All About Targeted Therapy

What is targeted therapy?

Targeted therapy is a type of cancer treatment. Chemotherapy works by killing cells that divide rapidly. This includes cancer cells and many types of healthy cells (hair, GI tract, blood cells, etc). Targeted therapies work by targeting something specific to a cancer cell. This allows the medication to kill cancer cells and to preserve the health of most normal cells. Sometimes the “target” is found on some healthy cells as well, and side effects can happen.

Targeted therapy can be called precision medicine or personalized medicine. This is because one person’s cancer may be treated differently than another based on the targets found on their tumor.

Targeted therapy medications work by stopping molecular targets in the cancer cell that lead to the growth, spread, and progression of cancer. In many cases, your healthcare provider will have to test your tumor to see if a specific target is present. Even though people may have the same type of cancer, they may not have the same molecular targets. The same targeted treatment doesn’t work for everyone with that type of cancer. Also, just because the target is present, doesn’t mean the tumor will respond to the targeted therapy.

Common molecular targets (mutations or changes) that are treated with targeted therapies include HER2, EGFR, KRAS, VEGF, ALK, JAK 1 and 2, BTK, and BRAF. Your healthcare team may test you for these mutations, depending on your cancer type and if a mutation is known in that cancer type.

Targeted therapies are currently FDA approved for the treatment of many cancers including breast, colorectal, lung, thyroid, prostate cancers, lymphoma, leukemia, myeloma, CLL, and melanoma. Targeted therapy may be given alone or in combination with chemotherapy, radiation, and/or surgery. Clinical trials studying other potential targeted therapies are in progress for many other cancer types.

What are the different types of targeted therapies?

Targeted therapies are classified as either small molecule drugs or large molecule drugs.

- Small molecule drugs can enter a cancer cell because of how small they are. They find the target, enter the cell and block it.
- Large molecule drugs often don’t fit into a cell. They instead attack proteins or enzymes on the surface of the cell.

There are many types of targeted therapies. Examples include:

- **Kinase Inhibitors**: Cell growth is controlled by growth factors. They attach to the surface of cells triggering a series of chemical reactions that allow the cell to grow and divide. Cancer cells do not work properly and are able to grow and divide even when growth factors are not present. Kinase inhibitors work by blocking signals within cancer cells, preventing a step necessary for the cell to grow and divide. Examples of kinase inhibitors include dabrafenib (Tafinlar®), imatinib (Gleevec®), sorafenib (Nexavar®), ibrutinib (Imbruvica), and cabozantinib (Cometriq).
- **Angiogenesis Inhibitors**: Angiogenesis is the development of blood vessels to supply the tumor with nutrients it needs to grow. These medications work to block the formation of this blood supply and cut off the tumor’s source of nutrients. Some kinase inhibitors also act as angiogenesis inhibitors (examples: sorafenib (Nexavar), sunitinib (Sutent®), everolimus (Afinitor®). Examples of angiogenesis inhibitors include ziv-aflibercept (Zaltrap®), lenalidomide (Revlimid®), and vandetanib (Caprelsa®).
- **Monoclonal antibodies**: These antibodies are made in a lab and target a specific antigen (protein). They work in a few
different ways. They can target a specific cell (the cancer cell), sending a message to the immune system to destroy the targeted cell. Some monoclonal antibodies slow or stop the growth of cancer cells by interfering with functions necessary for cell growth. Examples of monoclonal antibodies are bevacizumab (Avastin®), trastuzumab (Herceptin®), and denosumab (Xgeva®, Prolia®).

- **Radioimmunotherapy**: This is a combination of a monoclonal antibody and a radiation source, which permits radiation to be delivered directly to the targeted cells, but often in lower doses and over a longer period of time. An example is ibritumomab tiuxetan (Zevalin®).

### How are targeted therapies given?

Some targeted therapies are given by pill, others are given by vein (IV). Be sure to pay attention to storage and handling recommendations for oral medications. It is also extremely important that you take your oral medications as prescribed. Some of these oral medications are very expensive. Be sure to talk with your healthcare team if you can’t afford your medication, as assistance may be available.

### What are the side effects of targeted therapies?

There are side effects to targeted therapies. Not everyone will experience these side effects and the severity of the side effects can vary from person to person. Be sure to talk with your healthcare team about side effects you may be experiencing. Do not stop taking your oral medications due to side effects without talking to your healthcare team.

Some targeted therapies impact the skin, causing an acne-like rash or other skin changes. These are not the same as experiencing an allergy to the medication, but a direct effect of the medication. These skin changes happen in particular with EGFR and VEGF targeted therapies as these medications can also impact skin cells.

Skin side effects can exhibit in many different ways including, a sunburn-like sensation (not necessarily appearance); your skin may feel irritated and angry, be sensitive to sunlight, develop a rash, dry skin, hair loss or changes to hair texture, hand-foot syndrome, and other nail and skin changes.

Because many of these drugs are relatively new, we don’t know a lot about their potential for long term side effects. Be sure to talk with your healthcare team about fertility preservation before starting any targeted therapy, as these medications may impact your future ability to have a child. Certain targeted therapies like thalidomide and lenalidomide can cause serious birth defects and have special programs in place to educate patients and encourage safe distribution to patients of childbearing age.

Other side effects that patients on targeted therapies will be monitored for include problems with wound healing, blood clotting, high blood pressure, and gastrointestinal (GI) perforation.

It is possible that over time, you may build up a resistance to the targeted medication you are receiving. This may happen more frequently when targeted therapy is the only therapy being received.

### How will I know if targeted therapy is working for me?

Your healthcare team will continue to monitor your disease closely throughout your treatment. You will have regular blood and imaging (CT scan, PET scan) tests that will tell how your body is responding to treatment.

### Resources for More Information

- American Cancer Society: Targeted Therapy
- National Cancer Institute: Targeted Therapy Fact Sheet
- American Society of Clinical Oncology (ASCO): Understanding Targeted Therapy
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