All About Immunotherapy

What is immunotherapy?

All individuals have an immune system. This system helps protect us from infections and other threats to the health of the body. These threats include viruses, toxins, allergens and bacteria. In most cases, the immune system is not able to identify cancer as a threat to the body. Cancer arises from cells within the body, whereas viruses, bacteria, allergens and toxins come from outside the body. Cancer cells are mutated versions of normal cells. Thus, the immune system doesn’t recognize them as threats and a response is not activated. In addition, some types of cancer can interfere with the immune system’s ability to function correctly. Only recently did scientists start to realize the potential of the immune system to fight certain diseases, including some cancers.

Immunotherapy is a method of treating cancer that uses the body’s own capabilities to identify and kill cancer cells. Immunotherapy may also be called biologic therapy. Immunotherapy treatments may be used to attack cancer cells directly, to stimulate the immune system to respond to the disease, or to prevent a cancer from returning after treatment. Immunotherapy can also work to strengthen or restore the body’s natural immune function to make it easier for the immune system to destroy cancer cells and to prevent cancer from spreading to other parts of the body.

Use of immunotherapy can actually be traced back to the 1890’s, when bacteria was injected into a tumor in an attempt to encourage a response by the immune system against the cancer. However, immunotherapy research and available treatment methods have grown greatly in the past 20 years.

Types of immunotherapy are currently approved to treat several different types of cancer, including leukemia, lymphoma, breast cancer, prostate cancer, lung cancer, bladder cancer, and melanoma. Immunotherapy is being studied in clinical trials for almost all other types of cancer.

What are the different types of immunotherapy?

Just as there are many different types of other chemotherapies, there are many different kinds of immunotherapy that act in different ways to kick the immune system into action against cancer.

Types of immunotherapy include:

- **Monoclonal antibodies (mABs):** Laboratory-created antibodies that target a specific antigen (protein). These medications work by targeting something found on the surface of the cancer cell, “marking” that cell to be destroyed by the immune system. These medications may also work by blocking a “receptor” found on cells that is important to growth. Examples of monoclonal antibodies are: rituximab (Rituxan®), bevacizumab (Avastin®), trastuzumab (Herceptin®), and denosumab (Xgeva®, Prolia®).

- **Cancer vaccines:** Like other vaccines we receive, cancer vaccines are comprised of cells that have been modified in the lab to direct an immune response. There are a few different types of cancer vaccines, but primarily they function either to prevent disease (example: the HPV vaccine) or to treat the cancer directly (tumor cell vaccines, antigen vaccines, dendritic cell vaccines or vector-based vaccines).

- **Cytokine therapies:** Cytokines play a very specific role in the immune system. They facilitate communication among different immune cells, while also assisting in the launch of an immune response. When cytokine therapy is used to fight cancer, it is focused on using the substances to promote immune system response. Examples of cytokines include interferon, interleukin, and colony stimulating factors such as sargramostim (Leukine®, GM-CSF).

- **Adoptive T-cell transfer:** This therapy encourages the bodies T-cells to fight cancer. There are two types of this...
treatment. The first removes T-cells directly from a patient's tumor, produces large quantities of these cells outside the body and then re-infuses them back to the patient. The second method also removes T-cells from the patient, but the cells are then enhanced in the lab with new receptors, called chimeric antigen receptors (CAR-T). These receptors target specific antigens in the patient’s cancer cells, stimulating the immune response against the cancer. Examples of CAR-T treatments include tisagenlecleucel and axicabtagene ciloleucel.

- **Donor lymphocyte therapy (DLI):** DLI involves the infusion of lymphocytes (type of white blood cell) from a donor to a patient who has already had an allogenic bone marrow transplant from the same donor. The donor lymphocytes may assist in identifying targets for immune system attack. This can induce remission or potentially prevent relapse in patients who are at high risk for relapse after bone marrow transplant. DLI can also cause graft versus host disease (GVHD), a potentially serious side effect in which the recipient's cells/tissues are attacked by the donor immune cells.

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

- **Virus Immunotherapy:** This type of therapy uses viruses to deliberately infect the cancer cells, which then triggers an immune system response against the virus (and the virus infected cancer cells). Examples of viruses being used to study this therapy include the polio virus and the herpes simplex virus. These methods are still being studied in clinical trials.

- **Immune Checkpoint Inhibitors:** These medications block tumor cells from inactivating T cells. This allows the T cell (and the immune system) to remain active in fighting the tumor. Examples of immune checkpoint inhibitors include: ipilimumab (Yervoy®), nivolumab (Opdivo®) and pembrolizumab (Keytruda®).

### How is immunotherapy given?

Immunotherapies may be given into a vein (intravenously), or by injection, either under the skin (subcutaneous) or into a muscle (intramuscular). Therapies may also be given directly into a body cavity to treat a specific site. For example, bladder cancer can be treated with a Bacillus Calmette-Guerin (BCG, TICE®, TheraCys®) administered into the bladder. Many immunotherapies are approved by the U.S. Food and Drug Administration, but many more are still being tested in clinical trials. Depending on the type and stage of cancer, some patients may be treated with immunotherapy alone, while others may receive this in conjunction with other therapies (i.e. chemotherapy, surgery, or radiation therapy).

### What are the side effects of immunotherapy?

Although many immunotherapies use substances that occur naturally in the body, side effects can occur as a result of the increased production or the higher-than-normal levels of these substances. The most common side effects are the result of the “revving up” and stimulation of the immune system. They include fever, chills, body aches (flu-like symptoms), nausea/vomiting, loss of appetite, and fatigue. Depending on the doses and how the therapy is administered, patients may experience an allergic type reaction that may cause a decrease in blood pressure, difficulty breathing, rash or swelling at the injection site. Each therapy may have side effects specific to the cells that are being affected by the therapy. Your healthcare team will review potential side effects of the therapy you are receiving. Immunotherapy is relatively new, and we are still learning what long-term side effects they may lead to years later.

### How will I know if immunotherapy is working for me?

Chemotherapy and radiation often cause a rapid change in the size of tumors, which is measurable and can be seen on CT/MRI/Pet Scan and through changes in tumor marker levels in the blood. Immunotherapy responses are not measured in the same way. First, immunotherapy methods can take much more time to work as they encourage the immune system to mount its attack on the tumor. Thus, the tumor may continue to grow, despite the fact that therapy is being delivered. In addition, the speed of response may be influenced by the type of immunotherapy received. Your healthcare team will monitor your disease status and side effects throughout the course of treatment, though it may take weeks or even months for a measurable response from your immune system.

### Resources for More Information

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Cancer Immunotherapy, American Cancer Society
http://www.cancer.org/treatment/treatmentsandsideeffects/treatmenttypes/immunotherapy/immunotherapy-toc

Immunotherapy, Leukemia and Lymphoma Society
https://www.lls.org/treatment/types-of-treatment/immunotherapy

Understanding Cancer Immunotherapy, Society for Immunotherapy of Cancer (SITC)
http://www.sitcancer.org/resources/patient-information

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