Biomarkers
What you and your family need to know

FACTS YOU SHOULD KNOW
The GI Cancer Institute is Australia’s only independent, non-government, non-profit organisation with the specific aim of raising funds to carry out clinical research trials to test and improve treatments for gastro-intestinal (GI) cancers: those of the oesophagus, stomach, liver, pancreas, gallbladder and bowel (including rectum and anus).

These trials are conducted by the Australasian Gastro-Intestinal Trials Group (AGITG), a multi-disciplinary collaborative group of medical and research professionals. Since 1991 this group has been working to improve medical treatments for people with GI cancers. The GI Cancer Institute was established by the AGITG to raise funds for these trials, and also to raise public awareness about these cancers.

This brochure provides information to help patients with metastatic colorectal cancer, as well as their families and friends, learn more about the role of biomarker testing and what this means for personalised treatment.

What is a biomarker?

Biomarkers, short for biological markers, are biological molecules, cells or genes found in blood, other body fluids or tumour tissue itself, that may be assessed to provide more information about a tumour.¹

Personalised cancer medicine is advancing²³

A diagnosis of secondary or metastatic colorectal cancer means the primary cancer has spread (metastasised) beyond the bowel (colon or rectum) into other parts of the body, such as the liver or lungs.⁴ A number of investigations are carried out before starting treatment for metastatic colorectal cancer to ensure patients receive the most appropriate treatment.⁵

The aim of personalised medicine is to help doctors select the best treatment for each patient.²³ Steps can be taken to identify patients who may be more likely to benefit, or may be at greater risk of adverse effects, from one particular treatment compared to another.²³

Treatment for metastatic colorectal cancer can include surgery, radiotherapy, chemotherapy and/or targeted therapy.⁶ Combination treatment with surgery, chemotherapy and/or targeted therapy has been successful in improving treatment outcomes in patients with a metastatic colorectal cancer.⁷

Chemotherapy is a type of cancer treatment that works by killing the rapidly dividing cells that are found in cancer.⁸ Chemotherapy can also affect other healthy fast-growing cells which causes some of the side effects of chemotherapy such as hair loss.⁹

A ‘targeted therapy’ is a type of cancer treatment that works by targeting specific cancer cell genes or proteins involved in cancer cell growth. Some targeted therapy may be used alone and some only in combination with chemotherapy.⁹

Radiotherapy uses radiation, such as x-rays, to kill or damage cancer cells to stop them from growing and multiplying. It is a localised treatment, which means it usually only affects the part of the body where the radiation is directed.¹⁰

15,840 Australians were diagnosed with bowel cancer in 2012
How the biomarker test is used

The results of a biomarker test may:

- Indicate normal or abnormal cell function
- Provide a general insight into how likely the cancer is to progress and cause harm (i.e., prognostic biomarker)
- Predict the likelihood of the cancer’s response to a specific treatment (i.e., predictive biomarker)
- Help the patient and their doctor make decisions about how best to treat their cancer

Testing can determine a patient’s biomarker status

Taking a sample and testing colorectal cancer tissue can show if the tumour contains cells with certain genes that are normally functioning, known as ‘wild type’ genes, or genes that have changed, ‘mutated’.

Patients with metastatic colorectal cancer

Biomarker Testing

Biomarker-Negative (Wild-type)

Biomarker-Positive (Mutant-type)

Knowing their biomarker status can help the patient and their doctor decide on the most appropriate treatment plan, and possibly provide some information about expected outcomes in general regardless of treatment.
Some commonly tested biomarkers in colorectal cancer are RAS* (KRAS, NRAS) and BRAF. Biomarker test results will show if a patient’s tumour has no mutations (RAS and BRAF wildtype) and one or more of these mutations (RAS mutant and/or BRAF mutant).

**Biomarker status**

- **RAS* genes including KRAS and NRAS.**
  - RAS* is a family of genes that includes KRAS and NRAS. RAS biomarkers provide information to guide a patient's treatment and which therapies may or may not be appropriate.
  - The RAS family of genes also includes HRAS; however, mutations in HRAS are rarely found in metastatic colorectal cancer.

- **BRAF gene.** BRAF biomarkers provide information that has implications for treatment choice.

**What the results indicate**

- **About 50% of patients with metastatic colorectal cancer have RAS mutant tumours**
- **Patients with wild-type RAS genes in their tumours may be more likely to respond to certain treatments than those with mutated RAS genes in their tumours.**
- **5–10% of patients with metastatic colorectal cancer have BRAF mutant tumours**
- **Patients with metastatic colorectal cancer who have BRAF wild-type tumours have been shown to have better outcomes compared with patients with mutated BRAF tumours.**
- **90-95% of patients with metastatic colorectal cancer have BRAF wild-type tumours**

Biomarker testing provides knowledge about the genetic profile of a tumour to enable a patient and their doctor to decide on appropriate treatment.
Knowing your biomarker status may help you and your doctor make important disease management and treatment decisions.\textsuperscript{1,14}

The genetic makeup of each patient’s tumour is unique. Knowing your biomarker status — in this case the genetic properties of your tumour — may help you and your doctor select the most appropriate treatment.\textsuperscript{1}

1. Talk to your doctor about biomarker testing soon after your diagnosis of metastatic colorectal cancer so that you can make an informed decision regarding treatment.

2. Ask your doctor whether your tumour has been tested for biomarkers:
   If YES: What is your status for each of these biomarkers?
   If NO: Will your tumour be tested and when?

3. Ask your doctor how your biomarker status will affect your management.

When you’re diagnosed with metastatic colorectal cancer, you and your doctor want to get as much information as you can to make appropriate disease management decisions. It’s important to know your tumour biomarker status early, soon after the diagnosis of metastatic disease. When you understand your disease and how it affects your body, you can work with your doctor to plan your disease management.\textsuperscript{1,11}

As a patient with metastatic colorectal cancer, you and your caregivers are encouraged to keep an open dialogue with your doctors to keep up-to-date with genetic testing and what this means for your treatment.

Summary
1. Personalised medicine is advancing.\textsuperscript{2,3}

2. For patients with metastatic colorectal cancer, biomarker testing is an important tool that may be used to personalise treatment.\textsuperscript{1}

3. KRAS and NRAS are important biomarkers in metastatic colorectal cancer as they can predict whether a patient will respond to a particular treatment. BRAF may be important, as patients with a BRAF mutation may have a worse prognosis.\textsuperscript{1}

4. Knowing your biomarker status will help you and your doctor make important individualised decisions about the most appropriate treatment plan for you.\textsuperscript{1,14}
We need to raise community awareness of gastrointestinal cancers, and their research funding – to match their devastating burden of death and disease.

Russell Conley, Executive Officer, GI Cancer Institute / AGITG

The funding gap

GI cancers are amongst the least funded in Australia, compared to their impact in lives lost, according to a report from Cancer Australia published in 2014.

Analysis of data from the report shows that from 2009-11, pancreas, liver, oesophagus, stomach and bowel cancer all fared significantly worse in funding than other major cancers such as leukaemia, melanoma, breast and prostate cancers, when compared to the number of deaths they caused.

Cancer Australia, Cancer Research in Australia 2006-11; AIHW, Cancer Survival and Prevalence in Australia 1982-2010

References used in the development of this booklet


Ways to help

- Make a donation, online at www.gicancer.org.au or by phone 1300 666 769
- Run your own fundraising event or take the Gutsy Challenge. Call 1300 666 769
- Make a gift in your Will – for more information, call us (above) and ask for a confidential discussion
- Consider In Memory donations to honour a loved one
- Volunteer

Donations of $2 or more are tax deductible
FACTS YOU SHOULD KNOW ABOUT GI CANCER

3 people are diagnosed with GI cancer every hour

24,600 families are affected by GI cancer each year

33 Australians die every day of GI cancer

Source: AIHW Australian Cancer Database 2011, unpublished data

Locked Bag M250, Camperdown NSW 2050
P: 1300 666 769
E: info@gicancer.org.au

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GI CANCER INSTITUTE
GASTRO-INTESTINAL CANCER RESEARCH