

Backgrounder: Complete Biomarker Testing in Colorectal Cancer (CRC)

First-line treatment decisions for advanced colorectal cancer (CRC) lag behind recommended medical guidelines

Many advanced CRC patients may be receiving inappropriate therapy due to guideline non-adherence to biomarker testing before starting first-line treatment

- Medical guidelines have expanded over the past 10 years and now recommend all patients with metastatic colon cancer be tested for 6 genomic alterations or biomarkers: *KRAS*, *NRAS*, *BRAF*, *ERBB2 (HER2)*, and *NTRK* as well as microsatellite instability (MSI)¹ to help inform first-line treatment decisions
- Biomarker-driven therapy selection can improve survival for advanced CRC patients.² Testing for all biomarkers can help predict which treatment will respond and which won't, and is the only way to help ensure the right treatment from the start
- Only 40% of patients with advanced CRC receive complete guideline-recommended biomarker testing, putting many advanced CRC patients at risk for inappropriate treatment³
- As an example, 72% of patients who received anti-*EGFR* therapy did not have guideline-aligned *RAS* and *BRAF* testing to determine eligibility for that treatment³
- Various factors contribute to clinical adoption of precision oncology lagging behind recommended medical guidelines, including: physician-reported gaps in the knowledge and skills needed to incorporate genotyping into clinical practice; challenges in keeping track of the latest recommendations; the time frame associated with getting complete genotyping results using tissue biopsies; and the cost of tests when not covered by insurance³⁻⁵

Testing every newly diagnosed advanced CRC patient for all 6 guideline-recommended biomarkers is crucial⁶

Genetic mutation	Associated therapy information
<i>KRAS</i>	Poor response to anti- <i>EGFR</i> therapy. <i>KRAS</i> mutations, which appear in ~50% of patients, convey a lack of response to anti- <i>EGFR</i> therapies. ⁷⁻⁸
<i>NRAS</i>	Poor response to anti- <i>EGFR</i> therapy. <i>NRAS</i> mutations, which appear in ~50% of patients, convey a lack of response to anti- <i>EGFR</i> therapies. ⁷⁻⁸
<i>BRAF</i> V600E	Poor response to anti- <i>EGFR</i> therapy. <i>BRAF</i> V600E can be targeted with encorafenib. In combination with other therapies, it results in longer overall survival and higher response rate than standard therapy. ²
MSI (microsatellite instability)	Responds to immunotherapy. MSI-High status improves the likelihood of response to immune checkpoint inhibitors. ^{9-12, 3}
<i>NTRK</i> fusions	Respond to tumor-agnostic <i>NTRK</i> inhibitors.
<i>ERBB2 (HER2)</i> amplification	Anti- <i>HER2</i> therapy may have a beneficial role in the treatment of <i>HER2</i> -positive metastatic CRC.

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