Understanding the Role of Immuno-Oncology in Treating Cancer

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Immuno-oncology is the study and development of treatments that take advantage of the body's immune system to fight cancer.

Our immune system is a complex network of organs, cells and molecules that protects us from foreign substances that can cause infection, such as bacteria, fungi and viruses. In addition to finding and destroying foreign substances, the immune system can also locate and attack abnormal cells.

There are two main parts of the immune system:

- **Innate immunity,** a defense system we are born with, is the ability of the body to immediately protect itself against cancer, foreign organisms and toxins.
- **Adaptive immunity** is a learned defense system that develops in response to exposure to a specific foreign substance. The adaptive immune system works in one of two ways:
  - **Humoral,** also called antibody-mediated, in which B-cells (a type of white blood cell called a lymphocyte) make antibodies (specific blood proteins) that identify and destroy foreign substances.
  - **Cell-mediated,** in which T-cells (another type of white blood cell) identify and destroy abnormal cells, including cancer cells.

  Both an overactive and an underactive immune system can be harmful. Our growing understanding of the health benefits of a balanced immune system has led to he development of immunotherapies as a treatment approach for many types of cancer.

Types of Immunotherapy

General Immunotherapies

Some immunotherapies work by enhancing the immune system overall, without targeting specific cancer cells. These types of immunotherapies include:

- **Interleukins,** which are naturally occurring proteins that help cells communicate, in order to regulate cell growth and immune response. Interleukins are a subset of cytokines, molecules which modulate how cells behave and stimulate other types of immune cells to further enhance treatment response. Interleukins made in the laboratory are used to modify biological responses to boost the immune system. More than fifteen types of interleukins have been identified, each with its own immunological function.
- **Interferons,** another type of cytokine, which play an important role in regulating many types of cell function. Interferons can help the immune system fight cancer by inhibiting cell division, which can slow or stop the growth of cancer.
- **Colony stimulating factors** that can strengthen the immune system and protect against infection by increasing the number of white blood cells produced in bone marrow.

Cancer-Targeting Immunotherapies

The purpose of cancer-targeting immunotherapy is to modify the immune system to recognize that the cancer is foreign to the body and needs to be attacked. This can be difficult, because the differences between cancer cells and healthy cells are often quite small and hard to detect.

Additionally, white blood cells have "immune checkpoint" molecules that alert cells to either "engage and fight" or "ignore and rest" when it recognizes something in the body as being foreign. The checkpoint molecules prevent our immune system from attacking normal cells. Drugs called checkpoint inhibitors block these molecules, allowing the immune cells to attack cancer cells.

One type of immune checkpoint inhibitor works by interfering with PD-1 or PDL-1 proteins that prevent the body's immune system from attacking cancer cells. Drugs in this category currently approved by the U.S. Food and Drug Administration (FDA) are nivolumab (Opdivo), atezolizumab (Tecentriq), pembrolizumab (Keytruda), avelumab (Bavencio), durvalumab (Imfinzi) and cemiplimab (Libtayo).

Another type of immune checkpoint inhibitor seeks out and locks onto cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), a protein that normally helps keep immune system cells deactivated. The drug ipilimumab (Yervoy) is designed to help the immune system destroy cancer cells by blocking the action of CTLA-4.

In addition to checkpoint inhibitors, immunotherapy approaches fall into the following main categories:

- **Monoclonal antibodies** are lab-generated proteins that target specific tumor antigens (substances that the immune system sees as being foreign or dangerous). Some monoclonal antibodies help the immune system recognize and destroy cancer cells. Monoclonal antibodies used in the treatment of certain cancers include rituximab (Rituxan) and trastuzumab (Herceptin).

- **Bispecific antibodies** are lab-generated proteins that target specific tumor antigens (as do monoclonal antibodies) but also bind proteins on the surface of immune cells (T-cells). This allows the T-cells to get close to and destroy the cancer cells. Blinatumomab (Blincyto) is an example of a bispecific antibody.
- **Therapeutic vaccines** can boost the immune system and have the potential to treat cancer or prevent it from recurring (coming back) after treatment. The FDA has approved vaccines for certain cancers. Additionally, a number of types of vaccines are being studied in clinical trials.
- **Adoptive T-cell transfer** (also called cellular adoptive immunotherapy) is an approach in which T-cells are removed from the individual, grown to an increased number in a laboratory and infused back into the individual with the goal of improving the immune system's anti-cancer response. One type of adoptive T-cell transfer is chimeric antigen receptor (CAR)T-cell therapy, which is used to treat certain blood cancers.

Immunotherapies can sometimes work well in combination with other treatment types, such as surgery, radiation, chemotherapy and targeted therapy (treatments designed to target the specific cell mechanisms that are important for the growth and survival of cancer cells).

Immunotherapies can be used as a delivery mechanism by attaching a monoclonal antibody to a chemotherapy drug to make an antibody drug conjugate (ADC). The antibody seeks out and hones in on a specific molecule on the tumor cell, bringing the chemotherapy with it. This approach can kill tumor cells or stop them from dividing while limiting the harm to normal cells. Brentuximab vedotin (Adcetris) and ado-trastuzumab emtansine (Kadcyla) are examples of ADCs.

The Importance of Clinical Trials

Clinical trials are the standard by which we measure the worth of new treatments and the quality of life of individuals as they receive those treatments. For this reason, doctors and researchers urge people with cancer to take part in clinical trials.

Your doctor can guide you in making a decision about whether a clinical trial is right for you. Here are a few things that you should know:

- Often, people who take part in clinical trials gain access to and benefit from new treatments.
- Before you participate in a clinical trial, you will be fully informed as to the risks and benefits of the trial, including any possible side effects.
- Most clinical trials are designed to test a new treatment against a standard treatment to find out whether the new treatment has any added benefit.
- You can stop taking part in a clinical trial at any time for any reason.

Side Effects of Immunotherapy

Immunotherapy travels through the bloodstream, helping to prompt what is called an "immune response." Because immunotherapy can attack healthy cells as well as cancer cells, certain side effects may be experienced, including digestive tract symptoms, loss of appetite, fatigue, flu-like symptoms and changes to the skin.

Report any side effects that you experience to your health care team right away so they can help you manage them. The side effects can range in severity; reporting them early can minimize their intensity and seriousness, allowing you to keep to your treatment plan. It's important to remember that not all individuals experience all side effects, and individuals may experience side effects not listed here.

Following are tips and guidance for managing these side effects.

Managing Digestive Tract Symptoms

Nausea and vomiting

- Avoid food with strong odors, as well as overly sweet, greasy, fried or highly seasoned food.
- Nibble on dry crackers or toast. These bland foods are easy on the stomach.
- Having something in your stomach when you take medication may help ease nausea.
- Do not lie down within two hours after eating.

Loss of appetite

- Eating small meals throughout the day is an easy way to take in more protein and calories, which will help maintain your weight. Try to include protein in every meal.
- To keep from feeling full early, avoid liquids with meals or take only small sips (unless you need liquids to help swallow). Drink most of your liquids between meals.
- Keep high-calorie, high-protein snacks on hand such as hard-boiled eggs, peanut butter, cheese, ice cream, granola bars, liquid nutritional supplements, puddings, nuts, canned tuna or trail mix.
- If you are struggling to maintain your appetite, talk to your health care team about whether appetite-building medication could be right for you.

Constipation

- As hydration is important to avoid constipation, make sure to drink plenty of fluids. Also, limit your intake of caffeine and alcoholic beverages, as they can cause dehydration.
- Include foods high in fiber in your daily diet, such as fruit (especially pears and prunes), vegetables and cereals. If your health care team approves, you may want to add synthetic fiber to your diet, such as Metamucil, Citrucel or FiberCon.
- Be as physically active as you can, after checking with your health care team on the level of physical activity that is right for you.
- If your doctor has prescribed a "bowel regimen," make sure to follow it exactly.

Diarrhea

- Drink plenty of water. Ask your doctor about using drinks such as Gatorade which provide electrolytes. Electrolytes are body salts that must stay in balance for cells to work properly.
- Over-the-counter medicines such as loperamide (Imodium A-D and others) and prescription drugs are available for diarrhea but should be used only if necessary. If the diarrhea is bad enough that you need medicine, discuss it with your doctor or nurse.
- Choose fiber-dense foods such as whole grains, fruits and vegetables, all of which help form stools.
- Avoid food high in refined sugar and those sweetened with sugar alcohols such as sorbitol and mannitol.

Managing Fatigue

Fatigue (extreme tiredness not helped by sleep) is one of the most common side effects of many cancer treatments. Your doctor may lower the dose of your immunotherapy, as long as it does not make the treatment less effective. If you are experiencing fatigue, talk to your doctor about whether taking a smaller dose is right for you.

There are a number of other tips for reducing fatigue:

- Take several short naps or breaks during the day.
- Take short walks or do some light exercise, if possible.
- Try easier or shorter versions of the activities you enjoy.
- Ask your family or friends to help you with tasks you find difficult or tiring.
- Save your energy for things you find most important.

There are also prescription medications that may help. Your health care team can provide guidance on whether medication is the right approach for your individual circumstances.

Fatigue can be a symptom of other illnesses, such as anemia, diabetes, thyroid problems, heart disease, rheumatoid arthritis or depression. Be sure to ask your doctor if they think any of these conditions may be contributing to your fatigue.

It can also be beneficial to speak with an oncology social worker or oncology nurse to help manage your fatigue. These professionals can work with you to manage any emotional or practical concerns that may be causing symptoms and help you find ways to cope.

Managing Flu-Like Symptoms

The fever and aches that may occur with immunotherapy treatments can be managed with a combination of rest and medication. Acetaminophen (such as Tylenol) is often a doctor's first choice to treat these symptoms. Nonsteroidal anti-inflammatory drugs (NSAIDs) can also help, but should be taken only if recommended by your doctor, as they can cause other side effects. NSAIDs include aspirin, ibuprofen (Motrin and others) and naproxen (Naprelan, Midol, Aleve and others).

Managing Changes to the Skin

About 20 to 30 percent of people being treated with immunotherapy experience changes to the skin, such as a flat or raised itchy rash. The rash and itching can be treated with prescription-strength medications that are applied directly to the skin or taken as tablets. These medications are typically either antihistamines (drugs used to treat allergic reactions) or corticosteroids (drugs that act against inflammation).

Managing Pain

Both cancer itself and the side effects of treatment can sometimes cause pain. To help your doctor prescribe the best medication, it's useful to give an accurate report of your pain. Keep a journal that includes information on:

- Where the pain occurs
- When the pain occurs
- How long the pain lasts
- How strong the pain is on a scale of 1 to 10, with 1 being the least amount of pain and 10 the most intense
- What makes the pain feel better and what makes it feel more intense

There are a number of options for pain relief, including prescription and over-the-counter medications. It's important to talk to a member of your health care team before taking any over-the-counter medication in order to determine if it is safe and will not interfere with your treatments.

Physical therapy, acupuncture and massage may also be of help in managing your pain. Other techniques, such as mindfulness meditation, deep breathing exercises and yoga may also be helpful. Consult with a member of your health care team before beginning any of these activities.

Side Effects of Other Treatment Approaches

Immunotherapy is often given in combination with other types of treatments, which can have their own side effects.

Side Effects of Chemotherapy

The side effects of chemotherapy depend on the type and dose of drugs given and the length of time they are used, and can include:

- Hair loss
- Increased risk of infection (from having too few white blood cells)
- Easy bruising or bleeding
- Changes in memory or thinking
- Peripheral neuropathy (numbness or tingling in hands and feet)

Side Effects of Targeted Therapy

Targeted therapy doesn't have the same effect on the body as do chemotherapy drugs, but it can still cause side effects. Side effects of targeted therapies can include diarrhea, liver problems (such as hepatitis and elevated liver enzymes), nerve damage, high blood pressure and problems with blood clotting and wound healing.

Side Effects of Radiation Therapy

Changes to the skin are the most common side effects of radiation therapy. Those changes can include dryness, swelling, peeling, redness, and blistering. Sun exposure should be avoided, as it can worsen this side effect. If a reaction occurs, contact your health care team so the appropriate treatment can be prescribed. It's especially important to contact your health care team if there is any open skin or painful area, as this could indicate an infection. Infections can be treated with an oral antibiotic or topical antibiotic cream.

Communicating With Your Health Care Team

As you manage your cancer, it's important to remember that you are a consumer of health care. The best way to make decisions about health care is to educate yourself about your diagnosis and the members of your health care team, including doctors, nurses, nurse practitioners, physician assistants, dietitians, social workers and patient navigators.

Here are some tips for improving communication with your health care team:

Start a health care journal. Having a health care journal or notebook will allow you to keep all of your health information in one place. You may want to write down the names and contact information of the members of your health care team, as well as any questions for your doctor. Keep a diary of your daily experiences with cancer and treatment. You can separate your journal or notebook into different sections to help keep it organized.

Prepare a list of questions. Before your next medical appointment, write down your questions and concerns. Because your doctor may have limited time, you should ask your most important questions first, and be as specific as possible.

Bring someone with you to your appointments. Even if you have a journal and a prepared list of questions or concerns, it's always helpful to have support when you go to your appointments. The person who accompanies you can serve as a second set of ears. He or she may also think of questions to ask your doctor or remember details about your symptoms or treatment that you may have forgotten.

Write down your doctor's answers. Taking notes will help you remember your doctor's responses, advice and instructions. If you cannot write down the answers, ask the person who accompanies you to do that for you. If you have a mobile device, like a tablet or smartphone, ask if you can use it to take notes. Writing notes will help you review the information later.

Record your visit if your doctor allows it. Recording the conversation with your doctor gives you a chance to hear specific information again or share it with family members or friends.

Incorporate other health care professionals into your team. Your medical oncologist is an essential member of your health care team, but there are other health care professionals who can help you manage your diagnosis and treatment:

- Your primary care physician should be kept updated about your cancer treatment and any test results.
- Your local pharmacist is a great source of knowledge about the medications you are taking. Have all of your prescriptions filled at the same pharmacy to avoid the possibility of harmful drug interactions.
- Make sure your oncologist knows of any other medical conditions you have, or any pain you are experiencing, so that he or she can consult with your primary care physician or your specialist if needed.
- Ask your oncologist to send a summary of your visits to your primary care physician and all doctors involved in your care.

Remember, there is no such thing as over-communication.

Cancer*Care*'s Free Support Services and Programs

It can be very difficult to receive a diagnosis of cancer, and adjusting to the necessary changes in your life can be challenging.

Cancer*Care* can help. We are a national nonprofit organization providing free, professional services to anyone affected by cancer. Our licensed oncology social workers can provide support and education, help in navigating the complicated health care system, and offer information on support groups and other resources.

To learn more about how Cancer*Care* can help, call us at 800-813-HOPE (4673) or visit www.cancercare.org.

You will likely also build your own personal support network composed of family and friends. In doing so, it's best to take some time to think about the people in your life and how they are best suited to help. Match the task to their strengths—ask a family member who loves to shop to pick up something for you at the store; ask a friend who's a good listener to come over for a chat.

Frequently Asked Questions

Q: I've recently been diagnosed with cancer. What questions should I ask my oncologist about immunotherapy as a possible treatment approach?

A: Specific questions to discuss with your oncologist include:

- Does immunotherapy have a role in treating my type of cancer, alone or in combination with other treatments?
- Are there FDA-approved immunotherapies for my type of cancer?
- Are there any immunotherapies currently being studied in clinical trials for my type of cancer?
- What are the possible side effects of the immunotherapy approaches for my type of cancer?

Q: Will immunotherapy replace other types of cancer treatments?

A: There is much enthusiasm for immunotherapy as a treatment approach for many types of cancer. However, other forms of treatment are still considered to be effective, depending on the individual's specific circumstances. This includes treatments that have been used for many years, such as radiation and chemotherapy, and newer approaches such as targeted therapy. It's also important to note that immunotherapy can often be most effective when used in combination with other forms of treatment. Additionally, not all cancers survive and grow by evading the immune system. For those types of cancer, immunotherapy is not the right treatment approach. the right treatment approach.

Q: I am being treated with a vaccine for my cancer. Will this interfere with the other vaccines I usually get?

A: In order to stay as healthy as possible during any type of cancer treatment, it is generally recommended that you continue to receive the vaccines recommended for your specific situation, which can include shots for influenza, pneumonia and herpes zoster (shingles). However, this is an important issue to discuss with your health care team, as there can be exceptions to this general guidance.

Q: Is immunotherapy safe for people with an underlying autoimmune disease?

A: Common autoimmune diseases include diabetes, rheumatoid arthritis, multiple sclerosis, inflammatory bowel disease and lupus. Studies have shown that people with an autoimmune disease can respond well to immunotherapy. However, the potential benefits must be measured against the potential risk, as the underlying condition may temporarily worsen during the course of immunotherapy. People with an autoimmune disease who are being treated with immunotherapy for cancer should be closely monitored by their health care team (including their oncologist and the specialist treating the underlying condition).

Q: How long do I have to stay on my immunotherapy treatment?

A: The duration of immunotherapy treatments depends on a number of factors, including the type of immunotherapy being received. For instance, a vaccine might be given just once, while other medications may be given at set intervals over a number of weeks. How long to continue certain immunotherapies is an area of ongoing research in clinical studies.

Notes

Resources

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American Cancer Society
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Patient information from the American Society of Clinical Oncology
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Cancer Support Community
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215-690-0300
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