

Helping you understand the importance of
**Predictive RAS Biomarkers in Colorectal
Cancer Treatment**

Aims of this leaflet

This leaflet has been written to help you understand your medicine options after being diagnosed with colorectal cancer.

Introduction

Advances in medicine, not only in cancer, are happening at a considerable speed bringing changes to many areas of care. One of these is known as personalised medicine, or the development of medicines and treatment options that specifically target the individual needs of the patient. Research is showing that choosing a medicine that reflects the biology of the patient will probably result in fewer side effects and better outcomes. As a result every colorectal cancer tumour should be tested for the relevant biomarker before any medicine is prescribed.

What is a biomarker?

Biomarkers (short for biological markers) are molecules or genes found in the body that provide doctors with important information about a disease. In patients with cancer, biomarkers can be produced by the tumour itself and, in some cases, by other tissues in response to the presence of a tumour.

Biomarkers indicate whether a specific treatment is likely to work for you, allowing your doctor to tailor your treatment accordingly¹; this is known as personalised medicine. Testing for predictive biomarkers can help your doctor to select the most effective treatment for you, and to avoid unnecessary treatments which will not work for you.

Different types of biomarker work in different ways:

- **Diagnostic biomarkers** are used to screen and diagnose particular types of cancer
- **Prognostic biomarkers** provide insight into how a patient's disease may progress
- **Predictive biomarkers** assess the likely benefit, or lack of benefit, of a specific treatment for a specific patient

What are RAS biomarkers?

There are many different predictive biomarkers that are used to help doctors make treatment decisions for various types of cancer. In colorectal cancer, the RAS genes (including KRAS and NRAS) are important predictive biomarkers for helping doctors determine the right medicine. Both are now authorised in the European Union for all patients with metastatic colorectal cancer^{1,3}.

There are two different types of RAS gene that doctors test for. Normal RAS genes (KRAS and NRAS) are called 'wild-type' and occur in approximately 50% of colorectal tumours. The remaining 50% of tumours have mutated RAS genes and are called RAS mutant. Treatment decisions are made based on whether the tumour harbours a wild-type or mutated RAS gene.

How and when should I have a biomarker test?

Testing is performed on cancer cells that are removed either during a biopsy (a localised investigation) or during surgery.

Tests for your KRAS status (wild-type or mutated) and for NRAS, will probably be completed soon after you are diagnosed with metastatic colorectal cancer. The results will inform your oncologist about the best treatment for you thereafter.

You should expect to have the tests completed in a centre that is working to approved guidelines, such as those of the European Society of Medical Oncology³.

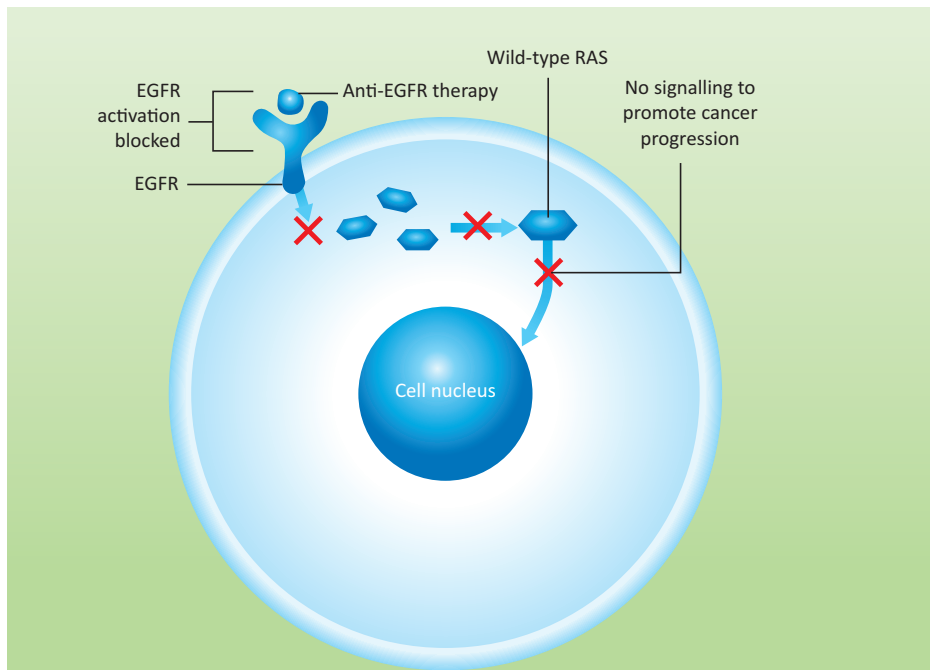
Which treatments are used after RAS status is known?

Wild-type RAS

Patients with wild-type RAS are more likely to benefit from anti-epidermal growth factor receptor (EGFR) treatment.

Anti-EGFR therapies bind to EGFR proteins on the surface of cancer cells. When wild-type RAS is present, this interaction blocks the signals that tell the cancer cell to grow and divide, and so stops further growth.

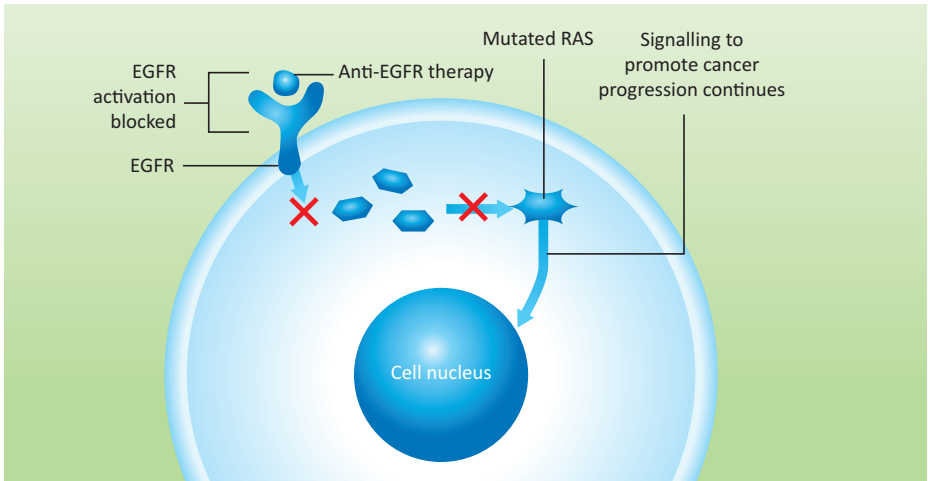
Current medicines for treating wild-type RAS tumours are: Cetuximab (Erbix) and Panitumumab (Vectibix).



Mutated RAS

Patients with mutated RAS types do not respond to anti-EGFR therapies.

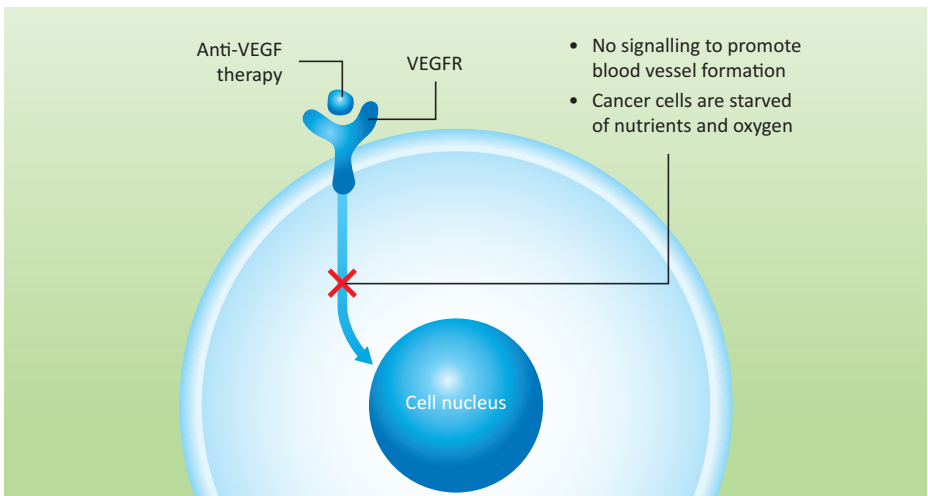
This is because when mutant RAS is present, EGFR signals are 'switched on' all the time, and anti-EGFR therapies cannot switch them off. The cancer cells continue to receive the signals they need to grow despite therapy.



Treating patients with mutant RAS

For patients with mutant RAS, other therapies might be more effective, one potential option for example is anti-VEGF (Vascular Endothelial Growth Factor). This treatment works by preventing new blood vessels from forming towards and within tumours, decreasing their blood supply⁴. The tumour, therefore, receives fewer nutrients and less oxygen, and consequently cannot grow as quickly, or at all.

Anti-VEGF therapy starves cancer cells from nutrients and oxygen.



Questions to ask your doctor

1. Has my tumour been tested for RAS status?
2. If so, is my tumour RAS wild-type or RAS mutated?
3. If not, where and when will the testing be completed?
4. How will the results from the test affect my treatment?
5. What will my treatment options be?

Take control of your disease and be informed

Personalised medicine will deliver its benefits through the greater involvement of patients in treatment decision-making and health management.

Learn more about your disease through reading relevant healthcare information and by talking to other patients. When you understand your disease, how it affects your body and how each treatment works, you are more in control of your cancer. You will be empowered to ask the questions that you need answered. You can be part of the decision-making process and make informed choices on matters that affect your life.

So talk to your doctor about biomarker tests, and remember:

YOUR HEALTH IS YOUR RESPONSIBILITY

Glossary

Gene Genes are parts of chromosomes that influence and control how cells behave. Genes are made up of DNA and act as instructions to make molecules called proteins.

EGFR A protein that is found on the surface of the cell and receives signals from outside the cell. Signals received by EGFR are transmitted to the cell and instruct it on whether to grow and divide.

VEGF A protein that binds to VEGF-R (VEGF Receptor) on the surface of the cell and stimulates the production of blood vessels.

About EuropaColon

EuropaColon is the voice of the European colorectal cancer community. We aim to save lives by bringing together the key stakeholders in the fight against this deadly disease, which is highly treatable if diagnosed early.

We work closely with our Affiliate and Associate groups in Europe to raise the profile of colorectal cancer, to support patients and their families and promote and encourage increased awareness of the symptoms and prevention of the disease. In addition, we promote formal population screening and campaign for access to best treatment and care.

References

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This leaflet was developed by the EuropaColon Expert Patient Advisory Group and supported by an educational grant from Amgen Europe GmbH



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May 2014 Registration No: 5314195 Registered Office: 92 Palatine Road, London N16 8ST.



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