
CANCER FACTS

National Cancer Institute • National Institutes of Health
Department of Health and Human Services

Targeted Cancer Therapies: Questions and Answers

Key Points

- Targeted cancer therapies use drugs that block the growth and spread of cancer by interfering with specific molecules involved in carcinogenesis (the process by which normal cells become cancer cells) and tumor growth (see Questions 1, 2, and 3).
- Because scientists call these molecules “molecular targets,” therapies that interfere with them are sometimes called “molecular-targeted drugs,” “molecularly targeted therapies,” or other similar names (see Question 1).
- The National Cancer Institute’s Molecular Targets Development Program is working to identify and evaluate molecular targets (see Question 6).

1. What are targeted cancer therapies?

Targeted cancer therapies use drugs that block the growth and spread of cancer. They interfere with specific molecules involved in carcinogenesis (the process by which normal cells become cancer cells) and tumor growth. Because scientists call these molecules “molecular targets,” these therapies are sometimes called “molecular-targeted drugs,” “molecularly targeted therapies,” or other similar names. By focusing on molecular and cellular changes that are specific to cancer, targeted cancer therapies may be more effective than current treatments and less harmful to normal cells.

Most targeted cancer therapies are in preclinical testing (research with animals), but some are in clinical trials (research studies with people), or have been approved by the U.S. Food and Drug Administration (FDA). Targeted cancer therapies are being studied for use alone, in combination with each other, and in combination with other cancer treatments, such as chemotherapy.



2. What are some of the cellular changes that lead to cancer?

Normally, cells grow and divide to form new cells as the body needs them. When cells grow old, they die, and new cells take their place. Sometimes this orderly process goes wrong. New cells form when the body does not need them, and old cells do not die when they should. These extra cells can form a mass of tissue called a growth or tumor. The cells in malignant (cancerous) tumors are abnormal and divide without control or order. They can invade and damage nearby tissues and organs. Also, cancer cells can break away from a malignant tumor and spread to other parts of the body.

Normal cell growth and division are largely under the control of a network of chemical and molecular signals that give instructions to cells. Genetic alterations (changes) can disrupt the signaling process so that cells no longer grow and divide normally, or no longer die when they should. Alterations in two types of genes can contribute to the cancer process. Proto-oncogenes are normal genes that are involved in cell growth and division. Changes in these genes lead to the development of *oncogenes*, which can promote or allow excessive and continuous cell growth and division. *Tumor suppressor genes* are normal genes that slow down cell growth and division. When a tumor suppressor gene does not work properly, cells may be unable to stop growing and dividing, which leads to tumor growth.

To use the metaphor of a car, the presence of an oncogene is like having a gas pedal that is stuck to the floorboard, causing cells to continually grow and divide. Tumor suppressor genes act like a brake pedal. The loss of a functioning tumor suppressor gene is like having a brake pedal that does not work properly, allowing cells to continually grow and divide.

Genetic changes that are not corrected by the cell can lead to the production of abnormal proteins. Normally, proteins interact with each other as a kind of relay team to carry out the work of the cell. For example, when molecules called growth factors (GFs) attach to their corresponding growth factor receptors (GFRs) on the surface of the cell, a process carried out by proteins signals the cell to divide. Damaged proteins may not respond to normal signals, may over-respond to normal signals, or otherwise fail to carry out their normal functions. Cancer develops when abnormal proteins inside a cell cause it to reproduce excessively and allow that cell to live longer than normal cells.

3. How do targeted cancer therapies work?

Targeted cancer therapies interfere with cancer cell growth and division in different ways and at various points during the development, growth, and spread of cancer. Many of these therapies focus on proteins that are involved in the signaling process. By blocking the signals that tell cancer cells to grow and divide uncontrollably, targeted cancer therapies can help to stop the growth and division of cancer cells.

4. What are some types of targeted cancer therapies?

Targeted cancer therapies include several types of drugs. Some examples are listed below:

- “Small-molecule” drugs block specific enzymes and GFRs involved in cancer cell growth. These drugs are also called signal-transduction inhibitors. Gleevec® (STI-571 or imatinab mesylate) is a small-molecule drug approved by the FDA to treat gastrointestinal stromal tumor (a rare cancer of the gastrointestinal tract) and certain kinds of chronic myeloid leukemia (1, 2). Gleevec targets abnormal proteins, or enzymes, that form inside cancer cells and stimulate uncontrolled growth. Iressa® (ZD1839 or gefitinib) is approved by the FDA to treat advanced non-small cell lung cancer. This drug targets the epidermal growth factor receptor (EGFR), which is overproduced by many types of cancer cells. Other small-molecule drugs are being studied in clinical trials in the United States.
- “Apoptosis-inducing” drugs cause cancer cells to undergo apoptosis (cell death) by interfering with proteins involved in the process. Velcade® (bortezomib) is approved by the FDA to treat multiple myeloma that has not responded to other treatments (3). Velcade causes cancer cells to die by blocking enzymes called proteasomes, which help to regulate cell function and growth. Another apoptosis-inducing drug called Genasense™ (oblimersen), which is only available in clinical trials, is being studied to treat leukemia, non-Hodgkin’s lymphoma, and solid tumors. Genasense blocks the production of a protein known as BCL-2, which promotes the survival of tumor cells. By blocking BCL-2, Genasense leaves the cancer cells more vulnerable to anticancer drugs.
- Monoclonal antibodies, cancer vaccines, angiogenesis inhibitors, and gene therapy are considered by some to be targeted therapies because they interfere with the growth of cancer cells. Information about these treatments can be found in the following NCI fact sheets, which are available on the Internet or by calling the Cancer Information Service (CIS) (see below):

—*Biological Therapies: Using the Immune System To Treat Cancer* includes information about monoclonal antibodies and cancer vaccines. This fact sheet is available at http://cis.nci.nih.gov/fact/7_2.htm on the Internet.

—*Herceptin® (Trastuzumab): Questions and Answers* contains information about Herceptin, which is a monoclonal antibody. This fact sheet can be found at http://cis.nci.nih.gov/fact/7_45.htm on the Internet.

—*Angiogenesis Inhibitors in the Treatment of Cancer* is available at http://cis.nci.nih.gov/fact/7_42.htm on the Internet.

—*Gene Therapy for Cancer: Questions and Answers* can be found at http://cis.nci.nih.gov/fact/7_18.htm on the Internet.

5. What impact will targeted therapies have on cancer treatment?

Targeted cancer therapies will give doctors a better way to tailor cancer treatment. Eventually, treatments may be individualized based on the unique set of molecular targets produced by the patient's tumor. Targeted cancer therapies also hold the promise of being more selective, thus harming fewer normal cells, reducing side effects, and improving the quality of life.

6. What are some resources for more information?

The NCI's Molecular Targets Development Program (MTDP) is working to identify and evaluate molecular targets that may be candidates for drug development. As part of the NCI's Center for Cancer Research, the MTDP provides research support for NCI-designated, high-priority drug discovery, development, and research focused on specific molecular targets, pathways, or processes. The MTDP's Web site is <http://home.ncifcrf.gov/mtdp/> on the Internet.

Information about clinical trials is available from the CIS (see below). Information specialists at the CIS use PDQ®, the NCI's cancer information database, to identify and provide detailed information about specific ongoing clinical trials. PDQ includes all NCI-funded clinical trials and some studies conducted by independent investigators at hospitals and medical centers in the United States and other countries around the world.

People also have the option of searching for clinical trials on their own. The clinical trials page of the NCI's Web site, located at <http://cancer.gov/clinicaltrials/> on the Internet, provides information about clinical trials and links to PDQ.

Selected References

1. Demetri GD, von Mehren M, Blanke CD, et al. Efficacy and safety of imatinib mesylate in advanced gastrointestinal stromal tumors. *New England Journal of Medicine* 2002; 347(7):472–480.
2. Kantarjian H, Sawyers C, Hochhaus A, et al. Hematologic and cytogenetic responses to imatinib mesylate in chronic myelogenous leukemia. *New England Journal of Medicine* 2002; 346(9):645–652.
3. Richardson PG, Barlogie B, Berenson J, et al. A phase 2 study of bortezomib in relapsed, refractory myeloma. *New England Journal of Medicine* 2003; 348(26):2609–2617.

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Related Resources

Publications (available at <http://cancer.gov/publications>)

- Cancer Facts 2.11, *Clinical Trials: Questions and Answers*
- Cancer Facts 7.2, *Biological Therapies: Using the Immune System To Treat Cancer*
- Cancer Facts 7.18, *Gene Therapy for Cancer: Questions and Answers*
- Cancer Facts 7.42, *Angiogenesis Inhibitors in the Treatment of Cancer*
- Cancer Facts 7.45, *Herceptin® (Trastuzumab): Questions and Answers*
- *What You Need To Know About™ Cancer*

National Cancer Institute (NCI) Resources

Cancer Information Service (toll-free)

Telephone: 1-800-4-CANCER (1-800-422-6237)

TTY: 1-800-332-8615

Online

NCI's Web site: <http://cancer.gov>

LiveHelp, NCI's live online assistance:

<https://cissecure.nci.nih.gov/livehelp/welcome.asp>

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