



# BIOMARKERS.

By choosing a treatment plan that best matches your tumor type, this may result in fewer side effects and improved health after cancer treatment.

Personalized medicine uses specific information about your tumor to help diagnose, plan treatment and find out how well treatment is working based on your own biology. The information (also called biomarkers) can be genes or other parts of a cell. Genes are referred to typically as wild type (normal) or mutated (abnormal).

## EGFR INHIBITORS

Research has shown that **if your tumor is KRAS/NRAS wild type, you will likely benefit from cetuximab (Erbix®) or panitumumab (Vectibix®).** These treatments, also called EGFR inhibitor treatments, are used only in patients with metastatic colorectal cancer (cancer that has spread to distant organs).

However, if there are KRAS/NRAS gene mutations, **you will not benefit from EGFR inhibitor treatments.**

If you have KRAS and NRAS mutations, you may benefit from other treatments, including chemotherapy and targeted therapies. As many as **half of patients may have mutated KRAS genes.** NRAS mutations are less frequent.

If you have metastatic colorectal cancer and a BRAF mutation you may not demonstrate a strong response to the EGFR inhibitor therapies.

“Epidermal Growth Factor Receptor (EGFR) cells have numerous receptors that tell it to divide. The drugs cetuximab and panitumumab keep the receptors from signaling.”

## COMMON CRC BIOMARKERS

KRAS	The Kirsten Rat Sarcoma Viral Oncogene Homolog (KRAS) gene provides instructions for making a protein called KRAS that is involved in normal cell division. When this gene is mutated, cell division increases abnormally.
NRAS	The Neuroblastoma RAS Viral Oncogene Homolog (NRAS) gene provides instructions for making a protein called N-Ras that is involved primarily in regulating cell division. When the RAS genes are mutated, the cancer cells keep dividing and growing.
BRAF	V-raf Murine Sarcoma Viral Oncogene Homolog B (BRAF) gene provides instructions for making a protein called BRAF that helps with cell function and cell division. When the BRAF genes are mutated, the cells divide rapidly and abnormally.
*KRAS, NRAS and BRAF are genes that belong to a class of genes known as oncogenes. When mutated, oncogenes have the potential to cause normal cells to become cancerous.	

## IMPLICATIONS

Dr. Axel Grothey, of Mayo Clinic and an active member of Fight Colorectal Cancer’s Medical Advisory Board, shared his insight on the research about NRAS mutations not responding to EGFR inhibitor treatments:

*“This research has immediate implications for clinical practice, and the results are so consistent across clinical trials that they’re indisputable and really very solid. We’ll soon make inroads into practice guidelines and prescribing information.”*

Change is already happening.



## Biomarkers Fact Sheet

The NCCN (National Comprehensive Cancer Network) recently changed their physician treatment guidelines to reflect this data. They now strongly recommend **KRAS/NRAS testing on ALL patients with metastatic CRC**. If you have either KRAS or NRAS mutations, you should not be treated with either cetuximab or panitumumab, either alone or in combination with other anticancer drugs.

## NOW WHAT?

### Common questions regarding CRC Biomarkers and EGFR inhibitors

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#### What does this mean for me?

If you've been diagnosed with metastatic colorectal cancer, you need your tumor tested for all RAS mutations, including KRAS and NRAS. This should be covered by insurance. If you have a BRAF mutation

#### What will my results look like?

Your test results will show whether your tumor has a mutation in the KRAS/NRAS genes. Tumors with neither mutation are sometimes called wild type. Only patients with KRAS/NRAS wild-type should receive treatment with an EGFR inhibitor.

#### When should I talk to my doctor?

Talk with your healthcare team about RAS mutation testing before beginning chemotherapy - especially if a recommended drug includes an EGFR inhibitor.

#### Will I need another biopsy?

No. When you had surgery, some of the tumor tissue that was removed from your body was processed into a wax block and stored at the hospital where you had your operation. Your doctor will arrange to have part of the saved tissue block sent to a laboratory to be tested. Results will be sent to your doctor so you can discuss your treatment decisions. The sample to be tested can come either from the original cancer in your colon or rectum or from a metastatic tumor that has spread from that primary one.

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