

# Tissue Agnostic MSI

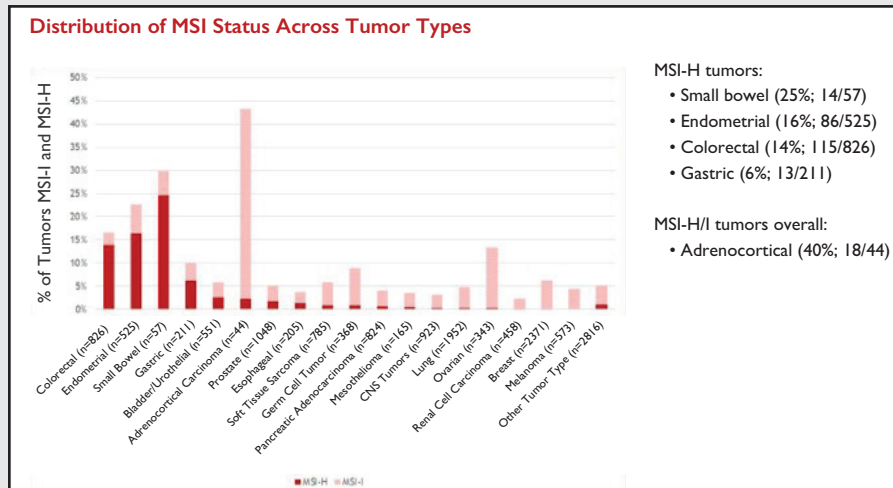
Getting MSI patients on the right treatment, faster

Microsatellite instability-high (MSI-H) cancers are “tissue-site agnostic,” reflecting a unique tumor biology, not an anatomical site of origin. This unique tumor biology sets up vastly different treatment approaches than non-MSI-H cancers. This unique MSI-H tumor biology portends chemotherapy ineffectiveness yet is very predictive of an excellent response and benefit from immune checkpoint inhibitors.

## J Clin Oncol.

2019 Apr 10;37(11):942. DOI: 10.1200/JCO.19.00517.

Microsatellite Instability Is Associated With the Presence of Lynch Syndrome Pan-Cancer (as synthesized and presented at ASCO 2018)

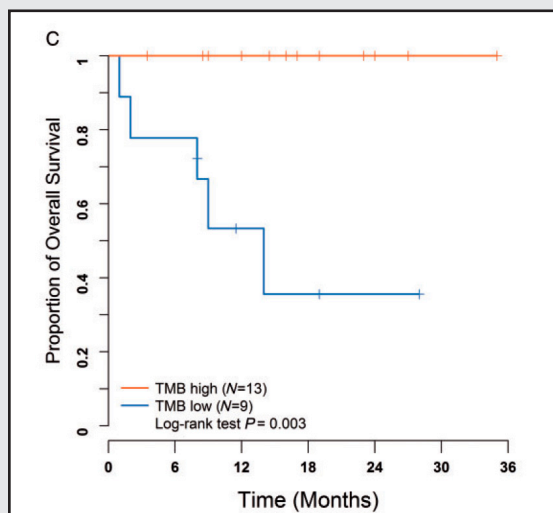


MSI-H is tissue agnostic and can occur in all carcinomas  
MSI-H can be present in both early and late stage cancers  
MSI-H can be determined in a liquid biopsy

## Ann Oncol. 30: 1096–1103, 2019

DOI:10.1093/annonc/mdz134, Published online 30 April 2019

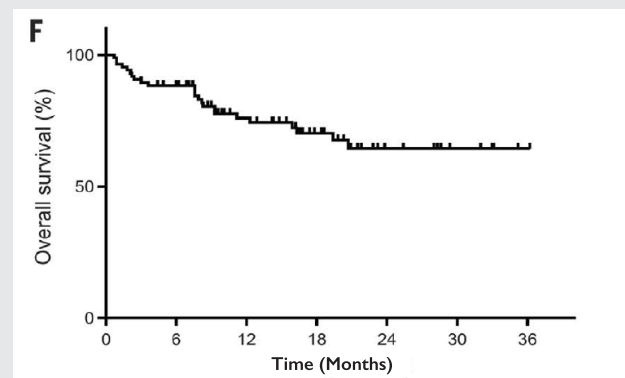
Tumor mutational burden is predictive of response to immune checkpoint inhibitors in MSI-high metastatic colorectal cancer



75% of MSI-H cancers are TMB high  
MSI-H cancers are best treated with immune checkpoint blockade  
MSI-H and TMB high are a powerful predictor of sustained immune therapy benefit

## Science

357 (6349), 409-413 DOI: 10.1126/science.aan6733  
Mismatch repair deficiency predicts response of solid tumors to PD-1 blockade



Tumor biology of MSI-H cancers predicts immune therapy benefit  
MSI-H and immune therapy benefit for your patients...testing MSI is the only way to know!

# Tissue Agnostic MSI

Getting MSI patients on the right treatment, faster



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The FDA granted its first “tissue-site agnostic” approval for anti-PD-1 therapy after standard chemotherapy across all MSI-H cancers, irrespective of the anatomical site of origin. There is now first-line approval of immunotherapy over chemotherapy in MSI-H metastatic colorectal cancers. It is vitally important for oncologists to not miss this potential immune therapy durability for their patients. This is a pan-cancer tumor biology, and all solid tumors should be tested for MSI-H.

## ESMO Ann Oncol. 30: 1096–1103, 2019

Tumor mutational burden is predictive of response to immune checkpoint inhibitors in MSI-high metastatic colorectal cancer

“Studies have found that 15% of all CRCs and 5% of all mCRCs are MSI-H.”

Immunotherapy with PD-1 inhibitors is currently FDA approved in first-line MSI-H metastatic CRC.

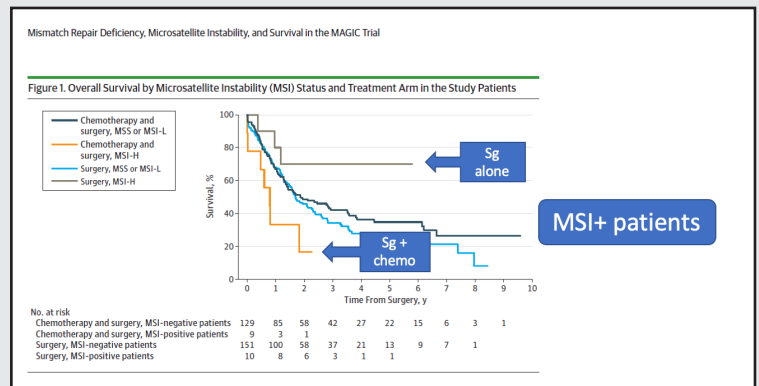
## JAMA Oncol.

2017;3(9):1197-1203. DOI:10.1001/jamaoncol.2016.6762

Published online February 23, 2017. Mismatch Repair Deficiency, Microsatellite Instability, and Survival

“No patient with MSI-H tumor treated with chemotherapy had significant pathologic response... ”

We found that patients with MSI-H or MMRD tumors have superior survival compared with patients with MSS/MSI-L or MMRP tumors when treated with surgery alone and conversely have inferior survival to patients with MSS/MSI-L or MMRP tumors when treated with perioperative chemotherapy plus surgery. Patients with MSI-H or MMRD may not benefit (or may experience a detrimental effect) from perioperative chemotherapy and may be better served by a surgery only approach.”



Chemotherapy is ineffective in MSI-H cancers

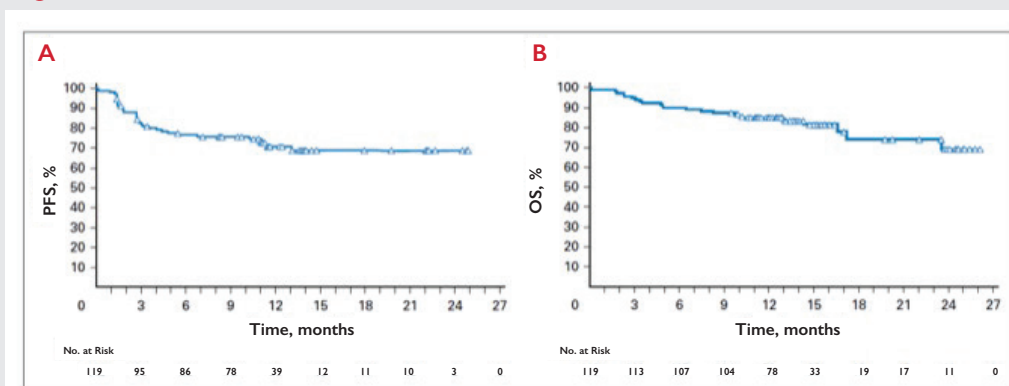
Chemotherapy was very detrimental to survival when added to surgery

MSI-H testing is vitally important to avoid chemotherapy harm

## J Clin Oncol.

2018 Mar 10;36(8):773-779. DOI: 10.1200/JCO.2017.76.9901

Durable Clinical Benefit With Nivolumab Plus Ipilimumab in DNA Mismatch Repair-Deficient/Microsatellite Instability-High Metastatic Colorectal Cancer



In 2018...dual immune checkpoint blockade...second line

119 patients

75% ≥ 2 prior rx

Overall response rate 55%

Durable clinical benefit with immune therapy relative to MSI-H

CIRCULOGENE'S ctDNA panel is a noninvasive technique that can be combined with traditional tissue biopsy to track cell-free DNA and detect disease biomarkers in blood faster and more accurately. MSI status can now easily and quickly be assessed by a liquid biopsy and plasma ctDNA. Clearance of the plasma MSI is also a dynamic marker to monitor immune therapy response whereas persistence of plasma MSI is a harbinger of progressing disease.