

Biomarker	About	Who should be tested	Prevalence	Heredity	Treatment Recommendations
MSS	The MSS (Microsatellite Stability) biomarker indicates that the patient is proficient in MMR (mismatch repair), and there are no mutations in the MMR gene. The MSS biomarker indicates a higher risk of reoccurrence of cancer. If there are mutations in the MMR gene, that indicates the patient is MSI-High. Colorectal cancer patients are either MSS or MSI-High.	All CRC patients	85% of all colorectal cancers	No	MSS patients do not respond well to immunotherapy and it is not recommended. MSS patients are treated with fluorouracil-based chemotherapy (5FU, FOLFOX, FOLFIRI).
MSI-H/MMR Deficiency	DNA Mismatch repair (MMR) is defective, the cells are deficient (dMMR), also known as High Microsatellite Instability MSI-High). Patients with MSI-High have a better prognosis than those with MSS.	All CRC patients	15% of all colorectal cancers, 4% of stage IV, metastatic colorectal cancer	No*	MSI-High / dMMR mutations respond well to immunotherapy treatments. Treatments with immune checkpoint inhibitors (Pembrolizumab or Nivolumab or a combination of Nivolumab and Ipilimumab) are recommended for MSI-H or dMMR. *3-5% of MSI-High/dMMR patients have Lynch Syndrome, which is a hereditary mutation. These patients are at higher risk for developing other cancers.
KRAS	KRAS is in the RAS family of genes. RAS mutations may indicate aggressive tumor and higher risk of reoccurrence. RAS testing must be performed prior to starting an EGFR inhibitor.	Stage IV, metastatic	~40% of all colorectal cancers	No	KRAS mutations do not respond well to EGFR inhibitors (cetuximab or panitumumab). Treatment options include chemotherapy (Folfox, Foliri, Capox), sometimes in combination with Bevacizumab. To date there are no approved anti-KRAS targeted therapies. Clinical trials for KRAS mutations should be discussed with the patient's medical team.
NRAS	NRAS is in the RAS family of genes. The NRAS mutation may indicate aggressive tumor growth and poorer outcomes than KRAS mutations. RAS testing must be performed prior to starting an EGFR inhibitor.	Stage IV, metastatic	5% of all colorectal cancers	No	NRAS mutations do not respond well to EGFR inhibitors (cetuximab or panitumumab). Treatment options include chemotherapy (Folfox, Foliri, Capox), sometimes in combination with Bevacizumab. To date there are no approved anti-NRAS targeted therapies. Clinical trials for NRAS mutations should be discussed with the patient's medical team.
BRAF V600E	The BRAF V600E mutation indicates aggressive tumor growth. The majority of BRAF mutations are V600E, but there are rare other mutations of the BRAF gene.	Stage IV, metastatic	10%-15% of colorectal cancers	No	BRAF V600E mutations do not respond to EGFR inhibitors on their own (cetuximab or panitumumab). Recommendations can include BRAF inhibitors in combination with MEK inhibitor and possibly also an EGFR inhibitor. BRAF Wild Type (No BRAF mutation present) are typically treated with EGFR-Inhibitors.
PIK3CA	PIK3CA mutations indicate an aggressive tumor with an increased risk of reoccurrence. For patients who have both the PIK3CA and the and a RAS mutation, their outcome is better than those with PIK3CA but not RAS.	No standard guidelines at this point. Stage IV, metastatic patients should speak to their medical professional.	17% of all colorectal cancers	No	Patients with PIK3CA do not respond well to anti-EGFR treatments, so cetuximab or panitumumab are not recommended. Treatment recommendations include chemotherapy (FOLFOX, CAPOX or FOLFIRI) with or without Bevacizumab. Clinical trials for PIK3CA mutations should be discussed with the patient's medical team.
HER2	HER2 amplification is more common in left-sided tumors. Those with KRAS wild-type or NRAS wild-type (no mutation present), are more likely to have HER2 amplification.	Stage IV, metastatic with wild-type KRAS, NRAS or BRAF (no mutation present).	5% of all stage III and stage IV colorectal cancers	No	HER2 amplifications do not respond well to EGFR inhibitors (cetuximab or panitumumab). Treatment options include trastuzumab with either pertuzumab or lapatinib alone or with chemotherapy. Clinical trials for patients with HER2 amplifications should be discussed with the patient's medical team.

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UGT1A1	The UGT1A1 gene helps break down toxic molecules (in this case from treatments) into non-toxic molecules. Patients with a UGT1A1 gene mutation are unable to break down toxic ingredients of Irinotecan chemotherapy. There are other variations of the UGT1A1 gene, with the most common being UGT1A1*28.	Patients experiencing severe toxicity to treatment.	UGT1A1*28 is fairly common in African Americans (45%) and individuals of European descent (31%)	Yes	Patients with the UGT1A1 gene mutation may have their doseage lowered or treatment plan altered.
DPYD	DPYD gene mutations either have a less efficient DPYD enzyme, or are entirely without the enzyme. 1 in 1000 have no enzyme activity, which could result in life-threatening toxicity to treatment.	Patients experiencing toxicity to treatment.	5-18% of all colorectal cancers have some level of DPYD mutations.	Yes	DPYD mutations are unable to metabolize drugs such as 5-Fluorouracil (5FU) and similar fluoropyrimidine-based chemotherapies (FOLFOX, FOLFIRI, FOLFIRINOX, and capecitabine). Based on reaction to treatment, dosage may be lowered or treatment may be changed.
CEA	CEA (Carcinoembryonic Antigen) is a protein that is high in colorectal cancer patients. Testing for CEA levels can help determine if cancer is growing or if the cancer has returned.	All colorectal cancer patients	~17-47% of colorectal cancers	No	Knowing your CEA levels can help your medical team determine treatment options. CEA testing is not 100% accurate and it is possible for colorectal cancer patients to have a low CEA.
Sidedness	Women are more likely to have tumors located on the right side, and individuals with right sided tumors tend to be more likely to have BRAF, KRAS or MSI-High. Right sided tumors tend to be more aggressive and larger than left sided tumors. Tumors on the left side are more common in men, and are also more likely to have HER2 amplification.	N/A, tumor location does not require biomarker testing	~70% of tumors are located in the left side of the colon, ~10% are located in the right side of the colon.	Patients with lynch syndrome, which is hereditary, are more likely to have right sided tumors	Metastatic tumors located on the right side of the colon respond differently to treatment than tumors located on the left side of the colon. EGFR Inhibitors are less successful in patients with right sided tumors, however MSI-High is more present in right sided tumors, where immunotherapy may be appropriate treatment. Traditionally, left-sided tumors had a better prognosis, but this may change as personalized medicine continues to develop.
TMB	Tumor Mutational Burden (TMB) is the measure of genetic mutations found in cancer cells. Patients with many tumor mutations are considered to have high TMB.	No standard guidelines at this point. Stage IV, metastatic patients should speak to their medical professional.	Not available	No	Patients with high TMB may respond well to immunotherapy treatments.
NTRK	NTRK genes fuse to other genes and create new fusion proteins that cause rapid cell growth. NTRK is very rare.	Stage IV, metastatic patients without KRAS,NRAS,BRAF, HER2 and experiencing cancer growth on chemotherapy	<1% off all colorectal cancers	No	For Stage IV/metastatic patients there are two NTRK inhibitor treatment options: larotrectinib or entrectinib. Patients with NTRK may have microsatellite instability (MSI-H) and should be tested for MSI-High.

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