions of each gene, and additional information on this test, see www.mayocliniclabs.com (Test ID MCSTP).

DISCLAIMER

CLINICAL CORRELATIONS

Test results should be interpreted in context of clinical findings, tumor sampling, histopathology, and other laboratory data. If results obtained do not match other clinical laboratory findings, please contact the laboratory for possible interpretation. Misinterpretation of results may occur if the information provided is inaccurate or incomplete.

This test is performed to evaluate for somatic (i.e., tumor-specific) variants. Although germline (i.e., inherited) alterations may be detected, this test cannot distinguish between germline and somatic alterations. Follow-up germline testing using non-neoplastic (normal) tissue can be performed for confirmation of suspected clinically relevant germline alterations. Germline testing should be performed along with genetic counselling.

The clinical trials provided are current as of the date that the report was generated and may not include all clinical trials available. Additional clinical trials can be found at clinicaltrials.gov. Data interpretation including therapeutic matching (FDA approved drugs, NCCN guidelines and clinical trials) with the variants identified are based on the primary tumor type.

The presence or absence of a genetic variant may not be predictive of response to therapy in all patients.

TECHNICAL LIMITATIONS

Variant Allele Frequency:

Variant allele frequency (VAF) is the percentage of sequencing reads supporting a specific variant divided by the total sequencing reads at that position. In somatic testing, VAF should be interpreted in the context of several factors including, but not limited to: tumor purity/heterogeneity/copy number status (ploidy, gains/losses, loss of heterozygosity) and sequencing artifact/misalignment [PMID: 27144058, PMID: 29769535].

Tumor Purity:

A tumor percentage of greater than or equal to 20% by morphological assessment is required to perform the assay and has shown to be sufficient for accurate detection of SNVs, insertions, deletions, fusions, and splice variants. However, a tumor percentage of greater than or equal to 40% is preferred to accurately detect copy number variants (CNVs), TMB, and MSI status. A tumor percentage lower than 40% may result in false negative results for MSI and/or copy number alterations and an underestimation of TMB. Performance characteristics (accuracy, reproducibility, and analytical sensitivity) are described in the laboratory test catalog.

Detection Thresholds:

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The sensitivity for SNVs, insertions, and deletions at or above 5% VAF was 97.9%. The sensitivity for variants with VAFs between 2-5% may be lower. Insertions and deletions are detected at 99.0% accuracy at or below 31 bp. The sensitivity for insertions and deletions larger than above 31 bps has not been determined. Tumor copy number variations can impact sequence coverage which in turn can impact the sensitivity for SNVs detection, and TMB calculation. A number of regions, originally included in this assay, are excluded from the reportable range due to low sequence coverage, or high background noise level. Gene amplifications and homozygous deletions are called by an in-house developed bioinformatics pipeline and are manually reviewed to optimize sensitivity and specificity. SNV, CNV, TMB and MSI markers calling may be impacted by suboptimal sequence coverage. Therefore, gene regions not achieving 100x coverage are disclaimed on the report. Amplification is defined as the presence of 6 or more copies of the gene for a diploid baseline genome. Reported copy numbers are an estimate of the identified gene copy number within the tumor purity of the specimen and are not adjusted to represent 100% tumor purity. Three supporting reads are required to call a gene fusion, and 10 supporting reads are required to call a splice/transcript variant. Tumor mutational burden (TMB) scores are classified as TMB-Low (less than 10 mutations/Mb) or TMB-High (greater than or equal to 10 mutations/Mb) in accordance with validation studies initially performed on lung cancer samples demonstrating a clinical response to immune checkpoint inhibitors, and more recently in multiple other solid tumor types, where TMB was evaluated by the TSO500 assay [PMID: 35218944]. MSI status is classified as MS-Stable (less than 20% unstable microsatellite sites) or MSI-High (greater than or equal to 20% unstable sites).

Rare polymorphisms may be present that could lead to false negative or false positive results.

A negative (wild-type) result does not rule out the presence of a mutation or rearrangement that may be present but below the limits of detection of the assay or not interrogated by the assay.

TEST CLASSIFICATION

The test was developed and its performance characteristics determined by Mayo Clinic in a manner consistent with CLIA requirements. This test has not been cleared or approved by the U.S. Food and Drug Administration.

RELEASED BY

HUSSAM AL KATEB

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