Overview

Useful For
Assisting in tumor profiling for diagnosis, predicting prognosis, and identifying targeted therapies for the treatment and management of patients with solid tumors

Identifying somatic alterations including single nucleotide variants (SNV), small insertions/deletions (INDEL), gene amplifications, fusions, and splice variants in genes known to be associated with the tumorigenesis of solid tumors

Assessment of microsatellite instability and tumor mutational burden status

Genetics Test Information
This test uses targeted next-generation sequencing to estimate tumor mutational burden (TMB), determine microsatellite instability (MSI) status, and identify somatic sequence variants, gene amplifications, fusions, and specific transcript variants in solid tumors. This panel includes a DNA subpanel for the detection of sequence alterations in 514 genes and amplification of 59 genes as well as an RNA subpanel for the detection of fusions involving 55 genes and specific splice variants involving EGFR, AR, and MET. See Genes Interrogated by MayoComplete Solid Tumor Panel in Special Instructions for details regarding genes interrogated by this test.

Note: This test is performed to evaluate for somatic (ie, tumor-specific) alterations within the genes listed. Although germline (ie, inherited) alterations may be detected, this test cannot distinguish between germline and somatic alterations with absolute certainty. Follow-up germline testing using whole blood can be performed for confirmation of suspected clinically relevant germline alterations. Germline testing should be performed along with genetic counselling.

Highlights
In addition to single nucleotide variants (SNV) and small insertions/deletions sequence variants, this test also identifies gene amplifications, fusions, and splice variants. Tumor mutational burden (TMB) and microsatellite instability (MSI) status are also determined as part of this test and are often clinically actionable for determining the efficacy of immunotherapy in solid tumors.

For each case, a quantitative value for TMB and qualitative assessments for TMB (TMB-Low, TMB-High) and MSI (MSS, MSI-H) are reported.

Additional Tests

<table>
<thead>
<tr>
<th>Test ID</th>
<th>Reporting Name</th>
<th>Available Separately</th>
<th>Always Performed</th>
</tr>
</thead>
<tbody>
<tr>
<td>SLIRV</td>
<td>Slide Review in MG</td>
<td>No, (Bill Only)</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Testing Algorithm
When this test is ordered, slide review will always be performed at an additional charge to ensure specimen adequacy.

Special Instructions
- Genes Interrogated by MayoComplete Solid Tumor Panel
- MayoComplete Solid Tumor Panel DNA Panel Excluded DNA Regions

Method Name
Sequence Capture and Targeted Next-Generation Sequencing (NGS)

NY State Available
No

Specimen

Specimen Type
Varies

Ordering Guidance
Multiple oncology (cancer) gene panels are available. For more information see Oncology Somatic NGS Testing Guide.

Necessary Information
Pathology report (final or preliminary) at minimum containing the following information must accompany specimen for testing to be performed:

1. Patient name
2. Block number—must be on all blocks, slides and paperwork (can be handwritten on the paperwork)
3. Tissue collection date
4. Source of the tissue

Specimen Required
This assay requires at least 20% tumor nuclei. However, 40% tumor is preferred.

-Preferred amount of tumor area: 720 mm\(^2\) tissue on up to 20 unstained slides
-Minimum amount of tumor area: 192 mm\(^2\) tissue on up to 20 unstained slides
-Tissue fixation: 10% neutral buffered formalin, not decalcified

-For this test, at least 6mm x 6mm areas on 20 unstained slides is preferred: this is approximately equivalent to 720 mm\(^2\). The minimum acceptable area is 3.1mm x 3.1mm on 15 unstained slides: approximately equivalent to 192 mm\(^2\).

Preferred:

Specimen Type: Tissue block

Collection Instructions: Submit a formalin-fixed, paraffin-embedded tissue block with acceptable amount of tumor tissue

Acceptable:

Specimen Type: Tissue slide
Test Definition: MCSTP
MayoComplete Solid Tumor Panel

Slides: 1 stained and 20 unstained

Collection Instructions: Submit 1 hematoxylin and eosin (H and E) stained slide and 20 unstained, nonbaked 5-micron thick sections

Note: The total amount of required tumor can be obtained by scraping up to 20 slides from the same block.

Specimen Type: Cytology slides (direct smears or ThinPrep)

Slides: 2 to 6 slides

Collection Instructions: Submit 2 to 6 stained and cover slipped slides with a preferred total of 10,000 nucleated cells or a minimum of at least 6,000 nucleated cells

Note: Glass coverslips are preferred; plastic coverslips are acceptable but will result in longer turnaround times.

Additional Information: Cytology slides will not be returned. An image of the slides will be stored per regulatory requirements.

Forms
If not ordering electronically, complete, print, and send a Oncology Test Request (T729) with the specimen.

Specimen Minimum Volume
See Specimen Required

Reject Due To

| Decalcified specimens | Bone marrow in EDTA | Reject |

Specimen Stability Information

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Temperature</th>
<th>Time</th>
<th>Special Container</th>
</tr>
</thead>
<tbody>
<tr>
<td>Varies</td>
<td>Ambient (preferred)</td>
<td></td>
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<tr>
<td></td>
<td>Refrigerated</td>
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</table>

Clinical and Interpretive

Clinical Information
Targeted cancer therapies are defined as antibody or small molecule drugs that block the growth and spread of cancer by interfering with specific cell molecules involved in tumor growth and progression. Multiple targeted therapies have been approved by the US Food and Drug Administration (FDA) for treatment of solid tumor malignancies. Molecular genetic profiling is often needed to identify targets amenable to targeted therapies and to minimize treatment costs and therapy-associated risks. Tumor mutational burden (TMB) and microsatellite instability (MSI) status are increasingly important biomarkers for determining effective immunotherapeutic treatment options for patients with solid tumors.(1,2)

In addition to providing therapeutic insight, molecular profiling of tumors often provides prognostic and diagnostic
information. Next-generation sequencing is an accurate, cost-effective method to identify variants across numerous genes known to be associated with response or resistance to specific targeted therapies. This test is a single assay that uses formalin-fixed paraffin-embedded tissue or cytology specimens to assess for Tier I and Tier II variants in 514 genes known to be associated with solid tumors.(3)

**Reference Values**
An interpretive report will be provided.

**Interpretation**
An interpretive report will be provided.

**Cautions**
Next-generation sequencing is performed to estimate tumor mutational burden (TMB) and microsatellite instability (MSI) status, somatic sequence variants, gene amplifications, fusions, and specific transcript variants in solid tumors. This test detects single nucleotide variants and small insertions and deletion within 514 genes, amplification of 59 genes, gene fusions involving 55 genes, and splice variants involving \( \text{EGFR}, \text{AR}, \) and \( \text{MET}. \)

See [Genes Interrogated by MayoComplete Solid Tumor Panel](#) in Special Instructions for details regarding genes interrogated by this test.

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

This test does not differentiate between somatic and germline alterations. Additional testing may be necessary to clarify the significance of results if there is a potential hereditary risk.

This test does not detect large structural variants, copy number changes, or insertions, deletions, or duplications greater than approximately 20 base pairs in size.

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

A negative (ie, wildtype) result does not rule out the presence of an alteration that may be present but below the limits of detection of this assay.

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

[A list of genomic regions in the DNA panel that have insufficient coverage to reliably detect](#) single nucleotide variants (SNV) and small insertions/deletions (INDEL) are listed in [MayoComplete Solid Tumor Panel DNA Panel Excluded DNA Regions](#) in Special Instructions.

**Supportive Data**

**Performance Characteristics**

The limit of detection for calling a somatic variant (single nucleotide variants [SNV] and small insertions/deletions [INDEL]) is 2% variant allele frequency (VAF) having at least 150X median exon coverage depth. To ensure accuracy, this test will be performed on cases that are estimated by a pathologist to have 20% or more tumor cells, however, for optimal performance of this assay, a tumor purity of 40% is recommended.

Verification studies demonstrated concordance between this test and the reference method for detection of SNV and
INDEL in 98.8% (503/509) and 98.6% (294/298) of variants, respectively. Detection accuracy of INDEL was 99.3% (277/279) in variants 1-10 base pairs (bp) in size, 93.3% (14/15) in variants 11-20 bp in size, and 75.0% (3/4) in variants greater than 20 bp in size.

Gene amplification is identified at a 2.2x fold change based on the normalized read depth over the copy number variant (CNV) target divided by the normalized read depth of the inferred diploid genome. Gene amplification detection is most accurate at 40% or more tumor cells. For gene amplifications, overall sensitivity was 98.7% (81/82), specificity was 92.3% (24/26), and concordance was 95.3% (105/108) during verification studies.

Of the 130 microsatellite sites available for evaluation in this assay, at least 20% of sites are required to be unstable to classify the case as MSI-High. Microsatellite instability (MSI) evaluation is most accurate at a tumor purity of 40% or more, although, highly unstable tumors may be detectable at 20% tumor. During verification studies, 100% concordance was observed between this test and orthogonal methods used to detect MSI status.

Tumor mutational burden (TMB) was measured as mutations per megabase for regions with greater than 50X coverage. When TMB scores were classified as TMB-Low (<10 mut/Mb) or TMB-High (> or =10 mut/Mb), 83% (50/60) concordance was achieved between this test and orthogonal assays detecting TMB status. Of the 10 samples with conflicting qualitative classification (ie, TMB-Low or TMB-High), the TMB quantitative values were near the 10 mut/Mb cutoff (3.9-11.8 mut/Mb). TMB values are most accurate at greater than or equal to 40% tumor purity.

Fusions are detected with the presence of 3 or more supporting reads passing pipeline filters and splice variants with 10 or more supporting reads. For fusions and splice variants, overall sensitivity was 98.0% (151/154), specificity was 94.8% (91/96), and overall concordance was 96.8% (242/250). Fusion and splice variant detection are most accurate at greater than or equal to 20% tumor purity.

Table 1. Analytical Sensitivity

<table>
<thead>
<tr>
<th>Variant type</th>
<th>Threshold for positivity</th>
<th>Recommended tumor purity</th>
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<tbody>
<tr>
<td>SNV</td>
<td>&gt; or =2% VAF &gt; or =150X median exon coverage</td>
<td>&gt; or =20%</td>
</tr>
<tr>
<td>INDEL</td>
<td>&gt; or =2% VAF, &lt; or =20 bp</td>
<td>&gt; or =20%</td>
</tr>
<tr>
<td>Gene amplification</td>
<td>&gt; or =2.2X fold change</td>
<td>&gt; or =40%</td>
</tr>
<tr>
<td>MSI status</td>
<td>&gt; or =20% sites unstable= MSI-H</td>
<td>&gt; or =40%</td>
</tr>
<tr>
<td>TMB status</td>
<td>&gt; or =10 variants per megabase TMB-H</td>
<td>&gt; or =40%</td>
</tr>
<tr>
<td>Fusion</td>
<td>&gt; or =3 supporting reads</td>
<td>&gt; or =20%</td>
</tr>
<tr>
<td>Splice variant</td>
<td>&gt; or =10 supporting reads</td>
<td>&gt; or =20%</td>
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Clinical Reference


4. Instruction manual: TruSight Oncology 500 High-Throughput. Illumina; 11/2020

**Performance**

**Method Description**

Next-generation sequencing is performed to estimate tumor mutational burden (TMB) and microsatellite instability (MSI) status, somatic sequence variants, gene amplifications, fusions, and specific transcript variants in solid tumors. This test detects single nucleotide variants and small insertions and deletion within 514 genes, amplification of 59 genes, gene fusions involving 55 genes, and splice variants involving EGFR, AR, and MET. (Instruction manual: TruSight Oncology 500 High-Throughput. Illumina; 11/2020)

See [Genes Interrogated by MayoComplete Solid Tumor Panel](#) in Special Instructions for details regarding genes interrogated by this test.

**PDF Report**

Supplemental

**Day(s) Performed**

Varies

**Report Available**

14 to 21 days

**Specimen Retention Time**

FFPE tissue: Unused portions of FFPE blocks will be returned. Unused, unstained slides: 5 years; Stained slides: Indefinitely.

**Performing Laboratory Location**

Rochester

**Fees and Codes**

**Fees**

- Authorized users can sign in to [Test Prices](#) for detailed fee information.
- Clients without access to Test Prices can contact [Customer Service](#) 24 hours a day, seven days a week.
- Prospective clients should contact their Regional Manager. For assistance, contact [Customer Service](#).

**Test Classification**

This 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 US Food and Drug Administration.

**CPT Code Information**

81455

81479 (if appropriate for gov't payors)
## LOINC® Information

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