Strand® Microsatellite Instability Test (PCR)

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Patient	**Sahabdeen Safan**	SampleID	**STRAN-2024-58182**	Test	**Strand MSI by PCR**
Gender	**Male**	Specimen Type	**FFPE Block**	Type	**Full Report**
Age	**40 Years**	Block ID	**JH1390 A5**	Sample Collected	**07-Sep-2024**
MRN	**NA**	Tumor Content	**75-80%**	Sample Received	**12-Sep-2024**
Clinician	**Dr. A. Iqbal**	Specimen Site	**Colon Caecum**	Report Generated	**27-Sep-2024**
Hospital	**Aegle Omics Private Limited**				

Clinical Indication

Colorectal carcinoma

Results

Total microsatelite loci analysed	5
Total microsatelite loci found instable	5
Status of microsatellite instability (MSI)	MSI-H

Interpretation Summary

This sample has tested positive for microsatellite instability. Microsatellite instability was detected at two or more of the five loci tested.

Microsatellite instability can result from germline or somatic mutations that cause a functional defect in mismatch repair. This can be primarily due to alterations in the mismatch repair genes MLH1, MSH6, MSH2 or PMS2.

Pembrolizumab is approved for the treatment of microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) unresectable or metastatic solid tumors that have progressed following prior treatment and who have no satisfactory alternative treatment options or microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) unresectable or metastatic colorectal cancer that has progressed following treatment with fluoropyrimidine, oxaliplatin, and irinotecan. [1]

Dostarlimab is approved for the treatment of mismatch repair deficient (dMMR) recurrent or advanced solid tumors that have progressed on or following prior treatment and who have no satisfactory alternative treatment options; and mismatch repair deficient (dMMR) or microsatellite instability-high (MSI-H) recurrent or advanced endometrial cancer in combination with platinum-containing regimen; or as single agent in mismatch repair deficient (dMMR) recurrent or advanced endometrial cancer that has progressed on or following prior treatment with a platinum-containing regimen. [2]

Nivolumab is approved for the treatment of microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR) metastatic colorectal cancer that has progressed following treatment with fluoropyrimidine, oxaliplatin, and irinotecan. [3]

Patients with stage II MSI-H colorectal cancer show good prognosis and may not benefit additionally from adjuvant 5-FU therapy. Clinical studies in stage II colon cancer have demonstrated that patients with dMMR (MSI-H) tumors receiving 5-FU had poor overall survival (OS) and no improvement in disease free survival (DFS) compared with those randomly assigned to surgery alone. [4-7]

Clinical correlation is recommended. Additional testing including immunochemistry, BRAF mutational analysis and sequencing of DNA mismatch repair genes may be appropriate in certain cases where a diagnosis of Lynch syndrome is under consideration.

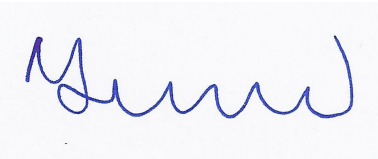
References

1. Keytruda FDA Label - https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125514s024lbl.pdf
2. Jemperli FDA Label - https://www.accessdata.fda.gov/drugsatfda_docs/label/2023/761174s006lbl.pdf
3. Opdivo FDA Label - https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/125554s055lbl.pdf
4. Benatti P et al. Microsatellite instability and colorectal cancer prognosis. Clin Cancer Res. 2005 Dec 1;11(23):8332-40. Erratum in: Clin Cancer Res. 2006 Jun 15;12(12):3868-9. PubMed PMID: 16322293.
5. Sinicrope FA. DNA mismatch repair and adjuvant chemotherapy in sporadic colon cancer. Nat Rev ClinOncol. 2010 Mar;7(3):174-7. doi: 10.1038/nrclinonc.2009.235. Review. PubMed PMID: 20190798; PubMed Central PMCID: PMC3767984.
6. Sargent DJ et al Defective mismatch repair as a predictive marker for lack of efficacy of fluorouracil-based adjuvant therapy in colon cancer. J Clin Oncol. 2010 Jul 10;28(20):3219-26. doi: 10.1200/JCO.2009.27.1825. Epub 2010 May 24. Erratum in: J Clin Oncol. 2010 Oct 20;28(30):4664. PubMed PMID: 20498393; PubMed Central PMCID: PMC2903323.
7. ASCO Abstract 15S - http://ascopubs.org/doi/abs/10.1200/jco.2008.26.15_suppl.4008

Sample Sufficiency for Testing

A histopathological review of this sample was conducted and the sample was deemed acceptable for testing. It has met our sample acceptance criterion of a minimum 20% tumor content.

Signatures



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Supplementary Section

Test Details

Methodology: Formalin fixed paraffin embedded (FFPE) samples with >20% tumor content were taken for the assay. Genomic DNA was extracted using commercial kits from FFPE sample (Qiagen, USA) and blood (germline sample) (Genfind, USA). The MSI PCR assay was performed using Promega MSI Analysis System, Version 1.2. and MSI amplification was performed as per manufacturer's protocol for 5 mononucleotide repeat marker (NR-21, BAT-26, BAT-25, NR-24, MONO-27) in tumor and germline sample. PCR products were resolved by capillary electrophoresis on the Genetic Analyzer (3500 DX, ThermoScientific, USA). The combination of a four-dye fluorescent system allows for simultaneous amplification and separation of different loci in the assay. The markers were analyzed by using GeneMapper v4.1 software (Applied Biosystems, USA). Results are reported as MSI-high (MSI-H) if 2 or more loci are positive; MSI-low (MSI-L) if 1 locus is positive; microsatellite stable (MSS) if all loci are negative.

Limitations and Disclaimer

As with any laboratory test, there is a small chance that this result may be inaccurate for a procedural reason, such as an error during specimen collection and labelling (incorrect patient identification), an error in processing, data collection or interpretation. Currently available data indicates that technical error rate for analysis involving DNA tests is anywhere between 1-3%. Accurate interpretation of this report is dependent on detailed clinical history of the patient. In the event of unavailability of detailed clinical history, the lab cannot guarantee the accuracy of the interpretation.

End of report