

## TARGETED THERAPY

Information and pictures from *National Cancer Institute* unless otherwise specified

### Quick Summary of Section

#### Targeted therapy

- Targeted therapy is a type of treatment that uses drugs or other substances to identify and attack specific cancer cells without harming normal cells.

#### Drugs used in Targeted Therapy (Breast Cancer)

- Monoclonal antibody therapy
- Tyrosine kinase inhibitors are targeted therapy drugs that block signals needed for tumors to grow.
- Cyclin-dependent kinase inhibitors are targeted therapy drugs that block proteins called cyclin-dependent kinases, which cause the growth of cancer cells.

#### Targeted therapy

##### What is targeted therapy?

Targeted therapy is a type of cancer treatment that targets proteins that control how cancer cells grow, divide, and spread. It is the foundation of precision medicine. As researchers learn more about the DNA changes and proteins that drive cancer, they are better able to design treatments that target these proteins. Targeted therapy is a type of treatment that uses drugs or other substances to identify and attack specific cancer cells without harming normal cells.

- Monoclonal antibodies, tyrosine kinase inhibitors, cyclin-dependent kinase inhibitors, mammalian target of rapamycin (mTOR) inhibitors, and PARP inhibitors are types of targeted therapies used in the treatment of breast cancer.
- Monoclonal antibody therapy is a cancer treatment that uses antibodies made in the laboratory, from a single type of immune system cell.

##### What are the types of targeted therapy?

- Most targeted therapies are either small-molecule drugs or monoclonal antibodies.
- Small-molecule drugs are small enough to enter cells easily, so they are used for targets that are inside cells.
- Monoclonal antibodies, also known as therapeutic antibodies, are proteins produced in the lab. These proteins are designed to attach to specific targets found on cancer cells. Some monoclonal antibodies mark cancer cells so that they will be better seen and destroyed by the immune system. Other monoclonal antibodies directly stop cancer cells from growing or cause them to self-destruct. Still others carry toxins to cancer cells.

##### Who is treated with targeted therapy?

- For some types of cancer, most patients with that cancer will have a target for a certain drug, so they can be treated with that drug. But, most of the time, your tumor will need to be tested to see if it contains targets for which we have drugs.
- Testing your cancer for targets that could help you and your doctor choose your treatment is called biomarker testing.
- You may need to have a biopsy for biomarker testing. A biopsy is a procedure in which your doctor removes a piece of the tumor for testing. There are some risks to having a biopsy. These risks vary depending on the size of the tumor and where

# LOST TEMPLE FITNESS

## Targeted therapy *Continued*

it is located. Your doctor will explain the risks of having a biopsy for your type of tumor.

### How does targeted therapy work against cancer?

Most types of targeted therapy help treat cancer by interfering with specific proteins that help tumors grow and spread throughout the body. They treat cancer in many ways. They can:

- Help the immune system destroy cancer cells. One reason that cancer cells thrive is because they can hide from your immune system. Certain targeted therapies can mark cancer cells so it is easier for the immune system to find and destroy them. Other targeted therapies help boost your immune system to work better against cancer.
- Stop cancer cells from growing. Healthy cells in your body usually divide to make new cells only when they receive strong signals to do so. These signals bind to proteins on the cell surface, telling the cells to divide. This process helps new cells form only as your body needs them. But, some cancer cells have changes in the proteins on their surface that tell them to divide whether or not signals are present. Some targeted therapies interfere with these proteins, preventing them from telling the cells to divide. This process helps slow cancer's uncontrolled growth.
- Stop signals that help form blood vessels. Tumors need to form new blood vessels to grow beyond a certain size. In a process called angiogenesis, these new blood vessels form in response to signals from the tumor. Some targeted therapies called angiogenesis inhibitors are designed to interfere with these signals to prevent a blood supply from forming. Without a blood supply, tumors stay small. Or, if a tumor already has a blood supply, these treatments can cause blood vessels to die, which causes the tumor to shrink. Learn more about Angiogenesis Inhibitors.
- Deliver cell-killing substances to cancer cells. Some monoclonal antibodies are combined with toxins, chemotherapy drugs, and radiation. Once these monoclonal antibodies attach to targets on the surface of cancer cells, the cells take up the cell-killing substances, causing them to die. Cells that don't have the target will not be harmed.
- Cause cancer cell death. Healthy cells die in an orderly manner when they become damaged or are no longer needed. But, cancer cells have ways of avoiding this dying process. Some targeted therapies can cause cancer cells to go through this process of cell death.
- Starve cancer of the hormones it needs to grow. Some breast and prostate cancers require certain hormones to grow. Hormone therapies are a type of targeted therapy that can work in two ways. Some hormone therapies prevent your body from making specific hormones. Others prevent the hormones from acting on your cells, including cancer cells.

### Are there drawbacks to targeted therapy?

- Targeted therapy does have some drawbacks. These include:
- Cancer cells can become resistant to targeted therapy. For this reason, they may work best when used with other types of targeted therapy or with other cancer treatments, such as chemotherapy and radiation.
- Drugs for some targets are hard to develop. Reasons include the target's structure, the target's function in the cell, or both.

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<p><b>Targeted therapy Continued</b></p>	<p><b>What are the side effects of targeted therapy?</b></p> <ul style="list-style-type: none"> <li>• Targeted therapy can cause side effects. The side effects you may have depend on the type of targeted therapy you receive and how your body reacts to the therapy.</li> <li>• The most common side effects of targeted therapy include diarrhea and liver problems. Other side effects might include problems with blood clotting and wound healing, high blood pressure, fatigue, mouth sores, nail changes, the loss of hair color, and skin problems. Skin problems might include rash or dry skin. Very rarely, a hole might form through the wall of the esophagus, stomach, small intestine, large bowel, rectum, or gallbladder.</li> <li>• There are medicines for many of these side effects. These medicines may prevent the side effects from happening or treat them once they occur.</li> <li>• Most side effects of targeted therapy go away after treatment ends.</li> </ul> <p><i>(Targeted Therapy to Treat Cancer)</i></p>
<p><b>Drugs used in Targeted Therapy For Breast Cancer</b></p>	<p><b>Types of monoclonal antibody therapy include the following:</b></p> <ul style="list-style-type: none"> <li>• <i>Trastuzumab</i> is a monoclonal antibody that blocks the effects of the growth factor protein HER2, which sends growth signals to breast cancer cells. It may be used with other therapies to treat HER2 positive breast cancer.</li> <li>• <i>Pertuzumab</i> is a monoclonal antibody that may be combined with trastuzumab and chemotherapy to treat breast cancer. It may be used to treat certain patients with HER2 positive breast cancer that has metastasized (spread to other parts of the body). It may also be used as neoadjuvant therapy in certain patients with early stage HER2 positive breast cancer.</li> <li>• <i>Ado-trastuzumab emtansine</i> is a monoclonal antibody linked to an anticancer drug. This is called an antibody-drug conjugate. It is used to treat HER2 positive breast cancer that has spread to other parts of the body or recurred (come back).</li> <li>• <i>Sacituzumab govitecan</i> is a monoclonal antibody that carries an anticancer drug to the tumor. This is called an antibody-drug conjugate. It is being studied to treat women with triple-negative breast cancer who have received at least two previous chemotherapy regimens.</li> </ul> <p><i>Tyrosine kinase inhibitors</i> are targeted therapy drugs that block signals needed for tumors to grow. Tyrosine kinase inhibitors may be used with other anticancer drugs as adjuvant therapy. Tyrosine kinase inhibitors include the following:</p> <ul style="list-style-type: none"> <li>• Lapatinib is a tyrosine kinase inhibitor that blocks the effects of the HER2 protein and other proteins inside tumor cells. It may be used with other drugs to treat patients with HER2 positive breast cancer that has progressed after treatment with trastuzumab.</li> <li>• Neratinib is a tyrosine kinase inhibitor that blocks the effects of the HER2 protein and other proteins inside tumor cells. It may be used to treat patients with early stage HER2 positive breast cancer after treatment with trastuzumab.</li> </ul> <p><i>Cyclin-dependent kinase inhibitors</i> are targeted therapy drugs that block proteins called cyclin-dependent kinases, which cause the growth of cancer cells. Cyclin-dependent kinase inhibitors include the following:</p> <ul style="list-style-type: none"> <li>• Palbociclib is a cyclin-dependent kinase inhibitor used with the drug letrozole to treat breast cancer that is estrogen receptor positive and HER2 negative and has spread to other parts of the body.             <ul style="list-style-type: none"> <li>○ It is used in postmenopausal women whose cancer has not been treated with hormone therapy.</li> <li>○ Palbociclib may also be used with fulvestrant in women whose disease has gotten worse after treatment with hormone therapy.</li> </ul> </li> </ul>

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<p><b>Drugs used in Targeted Therapy For Breast Cancer</b> <i>Continued</i></p>	<ul style="list-style-type: none"> <li>• <i>Ribociclib is a cyclin-dependent kinase inhibitor used with letrozole to treat breast cancer that is hormone receptor positive and HER2 negative and has come back or spread to other parts of the body.</i> <ul style="list-style-type: none"> <li>○ It is used in postmenopausal women whose cancer has not been treated with hormone therapy.</li> <li>○ It is also used with fulvestrant in postmenopausal women with hormone receptor positive and HER2 negative breast cancer that has spread to other parts of the body or has recurred.</li> <li>○ It is also used in premenopausal women with hormone receptor positive and HER2 negative breast cancer that has spread to other parts of the body or has recurred..</li> </ul> </li> <li>• <i>Abemaciclib is a cyclin-dependent kinase inhibitor used to treat hormone receptor positive and HER2 negative breast cancer that is advanced or has spread to other parts of the body. It may be used alone or with other drugs to treat breast cancer that has gotten worse after other treatment.</i></li> <li>• <i>Alpelisib is a cyclin-dependent kinase inhibitor used with the drug fulvestrant to treat hormone receptor positive and HER2 negative breast cancer that has a certain gene change and is advanced or has spread to other parts of the body.</i> <ul style="list-style-type: none"> <li>○ It is used in postmenopausal women whose breast cancer has gotten worse during or after treatment with hormone therapy.</li> </ul> </li> </ul> <p><i>Mammalian target of rapamycin (mTOR) inhibitors block a protein called mTOR, which may keep cancer cells from growing and prevent the growth of new blood vessels that tumors need to grow. mTOR inhibitors include the following:</i></p> <ul style="list-style-type: none"> <li>• Everolimus is an mTOR inhibitor used in postmenopausal women with advanced hormone receptor positive breast cancer that is also HER2 negative and has not gotten better with other treatment.</li> </ul> <p><i>PARP inhibitors are a type of targeted therapy that block DNA repair and may cause cancer cells to die. PARP inhibitors include the following:</i></p> <ul style="list-style-type: none"> <li>• Olaparib is a PARP inhibitor used to treat patients with mutations in the BRCA1 or BRCA2 gene and HER2 negative breast cancer that has spread to other parts of the body. PARP inhibitor therapy is being studied for the treatment of patients with triple-negative breast cancer.</li> <li>• Talazoparib is a PARP inhibitor used to treat patients with mutations in the BRCA1 or BRCA2 genes and HER2 negative breast cancer that is locally advanced or has spread to other parts of the body.</li> </ul> <p><i>NIH NCI (17)</i></p>
<p><b>References</b></p>	<p><i>NIH NCI (17) <a href="https://www.cancer.gov/types/breast/patient/breast-treatment-pdq#_185">https://www.cancer.gov/types/breast/patient/breast-treatment-pdq#_185</a></i></p> <p><i>Targeted Therapy to Treat Cancer – NCI <a href="https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies">https://www.cancer.gov/about-cancer/treatment/types/targeted-therapies</a></i></p>