

BIOMARKER	WHO SHOULD BE TESTED?	WHAT IS IT?	WHAT IS THE TREATMENT IMPACT?
<b>MSS AND MSI-HIGH</b>	<ul style="list-style-type: none"> <li>All colorectal cancer (bowel cancer) patients</li> <li>All patients with MSI-High results should also be tested for the hereditary Lynch Syndrome</li> </ul>	<ul style="list-style-type: none"> <li>MSS is microsatellite stability and MSI-High is microsatellite instability-high (also known as deficient mismatch repair, dMMR).</li> <li>MSS and MSI-High are assessments of your cells' ability to fix certain kinds of genetic mistakes.</li> </ul>	<ul style="list-style-type: none"> <li>CRC with MSS is treated with traditional chemotherapy.</li> <li>Immunotherapy is effective in MSI-High colorectal cancer.</li> </ul>
<b>KRAS</b>	<ul style="list-style-type: none"> <li>All stage IV/metastatic CRC patients</li> <li>All patients being considered for EGFR inhibitor treatment</li> </ul>	KRAS is a gene involved in controlling cell growth and cell survival. Mutations in KRAS may allow cells to grow out of control and become cancer.	<ul style="list-style-type: none"> <li>CRC without KRAS mutation (wild-type) is treated with EGFR inhibitors.</li> <li>EGFR inhibitors are not effective in tumors with KRAS mutation.</li> <li>Colorectal cancer with KRAS mutation is treated with traditional chemotherapy with or without bevacizumab added.</li> </ul>
<b>NRAS</b>	<ul style="list-style-type: none"> <li>All stage IV/metastatic CRC patients</li> <li>All patients being considered for EGFR inhibitor treatment</li> </ul>	NRAS is a gene involved in controlling cell growth and cell survival. Mutations in NRAS may allow cells to grow out of control and become cancer.	<ul style="list-style-type: none"> <li>CRC without NRAS mutation (wild-type) is treated with EGFR inhibitors.</li> <li>EGFR inhibitors are not effective in tumors with NRAS mutation.</li> <li>Colorectal cancer with NRAS mutation is treated with traditional chemotherapy with or without bevacizumab added.</li> </ul>
<b>HER2 (ERBB2)</b>	All stage IV/metastatic CRC patients, unless a KRAS, NRAS, or BRAF mutation has already been identified.	HER2 is a gene involved in control of cell growth and cell survival. An increased number of HER2 gene copies (amplification) and increased amount of HER2 protein (overexpression) can cause cancer by allowing abnormal control of cell growth and survival.	<ul style="list-style-type: none"> <li>CRC that is HER2 positive (has HER2 amplification or overexpression) may be treated with HER2 inhibitors with or without traditional chemotherapy.</li> <li>EGFR inhibitors are less effective in colorectal cancer with HER2 amplification.</li> <li>HER2 negative tumors are treated based on other patient and biomarker information.</li> </ul>
<b>BRAF (INCLUDING BRAF V600E)</b>	All stage IV/metastatic CRC patients	BRAF is a gene involved in controlling cell growth. Mutations in BRAF may allow cells to grow out of control and become cancer.	<ul style="list-style-type: none"> <li>Tumors without BRAF mutation (wild-type) are typically treated with EGFR inhibitors.</li> <li>CRC with BRAF mutation is treated with targeted therapy (BRAF inhibitors plus MEK inhibitors) with or without traditional chemotherapy.</li> <li>EGFR inhibitors alone are not effective in BRAF mutant tumors but may be added to other targeted therapy.</li> </ul>
<b>CEA</b>	All CRC patients	CEA is carcinoembryonic antigen, a substance produced by colorectal cancer cells and by intestinal cells in some other benign diseases.	<ul style="list-style-type: none"> <li>An increasing CEA level over time may indicate cancer progression on treatment or a return of cancer after treatment. Further testing is needed to confirm progression or recurrence.</li> <li>A decreasing CEA level during treatment is a sign that the treatment is effective.</li> </ul>

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<b>TUMOR LOCATION (TUMOR SIDEDNESS)</b>	<ul style="list-style-type: none"> <li>All CRC patients as part of initial diagnosis</li> <li>Does not require separate biomarker testing.</li> </ul>	<ul style="list-style-type: none"> <li>Right-sided colon cancer is located in the cecum (caecum), ascending colon, hepatic flexure (right colic flexure) or transverse colon.</li> <li>Left-sided CRC is located in the splenic flexure (left colic flexure), descending colon, sigmoid colon, or rectum.</li> </ul>	<ul style="list-style-type: none"> <li>Immunotherapy is effective in right-sided tumors.</li> <li>When added to traditional chemotherapy, bevacizumab is more effective than cetuximab in right-sided colon cancer.</li> <li>Adjuvant chemotherapy is effective in left-sided CRC.</li> <li>When added to traditional chemotherapy, cetuximab is more effective than bevacizumab in left-sided tumors.</li> </ul>
<b>PIK3CA</b>	No standardized guidelines, patients should discuss with medical team.	PIK3CA is a gene involved in controlling cell growth and migration. PIK3CA mutations may cause cancer as well as some rare diseases of abnormal growth.	<ul style="list-style-type: none"> <li>Tumors with mutation in PIK3CA exon 20 are less responsive to EGFR inhibitor treatment.</li> <li>Colorectal cancer with PIK3CA mutation may have a good response to aspirin or other NSAIDs as neoadjuvant or adjuvant treatment, or as recurrence prevention.</li> </ul>
<b>TMB</b>	No standardized guidelines, patients should discuss with medical team.	TMB is tumor mutational burden, a measurement of how many genetic mutations are present in tumor cells in a specific amount of DNA (a megabase).	<ul style="list-style-type: none"> <li>Immunotherapy is effective in CRC with TMB-High, even in some tumors with MSS.</li> <li>In colorectal cancer with TMB-Low, treatment is guided by other patient and biomarker information.</li> </ul>
<b>NTRK FUSION</b>	<ul style="list-style-type: none"> <li>Patients with stage IV/metastatic CRC that is progressing on chemotherapy and has no KRAS, NRAS, or BRAF mutation</li> <li>No standardized guidelines for patients with stage IV/metastatic CRC with MSI-High, patients should discuss with medical team</li> </ul>	NTRK genes encode TRK proteins which are involved in control of cell growth and cell survival. When a type of mutation called NTRK gene fusion occurs, TRK fusion proteins are made. TRK fusion proteins can cause cancer by allowing uncontrolled cell growth and survival.	<ul style="list-style-type: none"> <li>TRK inhibitors are used to treat CRC with NTRK fusion.</li> <li>Tumors without NTRK fusion are treated based on other patient and biomarker information.</li> </ul>
<b>DPYD</b>	<ul style="list-style-type: none"> <li>All CRC patients experiencing severe toxic effects of 5-FU related chemotherapy (5-FU and its combinations, capecitabine and its combinations).</li> <li>No standardized guidelines for pre-treatment DPYD testing, patients should discuss with medical team.</li> </ul>	DPYD is a treatment toxicity biomarker. DPYD is a gene encoding the enzyme DPD which is required to break down (metabolize) 5-FU related chemotherapy drugs. Mutations in DPYD may cause partial or complete DPD enzyme deficiency, leading to abnormal 5-FU metabolism and severe toxicity.	<ul style="list-style-type: none"> <li>In patients with DPYD mutations causing partial DPD enzyme deficiency, doses of 5-FU related drugs may be reduced to lower the risk of severe toxic effects.</li> <li>In patients with DPYD mutations causing complete DPD enzyme deficiency, different drugs may be used to avoid 5-FU related chemotherapy.</li> </ul>
<b>UGT1A1</b>	<ul style="list-style-type: none"> <li>All CRC patients experiencing severe toxic effects of irinotecan chemotherapy.</li> <li>No standardized guidelines for pre-treatment UGT1A1 testing, patients should discuss with medical team.</li> </ul>	UGT1A1 is a treatment toxicity biomarker. It is a gene encoding the enzyme which is required to metabolize irinotecan. Mutations in UGT1A1 may cause decreased enzyme level or function, leading to abnormal irinotecan metabolism and severe toxicity.	<ul style="list-style-type: none"> <li>In patients with UGT1A1 mutations, irinotecan dose may be reduced to lower the risk of severe toxic effects.</li> </ul>

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