



The role of biomarkers in planning treatment for metastatic breast cancer (MBC)

About this brochure

The purpose of the brochure is to explain biomarker testing and its important role in managing metastatic breast cancer (MBC).

This brochure will give you important information about:

- ✓ What MBC is
- ✓ What biomarkers are
- ✓ How biomarker testing works
- ✓ How biomarker testing can help your doctor choose the right treatment for you
- ✓ A specific biomarker known as “PIK3CA mutation”

What is MBC?

Breast cancer starts when cells in the breast grow out of control. When this happens, the cells can build up to form a malignant (cancerous) tumor.^{1,2} MBC happens when those cells spread to other parts of the body, including the bones, brain, lungs, and liver. MBC is sometimes called advanced or stage 4 cancer, and although it has spread to another part of the body, it’s still treated as breast cancer. About 30% of women diagnosed with early stage breast cancer will develop metastatic disease.^{3,4}

Your MBC subtype can help determine the best treatment for you

Understanding your diagnosis is an important first step to managing your condition.⁵ Knowing your breast cancer subtype can help determine your treatment.³

Your doctor may perform laboratory tests to determine your subtype.⁵

The following pages will help you understand more about the role of biomarkers in planning your treatment for MBC.

What is a biomarker?

A biomarker is a substance found in blood, urine, or body tissue that can give your doctor useful information about a cancer. It helps your doctor know which treatments might work best for that specific cancer.⁶⁻⁸ Important biomarkers in breast cancer include hormone receptors (HRs), the protein HER2, and PIK3CA mutations.⁸⁻¹⁰

Biomarker testing may help your doctor determine and discuss with you the appropriate treatment plan for your type of cancer.^{8,11,12}

HRs

(hormone receptors)

Some breast cancer cells use hormones, such as estrogen or progesterone, to grow. These hormones bind to cells using docking stations known as receptors.⁵

- HR+ (hormone receptor–positive): hormone receptors are found on the breast cancer cell⁵

HER2

(human epidermal growth factor receptor 2)

HER2 is a protein that helps cells grow and divide. When there is too much HER2, cancer cells may grow more quickly and be more likely to spread to other parts of the body.¹³

- HER2+ (HER2-positive): breast cancer cells that have high levels of HER2
- HER2- (HER2-negative): breast cancer cells that do not have high levels of HER2

If your MBC has HRs and no HER2 protein (HR+/HER2-), you may be prescribed medications called aromatase inhibitors. These may be used in combination with another medication called CDK4/6 or mTOR inhibitors to block the activity of an enzyme called aromatase. This makes less estrogen available to stimulate the growth of HR+ breast cancer cells.¹⁴

Gene mutations

Genes carry instructions that tell cells what to do. When genes are changed (mutated), cells can grow in the wrong ways. This can lead to medical conditions, such as breast cancer.¹⁵

The most common type of mutation to cause cancer is called “somatic.”¹⁵

Somatic mutations:

- Occur from damage to genes in a cell during a person’s life
- Are not passed down from parent to child (not inherited)

An example of a somatic mutation is a PIK3CA mutation. This is a change to the gene that tells cells what to do and how often to grow and divide.⁹

A far less common mutation to cause cancer is called “germline.”¹⁵

Germline mutations:

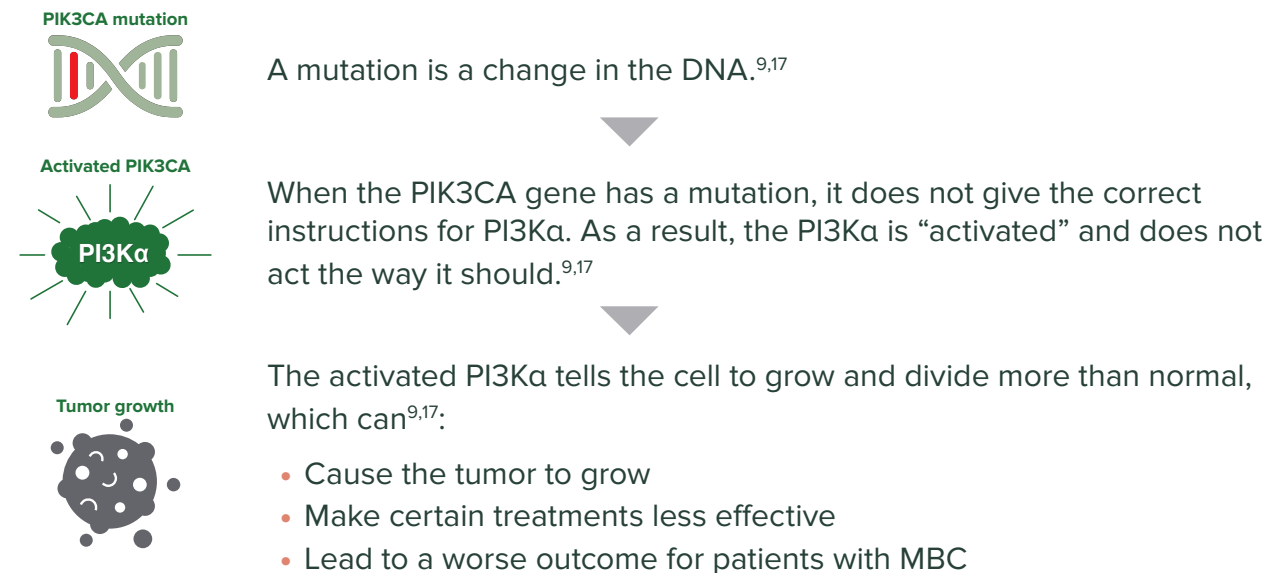
- Occur in a sperm cell or egg cell
- Can pass from parent to child (inherited)

BRCA1 and BRCA2 are germline mutations associated with some types of breast cancer. These are changes to the genes that help cells grow normally and help repair damaged DNA (the genetic information inside cells).^{5,16}

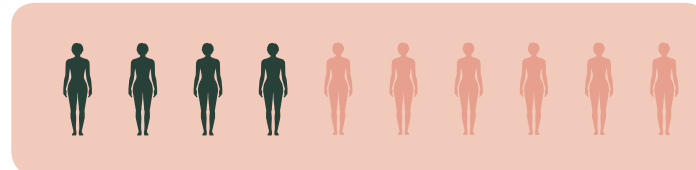
Understanding more about the PIK3CA mutation

[Include PIK3CA content according to regulations in your country]

DNA is found in all cells and is made up of a variety of different “genes.” Each gene is a set of instructions for making a different part of the cell. The PIK3CA gene gives instructions for part of the cell known as “PI3K α ” (PI3K-alpha).^{9,17}



**About 40% of HR+/HER2-
MBC patients have a PIK3CA
mutation in their tumors^{18,19}**



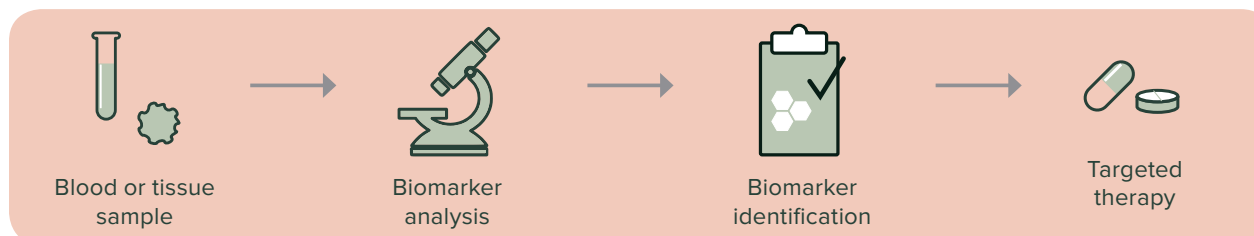
What should I know about testing for biomarkers like PIK3CA?

Biomarker testing may be done when your doctor first discovers that the cancer has spread (metastasized).²⁰ Testing can also be done when the cancer starts growing or spreading again after a treatment is given (also called progression), if it was not done earlier.^{8,21}

A biomarker may be found or measured by testing blood (plasma) or tissue.⁸ Biomarkers reveal “targets” for the most precise treatments, which are known as targeted therapies.^{6,7}

Biomarkers help to^{8,11,12}:

- ✓ Guide treatment decisions
- ✓ Predict how the cancer may respond to treatment
- ✓ Determine how well treatment is working
- ✓ Signal that the cancer is returning



What treatment makes the most sense for me?

Biomarker testing may help your doctor gather as much information as possible about your specific type of breast cancer. You can work with your doctor to determine what tests and treatments will be the most helpful. By talking openly with your doctor, you can be more engaged in your treatment plan.⁸



Hormone (endocrine) therapy

- Works by stopping cancer growth that is caused by hormones⁵
- May be used by women and adult men with hormone receptor–positive (HR+) breast cancer^{8,22}

Targeted therapy

- Works by finding and attacking specific types of cancer cells, while causing less harm to normal cells⁵
- In HR+/HER2- MBC, therapy sometimes targets CDK4/6 or mTOR proteins, which control cell growth and division, to block or slow their activity and control the cancer longer^{14,23}
- In HER2- MBC, when a person has a BRCA1 or BRCA2 mutation, therapy sometimes targets the PARP protein, which allows cancer cells to repair themselves^{5,6,24}
- For patients with HR+/HER2- MBC with a PIK3CA mutation, PI3K inhibitors may slow down or stop cancer cell growth²²

Chemotherapy

- Damages the cancer cell’s DNA in order to kill the cancer cells and/or prevent them from growing and dividing^{5,25}
- Used for many types of MBC, including HR+/HR- and HER2+/HER2-^{5,26}

Radiation therapy

- Destroys and/or damages cancer cells in a localized area⁵
- Used to prevent or manage the symptoms of specific sites where the cancer has metastasized/spread, such as pain⁵

Working with your doctor

Your doctor is your best resource throughout your treatment. Talk openly and often with your doctor about your doubts, questions, or concerns. That can help you feel more in control and get the information you need to best manage your treatment.²⁷



Before your visit

- Keep a log of your symptoms and side effects. Bring it with you to discuss with your doctor²⁸
- Write down any questions you have. Mark the most important ones to remind yourself to ask those first²⁸

During your visit

- Tell your doctor at the beginning of the appointment about the topics you want to discuss²⁷
- Take notes during the appointment to help you remember important information. Ask a friend, family member, or nurse to help if needed²⁷
- Ask questions and talk openly about²⁷:
 - Your breast cancer
 - Your treatment
 - How you're feeling—both physically and emotionally



All the members of your healthcare team work with one another and with you to help you get the best care possible. Asking them questions during your visits can help you get the information and support you need.²⁷

What questions should I ask my HCP at my next visit?

Below are questions that you may have about breast cancer and your treatment. Insert a check mark (✓) next to each one you'd like to discuss with your doctor. That way, you can get the conversation started and take a more active role in your care.²⁸⁻³⁰

Biomarkers and testing

- Where has the cancer spread?
- What is my biomarker status?
- What test can tell me if I have a biomarker or mutation?
- Where is this test available?
- What kind of sample is needed: blood or tumor tissue?
- How will you get tumor tissue for testing? What is involved in the biopsy procedure?
- If the test shows I have a biomarker or mutation, what does this mean for my treatment?

Targeted therapies

- Will a targeted therapy affect any other medicines I am taking?

My treatment plan

- What is my prognosis?
- Are there any tests and procedures I need to have done to help determine the best treatment?
- What are my treatment options; which do you recommend and why?
- What is the goal of my treatment?
- What are the risks of treatment?
- When do I need to make a treatment decision?
- How does reaching menopause affect my treatment options?
- How long will treatment last? What will it be like? Where will it be done?
- What tests will I need and how often to monitor treatment?
- What will happen if the treatment doesn't work or the cancer comes back?

During treatment

- What are the potential side effects of treatment? How long will they last? Is there anything I can do to reduce them?
- How will treatment affect my daily life? Will I be able to work, exercise, and go about my normal routine?
- How will I know if treatment is working?
- What can be done to help me feel more comfortable during treatment?

Finding support

- Who should I call if I have questions or problems?
- Do you communicate with your patients via email, phone, or an electronic record system?
- What support is available for me and my family?
- Where else can I look for information on my diagnosis and treatment?

After your visit

- Follow up on any instructions from your doctor, such as scheduling future appointments or filling a prescription^{30,31}
- Share your notes and talk about your doctor visit with family members or friends who support you

Glossary of terms

- **Advanced breast cancer:** Breast cancer that has spread to a nearby part of the body. It can be classified as either stage 3 or stage 4. It can also be called metastatic breast cancer (MBC)³²
- **Biomarker:** A substance found in blood, urine, or body tissue that can give doctors useful information about a cancer.⁸ In breast cancer, biomarkers provide important information often used to describe cancer subtypes⁶
- **De novo metastatic breast cancer:** Breast cancer that wasn't detected until it had spread to another part of the body³³
- **DNA:** Molecules inside cells that carry genetic information and pass it from one generation to the next³⁴
- **Endocrine (therapy):** Treatment that adds, blocks, or removes hormones³⁵
- **Estrogen:** A type of hormone made by the body that helps develop and maintain female sex characteristics³⁶
- **Fatigue:** Extreme tiredness and an inability to function due to a lack of energy³⁷
- **Genes:** Units of heredity passed from parents to their offspring; pieces of DNA that contain information for making a specific protein³⁸
- **HER2-/human epidermal growth factor receptor 2 negative:** The description of a type of cancer that does not contain high amounts of the HER2 protein. This protein helps the cancer cell grow and divide. When there is too much HER2, cancer cells may grow more quickly and be more likely to spread to other parts of the body. HER2 is a biomarker and is targeted by certain treatments^{8,13,39}
- **HR+/hormone receptor positive:** A type of cancer where hormone receptors that act as docking stations are found on the outside of the cancer cell. Hormones, such as estrogen and progesterone, attach to these receptors and cause the cancer cell to grow^{5,40}
- **Immune system:** A complex network of cells, tissues, organs, and the substances they make. They help the body fight infections and other diseases⁴¹
- **Malignant:** Cancerous. Cells that are malignant can spread to other parts of the body²
- **Metastatic:** Cancer that has spread from the primary site (where it started) to other places in the body. This is sometimes referred to as advanced or stage 4 cancer^{42,43}
- **Metastatic breast cancer:** Breast cancer that has spread from the primary site (the breast) to other places in the body, such as the bones, brain, lungs, or liver. Metastatic breast cancer is sometimes called advanced or stage 4 breast cancer^{3,4}
- **Mutation:** Any change in the DNA sequence of a cell. Mutations can have a positive effect, a negative effect, or no effect. Some mutations may lead to cancer or other diseases⁴⁴
- **PIK3CA:** A gene that sends signals to an enzyme that is an important part of the PI3K α pathway, which instructs cells on what to do and how often to grow and divide⁹
- **Progression:** When cancer grows and spreads after being treated⁴⁵

- **Postmenopausal:** The time in a woman's life when her menstrual periods no longer happen⁴⁶
- **Recur/recurrent:** When cancer comes back after it is treated. It may also be called advanced⁴⁷
- **Stage:** A number, and sometimes also a letter, that describes the extent of a cancer in the body⁴⁸
- **Targeted therapy:** A type of treatment that uses drugs or other substances to find and attack specific types of cancer cells with less harm to normal cells.⁴⁹ Targeted therapy is sometimes given in combination with hormone therapy.¹⁶ Ribociclib, everolimus, palbociclib, trastuzumab, pertuzumab, lapatinib, and alpelisib are examples of targeted therapies⁵⁰
- **Tumor:** An abnormal mass of tissue that forms when cells divide more than they should or do not die when they should. Tumors may be benign (not cancer) or malignant (cancer)⁵¹

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