Targeted Treatments [1]

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Watch theCancer.Net Video: What is Targeted Therapy? with Nicholas Vogelzang, MD[3] , adapted from this content.

Key Messages:

- Targeted therapy is a type of treatment that targets a cancer?s specific genes, proteins, or the tissue environment that contributes to cancer growth and survival.
- Not all tumors have the same targets, so doctors may run tests to match a cancer with the most effective treatment.
- A number of targeted therapies are being used to treat cancer, and many more are being tested in clinical trials.
- Although targeted therapies are a promising way to personalize cancer treatment, resistance to treatment often develops and side effects can be an issue.

Targeted therapy includes drugs that are aimed at specific genes or proteins that are only found in cancer cells or the tissue environment that contributes to cancer growth and survival. It is often used along with chemotherapy and other cancer treatments to block the growth and spread of cancer cells. Currently there are a number of targeted therapies approved by the U.S. Food and Drug Administration (FDA) to treat many types of cancer. In addition, clinical trials [4] are continuing to look for additional drugs aimed at new targets that have recently been discovered.

The ?targets? of targeted therapy

To understand targeted therapy, it helps to understand how cancer cells develop. Cells are the building blocks of every tissue in the body. There are many different types of cells, such as blood cells, brain cells, and skin cells, which each have specific functions. Cancer begins when specific genes in healthy cells mutate (change). Genes tell cells how to produce proteins, many of which help a cell function normally. If the genes are mutated, the proteins will be changed as well, resulting in abnormal cell division or delayed cell death. This causes the cells to grow uncontrollably, forming a mass called a tumor. Learn more about the genetics of cancer [5].

By studying cancer cells and how they react to their environment, researchers are finding that

specific gene mutations contribute to the development of specific cancers. With this knowledge, they are developing drugs that:

- Block or turn off signals that tell cancer cells to grow and divide
- Turn on or promote processes that result in natural cell death
- Deliver toxic substances specifically to cancer cells to destroy them

Types of targeted therapy

There are two main types of targeted therapy:

Monoclonal antibodies. These substances, which are made in the laboratory, block a specific target on the outside of cancer cells or in the tissue surrounding the cancer. Think of this as placing a protective plastic plug into an electrical socket to prevent electricity from flowing. Monoclonal antibodies can also deliver toxic substances, such as chemotherapy and radioactive substances, directly to cancer cells. These drugs are usually given intravenously (IV) because they are large compounds that are not absorbed well by the body.

Oral small drugs. These drugs are usually given in the form of a pill that a patient takes by mouth. Because they contain smaller chemical components than monoclonal antibodies, the body absorbs them better. These drugs usually block processes inside cancer cells that stimulate them to multiply and spread.

There is also a class of targeted therapy drugs called angiogenesis inhibitors [6] that target the tissue that surrounds a tumor. These drugs focus on stopping angiogenesis, which is the process of making new blood vessels. Because a tumor needs the nutrients delivered by blood vessels to grow and spread, the goal of anti-angiogenesis therapies is to essentially ?starve? the tumor by blocking the development of these new blood vessels.

Matching a patient to treatment

Recent studies show that not all tumors have the same targets, which explains why a targeted treatment does not work for every person. One example is a gene called *KRAS* (pronounced kay-rass), which controls tumor growth and spread. This gene is mutated in about 40% of colorectal cancers. When this happens, the targeted therapies cetuximab (Erbitux) and panitumumab (Vectibix) do not work. The American Society of Clinical Oncology (ASCO) recommends that patients with metastatic colorectal cancer have their tumors tested for *KRAS* mutations so doctors can provide the most effective treatment and not expose patients to unnecessary side effects and costs with drugs that are not likely to be helpful.

To find the most effective treatment, your doctor may order tests to identify the genes, proteins, and other factors unique to your tumor. Because many of these treatments have some degree of side effects and the treatments can be expensive, doctors are making efforts to match each patient?s tumor to the most effective treatment whenever possible. Learn more about the importance of molecular testing [7].

Examples of targeted therapies

There are a number of targeted therapies that have been approved to treat different types of cancer. Below are just a few examples. Remember, a targeted treatment will not work if the tumor does not contain the target; however, the presence of the target also does not guarantee that the treatment will work. Talk with your doctor or another member of your health care team for more information about your treatment options.

Breast cancer. Researchers have learned that about 20% to 25% of all breast cancers have too much of a protein called human epidermal growth factor receptor 2 (HER2), which fuels tumor cell growth. ASCO and the College of American Pathologists recommend that all people with invasive breast cancer have their tumors tested for HER2 [8]. If the results show the cancer is HER2 positive, there are several FDA-approved drugs that may be recommended as treatment options.

Colorectal cancer. Researchers have found that drugs that block the epidermal growth factor receptor (EGFR), which is often overproduced in this type of cancer, may be effective for stopping or slowing the growth of colorectal cancer if the cancer does not have a mutation in the *KRAS* gene. In addition, targeted therapy may also be directed at vascular endothelial growth factor (VEGF), a protein that helps new blood vessels to form.

Lung cancer. Researchers have found that drugs that block EGFR may be effective for stopping or slowing the growth of lung cancer, particularly if the *EGFR* gene contains certain mutations. Targeted therapy is also available to treat lung cancer that is driven by a mutated *ALK* gene. Angiogenesis inhibitors are also approved for treatment of specific types of lung cancer.

Melanoma. Approximately 50% of melanomas have a mutated or activated *BRAF* gene. Research has shown that specific *BRAF* mutations make good drug targets, and the FDA has approved several *BRAF* inhibitors. However, these drugs should not be used by patients whose tumors do not have these mutations as it can actually be harmful.

Currently there are a number of clinical trials underway in many different types of cancer to investigate new targets and drugs aimed at them. This is not an exhaustive list. More information about specific drugs and the use of targeted therapy in other types of cancer not listed in this article are available in the Treatment Options or Latest Research sections of the individual cancer type guides [9].

Challenges of targeted therapies

Although the idea of targeting a drug to a tumor seems straightforward, this approach is complicated and not always effective. For example, the target in the cancer cell may turn out not to be as important as first thought, and the drug will not provide much benefit to patients. Or, the cancer may become resistant to the treatment, meaning it no longer works, even if it did at first. Finally, these drugs may cause serious side effects, although the side effects are usually different than those seen with traditional chemotherapy. For example, patients receiving a targeted therapy often develop skin, hair, nail, and/or eye problems [10].

Although the development of targeted treatments is a breakthrough in cancer treatment, only a few cancers can be eliminated with these drugs alone. With a few exceptions, patients with cancer usually receive a combination of targeted therapy and surgery, chemotherapy, radiation

therapy, and/or hormonal therapy. As doctors gain more knowledge about specific changes in cancer cells, more targeted treatments will be developed. Find more information about the latest research on targeted therapies presented at the ASCO Annual Meeting [11].

More Information

Facts About Personalized Cancer Medicine [12]

Understanding Pharmacogenomics [13]

Explaining Cancer Genome Research [14]

Understanding Immunotherapy [15]

Additional Resources

National Cancer Institute: Targeted Cancer Therapies [16]

My Cancer Genome: Overview of Targeted Therapies for Cancer [17]

Links:
[1] http://www.cancer.net/navigating-cancer-care/how-cancer-treated/personalized-and-targeted-therapies/targeted-treatments
[2] http://www.cancer.net/about-us
[3] http://www.cancer.net/node/27356
[4] http://www.cancer.net/node/24876
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