

# KRAS and the Biological Agents

This factsheet has been written to give you information about the latest treatments for advanced bowel cancer and for which patients they might be suitable. If you have any questions about these or have concerns about any other aspect of bowel cancer, please call our **Bowel Cancer Advisory Service on freephone 0800 8 40 35 40**.

## The biological agents

Over the last decade, significant advances have been made in the development of new cancer treatments. One of the most exciting of these is the development of biological agents which work in combination with chemotherapy.

The biological agents can be particularly effective in reducing tumours that have spread to other parts of the body (metastatic tumours). In the case of bowel cancer, the disease usually spreads to the liver and the lungs. Biological agents are substances made from a living organism or its products and are often less toxic than chemotherapy, with less severe side effects. However, biological agents are not effective for all patients.

## The KRAS gene

Patients with bowel cancer have either the 'normal' [wild-type] KRAS (pronounced K-RAS) gene or 'mutant' [abnormal] KRAS gene. Two of the biological agents currently available for the treatment of bowel cancer – Cetuximab (Erbix) and Panitumumab (Vectibix) – are only effective for patients with the 'normal' KRAS gene. Neither drug works for patients who have the KRAS 'mutant' gene.

Approximately 65% of bowel cancer patients will have the 'normal' KRAS gene and of these approximately 60% will respond to Cetuximab, given in combination with chemotherapy. In trials it has been shown that patients who responded to the treatment lived longer with the disease and had an improved quality of life. Panitumumab is currently only given to patients after other drug treatments have failed or are no longer producing an effect to slow the progression of the disease, as this has a lower response rate than Cetuximab.

## Testing for which KRAS gene you have

Patients can find out which KRAS gene they have by having a sample of their primary colorectal tumour taken and analysed for its KRAS status ('normal' or 'mutant'). The KRAS test is performed on a sample of tumour tissue, which is sent to a laboratory for DNA analysis. Knowing the results of a patient's KRAS test enables the medical team to select the most effective treatment for them and, for those with the 'mutant' KRAS gene, to avoid giving patients a biological agent that will be of no benefit to them.

## How KRAS and the biological agents work

KRAS is a gene that provides instruction for making a protein primarily involved in regulating cell growth. This protein is critical to the communication between cells (cellular communication) and plays an important role in the epidermal growth factor receptors (EGFR) pathway. Epidermal growth factor receptors are proteins that are found on the surface of cells and the EGFR pathway is a signaling sequence which is involved in the development and progression of cancer. Cetuximab (Erbix) and Panitumumab (Vectibix) target the cancer by specifically binding to the EGF receptor and inhibiting the activation of the EGFR, thereby disrupting the signaling pathway and inhibiting the division and growth of tumour cells.



## NICE's approval of Cetuximab (Erbix) 'first line'

In June 2009, NICE (The National Institute for Health and Clinical Excellence) approved the use of Cetuximab 'first line' for a specific group of patients. These are patients who have the 'normal' KRAS gene, whose cancer has only spread to their liver and whose primary bowel cancer tumour has already been completely removed. First line therapy is the initial treatment given soon after surgery – usually six weeks post operation.

If a patient responds to Cetuximab, their liver tumours may shrink to such an extent that they can be removed by surgery in a process known as resection.

Cetuximab is currently not approved by NICE for second or third line use. However, following the above positive decision for 'first line' use with certain criteria fulfilled, it is likely that its manufacturers will re-apply for it to be approved for 'second' and 'third line' use.

## A combination of treatments

Patients will usually be given Cetuximab with a combination of chemotherapy agents: either a combination called the FOLFOX regime, which comprises two chemotherapy drugs – 5-FU and Oxaliplatin – and a vitamin called Leucovorin; or one called the FOLFIRI regime, which comprises 5-FU, Leucovorin and a chemotherapy drug called Irinotecan.

In the first instance patients will usually be given Cetuximab with FOLFOX. If FOLFOX doesn't work for a patient, or if they react badly with side effects, they can be given Cetuximab with FOLFIRI instead. In certain circumstances, patients can be given Cetuximab on its own, but it is less likely to be effective as a sole agent than in a combination of treatments.

Information correct as at date of publication (September 2009)

For further information contact the Bowel Cancer  
Advisory Service on: (Freephone) 0800 8 40 35 40

Email: [advisory@bowelcanceruk.org.uk](mailto:advisory@bowelcanceruk.org.uk)

Website: [www.bowelcanceruk.org.uk](http://www.bowelcanceruk.org.uk)

Registered Charity Number: 1071038

London office

7 Rickett Street

London SW6 1RU

Tel: 020 7381 9711

Fax: 020 7381 5752

Edinburgh Office

20 Queen Street

Edinburgh EH2 1JX

Tel: 0131 225 5333

Fax: 0131 225 2206