LITESPARK 029
ONCOLOGY CLINICAL TRIALS

Learn about a clinical trial for metastatic breast cancer

In this brochure, you will learn about **ER+/HER2- unresectable locally advanced or metastatic breast cancer** and a clinical trial for this disease. In this trial, researchers are trying to find out if an investigational combination of trial drugs is safe and may help slow down or stop the growth of this cancer. Researchers are studying this investigational combination in people who have already received certain types of treatments, but their cancer has gotten worse.

You can also use this brochure to talk with your doctor about this trial.

What is ER+/HER2- breast cancer?

ER+/HER2- breast cancer is the most common type of breast cancer.

- ER+ (estrogen receptor positive) means the breast cancer cells have receptors that attach to the estrogen hormones, which can help cancer cells grow.
- HER2- (human epidermal growth factor receptor 2 negative) means the cancer cells do not make high levels of a protein called HER2. HER2- cancer cells grow and spread slower than HER2+ cancer cells.

When ER+/HER2- breast cancer is found early and treated, there is a low chance that it will come back. However, sometimes it comes back after treatment, starts to spread, and can't be removed by surgery.

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What is locally advanced or metastatic breast cancer?

Locally advanced cancer means the cancer is in the early stages of spreading. Metastatic means the cancer has spread to other parts of the body. Some locally advanced or metastatic cancer is unresectable, meaning it cannot be removed by surgery.

What are my treatment options?

If you have unresectable locally advanced or metastatic breast cancer, your care team will talk about your treatment options with you and those close to you. Your options will depend on a few things:

- Your overall health
- The stage of your cancer, which tells you if the cancer has spread and how far
- Chance of the cancer coming back

- Side effects you might have from the treatment
- What chance the treatment has of slowing down or stopping the cancer
- How long the treatment might help extend your life
- How much the treatment might help improve your symptoms

Your care team may offer you 1 or more of these treatments:

Local therapies – treatment directed at the site of the cancer to destroy it

Targeted therapy – treatment that works on specific cells to stop them from growing

Immunotherapy – medicines that help your immune system fight the cancer

Chemotherapy – medicine to kill cancer cells or stop them from growing

Radiation therapy – treatment that uses beams of intense energy (like X-rays) to shrink or get rid of tumors. This would only be used to treat symptoms related to tumor growth.

Hormone therapy – also called endocrine therapy. These are medicines that block or lower the level of hormones that cause certain breast cancers to grow.

Palliative care – also called comfort care. This is special care to help ease pain and symptoms with a focus on the person's quality of life. This does not directly treat metastatic breast cancer, but it helps keep you as comfortable as possible.

Clinical trials, such as this one

Talk to your doctor to find out which treatment is right for you.

What is a clinical trial?

Clinical trials are research studies that help doctors find out if study drugs (alone or with other treatments) are safe and if they can help prevent, find, or treat diseases or conditions. Clinical trials are carefully controlled research studies that are done to get a closer look at investigational treatments and procedures.

All about this clinical trial

What is the goal of this clinical trial?

The goal of this trial is to learn if the investigational combination of the trial drug belzutifan with fulvestrant may help stop or slow down unresectable local advanced or metastatic ER+/HER2- breast cancer. Researchers are studying the investigational combination in people who have received previous treatment for this disease with endocrine therapy.

This trial is testing the investigational combination of belzutifan and fulvestrant and comparing it to everolimus plus fulvestrant or exemestane. Belzutifan is experimental. It has not been approved to use alone or in combination with fulvestrant for breast cancer. Fulvestrant, everolimus, and exemestane have been approved as independent treatments by certain health authorities for treatment of various cancers, including some types of breast cancer. These drugs and combinations of these drugs may not be approved in your country or to treat your type of breast cancer.

What treatment is being studied?

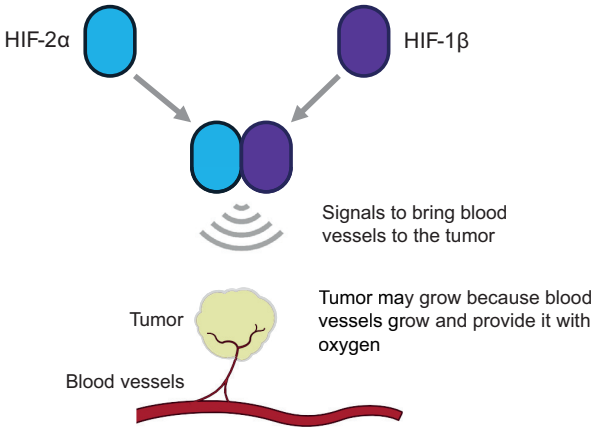
The trial medicine is belzutifan. It has been approved by some health authorities for treating some types of cancers, including kidney cancer in adults with a rare disease called von Hipple-Lindau (VHL). It may not be approved in your country for your type of cancer. Researchers are testing belzutifan in combination with fulvestrant and comparing it to everolimus plus fulvestrant or exemestane.

About Belzutifan:

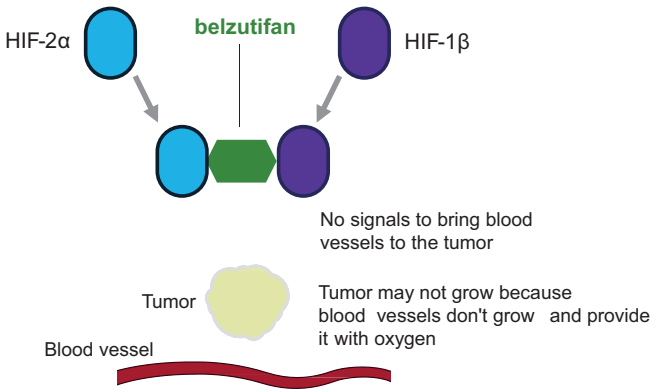
Belzutifan (also known as MK-6482) is an investigational trial drug that may help stack cancer cells. Belzutifan is approved in some countries to treat some types of kidney cancer.

1. The hypoxia-inducible factor, HIF-2α, is believed to play a critical role in tumor creations and tumor progression in certain types of cancers.
2. When the body experiences hypoxia (low oxygen), HIF-2α and HIF-1B can bind together and cause the increased creation of red blood cells and blood vessels that go to the tumor and help it grow. This also may prevent the cell from naturally dying on its own.
3. The investigational trial drug belzutifan comes in and may help stop HIF-2α and HIF-1B from binding to each other.
4. This study is evaluating whether blocking the binding will allow the cell to naturally go through its lifecycle, die off and cause the tumor cells to stop growing.

Another way to think about Belzutifan



When HIF-2αand HIF-1β bind together, it brings oxygen and blood to tumor cells. This helps cancer cells grow and survive.



This clinical trial looks at whether belzutifan can block HIF-2α and HIF-1β from binding, so that the cancer cells don't get oxygen and blood.

Deciding to join a clinical trial is something only you, those close to you, and your care team can decide together. If there is anything you do not understand, ask the trial doctor.

Who can join this trial?

There are eligibility criteria that will determine if you will quality for participation. For example, you must:

- Have ER+/HER2- unresectable locally advanced or metastatic breast cancer
- Had the cancer grow or spread during endocrine treatment
- Have received prior treatment with a CDK4/6 Inhibitor

Your trial staff will do tests to see if you are able to join this trial.

You and your trial doctor will discuss:

- All the requirements to join this trial
- Possible benefits, risks, and side effects of being in this trial

If I join, how long will I be in the trial?

How long you will be in the trial depends on:

- Your health
- What type of cancer you have
- How well you tolerate the study treatments

What will happen during trial visits?

You will visit the trial site on a regular schedule so that the trial doctors can see how the investigational trial drugs are working for you. During your trial visits, you may get:

- Your trial treatments
- Blood and urine tests
- Physical exams
- IV administration
- Imaging scans such as CT scans or MRIs (scans that help the doctor see the cancer inside your body)

You can ask your trial doctor any questions you have about what happens during trial visits and how often they will happen.

If you are able to join the trial, your trial doctor will need to stay in contact with you even after your trial visits are over. This is very important because this clinical trial is studying how well the study treatment works over time.

What treatments will I get?

The investigational trial drug combination you get will depend on which group you are randomly placed in. This trial has two groups:

Group	Treatment	Chance of being in this group
Group 1	Belzutifan plus fulvestrant	1 out of 2
Group 2	Everolimus plus (fulvestrant or exemestane)	1 out of 2

A computer will decide which group you are put in. You have an equal chance of getting put in each group.

You, your trial doctor, and the trial staff will know what treatments you are getting.

Thank you for learning about metastatic breast cancer and this clinical trial

You can use this brochure to talk with your doctor about this trial.

Your questions and notes:

You can use this space to write down notes or questions about this trial.

To learn more

To learn more about this trial, you can

- Talk to your doctor
- Contact Merck by
  - Visiting **www.merckoncologyclinicaltrials.com**
  - Scanning this QR code:

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