



Media Backgrounder:

Promega OncoMate™ MSI Dx Analysis System

CE marked *in vitro* diagnostic for microsatellite instability status detection

Executive Summary

- OncoMate™ MSI Dx Analysis System (OncoMate™ MSI) is a polymerase chain reaction (PCR)-based, validated gold standard for determining microsatellite instability (MSI) status in solid tumors.^{1,2,3} It offers analytical sensitivity and unsurpassed specificity with a short turn-around time.^{4,5}
- In patients with certain types of cancer, loss of mismatch repair (MMR) protein function results in tumor cells with MSI.⁶ Screening cancer patients with reliable markers to assess MSI can provide pathologists, oncologists and patients with information that characterizes tumors and guides care and treatment decisions.⁷
- OncoMate™ MSI uses the most sensitive panel of markers for MSI status detection.^{4,5} Promega MSI technology has been used extensively in clinical research for more than 15 years and is supported by more than 140 peer-reviewed publications.^{1,2,3}

OncoMate™ MSI Dx Analysis System

OncoMate™ MSI is a CE marked *in vitro* diagnostic (IVD) medical device in Europe. The PCR-based test determines MSI status in DNA purified from tissue samples derived from solid tumors. Multiplex analysis allows OncoMate™ MSI to deliver a fast turn-around time, to be economical with precious patient samples, and to be easy to perform and interpret.^{4,5}

Promega MSI technology has been used extensively in clinical research for more than 15 years. With the CE marking in Europe for OncoMate™ MSI, this technology is now accessible for clinical laboratories as a diagnostic tool, offering valuable insight to help inform patient treatment decisions.⁷

Numerous peer-reviewed journal articles refer to Promega MSI technology as the gold standard, most widely used MSI testing method.^{1,2,3} OncoMate™ MSI uses the same sensitive and specific panel of markers for detection of MSI status, in an improved format, appropriate for clinical testing use.⁴ These include five monomorphic mononucleotides, which are recommended by the European Society for Medical Oncology (ESMO)⁸ and other leading cancer organizations.^{8,9} OncoMate™ MSI is highly accurate in identifying tumors with MMR deficiency. In a method comparison study, OncoMate™ MSI showed strong agreement with an immunohistochemistry (IHC) panel. The Overall Percent Agreement (OPA) was 97.3% between the two test methods.¹⁰

About MSI

Microsatellites are short, repeated sequences of nucleotides/bases in DNA that are randomly distributed in the human genome. MMR is a DNA repair system that works by identifying errors and removing them from DNA. When the MMR system becomes deficient (dMMR), microsatellites develop an accumulation of uncorrected errors (mutations) that lead to instability – this is known as MSI.^{11,12}

MMR can play a role in cancer because tumors divide rapidly, creating many opportunities for DNA copy errors. People with a genetic condition, known as Lynch Syndrome, have inherited mutations in the MMR system, which places them at higher risk to develop certain cancers compared with people with a normally functioning MMR system.¹³ However, even if an individual does not have Lynch Syndrome, certain kinds of solid tumor cells can acquire mutations that affect their ability to repair mismatch copy errors.¹⁴ Tumor cells that develop these sporadic mutations in the MMR system also show increased MSI or are said to be MSI-High.¹¹

European guidelines recommend MSI testing to assess dMMR function of solid tumors for a spectrum of cancers, including colorectal cancer and endometrial cancer, to reduce morbidity and mortality.⁸ An accurate MSI result can be used as a marker to predict response with immuno-oncology therapies.⁷ Furthermore, cancer patients with MSI-High tumors can undergo further genetic testing to identify Lynch Syndrome. In addition, genetic testing of relatives of patients with Lynch Syndrome can help identify hereditary predisposition for cancers and potentially save lives by prompting improved surveillance and early detection of cancer.

MSI-High is found in around 15% of all colorectal cancers,¹⁵ 30% of endometrial cancers¹⁶ and up to 37% of gastric cancers,¹² although it can be found in other cancers.¹⁴

Unmet Need in Cancer Diagnostics

More can be done to screen cancer patients with reliable markers to support treatment decisions and improve surveillance, according to European guidelines.⁸

A lot is at stake. Scientific breakthroughs in our understanding of interactions between tumor cells and the host immune system have led to development of immuno-oncology therapies that have demonstrated remarkable efficacy in some sets of patients.⁷ But suboptimal MSI testing can reduce access to these life-saving immunotherapies for cancer patients, as

clinicians lack information to be able to predict which patients are likely to respond to these new therapies.

Our Work in Clinical Diagnostics

Today, Promega is a global clinical leader in manufacturing tools for biotechnology and molecular biology with a portfolio spanning genomics, protein analysis and expression, cellular analysis, drug discovery and genetic identity and *in vitro* diagnostics.

Our ambition is to make MSI testing accessible to every laboratory, thereby offering physicians a vital tool with which to make strategic decisions in cancer patient care and treatment.

¹ Baudrin LG, *et al.* Molecular and Computational Methods for the Detection of Microsatellite Instability in Cancer. *Frontiers in Oncology*. 2018; 8: 621.

² Svrcek M, Lascols O, Cohen R, *et al.* MSI/MMR-deficient tumor diagnosis: Which standard for screening and for diagnosis? Diagnostic modalities for the colon and other sites: Differences between tumors. *Bull Cancer*. 2019;106(2):119–128.

³ Fuchs CS, Doi T, Jang RW, *et al.* Safety and Efficacy of Pembrolizumab Monotherapy in Patients With Previously Treated Advanced Gastric and Gastroesophageal Junction Cancer: Phase 2 Clinical KEYNOTE-059 Trial. *JAMA Oncology*. 2018;4:e180013. Epub 2018 May 10. Erratum in: *JAMA Oncology*. 2019 ;1;5:579.

⁴ Bacher J.W., *et al.* Development of a fluorescent multiplex assay for detection of MSI-High tumors. *Disease Markers*. 2004; 20(4-5): 237-250.

⁵ Murphy K.M., *et al.* Comparison of the Microsatellite Instability Analysis System and the Bethesda Panel for the Determination of Microsatellite Instability in Colorectal Cancers. *Journal of Molecular Diagnostics*. 2006; 8(3): 305-11.

⁶ Richman S., *et al.* Deficient mismatch repair: Read all about it (Review). *International Journal of Oncology*. 2015;47(4):1189-202.

⁷ Le D.T, Mismatch repair deficiency predicts response of solid tumours to PD-1 blockade. *Science*. 2017; 357: 409.

⁸ Luchini C., *et al.* ESMO recommendations on microsatellite instability testing for immunotherapy in cancer, and its relationship with PD-1/PD-L1 expression and tumor mutational burden: a systematic review-based approach. *Annals of Oncology*. 2019; 30: 1232-1243.

⁹ NCCN Clinical Practice Guidelines in Oncology, Genetic/Familial High-Risk Assessment: Colorectal Version 3.2019.

¹⁰ OncoMate™ MSI Dx Analysis System Instructions for Use of Product MD2140

¹¹ Cancer Institute. Microsatellite instability-high cancer. Available from:

<https://www.cancer.gov/publications/dictionaries/cancer-terms/def/microsatellite-instability-high-cancer>. Last accessed February 2020.

¹² Zhu L., *et al.* Microsatellite instability and survival in gastric cancer: A systematic review and meta-analysis. *Mol and Clin Onco*. 2015; 3(3): 699-705.

¹³ Latham, A. *et al.* Microsatellite Instability Is Associated With the Presence of Lynch Syndrome Pan-Cancer. *J Clin Oncol*. 2018; 37:286-295.

¹⁴ Kok M., *et al.* How I treat MSI cancers with advanced disease. *ESMO Open*. 2019; 4.

¹⁵ Sinicrope F. A. The role of microsatellite instability testing in the management of colorectal cancer. *Clinical Advances in Hematology & Oncology*. 2016; 14(7): 476-9.

¹⁶ Kunitomi H *et al.* New use of microsatellite instability analysis in endometrial cancer. *Oncol Lett* 2017; 14(3): 3297-3301.