Biological Therapies for Cancer: Questions and Answers

Key Points

- Biological therapies use the body's immune system to fight cancer or to lessen the side effects that may be caused by some cancer treatments (see Question 1).
- Biological response modifiers (BRMs) occur naturally in the body and can be produced in the laboratory. BRMs alter the interaction between the body's immune defenses and cancer cells to boost, direct, or restore the body's ability to fight the disease (see Question 3).
- Biological therapies include interferons, interleukins, colony-stimulating factors, monoclonal antibodies, vaccines, gene therapy, and nonspecific immunomodulating agents (see Questions 4 to 10).
- Biological therapies can cause a number of side effects, which can vary widely from agent to agent and patient to patient (see Question 11).

1. What is biological therapy?

Biological therapy (sometimes called immunotherapy, biotherapy, or biological response modifier therapy) is a relatively new addition to the family of cancer treatments that also includes surgery, chemotherapy, and radiation therapy. Biological therapies use the body's immune system, either directly or indirectly, to fight cancer or to lessen the side effects that may be caused by some cancer treatments.

2. What is the immune system and what are its components?

The immune system is a complex network of cells and organs that work together to defend the body against attacks by "foreign" or "non-self" invaders. This network is one of the body's main defenses against infection and disease. The immune system works against diseases, including cancer, in a variety of ways. For example, the immune system may recognize the difference between healthy cells and cancer cells in the body and works to eliminate cancerous cells. However, the immune system does not always recognize cancer cells as "foreign." Also, cancer may develop when the immune system

breaks down or does not function adequately. Biological therapies are designed to repair, stimulate, or enhance the immune system's responses.

Immune system cells include the following:

- **Lymphocytes** are a type of white blood cell found in the blood and many other parts of the body. Types of lymphocytes include B cells, T cells, and Natural Killer cells.

  B cells (B lymphocytes) mature into plasma cells that secrete proteins called antibodies (immunoglobulins). Antibodies recognize and attach to foreign substances known as antigens, fitting together much the way a key fits a lock. Each type of B cell makes one specific antibody, which recognizes one specific antigen.

  T cells (T lymphocytes) work primarily by producing proteins called cytokines. Cytokines allow immune system cells to communicate with each other and include lymphokines, interferons, interleukins, and colony-stimulating factors. Some T cells, called cytotoxic T cells, release pore-forming proteins that directly attack infected, foreign, or cancerous cells. Other T cells, called helper T cells, regulate the immune response by releasing cytokines to signal other immune system defenders.

  Natural Killer cells (NK cells) produce powerful cytokines and pore-forming proteins that bind to and kill many foreign invaders, infected cells, and tumor cells. Unlike cytotoxic T cells, they are poised to attack quickly, upon their first encounter with their targets.

- **Phagocytes** are white blood cells that can swallow and digest microscopic organisms and particles in a process known as phagocytosis. There are several types of phagocytes, including **monocytes**, which circulate in the blood, and **macrophages**, which are located in tissues throughout the body.

3. What are biological response modifiers, and how can they be used to treat cancer?

Some antibodies, cytokines, and other immune system substances can be produced in the laboratory for use in cancer treatment. These substances are often called biological response modifiers (BRMs). They alter the interaction between the body's immune defenses and cancer cells to boost, direct, or restore the body's ability to fight the disease. BRMs include interferons, interleukins, colony-stimulating factors, monoclonal antibodies, vaccines, gene therapy, and nonspecific immunomodulating agents. Each of these BRMs is described in Questions 4 to 10.

Researchers continue to discover new BRMs, to learn more about how they function, and to develop ways to use them in cancer therapy. Biological therapies may be used to:

- Stop, control, or suppress processes that permit cancer growth.
- Make cancer cells more recognizable and, therefore, more susceptible to destruction by the immune system.
- Boost the killing power of immune system cells, such as T cells, NK cells, and macrophages.
- Alter the growth patterns of cancer cells to promote behavior like that of healthy cells.
- Block or reverse the process that changes a normal cell or a precancerous cell into a cancerous cell.
- Enhance the body's ability to repair or replace normal cells damaged or destroyed by other forms of cancer treatment, such as chemotherapy or radiation.
- Prevent cancer cells from spreading to other parts of the body.

Some BRMs are a standard part of treatment for certain types of cancer, while others are being studied in clinical trials (research studies). BRMs are being used alone or in combination with each other. They are also being used with other treatments, such as radiation therapy and chemotherapy.

4. What are interferons?

Interferons (IFNs) are types of cytokines that occur naturally in the body. They were the first cytokines produced in the laboratory for use as BRMs. There are three major types of interferons—interferon alpha, interferon beta, and interferon gamma; interferon alpha is the type most widely used in cancer treatment.

Researchers have found that interferons can improve the way a cancer patient's immune system acts against cancer cells. In addition, interferons may act directly on cancer cells by slowing their growth or promoting their development into cells with more normal behavior. Researchers believe that some interferons may also stimulate NK cells, T cells, and macrophages, boosting the immune system's anticancer function.

The U.S. Food and Drug Administration (FDA) has approved the use of interferon alpha for the treatment of certain types of cancer, including hairy cell leukemia, melanoma, chronic myeloid leukemia, and AIDS-related Kaposi's sarcoma. Studies have shown that interferon alpha may also be effective in treating other cancers such as kidney cancer and non-Hodgkin lymphoma. Researchers are exploring combinations of interferon alpha and other BRMs or chemotherapy in clinical trials to treat a number of cancers.

5. What are interleukins?

Like interferons, interleukins (ILs) are cytokines that occur naturally in the body and can be made in the laboratory. Many interleukins have been identified; **interleukin-2** (**IL–2** or **aldesleukin**) has been the most widely studied in cancer treatment. IL–2 stimulates the growth and activity of many immune cells, such as lymphocytes, that can destroy

cancer cells. The FDA has approved IL–2 for the treatment of metastatic kidney cancer and metastatic melanoma.

Researchers continue to study the benefits of interleukins to treat a number of other cancers, including leukemia, lymphoma, and brain, colorectal, ovarian, breast, and prostate cancers.

6. What are colony-stimulating factors?

Colony-stimulating factors (CSFs) (sometimes called hematopoietic growth factors) usually do not directly affect tumor cells; rather, they encourage bone marrow stem cells to divide and develop into white blood cells, platelets, and red blood cells. Bone marrow is critical to the body's immune system because it is the source of all blood cells.

Stimulation of the immune system by CSFs may benefit patients undergoing cancer treatment. Because anticancer drugs can damage the body's ability to make white blood cells, red blood cells, and platelets, patients receiving anticancer drugs have an increased risk of developing infections, becoming anemic, and bleeding more easily. By using CSFs to stimulate blood cell production, doctors can increase the doses of anticancer drugs without increasing the risk of infection or the need for transfusion with blood products. As a result, researchers have found CSFs particularly useful when combined with high-dose chemotherapy.

Some examples of CSFs and their use in cancer therapy are as follows:

- **G–CSF (filgrastim)** and **GM–CSF (sargramostim)** can increase the number of white blood cells, thereby reducing the risk of infection in patients receiving chemotherapy. G–CSF and GM–CSF can also stimulate the production of stem cells in preparation for stem cell or bone marrow transplants.

- **Erythropoietin (epoetin)** can increase the number of red blood cells and reduce the need for red blood cell transfusions in patients receiving chemotherapy.

- **Interleukin-11 (oprelvekin)** helps the body make platelets and can reduce the need for platelet transfusions in patients receiving chemotherapy.

Researchers are studying CSFs in clinical trials to treat a large variety of cancers, including lymphoma, leukemia, multiple myeloma, melanoma, and cancers of the brain, lung, esophagus, breast, uterus, ovary, prostate, kidney, colon, and rectum.

7. What are monoclonal antibodies?

Researchers are evaluating the effectiveness of certain antibodies made in the laboratory called monoclonal antibodies (MOABs or MoABs). These antibodies are produced by a single type of cell and are specific for a particular antigen. Researchers are examining

ways to create MOABs specific to the antigens found on the surface of various cancer cells.

To create MOABs, scientists first inject human cancer cells into mice. In response, the mouse immune system makes antibodies against these cancer cells. The scientists then remove the mouse plasma cells that produce antibodies, and fuse them with laboratory-grown cells to create "hybrid" cells called hybridomas. Hybridomas can indefinitely produce large quantities of these pure antibodies, or MOABs.

MOABs may be used in cancer treatment in a number of ways:

- MOABs that react with specific types of cancer may enhance a patient's immune response to the cancer.

- MOABs can be programmed to act against cell growth factors, thus interfering with the growth of cancer cells.

- MOABs may be linked to anticancer drugs, radioisotopes (radioactive substances), other BRMs, or other toxins. When the antibodies latch onto cancer cells, they deliver these poisons directly to the tumor, helping to destroy it.

MOABs carrying radioisotopes may also prove useful in diagnosing certain cancers, such as colorectal, ovarian, and prostate.

Rituxan® (rituximab) and **Herceptin® (trastuzumab)** are examples of MOABs that have been approved by the FDA. Rituxan is used for the treatment of non-Hodgkin lymphoma. Herceptin is used to treat metastatic breast cancer in patients with tumors that produce excess amounts of a protein called HER–2. (More information about Herceptin is available in the National Cancer Institute (NCI) fact sheet *Herceptin® (Trastuzumab): Questions and Answers*, which can be found at http://www.cancer.gov/cancertopics/factsheet/Therapy/herceptin on the Internet.) In clinical trials, researchers are testing MOABs to treat lymphoma, leukemia, melanoma, and cancers of the brain, breast, lung, kidney, colon, rectum, ovary, prostate, and other areas.

8. What are cancer vaccines?

Cancer vaccines are another form of biological therapy currently under study. Vaccines for infectious diseases, such as measles, mumps, and tetanus, are injected into a person before the disease develops. These vaccines are effective because they expose the body's immune cells to weakened forms of antigens that are present on the surface of the infectious agent. This exposure causes the immune system to increase production of plasma cells that make antibodies specific to the infectious agent. The immune system also increases production of T cells that recognize the infectious agent. These activated

immune cells remember the exposure, so that the next time the agent enters the body, the immune system is already prepared to respond and stop the infection.

Researchers are developing vaccines that may encourage the patient's immune system to recognize cancer cells. Cancer vaccines are designed to treat existing cancers (therapeutic vaccines) or to prevent the development of cancer (prophylactic vaccines). Therapeutic vaccines are injected in a person after cancer is diagnosed. These vaccines may stop the growth of existing tumors, prevent cancer from recurring, or eliminate cancer cells not killed by prior treatments. Cancer vaccines given when the tumor is small may be able to eradicate the cancer. On the other hand, prophylactic vaccines are given to healthy individuals before cancer develops. These vaccines are designed to stimulate the immune system to attack viruses that can cause cancer. By targeting these cancer-causing viruses, doctors hope to prevent the development of certain cancers.

Early cancer vaccine clinical trials involved mainly patients with melanoma. Therapeutic vaccines are also being studied in the treatment of many other types of cancer, including lymphoma, leukemia, and cancers of the brain, breast, lung, kidney, ovary, prostate, pancreas, colon, and rectum. Researchers are also studying prophylactic vaccines to prevent cancers of the cervix and liver. Moreover, scientists are investigating ways that cancer vaccines can be used in combination with other BRMs.

9. What is gene therapy?

Gene therapy is an experimental treatment that involves introducing genetic material into a person's cells to fight disease. Researchers are studying gene therapy methods that can improve a patient's immune response to cancer. For example, a gene may be inserted into an immune cell to enhance its ability to recognize and attack cancer cells. In another approach, scientists inject cancer cells with genes that cause the cancer cells to produce cytokines and stimulate the immune system. A number of clinical trials are currently studying gene therapy and its potential application to the biological treatment of cancer. (More information about gene therapy is available in the NCI fact sheet *Gene Therapy for Cancer: Questions and Answers*, which can be found at http://www.cancer.gov/cancertopics/factsheet/Therapy/gene on the Internet.)

10. What are nonspecific immunomodulating agents?

Nonspecific immunomodulating agents are substances that stimulate or indirectly augment the immune system. Often, these agents target key immune system cells and cause secondary responses such as increased production of cytokines and immunoglobulins. Two nonspecific immunomodulating agents used in cancer treatment are **bacillus Calmette-Guerin (BCG)** and **levamisole**.

BCG, which has been widely used as a tuberculosis vaccine, is used in the treatment of superficial bladder cancer following surgery. BCG may work by stimulating an inflammatory, and possibly an immune, response. A solution of BCG is instilled in the

bladder and stays there for about 2 hours before the patient is allowed to empty the bladder by urinating. This treatment is usually performed once a week for 6 weeks.

Levamisole is sometimes used along with fluorouracil (5–FU) chemotherapy in the treatment of stage III (Dukes' C) colon cancer following surgery. Levamisole may act to restore depressed immune function.

11. Do biological therapies have any side effects?

Like other forms of cancer treatment, biological therapies can cause a number of side effects, which can vary widely from agent to agent and patient to patient. Rashes or swelling may develop at the site where the BRMs are injected. Several BRMs, including interferons and interleukins, may cause flu-like symptoms including fever, chills, nausea, vomiting, and appetite loss. Fatigue is another common side effect of some BRMs. Blood pressure may also be affected. The side effects of IL–2 can often be severe, depending on the dosage given. Patients need to be closely monitored during treatment with high doses of IL–2. Side effects of CSFs may include bone pain, fatigue, fever, and appetite loss. The side effects of MOABs vary, and serious allergic reactions may occur. Cancer vaccines can cause muscle aches and fever.

12. Where can a person get more information about clinical trials?

Information about ongoing clinical trials involving these and other biological therapies is available from the Cancer Information Service (see below) or the clinical trials page of the NCI's Web site at http://www.cancer.gov/clinicaltrials/ on the Internet.

# # #

Related NCI materials and Web pages:

- National Cancer Institute Fact Sheet 7.18, *Gene Therapy for Cancer: Questions and Answers* (http://www.cancer.gov/cancertopics/factsheet/Therapy/gene)
- National Cancer Institute Fact Sheet 7.45, *Herceptin® (Trastuzumab): Questions and Answers* (http://www.cancer.gov/cancertopics/factsheet/therapy/herceptin)
- National Cancer Institute Fact Sheet 7.46, *Access to Investigational Drugs: Questions and Answers* (http://www.cancer.gov/cancertopics/factsheet/Therapy/investigational-drug-access)
- *Biological Therapy* (http://www.cancer.gov/cancertopics/biologicaltherapy)
- *Taking Part in Cancer Treatment Research Studies* (http://www.cancer.gov/clinicaltrials/Taking-Part-in-Cancer-Treatment-Research-Studies)
- *What You Need To Know About™ Cancer* (http://www.cancer.gov/cancertopics/wyntk/overview)

For more help, contact:

NCI's Cancer Information Service
Telephone (toll-free): 1–800–4–CANCER (1–800–422–6237)
TTY (toll-free): 1–800–332–8615
LiveHelp® online chat: https://cissecure.nci.nih.gov/livehelp/welcome.asp

This fact sheet was reviewed on 6/13/06