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Third Edition

IMMUNOTHERAPY *for the treatment of* MELANOMA *& other skin cancers*

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Immunotherapy for the Treatment of Melanoma & other Skin Cancers

Third Edition

IN THIS GUIDE

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Society for Immunotherapy of Cancer

→ **The Society for Immunotherapy of Cancer (SITC)** is the world's leading member-driven organization specifically dedicated to improving cancer patient outcomes by advancing the science and application of cancer immunotherapy. Established in 1984, SITC, a 501(c)(3) not-for-profit organization, serves scientists, clinicians, academicians, patients, patient advocates, government representatives and industry leaders from around the world. Through educational programs that foster scientific exchange and collaboration, SITC aims to one day make the word "cure" a reality for cancer patients everywhere.

FOR MORE INFORMATION SEE PAGE 13

For more information on cancer immunotherapy...

Visit **sitcancer.org/patientcourse** for patient resources from the Society for Immunotherapy of Cancer (SITC)

Knowing more about immunotherapy can be empowering

Immunotherapy has revolutionized the treatment of certain types of melanoma and other skin cancers. Uniquely different from other types of cancer treatment, it uses the body's own immune system to recognize and attack cancer cells that have been hiding and targets them for destruction. This ability to harness the power of the immune system is making it increasingly possible for many people with these diagnoses to live longer, better-quality lives. Understanding immunotherapy and its impact are important especially for newly-diagnosed patients. As the world's leading member-driven organization specifically dedicated to improving cancer patient outcomes by advancing the science and application of cancer immunotherapy, the Society for Immunotherapy of Cancer (SITC) provides resources for patients to learn more about immunotherapy, its research and how it is improving outcomes for many cancer types (sitcancer.org/patient).

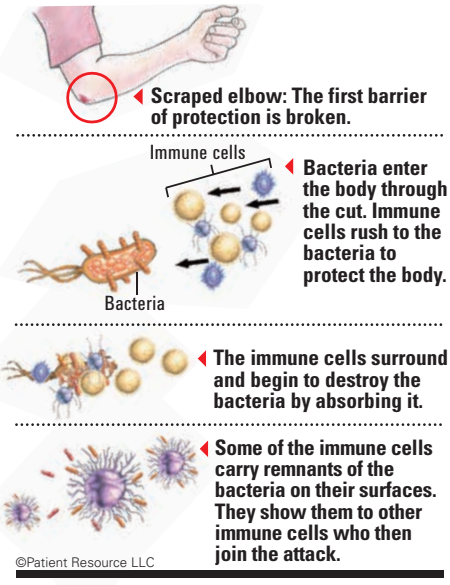
Even with treatment advances, receiving a cancer diagnosis can feel overwhelming. The first step toward understanding all the new information you'll hear is to know the specific type and stage of your diagnosis. This guide explains melanoma and other skin cancers, the immune system, immunotherapy and ways to help manage your treatment and follow-up care (see *Melanoma Overview,* page 3, and *Skin Cancer Overview*, page 5).

WHAT IS THE IMMUNE SYSTEM?

To understand how your immune system can be used to treat cancer, it's helpful to know it's a complex network of cells, molecules, organs and lymph tissues working together to defend the body against germs, microscopic invaders and even cancer cells.

The first job of the immune system is to distinguish between what is part of the body (self) and what is not part of the body (non-self or foreign). Viruses are one type of germ that can infect humans as they enter the normal cells of the body. The immune system has developed sophisticated ways to determine if a cell is normal or may contain a virus, or is abnormal for other reasons, such as injury or cancer. Once the immune system determines that a cell is not normal (or foreign to the body), it begins a series of reactions to identify, target and eliminate the abnormal cell. This process represents a way to protect against injury and foreign substances, such as germs. When you scrape your elbow, for example, the skin's protective barrier is broken, and harmful non-self substances can easily enter the body (see Figure 1).

FIGURE 1
NORMAL IMMUNE RESPONSE



The lymphatic system, which is made up of the spleen, thymus, adenoids, tonsils and lymph nodes, is a driving force in the immune system. Lymph, a clear fluid, is circulated throughout the body through the lymph nodes. It collects and filters bacteria, viruses, toxins and chemicals, which are circulating in the lymphatic system and bloodstream. Lymph nodes are located throughout the body, with large concentrations near the chest, abdomen, groin, pelvis, underarms and neck. The immune system recognizes abnormal cells or germs by "seeing" specific proteins or other molecules that are called antigens.

Lymph contains lymphocytes, a type of white blood cell that attacks infectious agents. The two main types of lymphocytes are B-lymphocytes (B-cells) and T-lymphocytes (T-cells).

B-cells develop in the bone marrow and mature into either plasma cells or memory cells. Plasma cells make antibodies to fight germs and infection. Memory B-cells help the immune system remember which antigens attacked the body so they can recognize them and respond if they return.

T-cells also develop in the bone marrow and mature into four cell types: helper, killer, regulatory and memory T-cells. Each responds to non-self antigens in different ways.

HOW THE IMMUNE SYSTEM WORKS

Each part of the immune system plays a role in defending the body. But, like any good team, these parts must be able to alert each other and communicate messages so the system can respond quickly to threats. Most cells communicate by sending chemical signals.

The surface of a cell is not completely round and smooth. It is covered with receptors and proteins, which work like puzzle pieces. Proteins have "tabs" that stick out, and receptors have "spaces" that curve inward. When the puzzle pieces fit together (known as binding), chemical signals and information are exchanged in a biochemical reaction. Cells also contain various proteins, sugars, fats and other molecules that stick out of their surfaces. These components contain information that is shared between cells.

An immune response typically begins when B-cells and helper T-cells identify a threat (non-self antigen) and tell the rest of the immune system. The body then ramps up its production of T-cells to fight. Killer T-cells are sent to destroy cells that contain the non-self antigens. Regulatory T-cells are sent to slow the immune system down once the cells that contain non-self antigens have been eliminated, to prevent the T-cells from attacking healthy parts of the body. T-cells then return to normal levels (see *How the Immune System Responds to a Threat,* page 2).

The immune system uses this same process

Questions for your doctor

- **Has immunotherapy successfully treated my type of melanoma/skin cancer?**
- **Am I a good candidate to receive immunotherapy?**

to recognize and eliminate cancer, but the process is more complicated. Cancer cells are created by the body, so the normal ways to find and fight invading cells from outside the body aren't always effective. The immune system may have difficulty identifying cancer cells as non-self. It may still see them as a normal part of the body and not coordinate an attack. If the body can't tell the difference between tumor cells and normal cells, the tumor cells may be able to "hide" from the immune system.

Cancer cells are smart. Over time, they can change and use multiple methods to escape or confuse the immune system. One way is to produce proteins on their surface to hide from the immune system, like camouflage. Another is to create their own messengers (cytokines), which means that the cancer cells can communicate and confuse the immune cells. That allows the cancer to take control of certain parts of the process that the body uses to regulate the immune response. So, even if the immune system recognizes the cancer, it may not be able to successfully start or maintain an attack long enough to kill the cancer cells.

The longer the cancer cells face a weakened immune response, the more they're able to adapt, and the easier it is for them to manipulate immune cells inside the tumor's location, sometimes called the tumor microenvironment.

Immunotherapy offers the immune system reinforcements to keep up its fight, whether that is by taking the brakes off the system, boosting it with modified T-cells or combining it with chemotherapy or radiation therapy.

IMMUNOTHERAPY FOR MELANOMA AND OTHER SKIN CANCERS

Some of the first types of immunotherapy approved by the U.S. Food and Drug Administration (FDA) for treating cancer were for melanoma. These approvals offered hope and durable responses to many who had Stage III and IV diagnoses, which had a poor prognosis, were difficult to treat and often spread quickly. Since then, the FDA has approved more immunotherapy drugs for both melanoma and other skin cancers, including cutaneous squamous cell and Merkel cell skin cancers. These drugs are considered breakthrough therapies that are offering a new way of treating these types of cancer.

Today, many immunotherapy options are available for people with melanoma and other skin cancers. These include cytokines, immune checkpoint inhibitors, immunomodulators and oncolytic virus therapy, which all work on different aspects of the immune system (see *Treatment Options*, page 6).

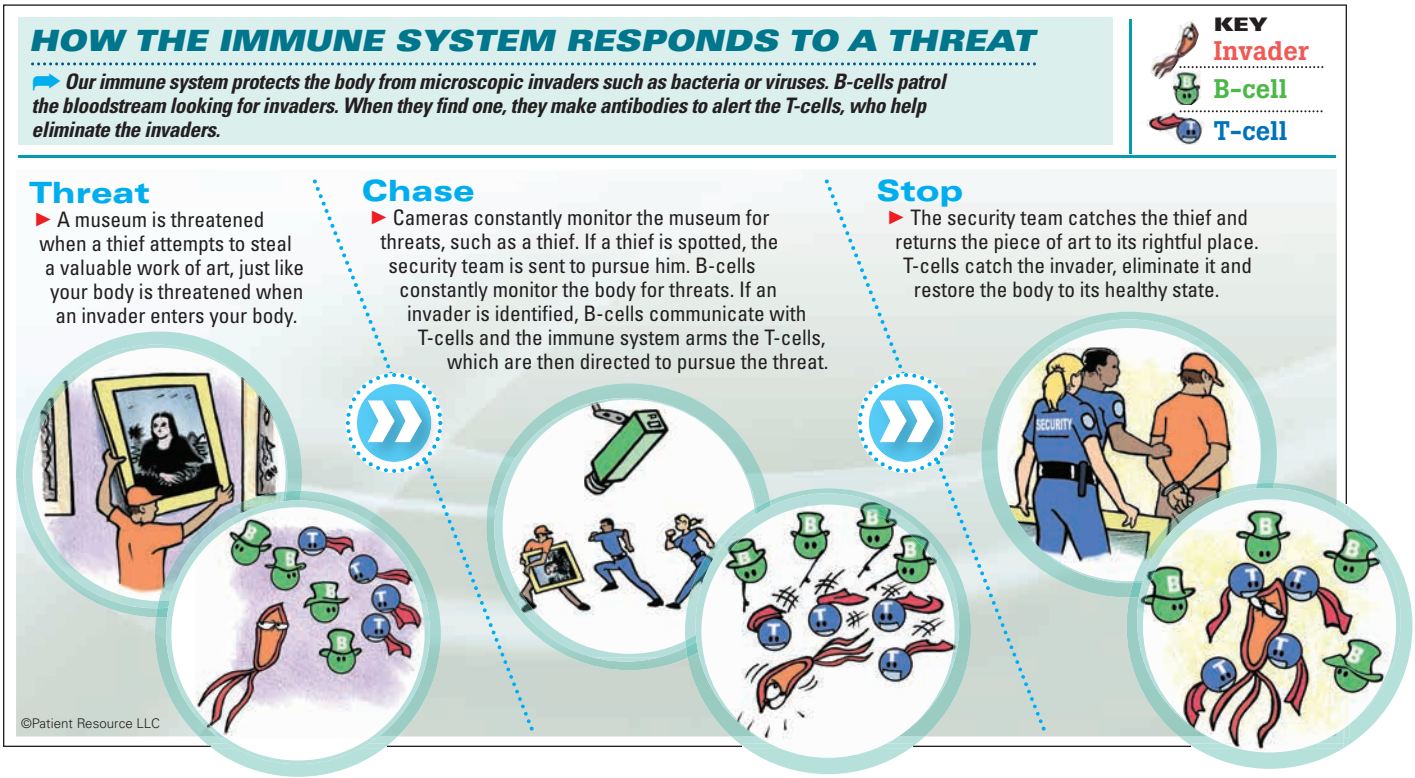
You may be a candidate for immunotherapy if you meet certain criteria. If you have a pre-existing autoimmune disorder, be sure to discuss it with your doctor. Immunotherapy is not effective for every person, even if it is approved for that person's cancer type. Scientists are studying patient responses to immunotherapy to find out why. Researchers are also investigating other methods for using the immune system to fight cancer to improve the effectiveness of this treatment (see *Clinical Trials*, page 9). ■

STAGING

➡ Staging helps your medical team develop a personalized treatment plan based on the extent of disease and how far it has progressed.

The TNM classification system developed by the American Joint Committee on Cancer (AJCC) is used to stage melanoma and other skin cancers. The T category specifies the primary tumor's size and location. The N category indicates whether lymph nodes show evidence of cancer cells. The location of these lymph nodes is important because it shows how far the disease has spread. The M category describes distant metastasis (spread) to other parts of the body, if any. The staging information for the types of melanoma and skin cancer discussed in this guide are available online using the links below:

- PatientResource.com/**Cutaneous**_Melanoma.aspx
- PatientResource.com/**Mucosal**_Melanoma.aspx
- PatientResource.com/**Ocular_Ciliary**_and_**Choroidal**_Melanoma.aspx
- PatientResource.com/**Ocular_Conjunctival**_Melanoma.aspx
- PatientResource.com/**Ocular_Iris**_Melanoma.aspx
- PatientResource.com/**Basal_Cell**_and_**Squamous_Cell**_Carcinoma.aspx
- PatientResource.com/**Merkel_Cell**_Carcinoma.aspx



Educate yourself about the basics of melanoma

Melanoma is a cancer that starts in skin cells known as melanocytes, which produce melanin, the substance that colors the skin, hair and eyes. Damaged DNA can cause the melanocytes to grow abnormally. When melanocytes become malignant (cancerous), they are called melanoma.

Melanomas can develop anywhere on the skin, in the eyes and in mucosal linings, such as in the mouth, genitals and anal area. The neck and face are common sites for melanoma of the skin. Melanocytes may also form moles that can turn into melanoma. Other names for this cancer of the skin include cutaneous melanoma and malignant melanoma.

TYPES OF MELANOMA

Although melanoma is the rarest of the skin cancers, it is considered the most serious type. It can easily spread into deep layers of skin as well as to lymph nodes and other organs. The skin's layers include the epidermis (outer layer), dermis (inner layer) and hypodermis (subcutaneous tissue). Melanoma typically develops in the epidermis, which contains melanocytes (see Figure 1).

Cutaneous melanoma includes four types:

- Acral lentiginous melanoma is found on the palms of the hands, soles of the feet or under the nail bed.
- Lentigo maligna melanoma typically begins on the face, ears and arms that have been exposed to the sun for long periods of time.
- Nodular melanoma usually appears suddenly as a bump on the skin.
- Superficial spreading melanoma develops from an existing mole.

Other rare subtypes of melanoma of the skin include amelanotic, which often lacks pigmentation, and desmoplastic, which is found in older adults and is distinguished by the presence of certain cell types.

Ocular melanoma develops in the eye. No screening tests are available for the disease, but routine eye exams help doctors find most ocular melanomas. Because they do not typically cause symptoms in the early stages, melanomas that develop as a dark spot in visible parts of your eye (primarily the iris) often have the best prognosis because they are caught the earliest. Other ocular melanomas may be found after they begin to cause symptoms or when the pupil is dilated during an eye exam.

The eye is composed of several layers and tissues, including the iris, ciliary body and choroid. The iris, which is the colored area of your eye, controls how much light enters the pupil. The ciliary body changes the shape of your lens when you focus on an object and makes the transparent liquid found between the outer layer of the eye and the iris. The choroid provides blood to the front part of the eye and to the retina, which is the light-sensitive ocular tissue.

Rarely, melanoma may also develop in the conjunctiva, the mucous membrane lining the eye, which keeps the eye lubricated.

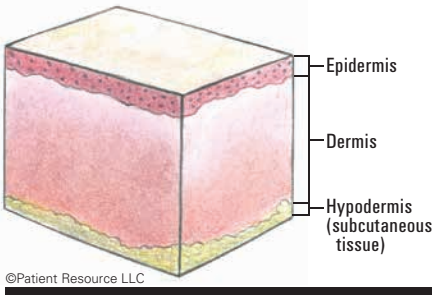
Mucosal melanoma develops in the mucosal lining of the body, a membrane that covers many body cavities and passageways. It is a rare disease accounting for around one percent of all melanomas. Because it often begins in concealed areas and causes no specific symptoms, many cases are diagnosed only after they have progressed to an advanced stage. The body's moist mucosal linings are:

- The respiratory tract, in areas such as the sinuses, nasal passages and mouth. Head and neck mucosal melanoma is the most common type.
- The gastrointestinal tract, including the anus and rectum (anorectal).
- The female genital tract, including the vagina and vulva.

HOW MELANOMA GROWS AND SPREADS

Melanoma cells may enter the lymphatic system, a network of vessels that carry lymph (a colorless fluid) throughout the body. Once in this system, melanoma cells can spread to nearby lymph nodes and also may enter the bloodstream and travel to other parts of the body. Early treatment can stop melanoma before it spreads through the lymphatic system to lymph nodes in the region or to distant organs, which is why early detection and treatment are so important.

FIGURE 1
ANATOMY OF THE SKIN



In the first growth stage, known as the radial growth phase, the melanoma grows horizontally, staying within the upper layer of the skin (epidermis). During this phase, melanomas are not likely to metastasize (spread to other areas).

In the next phase, the vertical growth phase, the melanoma begins to grow down into deeper layers, such as the dermis and hypodermis, as well as up into the epidermis, and the risk for metastasis increases. This occurs because the lymphatic vessels are located in the lower dermis and hypodermis, and melanoma cells can use these vessels to spread to lymph nodes. Because of this, the thickness is the most important factor in determining the prognosis of melanoma.

Melanomas are classified as thin (less than 1 millimeter, or about the thickness of a credit card), intermediate (1 to 4 mm) or thick (more than 4 mm).

Learn more about the forms of immunotherapy used to treat certain types of melanoma in *Treatment Options*, page 6. ■

Questions for your doctor

- **Is my melanoma thin, intermediate or thick, and how does that affect my prognosis?**
- **How will my melanoma be treated?**
- **I have a lot of moles and skin spots. Can they develop into melanoma?**

RESEARCH SAVED MY LIFE

After Bob Heffernan's cancer progressed to Stage IV, his doctor referred him to the National Institutes of Health where he joined an immunotherapy clinical trial and had a good response. Bob shares his wisdom with other melanoma survivors in his book, "Cancer's Gifts with Love & Hope" and is an advocate for cancer research and clinical trials.

Near the end of November 2006, I felt a bump on my scalp. I thought it was a pimple, so I put off seeing my dermatologist until January 2007. In the back of my mind, I worried it could be more serious, and it was. What I thought was a pimple turned out to be melanoma. Waiting that long was a mistake.

My dermatologist referred me to a well-known research hospital in my home state. A month after I was diagnosed, we discovered the cancer had spread to the lymph nodes in my neck, making it a Stage III melanoma. I was 52. My doctor started immunotherapy with a cytokine that was considered standard of care at the time. For the first year, I received a shot every two weeks, and I felt like I had the flu for the entire time.

The month after I stopped my cytokine treatment, scans found cancer in my lungs. I had surgery after diagnosis to remove the nodules in my lungs, and then had a year of clean scans. In the third year, the cancer appeared again. The doctor decided it was inoperable and tried a different cytokine for a month.

The side effects of the second cytokine were much harder. This treatment turns the immune system way up. It's like a scattershot approach to boost the immune system, but it required hospital inpatient treatment for two weeks. I recovered but I had exhausted all of the approved treatments, so I was referred to the National Institutes of Health (NIH), which was testing a new treatment. Back then, Stage IV melanoma had a 95 percent mortality rate, so I wanted to try all of my options. Luckily, I had some.

I joined NIH's clinical trial for a revolutionary treatment that involved tumor-infiltrating lymphocytes (TIL), which are immune cells that move from the blood into a tumor to try to attack it. Surgeons removed the largest tumor they could find and sent it to the lab to determine if it contained TILs. It did, so they sent the TILs to be multiplied, and more than 67 billion cells were generated. Four days later, I was able to see my TIL cells through a microscope.

While I waited for the new TILs to be ready, I underwent a procedure similar to a stem cell transplant to reduce my immune system. Three weeks later, the TIL cells were infused into my body to build back my immune system. It was a tough procedure, but it was a declaration that research saves lives. It certainly saved mine.

Never be afraid of research, especially if you have a rare cancer type. The researchers all talk to each other, and they know more about what's in the pipeline way before your oncologist does. You need to keep going as long as you can because you never know when that next breakthrough will be discovered.

Since the procedure, scans have shown two tiny lung tumors that remain small. The doctors are unsure if they are actually melanoma or scar tissue from the immune system attacking the lung tumors I had, so I can't be considered in full remission, but the cancer has been gone more than a year.

I believe there is a connection between body and mind. You have to have hope and determination. I notice that people who are fighting cancer on multiple fronts seem to have a greater chance at a better outcome than those who give up.

For me, patient group meetings were very helpful, as were my husband, who is a medical lab technician, and my mother. My work community enabled me to get to treatment and keep working from home. Everyone's support helped keep my life as normal as possible. Reach out to others. Have someone go with you to appointments because your mind races and can go on autopilot.

Also, I learned how very important it is to tell any doctor treating you that you've had immunotherapy. Serious side effects can occur even after treatment has stopped, and it's critical for the medical team to know your treatment history. In my case, I also let them know about my low platelet count, a long-term side effect I have.

Going through cancer was a wild experience. It taught me many lessons that I share in my book, "Cancer's Gifts with Love & Hope." Each chapter addresses feelings such as faith, hope and courage. As I write in my book, "Cancer is all about the intimate human experience. It brings out the best traits in so many of us. How we choose to handle a disease is just that — a choice." ■

Identifying the most common types of skin cancer

Your skin is your body's largest organ and your immune system's first line of defense against infection and injury. Its thin, outer layer is called the epidermis, with the dermis underneath it and the hypodermis (subcutaneous tissue) farther below (see Figure 1). More skin cancers are diagnosed in the United States each year than all other types of cancer combined.

Skin cancer can develop anywhere on the body and is most frequently found on the face, including the eyelids and outer lips; the head, including the tops of the ears; the neck; and the tops of the hands, as these areas usually receive the most exposure to ultraviolet (UV) rays from the sun and other sources.

The most common types of skin cancer are named for the cells in which they develop: basal cell carcinoma and squamous (SKWAY-mus) cell carcinoma. Melanoma is less common and forms in cells called melanocytes (see *Melanoma Overview,* page 3). Merkel cell carcinoma is among the many rare types, subtypes and variants of cancers that affect the skin.

Basal cell and squamous cell carcinomas behave very differently from melanoma, which is why they are often grouped together and referred to as non-melanoma skin cancers (NMSCs). Although most NMSCs are usually easily cured and rarely life-threatening, they can cause serious tissue damage, particularly to the face and head, if left untreated.

Basal cell carcinoma (BCC) is the most common form of skin cancer in the United States, with more than 20 subtypes and variants. It is most frequently diagnosed in Caucasians, but is also the most common type seen in Hispanic and Asian people. BCC forms in basal cells, which are round cells in the lower part of the epidermis, and begins when these cells become abnormal and grow out of control. BCC usually grows slowly and very rarely spreads beyond surrounding tissues. The most common site for BCC to occur is the nose.

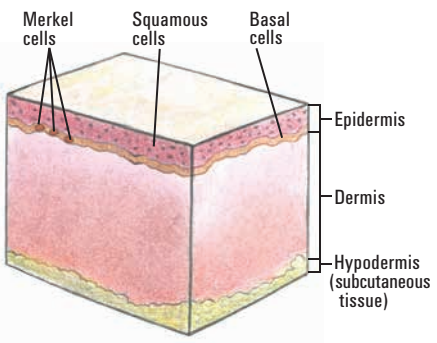
Squamous cell carcinoma (SCC) is less common than BCC. It is sometimes called squamous cell carcinoma of the skin, cutaneous squamous cell carcinoma (CSCC) or squamous cell skin cancer to differentiate it from SCC that develops in other parts of the body. SCC is commonly found on more sun-exposed areas of the skin, such as the face, ears, neck, lips and backs of the hands. It can also develop on scarred or damaged skin.

SCC develops in squamous cells, which form the outermost part of the epidermis. Under a microscope, these thin, flat cells resemble fish scales. SCC is more likely to spread than BCC, but it usually remains local, meaning it is confined to tissues surrounding the original site. Regional SCC has spread to nearby lymph nodes, and metastatic SCC has spread to distant parts of the body.

There are several SCC subtypes and related forms. Actinic keratosis (ak-TIH-nik KAYR-uh-TOH-sis) is a common skin condition also referred to as sun spots or age spots. These slow-growing lesions are most likely to appear on the face, balding scalp, forearms and backs of hands. Actinic keratosis is considered a precancer because it sometimes progresses to become SCC. Squamous cell skin cancer in situ (in SY-too), also called Bowen disease, is SCC in its very earliest form and involves only the superficial layer of skin. It grows very slowly, and without treatment, it may become SCC. Marjolin's ulcer, which can be aggressive, is SCC that develops at the site of an old scar, burn or non-healing wound.

Merkel cell carcinoma (MCC) is very rare. It forms in oval-shaped cells located in the basal layer in the lower part of the epidermis. These neuroendocrine cells are thought to be receptors that help produce the sensation of light touch. MCC begins when these cells become abnormal and grow out of control, most often in the head and neck area as well as the trunk, arms and legs.

FIGURE 1
ANATOMY OF THE SKIN



Because MCC is highly aggressive, it grows rapidly and is likely to spread, first to nearby lymph nodes and then to distant areas. These may include skin and lymph nodes elsewhere in the body, the brain, lungs, bones and other organs. MCC may also be referred to as neuroendocrine carcinoma of the skin.

Immunotherapy may be used to treat some types of skin cancers under certain conditions, such as when cancer is advanced and/or surgery isn't possible (see *Treatment Options*, page 6). Having a non-melanoma skin cancer significantly increases your risk of developing another skin cancer, so follow-up care is very important after being diagnosed with any type of skin cancer. This includes regularly scheduled appointments with a dermatologist (see *Follow-up Care is Essential,* page 11). ■

Questions for your doctor

- **How deeply has the cancer grown into my skin, and how does that affect my prognosis?**
- **How do we determine how serious my skin cancer is?**
- **How will my type of skin cancer be treated?**

Understanding the variety of immunotherapy options available

Using immunotherapy to treat melanoma and other skin cancers is a significant leap forward. The introduction of this class of drugs has changed how doctors treat these cancers, and it has improved the prognosis for many people with Stage III or IV disease. Some of the very first types of immunotherapy approved were for melanoma, and it remains a cancer that generally responds well to this treatment.

Research has discovered multiple ways to harness the potential of the body's own immune system and enable it to recognize and eliminate cancer cells. Today, several types of immunotherapy are approved to treat melanoma and other skin cancers, and all are a result of the research done in clinical trials.

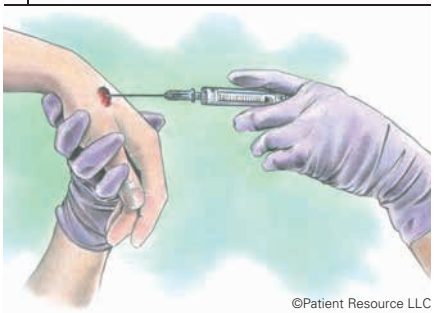
Once considered a last resort for metastatic cancers, immunotherapy may be used as a first-line therapy or second-line therapy. First-line therapy, also known as induction therapy, primary therapy or primary treatment, is the first treatment given and is usually part of the standard of care. Second-line therapy is treatment given after the first-line therapy doesn't work or stops working. Some may be used as local or systemic treatments. Local treatments are injected into a lesion or applied topically to the skin, and systemic treatments travel throughout your body (see Figures 1 and 2).

For early stage melanoma or skin cancer, treatment usually involves surgery only. For more advanced stages, additional treatment options may be necessary to prevent recurrence or to treat a metastasis. Immunotherapy strategies may be given after surgery (adjuvant treatment) with the goal of reducing the risk of disease recurrence. In more advanced cases or when the cancer is unresectable (unable to be removed with surgery), immunotherapy may be used as the first-line therapy. It may also be used in combination with other treatments such as chemotherapy, targeted therapy and radiation therapy.

Research in clinical trials is ongoing to determine if immunotherapy drugs approved for Stage III and IV cancers can be used in earlier stages and to discover new types of effective immunotherapy.

The following types of immunotherapy are currently approved by the U.S. Food and Drug Administration to treat melanoma and/or other skin cancers.

FIGURE 1
LOCAL THERAPY



CYTOKINES

Cytokine immunotherapy aids in immune cell communication and plays a big role in the full activation of an immune response. Remember, cytokines are how immune cells talk to one another. This approach works by introducing large amounts of laboratory-made cytokines to the immune system to promote immune responses as a systemic therapy. It is also considered a non-specific immune stimulator. Three types of cytokines are used in immunotherapy.

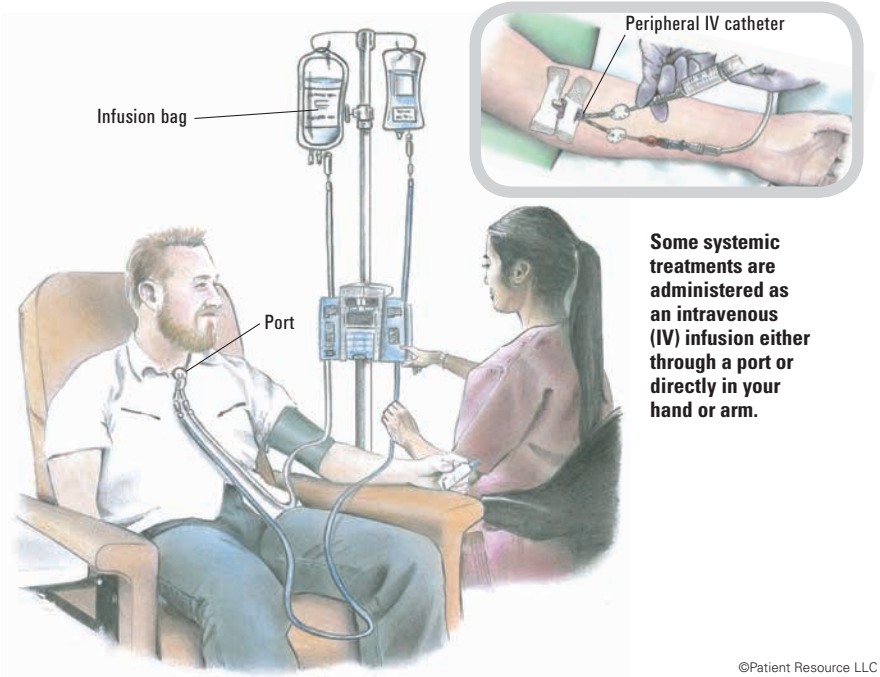
1. **Interleukins** help control the activation of certain immune cells. They are considered a first-generation immunotherapy.
2. **Interferons** boost the ability of certain immune cells to attack cancer cells. They are also a first-generation immunotherapy and may be given as adjuvant therapy (given after primary treatment).
3. **Granulocyte-macrophage colony stimulating factors** (GM-CSFs) stimulate the bone marrow, increasing the growth of immune and blood cells. This includes dendritic cells, which become antigen-presenting cells, which help start a T-cell immune response. An oncolytic virus that includes the GM-CSF cytokine to help activate a strong immune response is approved for melanoma treatment.

IMMUNE CHECKPOINT INHIBITORS

This type of immunotherapy was first approved in 2011 for melanoma and in 2017 for other skin cancers. These drugs are given as an infusion intravenously (IV) and are systemic. Some are approved to be used alone or in combination.

To understand how immune checkpoint inhibitors work, it is helpful to know how the immune system works in general. Because one of the primary functions of the immune system is to determine which cells or substances are self (normal) or non-self (foreign), the immune system contains cells, called B-cells and T-cells, which can recognize the foreign cells. These cells are part of the white blood cells that fight infections and eliminate cancer cells in the body. To prevent attack on normal cells, the immune system has a complex process that regulates the

FIGURE 2
SYSTEMIC THERAPY



Some systemic treatments are administered as an intravenous (IV) infusion either through a port or directly in your hand or arm.

activity of B-cells and T-cells. The immune cells are rapidly activated to clear an infection or kill a cancer cell. However, to prevent an attack on normal cells, the immune system must slow down. It does this through the use of checkpoints.

Checkpoints keep the immune system "in check" by turning off immune cells or killing the immune cells. This may be normal after an infection has been cleared, but, in cancer, this may occur prematurely, allowing the cancer to continue to grow. When the correct checkpoint proteins and cell receptors connect, a series of signals is sent to the immune system to slow down once an immune response is finished. So far, three checkpoint receptors that slow down the immune system have been used in cancer treatment.

1. **CTLA-4** (cytotoxic T-lymphocyte associated protein 4) is a receptor that binds with certain molecules to tell the immune system to slow down.
2. **PD-1** (programmed cell death protein 1) is a receptor involved with telling T-cells to die and reducing the death of regulatory T-cells (suppressor T-cells). Both of these effects slow down an immune response. PD-1 can tell the immune system to slow down only if it connects with PD-L1.
3. **PD-L1** (programmed death-ligand 1) is a protein that, when combined with PD-1, sends a signal to reduce the production of T-cells and enable more T-cells to die.

When PD-1 (the receptor) and PD-L1 (the protein) combine, the reaction signals it's time to slow down. CTLA-4, however, can connect with more than one protein, which is a more complex reaction than with PD-1 and PD-L1. When CTLA-4 combines with any of the various proteins, it also tells the immune system to slow down.

Checkpoint-inhibiting drugs prevent connections between checkpoints. This prevents the immune response from slowing down, which allows the immune cells to continue fighting the cancer. When an immune checkpoint inhibitor is given, the immune system can better recognize cancer cells as foreign cells.

The following types of immune checkpoint inhibitors are currently approved.

- **Anti-CTLA-4** antibodies allow T-cells to continue fighting cancer cells instead of shutting down.
- **Anti-PD-1** drugs allow for the continued or increased production of T-cells and enable them to continue fighting cancer.

FDA-APPROVED IMMUNOTHERAPIES FOR MELANOMA

Cytokines
- interferon alfa-2b (Intron A)
- interleukin-2 (Aldesleukin, Proleukin)
- peginterferon alfa-2b (Sylatron)

Immune Checkpoint Inhibitors
- ipilimumab (Yervoy)
- nivolumab (Opdivo)
- pembrolizumab (Keytruda)

Oncolytic Virus Therapy
- talimogene laherparepvec (Imlygic/T-VEC)

Combination
- ipilimumab (Yervoy) + nivolumab (Opdivo)

As of 2/11/20

FDA-APPROVED IMMUNOTHERAPIES FOR NON-MELANOMA SKIN CANCER

Immune Checkpoint Inhibitors
- avelumab (Bavencio)
- cemiplimab-rwlc (Libtayo)
- pembrolizumab (Keytruda)

Immunomodulator
- imiquimod (Aldara, Zyclara)

As of 2/11/20

Identifying Biomarkers to Detect Response to Immunotherapy

Most cancer is caused by genetic changes in DNA. Detecting these changes at the microscopic level with biomarkers is becoming an increasingly valuable part of diagnosing and treating melanomas and other skin cancers. As a result, the use of biomarkers is expanding rapidly. Biomarkers are substances, such as genes, proteins or molecules, produced by cancer cells or other cells in the body. Biomarkers are also called tumor markers, molecular markers, biological markers or serum markers. Other biomarkers may be cells, especially immune cells. Evidence suggests that certain T-cells, for example, when found at higher numbers in melanoma tumors are associated with a better prognosis and response to immunotherapy.

Biomarkers may be prognostic, predictive or diagnostic. A prognostic biomarker provides information about a person's overall cancer outcome, regardless of therapy, while a predictive biomarker gives information about the effect of a specific treatment approach. Diagnostic biomarkers help determine the type of tumor.

The following biomarkers may be used to make immunotherapy treatment decisions for melanoma and other skin cancers.

Lactate dehydrogenase (LDH) is the only accepted serum biomarker for melanoma, and it is tested to determine if a person has an elevated risk for metastasis. A decrease in LDH has been associated with response to immunotherapy. It is a prognostic biomarker that may be elevated if the cancer has progressed. It is released when melanoma cells are damaged or die.

PD-L1 expression may be tested to determine if the tumor cells or immune cells in the tumor's microenvironment contain a higher level, which may mean that a patient could be a good candidate for immune checkpoint inhibitors. However, testing this biomarker alone is not sufficient to determine a therapeutic response to immunotherapy in patients with melanoma or other skin cancers.

Tumor mutational burden (TMB) is an assessment of the number of genetic mutations in a tumor. It can help doctors determine if a patient will respond to immunotherapy. It is believed that the higher the TMB level is, the more likely the patient will respond to immunotherapy.

Tumor-infiltrating lymphocytes (TILs) are determined from a biopsy, and melanomas with higher numbers of TILs and those with TILs inside the tumor have been shown to have a better prognosis and may respond better to immunotherapy. Some treatments result in higher TILs and may be a biomarker for response with these therapies.

Doctors are also genetically testing melanoma tumors to identify subtypes and certain genetic mutations and to determine if any may predict if a person will respond to immunotherapy. This information aids your doctor in making treatment decisions. Some of the genetic factors that may be used more in the future to determine how a person will respond to treatment include *BRAF* (pronounced BEE-raff), *NRAS* (pronounced EN-rass) and *NF1* mutations. Targeted therapies have been developed to treat *BRAF* mutations, specifically *BRAF V600*, and more are expected in the future.

Not all patients who receive immunotherapy respond, and research is ongoing to find out why. Scientists are looking for more biomarkers that may indicate whether a patient is a good candidate for immunotherapy. Biomarkers are expected to be considered more commonly in the future so that immunotherapy is not given to someone who may not respond to it.

► **Learn more about immunotherapy treatments and ongoing research from the Society for Immunotherapy of Cancer (SITC) at sitcancer.org/patientcourse.**

- **Anti-PD-L1** molecules prevent the destruction of T-cells, allowing the T-cells to recognize tumor cells as the enemy and then attack them.

Monoclonal antibodies (mAbs) are a type of approved immune checkpoint inhibitor. Antibodies (a type of protein) are the body's way of tagging a specific antigen (foreign substance). They bind to the antigen, which allows the rest of the immune system to recognize the antigen as foreign and target it for destruction.

Laboratory-made antibodies that are designed to target specific tumor targets, such as antigens or other proteins found on the cancer cell, can work in different ways, including flagging targeted cancer cells for destruction, blocking growth signals and receptors and delivering other therapeutic agents directly to targeted cancer cells.

IMMUNOMODULATORS

Immunomodulatory drugs may stimulate or slow down the immune system in indirect ways. They may boost the immune system and the effects of other therapies on the tumor and the tumor microenvironment, slow or stop the growth of the tumor and its blood vessel formation, improve the bone marrow microenvironment or have an anti-inflammatory effect, slowing the growth of the cancer. They are generally considered systemic treatments, but some may be given directly into the tumor.

ONCOLYTIC VIRUS IMMUNOTHERAPY

This type of immunotherapy uses viruses that directly infect tumor cells to cause an immune response. It is typically given as a local treatment directly to the tumor. One oncolytic virus uses a weakened version of the herpes simplex virus. It has been changed from the original and contains the GM-CSF cytokine. The virus targets specific cancer cells, infects them and duplicates itself continuously within the cell until it ruptures. This rupture kills the cell and releases the GM-CSF cytokine produced by the virus to promote an overall immune boost. This process increases the chance that the attack can also begin killing cancer cells that have not been infected with the virus.

Other viruses are being evaluated as potential cancer treatments.

VACCINATIONS

Two types of vaccines are used against cancer: preventive and treatment. A preventive vaccine is given to a healthy person to keep a cancer from developing. A treatment vaccine, which is injected into the body to create an immune response, is currently being tested in patients with melanoma. Researchers are testing several other vaccines, given alone or with other therapies.

OTHER TREATMENT OPTIONS

Monoclonal antibodies can also be created to carry certain cancer drugs, radiation particles or laboratory-made cytokines (proteins that enable immune cells to send messages to each other) directly to cancer cells. ■

Questions for your doctor

What is the goal of my treatment plan?

What is the process for receiving my immunotherapy treatment?

How long will I be on treatment?

GLOSSARY

Words to know: These definitions may help as you discuss your diagnosis and treatment with your health care team.

Cutaneous: Related to the skin.

Dermatologist: A doctor trained in dermatology, a medical field dealing with skin function and diseases.

Dermis: The middle layer of the three main layers of the skin. The dermis has connective tissue, blood vessels, sebaceous (oil) and sweat glands, nerve endings, hair follicles and other structures.

Durable response: The disappearance of cancer in response to treatment that lasts for longer than a specified time, typically at least one year. This does not always mean the cancer has been cured.

Epidermis: The visible part of your skin; the thin, outermost layer that acts as a barrier to protect the body against infection, injury and the sun's ultraviolet (UV) rays.

First-generation immunotherapy: The first wave of approved treatments that involved stimulating or suppressing the body's immune system to fight cancer.

Hypodermis: The innermost of the three main layers of the skin, sometimes called subcutaneous tissue. It consists of fat, lymphatic vessels and connective tissue.

In-transit metastasis: A type of metastasis in which skin cancer spreads through a lymphatic vessel and begins to grow more than 2 centimeters away from the primary tumor but before it reaches the nearest lymph node.

Lymphocyte: A type of immune cell (white blood cell) in lymph tissue and blood that helps the immune system fight infections and cancer. The main types are B-lymphocytes (B-cells) and T-lymphocytes (T-cells).

Neuroendocrine tumor: Formed from cells that release hormones into the bloodstream in response to a signal from the nervous system. Merkel cell carcinoma is this type of tumor.

Pigment: A substance that gives color. In the body, the pigment melanin gives color to the skin, eyes and hair.

Progression-free survival: The length of time during and after treatment that a patient lives with the disease but it does not get worse.

Satellite tumor: A group of tumor cells in an area near the primary (original) tumor. In melanoma, satellite tumors occur within 2 centimeters of the primary tumor, on or under the skin, and can be seen without a microscope. Microsatellite tumors can be seen only with a microscope.

Sun protection factor (SPF): A rating scale for sunscreen products indicating how long a particular product provides protection against sunburn. The higher the SPF number, the longer the protection.

Topical: Refers to medication applied to a surface of the body, such as the skin or mucous membranes, usually as an ointment, cream, gel, foam, etc.

Tumor-infiltrating lymphocyte (TIL): A type of immune cell (T-cell) that has moved from the bloodstream into a tumor to try to attack cancer cells.

Tumor-infiltrating lymphocyte (TIL) therapy: A melanoma treatment being evaluated in clinical trials that involves obtaining T-cells from a biopsy of tumor cells and growing them in a lab to select specific TILs that can best recognize the cancer cells. These TILs are "activated," grown quickly in large numbers and infused back into the patient to help the immune system identify and fight the cancer cells.

Tumor microenvironment: The area that surrounds and sustains a tumor. It is made up of tumor cells, normal cells, immune cells, molecules and blood vessels.

Ultraviolet (UV) radiation: Invisible rays from the sun that can cause sunburn, premature aging of the skin, melanoma and other skin cancers, as well as eye problems. UV radiation also comes from tanning beds and sun lamps.

Some definitions courtesy of the website of the National Cancer Institute (www.cancer.gov)

SITC Guidelines: The Society for Immunotherapy of Cancer (SITC) offers guidelines for medical professionals regarding the recommended use of immunotherapy treatment and immune-related adverse event management. Guidelines for cutaneous melanoma and several other cancers are currently available at → **www.sitcancer.org/guidelines**

What everyone should know about clinical trials

Every cancer treatment being used today has been part of a clinical trial. Clinical trials allow patients access to treatments before they are approved, and they are considered experimental at that time. If a patient is interested in a clinical trial, it is important to understand the purpose of the study. The treatment being studied is offered to patients who meet certain criteria, with the goal of determining if a therapy, combination of drugs, dosage or procedure is safe; better than the current standard of care; or has other benefits to patients.

Groundbreaking research for immunotherapy is currently underway. One strategy involves adoptive T-cell therapy, in which a patient's T-cells are removed from his or her own blood or tumor tissue, grown in large numbers in a laboratory, then given back to the patient to help the immune system fight cancer. Types of adoptive cell therapy include tumor-infiltrating lymphocyte (TIL) therapy and chimeric antigen receptor T-cell (CAR T-cell) therapy. Other strategies involve identifying biomarkers to indicate which patients will benefit from immunotherapy, and investigating how age may affect patient response to checkpoint inhibitors. Other clinical trials are testing new immune checkpoint inhibitors, cytokines, oncolytic viruses, innate immune stimulators and new combinations of these agents.

As you weigh treatment options, consider clinical trials. Use the resources on this page and in the back of the guide to learn more about this potential option. ■

WHAT ARE CLINICAL TRIALS?

- Clinical trials are medical research studies that are frequently used to test new therapies.
- All participants enrolled are volunteers.
- The details of a trial are outlined in the Informed Consent form, which participants must sign before beginning a trial.
- Participants can withdraw from a clinical trial at any time for any reason.

MYTHS vs FACTS

A clinical trial is a last resort. In some situations, a clinical trial may offer the best option among treatments you're considering and may even be the first option to consider.

If my doctor doesn't bring it up, I can't participate. Thousands of trials take place at the same time, making it very difficult for your doctor to know about every trial. That's why you're encouraged to search for a clinical trial on your own.

I'll have to travel to a major city to take part in a trial. Not necessarily. Although people may travel to take advantage of some trials, more are available all over the country in hospitals, treatment centers and doctors' offices.

Once I start the trial, I have to finish it. Participation is always voluntary. You may choose to leave the trial at any time, for any reason, and opt for standard-of-care treatment.

I'm too old to be in a clinical trial. Seniors may respond differently to treatment and may develop different side effects. Having them enrolled in a trial helps researchers develop the right treatment for older people.

BENEFITS OF PARTICIPATION

- Access to leading-edge treatments that aren't yet available for your type or stage of disease.
- Higher level of care because you will be closely monitored by your oncologist and the clinical trial medical team.
- Being an active partner in your own care.
- Knowing you are contributing to the future of cancer care.

HOW TO FIND A CLINICAL TRIAL

- Ask your doctor about available trials for which you may qualify.
- Search online. Start with this list of clinical trial sites. Depending on your diagnosis, there could be hundreds. Ask friends and family to help.
- Have your exact diagnosis, pathology report and treatment details available to see if you meet a trial's criteria.
- Discuss possible trials with your doctor to determine whether they are an option for you.

CLINICAL TRIAL SITES

Center for Information & Study on Clinical Research Participation
www.searchclinicaltrials.org

CenterWatch
www.centerwatch.com

ClinicalTrials.gov
www.clinicaltrials.gov

Melanoma Research Foundation
www.melanoma.org
Participate in Clinical Trials

National Cancer Institute
www.cancer.gov
Steps to Find a Clinical Trial

See more on page 12.

QUESTIONS TO ASK YOUR DOCTOR

Should I consider a clinical trial?

What tests and treatments are involved?

Is travel required to participate?

Will you continue to manage my care?

Will it affect my daily life, such as my capability to work?

How long will the trial last?

Prepare for potential physical and emotional side effects

A wide-ranging group of services called supportive care can help address the physical, emotional, practical, spiritual, financial and family-related challenges you may experience. A primary focus is to help you prevent, minimize and manage treatment-related side effects. Research has shown that receiving these services as early as possible improves your overall quality of life and may make it easier to complete your therapies. Sometimes referred to as palliative care, these valuable resources are available from diagnosis through survivorship.

Side effects of immunotherapy may not appear until a few months into treatment – or even years afterward – and may affect one or more systems of the body not related to the cancer site. Each drug has a different side effect profile. Before treatment begins, ask your doctor for a list of symptoms to watch for and strategies for managing them. Determine when to contact your doctor's office about symptoms and when to seek emergency care. Alert your health care team as soon as symptoms arise, even those that seem trivial. Prompt treatment can help prevent more serious complications and can keep you more comfortable during treatment.

POTENTIALLY SEVERE SIDE EFFECTS

Although severe side effects are not common, they are possible. Called **immune-related adverse events** (irAEs), they can develop rapidly, becoming serious or even life-threatening without swift medical attention. They may occur if the treatment overstimulates the immune system (see Table 1).

You may not be able to physically feel these symptoms at first, so it's essential to schedule and keep all medical appointments. Routine laboratory tests and imaging may detect irAEs at an early stage. Be sure to contact your medical team if symptoms occur between appointments, and remain alert to the possibility of irAEs for two years after treatment ends. An important point is that many of the side effects associated with immunotherapy can be easily corrected if they are treated rapidly. Thus, it is very important that you contact your health care team as soon as possible if you do develop a side effect.

Infusion-related reactions may occur with immunotherapy given intravenously (by IV), usually soon after exposure to the drug. Common symptoms are itching, rash or fever; more serious symptoms include shaking, chills, low blood pressure, dizziness, breathing difficulties and irregular heartbeat. Reactions are generally mild but can become life-threatening if not promptly treated.

Cytokine release syndrome can occur if immune cells affected by treatment rapidly release a large amount of cytokines into the bloodstream. Symptoms may include fever, headache, nausea, rapid heartbeat, decreased blood pressure and difficulty breathing. Reactions are usually mild but can be life-threatening.

COMMON SIDE EFFECTS

Each type of immunotherapy has different side effects, and every individual responds differently. Symptoms are often more intense when immunotherapies are combined.

Constipation can occur at any time, and the best way to manage is to prevent it. Talk with your doctor about preventive medications or dietary and lifestyle changes you can make. If you are already constipated, ask your doctor before using over-the-counter remedies.

Coughing is a common symptom but may also signal pneumonitis (inflammation of the lungs) or a respiratory tract infection. Contact your doctor immediately so the cause of the cough can be determined and managed, particularly if the cough is new or changing.

Diarrhea, if left untreated, can lead to dehydration and loss of essential nutrients. It may also signal an immune system nearing overload. Ask your doctor about prevention medication before your treatment begins. If you have more than six episodes in 24 hours or diarrhea that routinely keeps you homebound, contact your health care team. Never use over-the-counter antidiarrheals without checking with your health care team.

Fatigue related to cancer treatment is more severe. It lasts longer than typical fatigue and may not be relieved by sleep. A proven remedy

TABLE 1
IMMUNE-RELATED ADVERSE EVENTS (irAEs)

Body System	irAE	Symptoms & Signs
Cardiovascular	Myocarditis	Chest pain, shortness of breath, leg swelling, rapid heartbeat, changes in EKG reading, impaired heart pumping function
Endocrine	Endocrinopathies	Hyperthyroidism, hypothyroidism, diabetes, extreme fatigue, persistent or unusual headaches, visual changes, alteration in mood, changes in menstrual cycle
Gastrointestinal	Colitis	Diarrhea with or without bleeding, abdominal pain and cramping, bowel perforation
Liver	Hepatitis	Yellow skin or eyes (jaundice), nausea, abdominal pain, fatigue, fever, poor appetite
Nervous system	Neuropathies	Numbness, tingling, pain, a burning sensation or loss of feeling in the hands or feet, sensory overload, sensory deprivation
Neurologic	Encephalitis	Confusion, hallucinations, seizures, changes in mood or behavior, neck stiffness, extreme sensitivity to light
	Headache	Pain that persists for more than 24 hours and does not respond to pain medications
Pulmonary/lung	Pneumonitis	Chest pain, shortness of breath, unexplained cough or fever
Renal/kidneys	Nephritis	Decreased urine output, blood in urine, swollen ankles, loss of appetite
Skin	Dermatitis	Rash, skin changes, itching, blisters, painful sores

is regular exercise. Even a daily 10-minute walk can make a difference. Aim for eight hours of sleep each night, pace yourself each day and save your energy for people and activities most important to you.

Flu-like symptoms may occur, including fever, chills, aches, headaches, drowsiness, nausea, vomiting, runny nose, loss of appetite and blood pressure changes. Report symptoms to your doctor immediately.

Headache can be a common side effect. A headache that occurs and does not go away within 24 hours could be a sign of inflammation of the pituitary gland. This should be reported to your health care team.

Heart palpitations may occur. Contact your doctor immediately about abnormal heart rhythm, dizziness or lightheadedness.

Joint pain (arthralgia), **muscle pain** (myalgia) and **pain in general** may occur and typically resolves when treatment ends. People with rheumatologic or other autoimmune conditions may see those symptoms worsen or "flare," so ensure your doctor is aware of all your medical conditions.

Mouth sores (oral mucositis) can begin as tiny sores in the lining of the mouth and may affect the gums, tongue, roof of mouth and/or lips. Pain may range from mild to severe, making it difficult to talk, eat or swallow. Ask your doctor about medications to prevent or minimize this condition. Mouth sores are much easier to treat early, so contact your health care team at the first sign of symptoms.

Nausea and **vomiting** can lead to dehydration in severe cases, interrupting your treatment. Both are easier to prevent than control. Ask your doctor about using antiemetics (anti-nausea drugs) before treatment begins. Non-drug approaches include progressive muscle relaxation, guided imagery, acupuncture, self-hypnosis and biofeedback.

Shortness of breath or trouble breathing after simple walking or exercise may be a sign of inflammation in the lungs or an infection. If this happens with or without a cough, you should inform your health care team.

Skin reactions can include redness and irritation similar to a sunburn, rashes that are bumpy or itchy, or dry, flaky skin that may itch. Be alert for changes in skin color, inflammation, blistering, hives, dryness, cracking around the fingertips or flushed appearance. Skin reactions can potentially become severe if not treated early, so contact your health care team about these symptoms.

Swelling (edema) in legs can be caused by fluid buildup. The effects may be reversed, so tell your health care team about recent weight gain or swelling, stiffness or a heavy feeling in your legs.

Vitiligo appears as white patches of skin that have lost pigmentation (coloration) and occurs when pigment-producing epidermal cells (melanocytes) are destroyed. It is most often seen on the face, backs of hands, knees, elbows and genitals. Affected areas may slowly become larger and are prone to sunburn. Talk with your doctor about treatment options. ■

Take care of your emotional well-being

Cancer can affect you emotionally as well as physically. It's common to experience anger, fear, guilt, insecurity and other emotions. Supportive care services can connect you with resources to help you work through your feelings. These suggestions may also help.

- Allow yourself to fully express your emotions when they occur to help you avoid releasing bottled-up feelings in unhealthy ways.
- Cancer survivors can be a great source of support, friendship and insight. Ask about cancer support groups available in your community, options for online support or phone-based peer support programs.
- Explore meditation, gentle yoga, massage therapy, deep breathing exercises, or other relaxation techniques.
- Get outside, regardless of the season. Fresh air and nature can be therapeutic.
- Express your feelings by writing in a journal.
- Take charge of things you can control. If decision-making feels overwhelming, ask loved ones to handle routine decisions for now.
- Give yourself permission to grieve the loss of the life you had before cancer. Share your feelings with someone you trust.
- Staying positive is important, but give yourself a break when you need it.
- Find something to laugh about every day.
- It's extremely important to talk with your doctor about feeling depressed, hopeless or desperate, particularly if these feelings last more than a few days. Seek medical attention immediately for thoughts of suicide.

FOLLOW-UP CARE IS ESSENTIAL

To help reduce your risk of another skin cancer, three things should be added to your routine.

1 **Tell every health care professional you see from now on that you received immunotherapy. This information may alter providers' recommendations and also alert them to consider whether any new symptoms are related to your immunotherapy treatment.**

2 **Make a follow-up care plan with your oncologist for routine monitoring for early signs of recurrence, as well as to check for late effects of immunotherapy. Ask for a referral to a dermatologist if you don't have one, and give yourself monthly full-body skin checks (learn to detect a melanoma at PatientResource.com/ABCDErule.aspx).**

3 **Be dedicated to protecting your skin. Wear daily moisturizer with built-in sunscreen of at least SPF 15. Generously apply sunscreen with 30+ SPF before going outside, and avoid direct sun between 10 a.m. and 4 p.m. in all seasons. Wear a wide-brimmed hat or billed cap, sunglasses and protective clothing.**

Questions for your doctor

- **Is supportive care/palliative care the same thing as hospice?**
- **Whom do I call if I experience side effects or feel depressed?**
- **What resources are available to help my loved ones cope with my diagnosis?**

Support and financial resources available for you

CANCER EDUCATION

American Cancer Society ..... www.cancer.org
American Society of Clinical Oncology ..... www.cancer.net
CANCER101 ..... www.cancer101.org
Cancer*Care* ..... www.cancercare.org
CancerQuest ..... www.cancerquest.org
Cancer Support Community ..... cancersupportcommunity.org
Centers for Disease Control and Prevention (CDC) ..... www.cdc.gov
The Gathering Place ..... www.touchedbycancer.org
Get Palliative Care ..... www.getpalliativecare.org
Global Resource for Advancing Cancer Education (GRACE) ..... www.cancergrace.org
The Hope Light Foundation ..... hopelightproject.com
LIVESTRONG Foundation ..... www.livestrong.org
National Cancer Institute ..... www.cancer.gov
National Comprehensive Cancer Network (NCCN) ..... www.nccn.org
NCI Contact Center (cancer information service) 800-422-6237
OncoLink ..... www.oncolink.org
Patient Power ..... www.patientpower.info
PearlPoint Nutrition Services ..... www.pearlpoint.org
Pine Street Foundation ..... pinestreetfoundation.org
Scott Hamilton Cares Foundation ..... www.scottcares.org
Triage Cancer ..... triagecancer.org
U.S. National Library of Medicine ..... www.nlm.nih.gov

CAREGIVERS & SUPPORT

4th Angel Patient & Caregiver Mentoring Program www.4thangel.org
CanCare ..... www.cancare.org
CANCER101 ..... www.cancer101.org
Cancer and Careers ..... www.cancerandcareers.org
Cancer*Care* ..... www.cancercare.org
Cancer Connection ..... www.cancer-connection.org
Cancer Hope Network ..... www.cancerhopenetwork.org
Cancer Information and Counseling Line 800-525-3777
Cancer Support Community ..... cancersupportcommunity.org
Cancer Support Helpline 888-793-9355
Cancer Survivors Network ..... csn.cancer.org
Caregiver Action Network ..... www.caregiveraction.org
CaringBridge ..... www.caringbridge.org
Center to Advance Palliative Care ..... www.capc.org
Chemo Angels ..... chemoangels.com
Cleaning For A Reason ..... www.cleaningforareason.org
Cooking with Cancer ..... www.cookingwithcancer.org
Connect Thru Cancer ..... www.connectthrucancer.org
Family Caregiver Alliance ..... www.caregiver.org
Fighting Chance ..... www.fightingchance.org
Friend for Life Cancer Support Network friend4life.org, 866-374-3634
The Gathering Place ..... www.touchedbycancer.org
Guide Posts of Strength, Inc. ..... www.cancergps.org
The Hope Light Foundation ..... hopelightproject.com
Imerman Angels ..... www.imermanangels.org
Lacuna Loft ..... www.lacunaloft.org
The LGBT Cancer Project – Out With Cancer ..... www.lgbtcancer.org
LIVESTRONG Foundation ..... www.livestrong.org
LivingWell Cancer Resource Center ..... www.livingwellcrc.org
Lotsa Helping Hands ..... www.lotsahelpinghands.com
The Lydia Project ..... thelydiaproject.org
Patient Empowerment Network ..... www.powerfulpatients.org
Patient Power ..... www.patientpower.info
SHARE Caregiver Circle ..... www.sharecancersupport.org/caregivers-support
Stronghold Ministry ..... www.mystronghold.org
Support Groups ..... www.supportgroups.com
Triage Cancer ..... www.triagecancer.org
Vital Options International ..... www.vitaloptions.org
Walk With Sally ..... www.walkwithsally.org
Well Spouse Association ..... www.wellspouse.org
weSPARK Cancer Support Center ..... www.wespark.org

CLINICAL TRIALS

ACT (About Clinical Trials) ..... www.learnaboutclinicaltrials.org
Cancer Support Community ..... cancersupportcommunity.org
Center for Information & Study on Clinical Research Participation ..... www.searchclinicaltrials.org
CenterWatch ..... www.centerwatch.com
ClinicalTrials.gov ..... www.clinicaltrials.gov
Lazarex Cancer Foundation ..... www.lazarex.org
LIVESTRONG Foundation ..... www.livestrong.org
National Cancer Institute ..... www.cancer.gov/clinicaltrials
NCI Contact Center (cancer information service) 800-422-6237

FERTILITY & CANCER

Alliance for Fertility Preservation ..... www.allianceforfertilitypreservation.org
American Society for Reproductive Medicine ..... www.reproductivefacts.org
LIVESTRONG Foundation ..... www.livestrong.org
RESOLVE: The National Infertility Association ..... www.resolve.org
SaveMyFertility ..... www.savemyfertility.org

FINANCIAL ASSISTANCE

BenefitsCheckUp ..... www.benefitscheckup.org
Bringing Hope Home ..... www.bringinghopehome.org
Cancer*Care* ..... www.cancercare.org/financial
Cancer*Care* Co-Payment Assistance Foundation ..... www.cancercarecopay.org, 866-552-6729
Cancer Financial Assistance Coalition ..... www.cancerfac.org
Cancer Warrior, Inc. ..... www.cancerwarriorinc.org, 323-578-5083
HealthWell Foundation ..... www.healthwellfoundation.org
Hope Lodge ..... www.cancer.org/hopelodge
Medicare.gov ..... www.medicare.gov
Medicine Assistance Tool ..... medicineassistancetool.org
NeedyMeds ..... www.needymeds.org
Patient Access Network Foundation ..... www.panfoundation.org
Patient Advocate Foundation ..... www.patientadvocate.org
Patient Services, Inc ..... www.patientservicesinc.org
RxAssist ..... www.rxassist.org
RxHope ..... www.rxhope.com
Singlecare ..... www.singlecare.com, 844-234-3057
Social Security Administration ..... www.ssa.gov
Social Security Disability Resource Center ..... www.ssdrc.com
State Health Insurance Assistance Programs ..... www.shiptacenter.org

IMMUNOTHERAPY

Cancer Research Institute ..... www.cancerresearch.org
Cancer Support Community ..... cancersupportcommunity.org
Immuno-Oncology ..... www.immunooncology.com
Society for Immunotherapy of Cancer ..... www.sitcancer.org

MELANOMA & OTHER SKIN CANCERS

A Cure in Sight (ocular melanoma) ..... acureinsight.org
AIM at Melanoma Foundation ..... www.aimatmelanoma.org
American Academy of Dermatology ..... www.aad.org
American Melanoma Foundation ..... www.melanomafoundation.org
Gorlin Syndrome Alliance ..... gorlinsyndrome.org
IMPACT Melanoma ..... www.impactmelanoma.org
Melanoma Hope Network ..... www.melanomahopenetwork.org
Melanoma International Foundation ..... www.melanomainternational.org
Melanoma Research Alliance ..... www.curemelanoma.org
Melanoma Research Foundation ..... www.melanoma.org
Mollie's Fund ..... molliesfund.org
National Council on Skin Cancer Prevention ..... www.skincancerprevention.org
Ocular Melanoma Foundation ..... www.ocularmelanoma.org
Outrun the Sun ..... www.outrunthesun.org
The Skin Cancer Foundation ..... www.skincancer.org
Skin of Steel ..... skinofsteel.org
SunWise ..... www.neefusa.org/sunwise

MENTAL HEALTH SERVICES

American Psychosocial Oncology Society Helpline 866-276-7443

NUTRITION

American Cancer Society ..... www.cancer.org
Cancer*Care* ..... www.cancercare.org
Cancer Support Community ..... cancersupportcommunity.org
LIVESTRONG Foundation ..... www.livestrong.org
OncoLink ..... www.oncolink.org
PearlPoint Nutrition Services ..... www.pearlpoint.org

PAIN MANAGEMENT

American Chronic Pain Association ..... theacpa.org
American Society of Anesthesiologists ..... www.asahq.org
LIVESTRONG Foundation ..... www.livestrong.org
The Resource Center of the Alliance of State Pain Initiatives ..... www.trc.wisc.edu
U.S. Pain Foundation ..... uspainfoundation.org

PRESCRIPTION EXPENSES

America's Pharmacy ..... americaspharmacy.com, 888-495-3181
Cancer*Care* Co-Payment Assistance Foundation ..... www.cancercarecopay.org, 866-552-6729
Cancer Financial Assistance Coalition ..... www.cancerfac.org
Foundation for Health Coverage Education ..... www.coverageforall.org
GoodDays ..... www.mygooddays.org, 972-608-7141
HealthWell Foundation ..... www.healthwellfoundation.org, 800-675-8416
Medicine Assistance Tool ..... medicineassistancetool.org
NeedyMeds ..... www.needymeds.org, 800-503-6897
Patient Access Network Foundation ..... www.panfoundation.org, 866-316-7263
Patient Advocate Foundation Co-Pay Relief ..... www.copays.org, 866-512-3861
Patient Services, Inc. ..... www.patientservicesinc.org, 800-366-7741
RxAssist ..... www.rxassist.org
RxHope ..... www.rxhope.org
RxOutreach ..... www.rxoutreach.com, 888-796-1234
Singlecare ..... www.singlecare.com, 844-234-3057
Together Rx Access ..... www.togetherrxaccess.com, 800-444-4106

REIMBURSEMENT & PATIENT ASSISTANCE PROGRAMS

Amgen Assist 360 ..... amgenassist360.com/patient, 888-427-7478
Bausch Health Patient Assistance Program ..... bauschhealthpap.com, 833-862-8727
Bavencio CoverOne ..... coverone.com, 844-826-8371
Bristol-Myers Squibb Access Support ..... bmsaccesssupport.bmscustomerconnect.com/patient, 800-861-0048
Bristol-Myers Squibb Patient Assistance Foundation ..... bmspaf.org, 800-736-0003
Imlygic Co-Pay and Reimbursement Resources ..... imlygic.com/savings-and-support, 888-657-8371
Intron A Patient Assistance Program merckhelps.com/intron%20%20a, 800-727-5400
Keytruda Patient Assistance ..... merckaccessprogram-keytruda.com/hcc/, 855-257-3932
Libtayo Surround ..... libtayo.com/support, 877-542-8296, option 1
Merck Access Program ..... merckaccessprogram.com/hcc/
Merck Helps ..... merckhelps.com, 800-727-5400
Opdivo with You ..... patientsupport.bmscustomerconnect.com/opdivo-with-you-registration, 855-673-4861
Pfizer Oncology Together ..... pfizeroncologytogether.com/patient, 877-744-5675
Pfizer RxPathways ..... pfizerrxpathways.com, 844-989-7284
Prometheus IV Bolus Proleukin Inpatient Reimbursement 877-776-5385
Sanofi Genzyme Patient Support Services ..... sanofigenzyme.com/en/patient-support/patient-services
Sanofi Patient Connection ..... sanofipatientconnection.com, 888-847-4877
Sylatron Patient Assistance ..... merckhelps.com/sylatron, 800-727-5400

STOPPING TOBACCO USE

American Cancer Society ..... www.cancer.org
BecomeAnEx ..... www.becomeanex.org
National Cancer Institute Smoking Quitline 877-448-7848
QuitSTART ..... teen.smokefree.gov
Smokefree.gov ..... smokefree.gov
SmokefreeTXT ..... smokefree.gov/smokefreetxt

➥ ***For more resources, go to*** PatientResource.com

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