DNA Test Report

MGM527: Microsatellite Instability (MSI) by fragment analysis

Patient P.W.B. RENUKA VITHANA /59 years **SID/OID:** 8840970/ 1128578

Patient Details		Specimen Information		Ordering Clinician	
Name	P.W.B. RENUKA VITHANA	**Sample ID**	8840970	**Clinician**	Dr. Mahendra Perera
		Order ID	1128578		
Gender/Age	Female / 59 Years	**Specimen Type**	FFPE Tumour	**Affiliation**	Aegle Omics Private Limited-Colombo
Patient ID	NA	**Date Received**	4th December 2024		
Tumor Type	Colorectal Neoplasms	**Date and Time of Report**	12th December 2024		

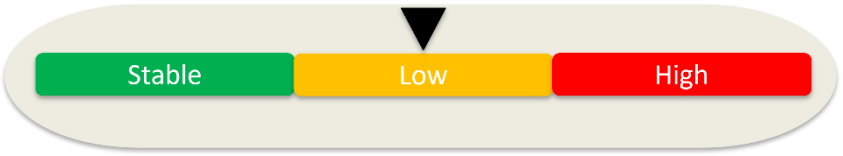
Test Code MGM527 **Test Name** **Microsatellite Instability (MSI) by fragment analysis**

CLINICAL DIAGNOSIS/INDICATIONS/HISTORY

Moderately differentiated adenocarcinoma of sigmoid colon and upper rectum; pT3N2aMx Stage IIIB. The tumor content estimated for the tissue available in the FFPE block [SK3020 (A4)] was adequate for further analysis.

TEST RESULT SUMMARY

Microsatellite Instability (MSI) Status –– MSI-L



Summary of Markers	
Count of markers reported Unstable	**01**
Count of markers reported Stable	**11**
Reported Unstable Rate	***8%***
Unstable Markers	***ABI-20B***

CLINICAL SIGNIFICANCE

- MSI screening has long been recognized as important in the care of patients with colorectal cancer (CRC) or endometrial cancer (EC).
- High-frequency MSI (MSI-H) is also recognized as a potential marker for germline mutations in certain DNA mismatch repair (MMR) genes associated with Lynch syndrome [PMID: 15872200].
- MSI has been found in several cancer types, including non-small cell lung cancer, melanoma, breast cancer, urothelial cancer, pancreatic ductal adenocarcinoma and brain cancer. The expansion of MSI clinical trials into other cancers may elucidate the prognostic and predictive value of MSI for non-colorectal [PMID: 35955855].
- NCCN® guidelines recommend universal screening for 15+ different cancer types by MSI and/or IHC analysis [www.nccn.org]
- MSI-H status is predictive of a positive response to immunotherapies such as immune checkpoint blockade inhibitors [PMID: 26028255]
- The 2015 paper by Le et al. reported the extended analysis on the efficacy of PD-1 blockade in patients with advanced mismatch repair-deficient cancers of both colorectal cancer and non-colorectal origins. Following 41 patients, the study found that patients with mismatch repair deficient

tumors, experienced an objective response rate of 40% and a progression-free survival rate of 78%. In contrast, the objective response rate was 0% and the progression-free survival rate was 11% for mismatch repair-proficient patients [PMID: 26028255].

- The College of American Pathologists (CAP), in collaboration with the Association of Molecular Pathology (AMP), American Society of Clinical Oncology (ASCO), and patient advocacy group Fight Colorectal Cancer (Fight CRC) convened a multidisciplinary expert and advisory panel to develop evidence-based guidelines to identify the optimal clinical laboratory test to identify defects in DNA mismatch repair (dMMR) in patients with solid tumor malignancies who are being considered for immune checkpoint inhibitor (ICI) therapy. MSI by PCR was recommended for colorectal cancer, patients with gastroesophageal and small bowel cancer and other solid malignancies [PMID: 35920830].
- On June 29, 2020, the Food and Drug Administration approved pembrolizumab (KEYTRUDA, Merck & Co.) for the first-line treatment of patients with unresectable or metastatic microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) colorectal cancer [www.fda.gov]
- The FDA approved pembrolizumab on May 23, 2017, for the treatment of adult and pediatric patients with unresectable or metastatic, microsatellite instability-high (MSI-H), or mismatch repair deficient (dMMR) solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options and for the treatment of unresectable or metastatic MSI-H or dMMR colorectal cancer that has progressed following treatment with a fluoropyrimidine, oxaliplatin, and irinotecan [www.fda.gov].

DISCLAIMER

- **Decisions regarding treatment action plan should not be solely based on these test results. These findings are highly recommended to be correlated with the patient's clinical, pathological, radiological and family history for decisions on diagnosis, prognosis, or therapeutics.**
- The therapy information provided in this report is based on FDA approved drugs data, NCCN guidelines, peer-reviewed published literature, standard clinical databases, and strength of biomarker results. These therapies may or may not be suitable/beneficial to a particular patient. This clinical report summarizes potentially effective medications, potentially ineffective medications, and medications that may pose a higher risk of adverse reactions by mapping the patient's genetic alterations to the biomedical reference information. The report may also provide prognostic and diagnostic biomarkers detected or shown for the given disease context.
- The identification of a genomic biomarker does not necessarily imply pharmacological effectiveness or ineffectiveness. The medications identified by the treating physician may or may not be suitable for use on a particular patient. Thus, the clinical report does not guarantee that any particular agent will be effective in the treatment of any particular condition. Also, the absence of a treatment option does not determine the effectiveness or predict an ineffective or safety-relevant effect of a medication selected by the treating physician.
- Due to poor quality of FFPE tissue blocks, the QC parameters for extracted DNA may not pass to proceed further with the testing, therefore there is a possibility of assay failure or compromised. However, sample status in such scenarios shall be sent through mail to the ordering clinician.
- This test has been validated at MedGenome Labs as per the CAP guidelines with 100% sensitivity and specificity.
- The results of this test are dependent on the tumor content in the tissue sample provided. A minimum of >10% tumour content is required for a successful testing.
- In case of MSI negative or MSS patients, if there is a co-existing strong personal or family history of HNPCC related cancers for this patient, consider microsatellite instability and IHC testing on a different tumor block to further evaluate the possible role of defective DNA mismatch repair.
- **Additional case specific disclaimer: In this case, the markers "*ABI-20A*" had failed in amplification. Hence, the MSI status of this subject has been interpreted based on the status of 11 out of 13 markers. Kindly correlate clinically.**

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TEST METHODOLOGY

This assay detects the presence of microsatellite instability (MSI) in DNA samples through multiplex PCR [1] and fragment analysis and screens for 13 mononucleotide markers listed in table below. Mononucleotide markers like BAT-25, BAT-26 and BAT-40 markers are selected as per the NCI guidelines. A revised guidelines suggests mononucleotide marker panel is more sensitive for MSI-H tumors than other microsatellite markers. Dinucleotide markers are less sensitive, and if only dinucleotide markers are positive, it is mandatory to test additional mononucleotide markers to rule out MSI-L [PMID: 14970275]. This kit contains 13 mononucleotide markers for higher resolution and two STR sequences that can be used to track sample identity [PMID: 35884597, PMID: 35982978].

BAT-25	*NR-21*	*ABI-16*	*ABI-20B*
BAT-26	*NR-22*	*ABI-17*	
BAT-40	*NR-24*	*ABI-19*	
CAT-25	*NR-27*	*ABI-20A*	

The primers are fluorophore tagged at the 5' end and the end-point PCR product is analyzed by Fluorophore Capillary Electrophoresis. The tumor tissue is classified as MSS/MSI-L/MSI-H as mentioned in the table below.

MSI Result	**Interpretation** [PMID: 35884597]
MSI-High	Unstable marker rate:- 30% - 100%
MSI-Low	Unstable marker rate:- 5% - 30%
MSS (Microsatellite Stable)	Unstable marker rate:- 0%

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

Reference:

1. Application note: TrueMark MSI Assay—a simplified solution for analyzing microsatellite instability in FFPE tumor samples, 2020.

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End of Report