

Why Getting Personal Can be Lifesaving?

A guide for healthcare professionals to address any questions patients with metastatic colorectal cancer may have on biomarkers

1. What are biomarkers?

A biomarker is a **biological molecule** found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. Biomarkers are widely used in medicine to evaluate different physiological and disease processes. They are a tool to measure how the body is doing. A biomarker can be a change in DNA, RNA, or protein. In mCRC they can be used to understand the characteristic of the tumour and the patient to help design a **personalized treatment** for each person.

2. What is precision medicine?

Precision medicine, sometimes known as "personalized medicine" is an innovative approach to **tailoring disease prevention and treatment** that takes into account differences in people's genes, environments, and lifestyles. The goal of precision medicine is to provide the **right treatment to the right patients at the right time**.

3. Why is it important to test tumour biomarkers?

Each tumour is unique. Knowing the tumour biomarkers is like knowing the fingerprints of a hand. It is a characterization of the tumour that can provide information to find the **most suitable treatment**.

4. How are biomarkers classified?

Biomarkers can be classified based on the information that their analysis can provide. A biomarker can be **diagnostic** and help to identify the cancer type. There are **prognostic** biomarkers used to learn about the estimated course of cancer if it goes independently from the treatment. **Predictive** biomarkers can predict whether the body will respond to a specific treatment or not. **Pharmacodynamic** biomarkers help with dosing decisions. Finally, **recurrence** biomarkers are used to monitor if the cancer is coming back after it has been treated. Some biomarkers can cover different information at the time.

5. How are biomarkers tested?

Biomarkers are tested on a sample of the tumour obtained through a biopsy or after the surgery. Some biomarkers can be tested using a sample of one's blood. Different techniques can be used to test the biomarkers depending on their nature. Proteins are usually detected by **immunohistochemistry**, and DNA and RNA are usually sequenced using **sequencing** or **next-generation sequencing (NSG)**.

6. How knowing the biomarkers will affect the treatment?

Biomarker analysis can provide information on the **effectiveness of specific drugs**. For example, RAS mutations (either KRAS or NRAS) will determine whether a specific class of drug namely anti-epidermal growth factor receptors might be effective or not. Also, having a specific mutation in a specific biomarker can make one a suitable candidate for a **clinical trial**.

7. What is microsatellite instability?

The DNA contains **short sequences repeated multiple times** that have different biological functions. These DNA regions are called microsatellites and tend to mutate easily due to their structure. Specific proteins have the ability to correct mistakes that occur during DNA replication and recombination and in case of DNA damage. If one or more of these proteins are mutated and lose their ability to correct mistakes, the DNA can accumulate **a large number of mutations**, causing an abnormal (increased or decreased) length of microsatellite repeats, which can lead to cancer formation.

8. What does it mean if the biomarkers are wild-type?

A biomarker is defined as wild-type if it presents the sequence or the structure that is shared among the majority of the population. Having a wild-type form of a biomarker means that **it is not mutated and it keeps its normal functions** within the body (it hasn't changed).

9. What does it mean if the biomarkers are mutated?

If one of the biomarkers tested presents a mutation it means that with a high probability **its biological function is altered**. Depending on the specific biomarker, the mutation can affect the development of the tumour, its growth and the response to treatment.

10. What is a sporadic mutation?

A sporadic mutation is a mutation affecting somatic cells which are all the cells and tissues in our body other than sperm and oocytes. This means that **only specific cells** of your body are affected by this mutation. **These mutations are not inherited**.

11. What is a germline mutation?

A **heritable change in the DNA** that occurred in a germ cell (a cell destined to become an egg or the sperm) or in the zygote at the single-cell stage. When transmitted to a child, a germline mutation is incorporated into **every cell of their body**.

In colorectal cancer, germline mutations can be associated with specific diseases (**Lynch syndrome** or **Familial Adenomatous Polyposis**) linked to a higher probability of developing cancer.

12. Should my family also be tested for biomarkers?

If you have found to have a **germline mutation**, you should be referred to a **genetic counsellor** who will determine which members of your family should be tested for the same mutation.

13. Can biomarkers be used to track my treatment?

The biomarker called Carcinoembryonic Antigen (CEA) can be used to monitor the progression of the tumour. It is a protein produced by cell tumours that can be measured in the blood. The levels of CEA should decrease after your tumour has been removed by surgery or after drug treatment. If this does not happen, it may be a sign that the tumour was not completely removed or has come back. Also, if CEA levels do not go down during chemotherapy, it could mean that the cancer is not responding to the current treatment.

It is good to remember that **CEA biomarker testing has some limitations because it is not always associated with cancer progression or recurrence**. It needs to be evaluated within the clinical context of each patient.

14. Can biomarkers change over time?

The biomarkers can change over time because new mutations occur or a group of preexisting cells with a mutation able to resist the treatment grow stronger. Biomarkers can be retested when treatment is not working as expected.

Remember:

- Use simple language when explaining medical terminology. You can try to use simple metaphors to explain complex concepts.
- Choose a private and quiet place for the discussion.
- Tailor your messages to the patient and consider specific factors when talking about biomarkers, such as the patient's age or cultural background.
- Answer questions until the patient begins to understand how biomarkers results can impact the treatment. Encourage the patient and his/her family to ask additional questions.
- For any further questions, provide the patient with a healthcare professional's updated contact details.
- Provide the patient with reliable and trustworthy information/tools on biomarkers (e.g. DiCE's [Patient Guide on Biomarkers in Metastatic Colorectal Cancer](#), ESMO guide for colorectal cancer patients).

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