MSI BY PCR ANALYSIS: MP24-190MP00053

Order: 9999999999 - Reflex for Order 0000000000

Collected **MM/DD/YYYY 0:00 PM** Status: **Final result** Visible to patient: **Yes (seen)**

Dx: **Person encountering health services t...**

Component

Microsatellite Status

PCR Analysis

Cleveland Clinic MSI PCR Analysis

Laboratory Accession Number: 0000000000
Case #: P00-000000
Part ID: XXXXX
Sample Type: FFPET

% Tumor: 15

RESULT:
Indeterminate

INTERPRETATION:
This sample is indeterminate for MSI testing by PCR. Microsatellite instability is NOT DETECTED in this specimen; however, the tumor purity was significantly less that required (<40%). As such, a negative result may be due to decreased sensitivity and is considered indeterminate. Testing of an alternative specimen is recommended. Clinical and pathological correlation required.

Microsatellite instability (MSI) is a hypermutator phenotype, caused by the loss of mismatch repair (MMR) gene function (MMR deficiency; dMMR). Tumor MSI-H/dMMR status can be due to germline genetic mutation (Lynch Syndrome) or, more commonly, somatic genetic and epigenetic changes. MSI/dMMR status is routinely assessed for any sporadic cancer type in the Lynch Syndrome spectrum (i.e., colorectal, endometrial, etc.), and MSI-H/dMMR status can predict clinical benefit of immune checkpoint blockade for solid tumors. Specifically, the anti-PD-1 antibody pembrolizumab is an FDA-approved drug for therapy of adult and pediatric patients with unresectable or metastatic MSI-H/dMMR solid cancers that have progressed following prior treatment. In addition, the anti-PD-1 antibody dostarlimab in combination with carboplatin and paclitaxel is FDA-approved for the treatment of patients with MSI-H/dMMR endometrial cancer. The anti-PD-1 antibodies pembrolizumab or nivolumab, as single-agents, and the anti-CTLA4 antibody ipilimumab in combination with nivolumab are FDA-approved for the treatment of patients with MSI-H/dMMR metastatic colorectal cancer.

METHODS:
The Idylla MSI PCR analysis assay is a rapid, automated, cartridge-based system to detect microsatellite instability in seven monomorphic DNA biomarkers (ACVR2A, BTBD7, DIDO1, MRE11, RYR3, SEC31A and SULF2) using real-time PCR from formalin-fixed paraffin embedded tissue specimens. The assay was performed according to manufacturer's instructions. Samples with less than 40 percent tumor purity undergo

macrodissection prior to analysis. This assay is performed on the Idylla system (Biocartis US, Itasca, IL). MSI PCR cartridges contain dried reagents (enzymes, primers, and probes), 1.7 ml liquefaction buffer and 2.2 ml dilution buffer to enable tissue to undergo liquefaction, cell lysis, extraction, real-time PCR amplification and detection. After PCR amplification, molecular beacons differentially dissociate from the wild type or mutated amplicons with increasing temperature. The MSI specific software included in the Idylla system checks the validity of the measured fluorescence profiles. These profiles are analyzed by the software to determine marker genotype. The MSI status of the sample can be determined if at least five valid marker-specific fluorescence profiles could be fully analyzed (otherwise the MSI status will be called "Invalid"). If the sample is valid for test resulting, at least two mutant markers will result in a status being MSI-H (Microsatellite Instability-High), otherwise the status will be scored as MSS (Microsatellite Stable).

LIMITATIONS:
Specimens must contain at least 40 percent tumor cells; if less than 40 percent tumor is utilized, a negative result is of indeterminate significance. Tumor heterogeneity, tumor burden, specimen degradation or other limitations of the technology may affect the sensitivity. Interfering substances, specifically formalin, decalcification agents, fixation agents containing heavy metals or preservation of buffy coats using Hank's Balanced Salt Solution (HBSS) can potentially affect assay performance. This test cannot distinguish between somatic and germline variants. Molecular microsatellite instability can be assessed by clinically validated IHC, PCR and NGS methods; discrepancies between these results can occur due to technical or biological reasons. Test results obtained using this assay must be interpreted by healthcare professionals in conjunction with other clinical findings, family history and other laboratory data.

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DISCLAIMER:
This test was developed and its performance characteristics determined by Cleveland Clinic's Robert J. Tomsich Pathology and Laboratory Medicine Institute (RT-PLMI). It has not been cleared or approved by the FDA. RT-PLMI is regulated under CLIA as certified to perform high-complexity testing. This test is used for clinical purposes. It should not be regarded as investigational or for research.

Testing and interpretation performed at Cleveland Clinic, 9500 Euclid Ave, Cleveland, OH 44195. CLIA Number: 36D0656094

As reviewed by Elizabeth Azzato, MD, PhD