NCCN GUIDELINES FOR PATIENTS®

2018

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Melanoma

Presented with support from:

NCCN FOUNDATION®
Guiding Treatment, Changing Lives.

Available online at NCCN.org/patients

LEARNING that you have cancer can be overwhelming.

The goal of this book is to help you get the best cancer treatment. It explains which tests and treatments are recommended by experts in melanoma.

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 27 leading cancer centers. Experts from NCCN have written treatment guidelines for doctors who treat melanoma. These treatment guidelines suggest what the best practice is for cancer care. The information in this patient book is based on the guidelines written for doctors.

This book focuses on the treatment of melanoma. Key points of the book are summarized in the NCCN Quick Guide™. NCCN also offers patient books on breast, lung, and pancreatic cancer, as well as many other cancer types. Visit NCCN.org/patients for the full library of patient books, summaries, and other resources.

About

National Comprehensive Cancer Network®

These patient guidelines for cancer care are produced by the National Comprehensive Cancer Network® (NCCN®).

The mission of NCCN is to improve cancer care so people can live better lives. At the core of NCCN are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). NCCN Guidelines® contain information to help health care workers plan the best cancer care. They list options for cancer care that are most likely to have the best results. The NCCN Guidelines for Patients® present the information from the NCCN Guidelines in an easy-to-learn format.

Panels of experts create the NCCN Guidelines. Most of the experts are from NCCN Member Institutions. Their areas of expertise are diverse. Many panels also include a patient advocate. Recommendations in the NCCN Guidelines are based on clinical trials and the experience of the panelists. The NCCN Guidelines are updated at least once a year. When funded, the patient books are updated to reflect the most recent version of the NCCN Guidelines for doctors.

For more information about the NCCN Guidelines, visit NCCN.org/clinical.asp.

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NCCN FOUNDATION®
Guiding Treatment, Changing Lives.

NCCN Foundation was founded by NCCN to raise funds for patient education based on the NCCN Guidelines. NCCN Foundation offers guidance to people with cancer and their caregivers at every step of their cancer journey. This is done by sharing key information from leading cancer experts. This information can be found in a library of NCCN Guidelines for Patients® and other patient education resources. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of cancer research, education, and progress of cancer therapies.

For more information about NCCN Foundation, visit NCCNFoundation.org.

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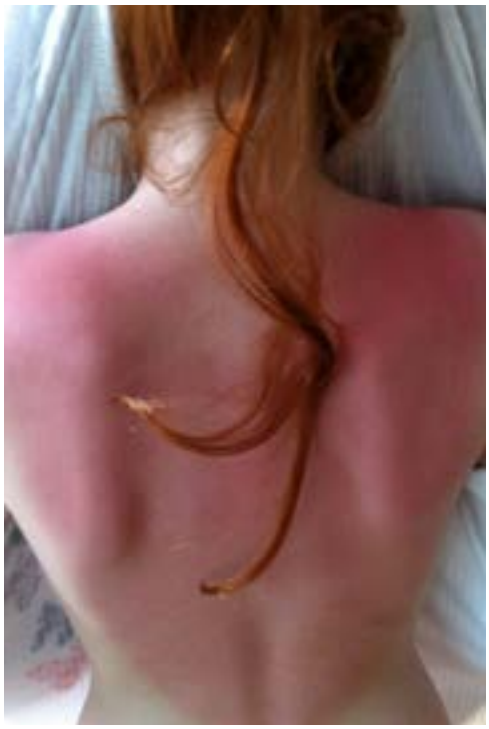
Endorsed by

AIM at Melanoma
Every hour someone in the United States dies from melanoma, the deadliest form of skin cancer. If caught in its early stages, chances of survival are excellent. However, once it has spread, survival rates drop dramatically. The NCCN Guidelines are an important tool for patients with melanoma to help educate them on the treatment options that are available for melanoma patients as well as follow-up care which is essential for their future health.

Melanoma Research Alliance
The MRA endorses the NCCN Guidelines for Patients with Melanoma. This is an important resource to assist patients or caregivers in understanding the treatment approaches available and the progress against this terrible disease.

Melanoma Research Foundation (MRF)
The Melanoma Research Foundation is very pleased to endorse the NCCN Guidelines for Patients, which provide people who are living with cancer the same information that for years has informed doctors about the current best practices in care. We believe that informed and empowered patients live longer, better lives and this information is critical in a time when the treatment landscape is changing so rapidly. www.melanoma.org



Contents

Who should read this book?

Melanoma is a type of cancer that starts in skin cells that give skin its color. Melanoma can also form in the eyes, nose, mouth, genitalia, or, rarely, in the internal organs. This book focuses on treatment for melanoma that starts in the skin. Patients and those who support them—caregivers, family, and friends—may find this book helpful. It may help you discuss and decide with your doctors what care is best.

Are the book chapters in a certain order?

Early chapters explain concepts that are repeated in later chapters. Starting with **Part 1** may be helpful for many people. It explains what melanoma is. Knowing more about this cancer may help you better understand its treatment.

Part 2 explains the tests doctors use to assess for this type of cancer and plan treatment. **Part 3** describes how doctors rate and describe the extent (stage) of the cancer. **Part 4** describes the types of treatments that may be used. **Part 5** is a guide to treatment options. **Part 6** offers some helpful tips for anyone making treatment decisions.

Does this book include all options?

This book includes information for many situations. Thus, you will likely not get every test and treatment listed. Your treatment team can point out what applies to you and give you more information. As you read through this book, you may find it helpful to make a list of questions to ask your doctors.

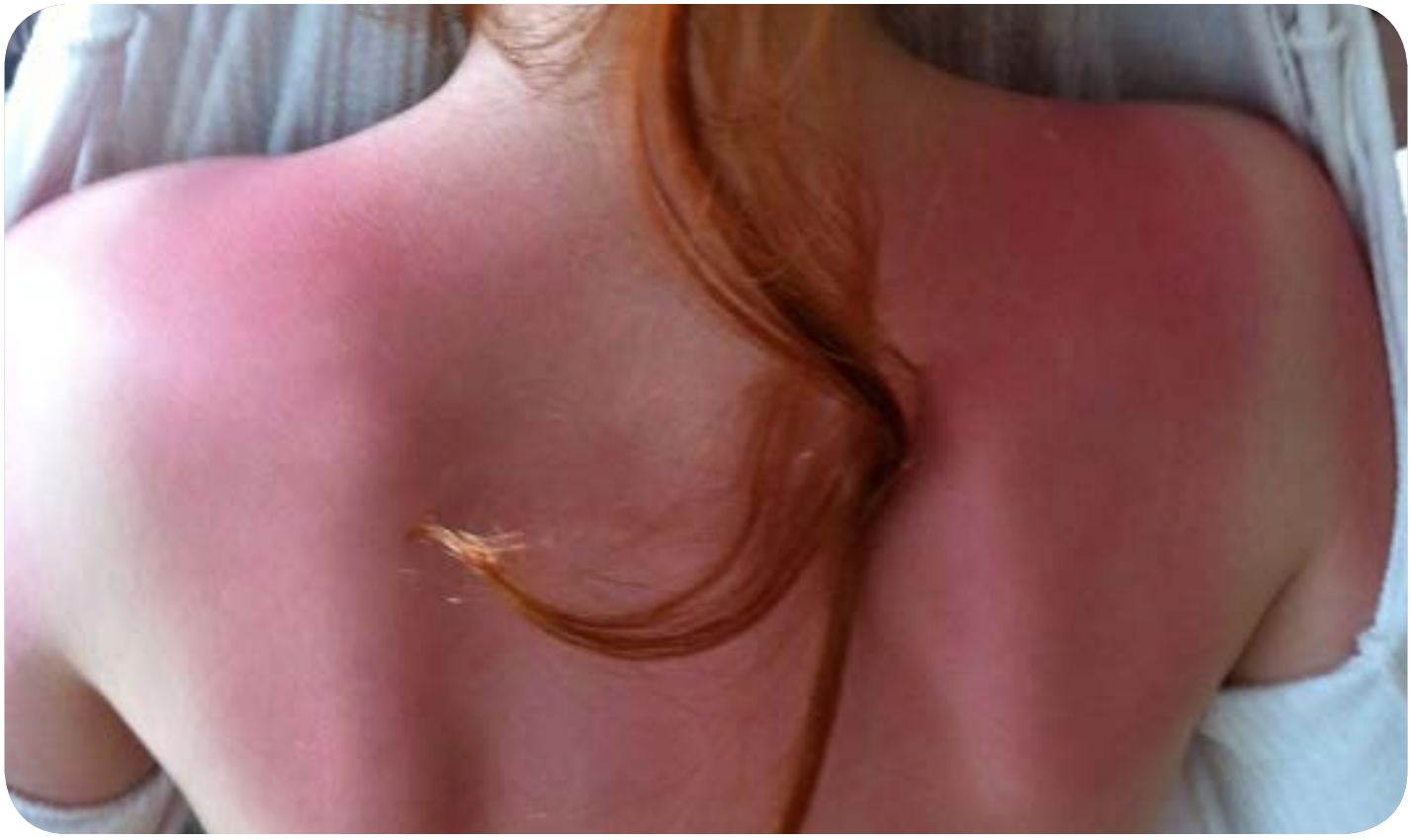
The recommendations in this book are based on science and the experience of NCCN experts. However, each patient is unique and these recommendations may not be right for you. Your doctors may suggest other tests or treatments based on your health and other factors. If other suggestions are given, feel free to ask your treatment team questions.

Help! What do the words mean?

In this book, many medical words are included. These are words you will likely hear from your treatment team. Most of these words may be new to you, and it may be a lot to learn.

Don’t be discouraged as you read. Keep reading and review the information. Feel free to ask your treatment team to explain a word or phrase that you don’t understand. Words that you may not know are defined in the text or in the *Dictionary*. Acronyms are also defined when first used and in the *Glossary*. One example is CBC for **c**omplete **b**lood **c**ount.

1
Melanoma basics



You've learned that you have or may have melanoma. Part 1 explains some basics about this cancer that may help you learn about it and start to cope. These basics may also help you start planning for treatment.

Layers of the skin

The skin is the largest organ of the body. The skin has two layers. The outer layer, which can be seen, is called the epidermis. The second layer, under the epidermis, is called the dermis. Under the dermis is the subcutaneous tissue. **See Figure 1**.

Epidermis

The main job of the epidermis is to protect the body and help control body temperature. It is made up of four types of cells, including pigment cells called melanocytes.

Melanocytes are located at the bottom of the epidermis. These cells make a pigment called melanin, which moves to the top of the epidermis and gives skin its color. People with darker skin have the same number of melanocytes as people with lighter skin. The darkness of skin is based on how much melanin is made by the melanocytes. Higher levels of melanin cause the skin to be darker.

Dermis

The dermis is much thicker than the epidermis. It contains hair roots, blood vessels, lymph vessels, glands, and nerve endings. Blood and lymph vessels in the dermis bring nutrients to the dermis and epidermis. Glands make fluids or chemicals the body needs. Connective tissue holds all these structures in place and allows the skin to stretch.

Under the dermis is the subcutaneous tissue. Subcutaneous means "below the skin." It is mostly made of fat and connective tissue. It is not part of the skin but connects the skin to muscles and bones. It also saves body heat, stores energy, and absorbs shock to protect the body from injury.

About melanoma

Cells are the building blocks that form tissue in the body. Genes are the instructions in cells for making new cells and controlling how cells behave. Abnormal changes (mutations) in genes can turn normal cells into cancer cells.

Normal cells divide to make new cells. New cells are made as the body needs them to replace injured or dying cells. Normal cells stay in one place and do not spread to other parts of the body. When normal cells grow old or get damaged, they die.

Cancer cells do not do this. Cancer cells don't stay in place as they should. Cancer cells make new cells that aren't needed and don't die quickly when old or damaged. Over time, cancer cells grow and divide enough to form a malignant tumor. **See Figure 2**. The first tumor formed by the overgrowth of cancer cells is called the primary tumor. Researchers are still trying to learn what causes genes to mutate and cause cancer.

Figure 1
Parts of the skin

The skin has two layers. The outer layer is called the epidermis. The second layer is called the dermis.

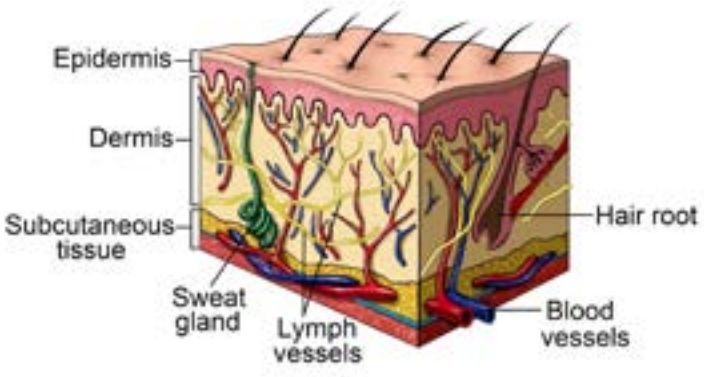
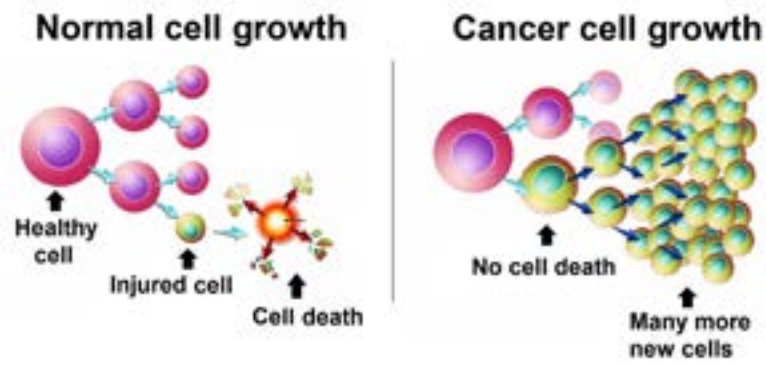


Figure 2
Normal versus cancer cell growth

Normal cells divide to make new cells as the body needs them. Normal cells die once they get old or damaged. Cancer cells make new cells that aren't needed and don't die quickly when old or damaged.



Melanoma skin tumors are made of abnormal pigment cells (melanocytes) that have become cancer cells. **See Figure 3**. These tumors are usually brown or black in color because the cells still make melanin. Melanoma is more dangerous than most other common skin cancers because it is more likely to spread if it isn't found early. However, most melanomas—about 84 out of 100—are found early before they have spread and so are likely to be cured with treatment.

Melanoma has the potential to spread through the dermis to nearby tissues and other parts of the body. The deeper a melanoma grows into the dermis, the higher the risk of spreading through lymph vessels or blood vessels. This is why finding melanoma as early as possible is so important. Most people can be cured if melanoma is found and treated early.

Melanocytes are located at the bottom of the epidermis. These cells make melanin, which spreads to the top of the epidermis and gives skin its color. Melanoma tumors are made of abnormal melanocytes that have become cancer cells.

How melanoma spreads

Unlike normal cells, cancer cells can spread to other parts of the body. This process is called metastasis. The uncontrolled growth and spread of cancer cells makes cancer dangerous. Cancer cells can replace or deform normal tissue causing organs to stop working.

Cancer cells often spread to nearby and distant sites through lymph or blood. Lymph is a clear fluid that gives cells water and food.

Lymph leaks out of blood vessels and then flows through tiny tubes called lymph vessels mostly in one direction toward the heart, where lymph re-enters the blood. Lymph also has white blood cells that fight germs.

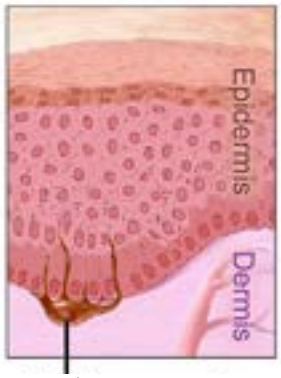
A lymph node is a small group of special disease-fighting cells. Lymph nodes filter lymph and remove germs. Lymph nodes are connected to each other by lymph vessels.

Lymph vessels and nodes are found throughout the body. But, the main nodal basins are found in the head and neck, armpits, and groin area. **See Figure 4.** Once melanoma has grown into the dermis, it can reach the lymph vessels. The melanoma cells can then travel through the lymph vessels to the lymph nodes and other parts of the body. Melanoma can spread anywhere in the body, including the brain. Cancer that spreads from the primary site to a new location is called metastasis.

- Metastasis to a nearby body part is called a local metastasis.
- Metastasis to a body part far from the first tumor is called a distant metastasis.
- Melanoma that has spread into a nearby lymph vessel, but not to lymph nodes, is called an in-transit metastasis.
- Melanoma that has spread to a small area of skin near the first tumor is called a satellite metastasis.

Figure 3
Melanocytes of the epidermis

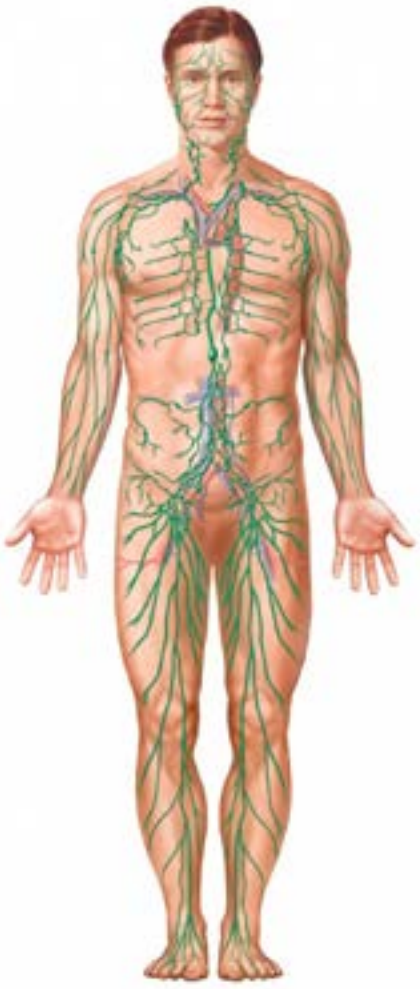
Melanocytes are located at the bottom of the epidermis. These cells make melanin, which spreads to the top of the epidermis and gives skin its color. Melanoma tumors are made of abnormal melanocytes that have become cancer cells.



Derivative work of Anatomy: The Skin by Don Bliss available at: http://visualsonline.cancer.gov/details.cfm?imageid=4366

Figure 4
Lymph nodes and vessels

Lymph nodes and lymph vessels are found throughout the body. A lymph node is a small group of special disease-fighting cells. Lymph nodes are connected to each other by tiny tubes called lymph vessels.



Types of melanoma

Melanoma may be found anywhere in the body. The most common area is the skin. Other rare types include mucosal melanoma and uveal melanoma. Mucosal melanoma may occur in the mucous membranes that line the sinuses, oral cavity, anus, vulva, vagina, GI (**g**astro**i**ntestinal) tract, and other areas of the reproductive tract. Uveal melanoma occurs in the uveal tract of the eyes. The uveal tract is the middle layer of the eye that contains the choroid, ciliary body, and iris.

This book focuses on melanoma that starts in the skin. Below is a list of the four major types of melanoma skin cancer. Learning the unique features of each can help you recognize these features, and may allow for earlier detection. These features include color, shape, location, and growth pattern.

Superficial spreading melanoma

Superficial spreading melanoma is the most common type of melanoma. It is also the most common type diagnosed in younger people. It usually looks like a brown-black stain that is spreading from a mole. But, most melanomas do not develop from a pre-existing mole. **See Figure 5**.

A mole is a spot on the skin formed by a cluster of melanocytes—cells that make melanin to give skin its color. This type of melanoma normally occurs on skin that is sometimes exposed to high levels of sunlight or artificial UV (**u**ltra**v**iolet) light (such as from tanning beds), including the trunk and legs.

Nodular melanoma

Nodular melanoma grows more quickly into the dermis than other types of melanoma. It tends to be deeper than other types of melanoma at the time it is found. The dermis is the second layer of skin, located under the epidermis. Once in the dermis, it can spread to other tissues.

Nodular melanoma looks like a dome-shaped bump and feels firm. It tends to ulcerate and bleed more often than other types of melanoma.

Lentigo maligna melanoma

Lentigo maligna melanoma is the slowest growing type of melanoma. It tends to develop in sites of chronic sun exposure in older adults. It is not generally associated with having a lot of moles. When it begins, it looks like a dark, flat stain with an uneven border and may be mistaken for a harmless sunspot. This type of melanoma usually occurs on chronically sun-exposed areas of the face, ears or arms.

Acral lentiginous melanoma

This type of melanoma is not related to UV light exposure. It occurs on the palms of the hands or soles of the feet, including fingernails and toenails. It can appear as a dark spot, like a bruise that doesn't go away. In a nail, it can look like a dark stripe. Acral lentiginous melanoma is the least common type of melanoma. But, in people with darker-colored skin such as Asians, Hispanics, and African Americans, it is the most common type of melanoma, since sun-related melanoma is less frequent.

Signs and symptoms

Often, the first sign of melanoma skin cancer is a mole or spot on the skin that looks abnormal—not normal. It may present as a new "mole" or an existing mole that has changed over the past few weeks or months. But, most melanomas do not arise from existing moles. Finding melanoma before it grows deep in the skin is important. This is because deeper melanomas are more likely to have spread to other parts of the body. Treatment is more likely to cure melanoma if it has not spread.

Skin self-exam: A mole that changes is very important

You should learn about the differences between normal and abnormal pigmented spots or lesions on the skin. The “ugly duckling rule” and the “ABCDE rule” are easy ways to remember how to tell a normal mole or spot (lesion) apart from a melanoma.

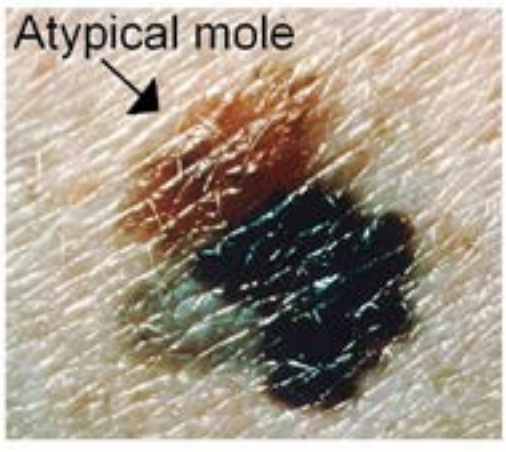
Normal moles tend to have an even tan, brown, or black color. Most normal moles are less than ¼ inch in size—about the width of a pencil eraser. However, normal moles may be larger than ¼ inch and some melanomas are smaller than ¼ inch. Normal moles are round or oval and can be either flat or raised. They stay the same size, shape, and color for many years. Later in life, they often fade away.

In contrast, melanoma often presents as a spot that does not “match” a person’s other moles. Or, it may cause an existing mole to change size, shape, or color. Itching, scaling, oozing, bleeding, redness, swelling, and tenderness are also possible but less common signs of melanoma.

You should check your skin on a regular basis to recognize abnormal spots from normal ones. Use a full-length mirror and a hand-held mirror for areas that are hard to see. A partner may be able to help. Inspect all areas of your body. Remember, change in any spot (lesion) on your skin is an important sign. Know your skin so you can tell if there are any changes in existing spots or new areas of concern. Be sure to show your doctor any spots that have changed or that concern you. **See Figure 6** on page 14.

Figure 5
Superficial spreading melanoma

Superficial spreading melanoma is the most common type of melanoma.



Melanoma courtesy of the National Cancer Institute
available at: http://visualsonline.cancer.gov/details.cfm?imageid=9189

ABCDE rule

Asymmetry: One half or side of the spot or lesion does not match the other half or side.

Border irregularity: The edges of the lesion are ragged or notched.

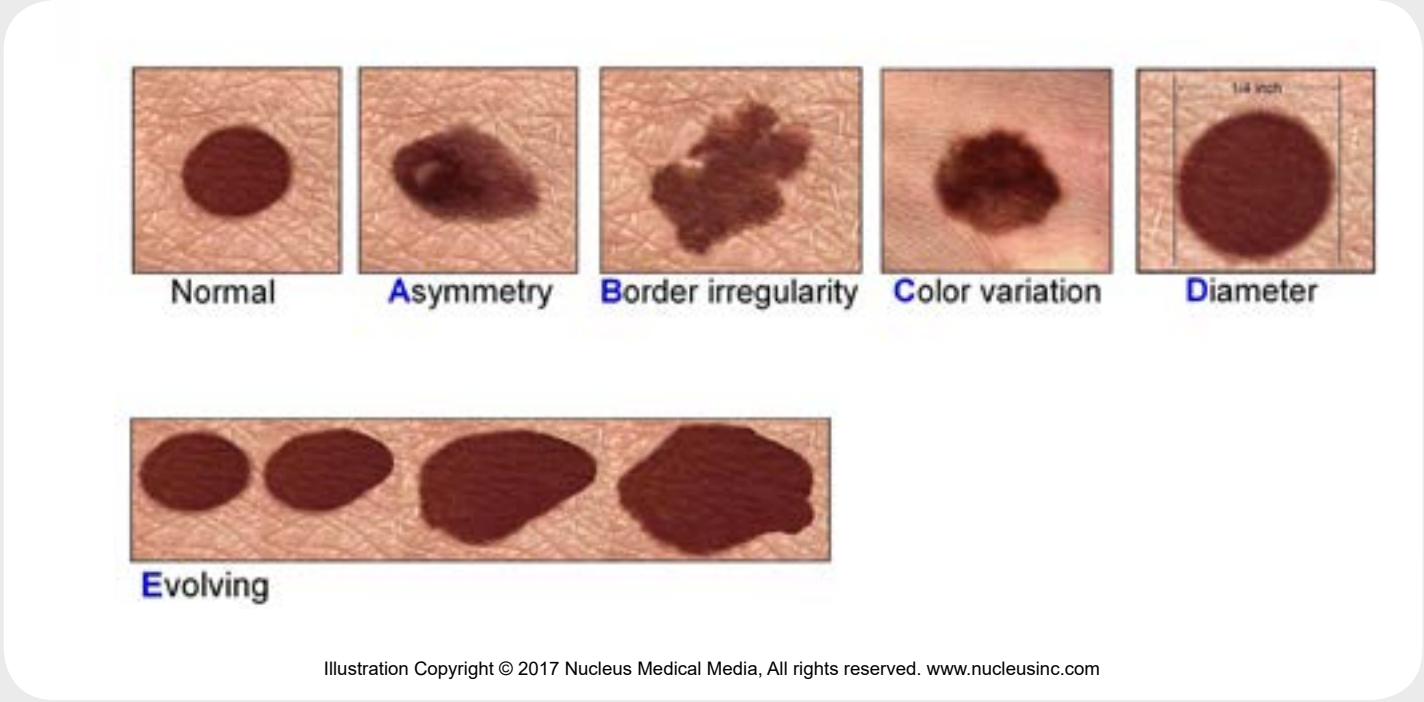
Color: The color of the lesion is not the same throughout. There may be different shades of tan, brown, or black and sometimes patches of red, blue, or white.

Diameter: The lesion is wider than a ¼ inch—the size of the top of a pencil eraser. However, doctors have found melanomas as small as ⅛ inch.

Evolving: The lesion has changed in size, shape, color, or texture over the past few weeks or months. This is a key factor for recognizing melanoma, especially when the lesion looks different from the rest of a person's moles, like an "ugly duckling."

Figure 6
ABCDE rule: Moles with and without signs of cancer

The ABCDE rule is an easy way to remember how to tell a normal spot on skin apart from a melanoma.



Risks and prevention

Exactly what causes melanoma is unknown. But, many risk factors for melanoma are known. A risk factor is anything that increases the chance of getting a disease. Some risk factors are passed down from parent to child through genes. Other risk factors are activities that people do. Having one or more risk factors doesn't mean you'll get melanoma. Likewise, melanoma occurs in some people who have no risk factors. Key melanoma risk factors are described next.

Ultraviolet energy

Melanoma often occurs on parts of the body exposed to UV energy. UV energy is an invisible light energy. The main source of UV energy or rays is sunlight. Tanning beds also expose the skin to UV rays and are known to cause skin cancer, including melanoma. Both UVA (**u**ltra**v**iolet-**A**) and UVB (**u**ltra**v**iolet-**B**) rays contribute to the development of melanoma and skin cancer. Too much exposure damages the skin and increases the risk for skin cancer. Whether sun exposure was too much depends on UV intensity, length of exposure, and how well the skin was protected. Severe sunburns with blisters, especially in youth, increase the risk for melanoma.

Many or atypical moles

Moles are made up of clusters of melanocytes. Babies usually don't have moles at birth. They first appear during youth and continue to appear until about age 40. Most adults have moles. Most moles don't turn into melanoma. But, having many moles, large moles, or atypical moles puts you at higher risk for melanoma. An atypical mole is a mole that has some features of melanoma listed in the "ABCDE rule" and looks different from a normal or common mole. Most atypical moles do not become cancer.

Fair complexion

Having a fair complexion raises your risk for developing melanoma. Examples of a fair complexion are red or blond hair, blue or green eyes, or skin that easily freckles or sunburns. Fair skin is less protective against UV energy because it has less melanin.

Family history

Although rare, melanoma can run in families. Thus, you have a higher risk of developing melanoma if a blood relative has had melanoma. The more family members with melanoma, the more you are at risk.

Tell your doctor if any of your family members had melanoma, pancreatic cancer, astrocytoma (brain tumor), uveal melanoma (in the eye), or mesothelioma. Your doctor can help you understand your risk and if needed, refer you to a qualified cancer genetics counselor for possible testing for gene mutations.

Xeroderma pigmentosum

Xeroderma pigmentosum is a very rare medical condition in which the skin can't repair itself from UV damage. It is passed down from parents to children. It causes an extreme skin reaction to UV energy because the skin can't heal itself well. Xeroderma pigmentosum increases the risk for both melanoma and other types of skin cancer.

Age

Most people who develop melanoma do so after age 60. But, melanoma is one of the most common cancers in people younger than age 30, particularly in young women who tan frequently or use tanning beds. People with a strong family history of melanoma may also develop melanoma at a young age.

Immune suppression

Some diseases and drugs weaken (suppress) the immune system—the body's natural defense against infection and disease. Individuals with a weakened immune system may have a higher risk of developing melanoma and other skin cancers.

Prevention

The number of people with melanoma is increasing, but there are ways to lower your risk. Check your skin and tell your doctor about any changes in your moles or skin. If you have many moles, a dermatologist should check your skin regularly. A dermatologist is a doctor who's an expert in skin diseases.

One of the most important ways to prevent melanoma skin cancer is to limit your sun exposure and to avoid tanning in the sun or in tanning beds. It is helpful to avoid peak sun exposure between the hours of 10:00 AM – 4:00 PM in the summer months or sunny climates.

Parents should make sure their children practice sun protection. Protecting children is very important since sunburns at an early age can greatly increase the risk for melanoma later in life.

There are many ways to protect your skin. Things you may find helpful are listed here.

- Stay in the shade. This is the best way to avoid UV light when outdoors.
- Wear clothes that protect your skin. Long-sleeved shirts, long pants, and hats with brims make a difference.
  - You can find clothing at sporting goods stores made from fabrics designed to limit UV exposure.
- Use broad-spectrum sunscreen with an SPF (**s**un **p**rotection **f**actor) of 30 or higher every day, because UV light is always present. Broad-spectrum sunscreen protects against UVA and UVB rays.
  - The SPF allows a person to spend longer time in the sun without burning. The SPF refers mainly to protection from UVB rays.
  - An SPF of at least 15 has been shown to reduce the risk of skin cancer and damage to the skin that causes it too look older (photoaging).
  - Re-apply sunscreen if you sweat and after swimming since it may have come off.
  - Don't use sunscreen to increase the time spent in the sun. UV light still reaches the skin when wearing sunscreen.
- Wear sunglasses with 99% to 100% UVA and UVB protection. These glasses provide the best protection for the eye area.
- Don't use tanning beds. They expose skin to higher levels of UV rays than natural sunlight and are not safer than sun exposure.
  - Tanning bed use is linked with a higher risk of melanoma and other types of skin cancer.

Review

- The skin has two layers. The top layer is the epidermis. The second layer is the dermis.
- Cells that give skin its color—called melanocytes—are in the top layer.
- Melanoma is a cancer of the cells that give skin its color.
- Melanoma can spread throughout the body if it grows into the second layer of skin.
- Your risk for melanoma is higher if your skin is fair, freckled, or has many moles.
- Lower your cancer risk by using sun protection and by not using tanning beds.
- Learn what skin cancer looks like so you can check your skin often.

I was stunned. I am too young, too busy, and too healthy to have melanoma! However, being diagnosed with melanoma has been a blessing. It has opened doors that have allowed me to help others. I now can empathize with so many people who have been in my shoes.

- Seth, current age 36
  diagnosed at age 33

2
Tests for melanoma

Treatment planning starts with testing. This chapter describes the tests that are used to confirm (diagnose) melanoma and plan treatment. This information can help you use the *Treatment guide* in Part 5. It may also help you know what to expect during testing. Not every person with melanoma will receive every test listed.

General health tests

Your doctor or health care provider may send you to a dermatologist if you have signs of skin cancer. A dermatologist is a doctor who's an expert in diseases of the skin. Most skin changes aren't cancer, but sometimes only a dermatologist will know. This section describes common exams and tests used by dermatologists.

Medical history

Your medical history includes any health events in your life and any medications you've taken. This information may affect which cancer treatment is best for you. It may help to make a list of old and new medications while at home to bring to your doctor's office.

Your doctor will ask about any symptoms and medical conditions that you have had. There will be specific questions about your skin and moles. Some health problems, including melanoma, can run in families. Therefore, your doctor will ask about the medical history of your immediate family and other risk factors you have for melanoma. A risk factor is something that increases the chance of getting a disease. (See page 15 for more details on risk factors.)

A medical history is needed for treatment planning. It may help to make a list of old and new medicines while at home to bring to your doctor's office.

Physical exam

Doctors often give a physical exam along with taking a medical history. A physical exam is a review of your body for signs of disease. Your doctor will also perform a medical skin exam.

For this, your doctor will carefully inspect your skin for lesions and areas that look abnormal (not normal). A lesion is an area of abnormal tissue that has been damaged by disease or injury.

- Your doctor will note the size, shape, color, and texture of any lesions.
- Your doctor will also feel for enlarged lymph nodes in the area where the melanoma lesion is or was located.

Unusual symptoms, such as bleeding or scaling, may be other signs of cancer. Be sure to have skin exams on a regular basis.

Besides your skin, other parts of your body may be examined to look for signs of cancer. During this exam:

- Your doctor may listen to your lungs, heart, and intestines.
- Parts of your body, such as your liver or spleen, may be felt to see if organs are of normal size, are soft of hard, or cause pain when touched.

Tumor tissue tests

To confirm if you have melanoma, a sample of tissue must be removed from the concerning spot on your skin to test for cancer cells with a microscope. This is called a biopsy. Based on the physical and skin exam, your doctor may perform a skin biopsy.

There are many types of skin biopsies used for melanoma. Most biopsies try to remove all (or mostly all) of the skin lesion at the outset—to allow for the most accurate diagnosis by the pathologist.

The type of biopsy you will have depends on the size and location of the concerning spot (lesion) on your skin. A skin biopsy is an important test that is needed for treatment planning. Other tests may also be needed. Types of skin biopsies include:

Excisional biopsy

An excisional biopsy attempts to remove the entire lesion and a small amount of normal-looking skin around the edge. The normal-looking skin removed is called the surgical margin. An excisional biopsy with 1- to 3-mm (**m**illi**m**eter) surgical margins is preferred to confirm (diagnose) melanoma.

An excisional biopsy for melanoma can be done using a surgical knife in an “elliptical” excision, where stitches (sutures) are placed. It can also be done with a deep shave/saucerization biopsy, which uses a different kind of surgical blade. Or, it can be done with a punch biopsy tool that is similar to a cookie cutter.

When an elliptical excisional biopsy is done, the direction and width of the surgical cut should be done in a way that it won’t affect future treatment. If this can’t be done, your doctor may perform an incisional biopsy instead.

Incisional biopsy

An incisional biopsy removes only part of the lesion with a surgical knife, surgical blade, or punch biopsy. This type of biopsy may be done for a very large lesion. It may also be used for a lesion that’s in a place where it can’t be easily removed such as your face, ear, palm of your hand, or sole of your foot.

Punch biopsy

A punch biopsy can be excisional for some melanomas or partial for larger lesions. It uses a sharp hollow device—like a cookie cutter—to remove a small but deep sample of both skin layers. **See Figure 7**. This kind of biopsy may be better for very large lesions or certain areas of the body. These areas include the face, ear, finger, toe, palm of the hand, or sole of the foot.

Shave biopsy

A superficial shave biopsy removes the epidermis and the top part of the dermis. The epidermis is the outer layer of skin. The dermis is the second layer of skin, under the epidermis. A superficial shave biopsy is usually not done if your doctor thinks the melanoma has grown deeply into the dermis.

A deep shave biopsy, also called a “saucerization," is used to remove the entire lesion and is the most common type of excisional biopsy performed. A deep shave biopsy should not be confused with a superficial biopsy. Superficial shave biopsies are often used to remove moles that look normal and for skin diseases other than melanoma.

What to expect during a skin biopsy

Before a biopsy, your doctor will numb your skin with local anesthesia. Local anesthesia is medicine that results in a temporary loss of feeling in a small area of the body to prevent pain during the procedure. Tell your doctor if you’ve had any reactions to anesthesia in the past.

With local anesthesia, you'll feel a small needle stick and a little burning with some pressure for less than a minute. Then, there will be a loss of feeling in that area for a short time. You may feel a little pressure during the biopsy, but no pain.

After the biopsy, your doctor may close the wound with sutures (for a punch or elliptical biopsy) and a bandage. There are usually no side effects, but scars can form after biopsies. If you are on blood thinners, adjustments may be needed before a biopsy can be done.

At the lab

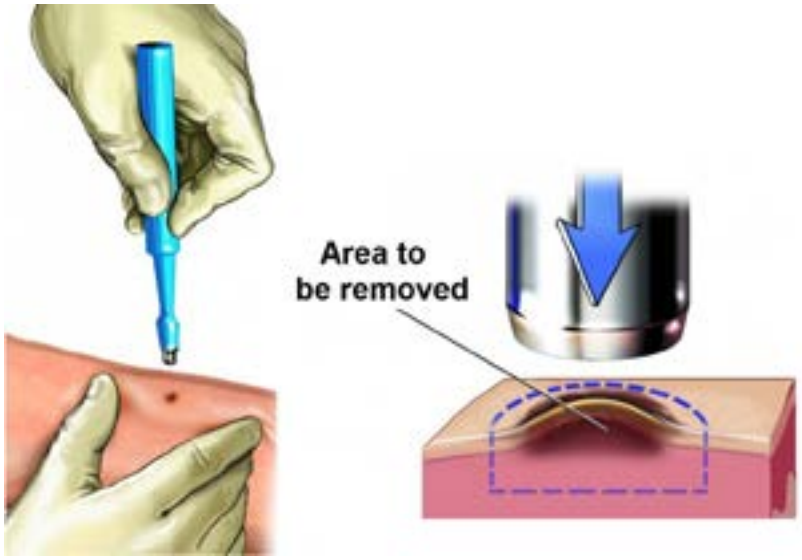
Your doctor will send the biopsy tissue sample to a lab so a pathologist can examine it with a microscope for cancer cells. A pathologist is a doctor who's an expert in testing cells and tissues for disease. A pathologist who has experience with skin lesions should examine the biopsy sample.

If the pathologist finds melanoma cells, he or she will assess if the cells are growing into the dermis and measure how deeply they are growing. The pathologist will also assess other features of the melanoma and describe them in the pathology report. If test results of the first biopsy are unclear, your doctor may perform another biopsy. Or, the pathologist may do other tests on the tissue sample.

If the pathologist finds cancer cells in the biopsy sample, your doctor may order more tests. Though rare, depending on the extent of the melanoma, other tests may be done to see if it has spread. Cancer that has spread from the first tumor to other sites in the body is called a metastasis. Metastases are more likely if the skin tumor has grown deep into the dermis—the second layer of skin. The next section describes how pathology results help to stage melanoma and the possible tests that may be used to check for metastases.

Figure 7. Punch biopsy

A punch biopsy uses a sharp hollow device—like a cookie cutter—to remove a deeper sample of both skin layers. As with a shave biopsy, it can be partial or excisional.



The pathology report

A pathology report is a document with information about tissue removed from your body during a biopsy or surgery. A pathologist examines the tissue with a microscope to check for cancer cells and then writes the results in the pathology report. Your doctors will use this information to decide which treatment is best for you.

The pathology report includes many important test results and details of the tumor. It states whether cancer cells were found and, if so, what types of cancer cells. Other findings in the pathology report are used to determine the extent of the cancer. This is called staging and it is explained in Part 3.

The process of preparing the tissue, examining it, and giving results to your doctor takes at least several days.

At times, the pathologist may have questions and request a 2nd opinion from another pathologist. For melanoma, the tissue samples should be sent to a dermatopathologist or pathologist experienced in pigmented skin lesions to examine. A dermatopathologist is a doctor who's an expert in testing skin cells and tissues for disease. Contact your treatment team if you have questions about your pathology report or if you would like a copy of it.

Pathology results

- **Diagnosis.** Whether melanoma is present and if so, the subtype, for example, superficial spreading melanoma.
- **Breslow thickness.** How deep the tumor has grown into the skin, measured in millimeters.
- **Ulceration status.** Whether or not the tumor's top skin layer is present and intact (not ulcerated) or is broken or missing (ulcerated).
- **Dermal mitotic rate.** A measure of how many melanoma cells are actually growing and dividing.
- **Peripheral margin status.** Presence or absence of cancer cells in the normal-looking tissue around the sides of a tumor removed during initial biopsy or subsequent surgery.
- **Deep margin status.** Presence or absence of cancer cells in the normal-looking tissue under a tumor removed during initial biopsy or subsequent surgery.
- **Microsatellitosis.** Tiny tumors (satellites) that have spread to skin near the first melanoma tumor and can only be seen with a microscope.
- **Tumor location.** The area of the body where the tumor is found.
- **Tumor regression.** The presence of white blood cells called lymphocytes and scar-like changes that suggest a person's immune system is attacking the skin melanoma.
- **Tumor-infiltrating lymphocytes.** Presence or absence of white blood cells that may be present in primary melanomas.
- **Vertical growth phase.** Direction of tumor growth is down into the skin.
- **Angiolymphatic invasion.** Melanoma has grown into (invaded) lymph vessels or blood vessels.
- **Neurotropism.** Melanoma cells are evident in or around nerves in the skin.
- **Histologic subtype.** Classification based on microscopic features of the melanoma.

Lymph node tissue tests

A biopsy is the removal of a small amount of tissue from your body to test for disease. After a skin biopsy confirms melanoma, a biopsy of the lymph nodes may be recommended to check if the cancer has spread.

- Lymph nodes are small groups of special disease-fighting cells located throughout the body.
- Lymph nodes are connected to one another by lymph vessels—tubes that carry a clear fluid called lymph throughout the body.

Most melanomas are found early, when the chance that cancer cells have spread to a lymph node is small. For early melanomas, lymph node testing is usually not recommended. Your doctor will discuss this with you based on the test results in the pathology report.

There is more than one type of lymph node biopsy. A lymph node biopsy may be done during surgery. Or, it may be done with a very thin needle. Which type of biopsy is recommended depends on certain factors such as whether or not there are signs of cancer spread.

Types of lymph node biopsies include:

Sentinel lymph node biopsy

A sentinel lymph node biopsy is a surgery that removes one or more nearby (regional) lymph node(s) to test for cancer cells. The sentinel lymph node is the first lymph node to which cancer cells will likely spread from the first (primary) tumor.

This type of lymph node biopsy is recommended when there's an increased chance that the melanoma has spread to a lymph node, but the physical exam did not find any enlarged lymph nodes that may be a sign of cancer spread. It is performed to find very tiny (microscopic) cancer cells in a lymph node that cannot be found by physical exam or imaging tests. Because this is a surgical test, it is not recommended when the chance of cancer spread is very small.

For this biopsy, a special dye is injected into the skin near the primary tumor. The dye follows the path the lymph takes in the lymph vessels in the area around the tumor. This allows your doctor to find the first lymph node to which lymph (and possibly a cancer cell) travels when it leaves the tumor. This is called the sentinel lymph node. The sentinel node is usually removed during the same surgery to remove the primary melanoma tumor.

Possible side effects of sentinel lymph node biopsy may include numbness, pain, bruising, and lymph fluid buildup near the biopsy site. Because only one or very few lymph nodes are removed, serious side effects such as lymphedema (swelling due to fluid buildup) are rare.

FNA (fine-needle aspiration) biopsy

This biopsy is often used when your doctor can feel an enlarged lymph node during the physical exam. An FNA biopsy uses a very thin needle to remove small pieces of a lymph node to test for cancer cells. An anesthetic may be applied or injected to numb the area before an FNA biopsy. An FNA biopsy causes little discomfort and doesn't leave a scar. Your doctor may use an ultrasound device or pictures from a test called a CT (**c**omputed **t**omography) scan to guide the needle into the lymph node.

Excisional lymph node biopsy

An excisional lymph node biopsy removes enlarged lymph nodes through a small surgical cut in the skin. This type of biopsy may be needed if your doctor finds an enlarged lymph node during the physical exam or imaging test and an FNA biopsy isn't possible or is unclear.

After removing the lymph node(s), your doctor will test the tissue for cancer cells. Local anesthesia or general anesthesia may be used for this surgery. Local anesthesia is medicine that results in a temporary loss of feeling in a small area of the body to prevent pain during the procedure. In contrast, general anesthesia is medicine that causes a temporary loss of feeling and a complete loss of awareness that feels like a very deep sleep.

Blood tests

Blood tests are not used to find or confirm (diagnose) melanoma. They are generally only used to monitor melanoma once it has spread from the skin and lymph nodes to other parts of the body. Or, they may be used to assess the response to drugs that are being used to treat melanoma. Abnormal levels of certain chemicals in the blood may be a sign that the cancer has spread to distant parts of the body.

One of the chemical levels that doctors look for is a high LDH (**l**actate **d**e**h**ydrogenase) level, but usually in the setting of advanced melanoma at the outset. This would be melanoma that has spread to other sites of the body. Doctors may also use LDH to follow treatment response. LDH is a substance found in the blood that is involved in energy production in cells. If blood test results are abnormal, your doctor may order other tests.

Imaging tests

Imaging tests take pictures of the inside of your body. Before the test, you may be asked to stop eating or drinking for several hours. You should also remove any metal objects that are on your body. Often there are no side effects.

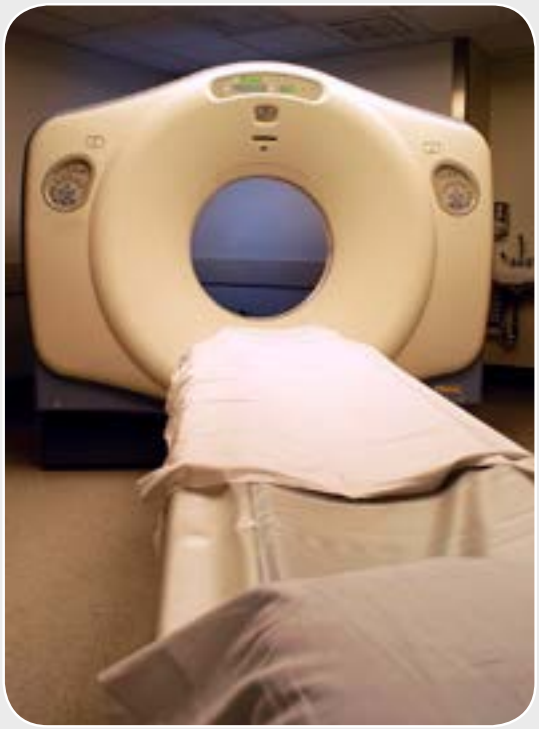
Imaging tests aren't used to find (diagnose) melanoma, but they may be used if you have signs or symptoms that the melanoma has spread. Such symptoms include pain that can't be explained. Imaging tests may be used during or after treatment to check that treatment worked. The imaging tests that may be used for melanoma are described next.

CT scan

CT takes many pictures of a part of the body from different angles using x-rays. A CT scan machine is large and has a tunnel in the middle. **See Figure 8**.

Figure 8. CT scan machine

A CT scan machine is large and has a tunnel in the middle. During the test, you will lie on a table that moves slowly through the tunnel.



During the test, you will lie on a table that will move slowly through the tunnel as the machine takes many pictures. Then a computer will combine all the pictures into one detailed picture. Imaging tests can take 15 to 60 minutes to complete.

A computer combines the x-ray pictures to make detailed pictures of organs and tissues inside the body. Before the test, you may be given a contrast dye to make the pictures clearer. The dye may be put in a glass of water for you to drink, or it may be injected into your vein. It may cause you to feel flushed or get hives. Rarely, serious allergic reactions occur. Tell your doctor if you have had bad reactions before.

MRI scan

MRI (**m**agnetic **r**esonance **i**maging) uses radio waves and powerful magnets to take pictures of the inside of the body. MRI is very useful for looking at the soft tissues, brain, spinal cord, and specific areas in the bone. An MRI scan may cause your body to feel a bit warm.

PET/CT scan

PET/CT (**p**ositron **e**mission tomography/**c**omputed **t**omography) shows how your cells are using a simple form of sugar. To make the pictures, a sugar radiotracer first needs to be injected into your vein. The radiotracer lets out a small amount of energy that is seen by the machine that takes pictures. PET scans are usually combined with CT (PET/CT).

Cancer cells use sugar faster than normal cells, so they look brighter in the pictures. The CT portion of the scanner allows the computer to make a three-dimensional picture of sugar use throughout the body.

Your medical records:

- ✓ Your doctors will order tests and schedule visits to talk about your care plan.
- ✓ It is helpful to keep track of your test results at all times. Ask your doctors questions about the results.

Ultrasound

An ultrasound is a test that uses sound waves to take pictures of the inside of the body. This test is sometimes used to get a better look at lymph nodes near the first (primary) melanoma tumor in certain cases. For example, your doctor may consider this test if findings during the physical lymph node exam were unclear. Or, it may be used if you opted not to have other lymph node tests or procedures such as a sentinel lymph node biopsy or lymph node dissection.

For this test, you will lie on a table and have a gel spread over your skin in the area of the lymph nodes. Your doctor will then glide a hand-held device back and forth over the gel area. This device sends out sound waves that bounce off the lymph nodes and other tissues in your body to make echoes. A computer uses the echoes to make a picture of the lymph nodes, shown on a computer screen.

Review

- Cancer tests are needed if your skin shows signs of cancer.
- Cancer tests are used to plan treatment.
- Your health history and body exam inform your doctor about your health.
- Testing tissue removed from your body is the only way to know if you have melanoma.
- Tests of lymph nodes can show if cancer has spread.
- Blood tests monitor melanoma that has spread far to other parts of the body.
- Tests that take pictures of the inside of your body may show if the cancer has spread.

3
Melanoma staging

Cancer staging is how your doctors rate and describe the extent of cancer in your body. The rating—called the cancer stage—is based on the results of certain tests. The cancer treatments that doctors recommend highly depend on cancer staging. Part 3 describes the staging system used for melanoma. It also explains the different stages of melanoma. Contact your treatment team if you don't know your cancer stage. This information will help you use the *Treatment guide* in Part 5.

Staging

Cancer staging is a way that doctors rate and describe the extent of cancer in your body. Cancer stages are defined by the growth of the first (primary) tumor and its spread to other sites in the body. Cancer staging is used by doctors to plan which treatment is best for you. Often, melanoma is staged twice.

- **The first staging is the clinical stage.** It is based on the physical exam and skin biopsy of the primary melanoma tumor. A skin biopsy is the removal of a sample of tissue from the concerning spot on your skin to test for cancer cells.
- **The second staging is the pathologic stage.** It is based on the clinical staging as well as results from biopsies of lymph nodes and other tissue removed during surgical treatment.

Most of the time, the pathologic stage is the most important stage. This is because your lymph nodes can only be completely examined for cancer cells by viewing the biopsy sample with a microscope.

Imaging tests might be used once pathologic staging is complete. Imaging tests take pictures of the inside of your body to look for signs of cancer.

TNM scores

The AJCC (**A**merican **J**oint **C**ommittee on **C**ancer) staging system is used to stage melanoma skin cancer. In this system, each of the letters—T, N, and M—describes a different area of cancer growth. Your doctor will assign a score to each letter. TNM scores are based on the tests described in Part 2. These scores are used to assign the cancer a stage.

T = Tumor

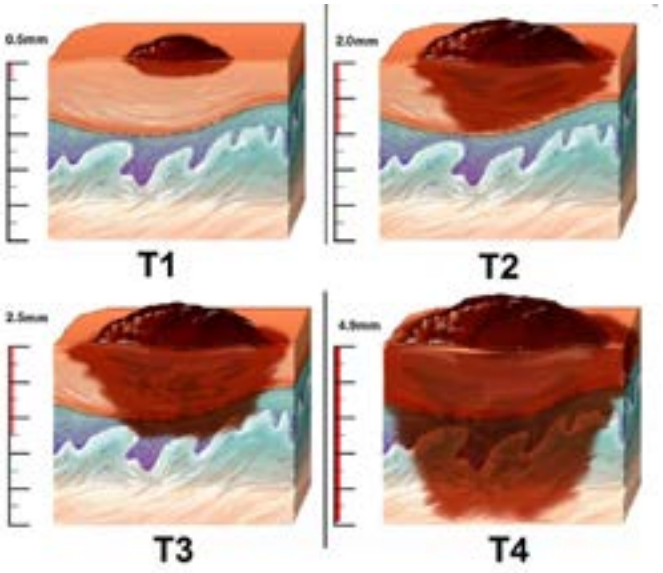
The T category tells you how thick the primary tumor is. The T category is given a score from 1 to 4 based on how deep the tumor has grown into the skin, measured in mm (**mi**lli**m**eters). **See Figure 9**. The sharp point of a pencil is about 1 mm.

For T1 to T4 melanomas, subcategories are given based on the ulceration. The ulceration status tells whether or not the tumor's top skin layer is present and intact (not ulcerated) or is broken or missing (ulcerated).

- TX means thickness can't be assessed.
- T0 means there is no evidence of a primary tumor.
- Tis means there are abnormal cells in the epidermis only.
- T1 tumors are ≤1.0 mm thick.
  - T1a tumors are <0.8 mm thick and do not have ulceration.
  - T1b tumors are <0.8 mm thick and have ulceration, or are 0.8 to 1.0 mm thick and with or without ulceration.
- T2 tumors are >1.0 to 2.0 mm thick.
  - T2a tumors are >1.0 to 2.0 mm thick and do not have ulceration.
  - T2b tumors are >1.0 to 2.0 mm thick and have ulceration.
- T3 tumors are 2.0 to 4.0 mm thick.
  - T3a tumors are 2.0 to 4.0 mm thick and do not have ulceration.
  - T3b tumors are 2.0 to 4.0 mm thick and have ulceration.
- T4 tumors are >4.0 mm thick.
  - T4a tumors are >4.0 mm thick and do not have ulceration.
  - T4b tumors are >4.0 mm thick and have ulceration.

Figure 9
Growth of melanoma into the skin

The T category is given a score from 1 to 4 based on how deep the melanoma tumor has grown into the skin.



N = Node

The N category reflects how far the melanoma has spread within nearby (regional) lymph nodes. Lymph nodes are small groups of special disease-fighting cells located throughout the body.

The main factor for the N score is the number of lymph nodes to which cancer cells have spread. For N1, N2, and N3 melanomas, subcategories are given based on how the lymph node metastases were found and whether cancer cells have spread to nearby skin or lymph vessels.

- NX means regional (nearby) lymph nodes have not been assessed.

- N0 means there is no cancer in nearby lymph nodes.

- N1 means that cancer cells have spread to only 1 lymph node or cancer cells are in the lymph vessels or nearby skin.
  - N1a means that 1 lymph node was found only by the pathologist.
  - N1b means that 1 lymph node was found during a physical exam or by imaging tests.
  - N1c means no regional lymph node disease.

- N2 means that cancer cells have spread to 2 to 3 lymph nodes or cancer cells are in the lymph vessels, or nearby skin along with 1 lymph node.
  - N2a means that the lymph node metastases were found only by the pathologist.
  - N2b means that the lymph node metastases were found and at least 1 was found during a physical exam or by imaging tests.
  - N2c means that cancer cells have spread to 1 known lymph node found by a pathologist or 1 lymph node was found during a physical exam or imaging test.

- N3 means that cancer cells have spread to ≥4 lymph nodes; the nodes stick together; or cancer cells have spread to both lymph nodes and to lymph vessels or nearby skin along with 2 or more lymph nodes.
  - N3a means that the lymph node metastases were found only by the pathologist.
  - N3b means that 4 or more lymph nodes were found and at least 1 was found during a physical exam or by imaging tests, or any number of nodes stick together.
  - N3c means that 2 or more lymph nodes were found by the pathologist or during a physical exam or imaging test, and/or any number of nodes stick together.

M = Metastasis

The M category tells you if cancer cells have spread to distant sites—called metastasis. Melanoma usually spreads to distant skin and lymph nodes first. The next pattern of spread is generally to the lungs, then to the liver, brain, bone, and/or intestines. Different patterns of melanoma spread are also possible. For metastases, subcategories are given based on where the cancer has spread, and those sub-categories also include whether LDH levels are normal or high (elevated).

- M0 means the melanoma hasn't spread to distant sites.

- M1 means the melanoma has spread to distant organs.

  - M1a means the cancer has spread to distant skin sites, areas under the skin, or distant lymph nodes.
    - M1a(0) LDH not elevated
    - M1a(1) LDH elevated

- M1b means the cancer has spread to the lungs with or without M1a areas of disease.
  - M1b(0) LDH not elevated
  - M1b(1) LDH elevated

- M1c means the cancer has spread to internal organs with or without M1a or M1b areas of disease.
  - M1c(0) LDH not elevated
  - M1c(1) LDH elevated

- M1d means the cancer has spread to the CNS (**c**entral **n**ervous **s**ystem) with or without M1a, M1b, or M1c areas of disease.
  - M1d(0) LDH normal
  - M1d(1) LDH elevated

Stages of melanoma

The TNM scores are combined to assign the cancer a stage. Guide 1 shows the melanoma stage groupings. The stages are labeled by Roman numerals 0 to IV. The stage groupings are defined by the TNM scores according to the AJCC staging system. In general, melanomas of the same stage will have a similar outcome (prognosis) and thus are treated in a similar way.

Most melanomas are found early, before they have spread beyond the primary tumor. Melanomas that are found and removed early may have a good prognosis and a low chance that they will come back (recur) after treatment. But, for melanomas that are thicker, are ulcerated, and/or have lymph node spread, the risk of recurrence after surgery goes up.

The 5 stages of melanoma

Stage 0

The melanoma is in situ—in its original place. The melanoma cells are only in the epidermis (the outer layer of skin) and have not invaded the dermis (the second layer of skin, under the epidermis).

Stage I

In stage IA, the tumor is thinner than 1.0 mm, the cells are dividing slowly, and there is no ulceration viewed under the microscope. Stage IB tumors are thinner than 1.0 mm and have ulceration, or 0.8 to 1.0 mm with or without ulceration, or they are a bit thicker (>1.0–2.0 mm) with no ulceration. In stage I, there is no cancer in the lymph vessels, lymph nodes, or distant organs.

Stage II

This stage is divided into 3 groups—A, B, and C—based on tumor thickness and ulceration status. In stage II, there is no cancer in the lymph vessels, lymph nodes, or distant organs.

Stage III

In stage III, melanoma has spread to nearby lymph vessels, lymph nodes, and/or nearby skin (satellites). The clinical stage includes tumors of any depth with metastases in lymph nodes and/or lymph vessels. Pathologic staging divides tumors of any size into 4 groups based on ulceration of the primary tumor and the extent of growth into the lymph vessels, lymph nodes, and nearby skin.

Stage IV

The melanoma has spread to one or more distant sites. The tumor may be of any thickness and with any range of spread in lymph vessels and lymph nodes.

Guide 1. Melanoma stages

Clinical staging*				Pathologic staging**			
Stage 0	Tis	N0	M0	**Stage 0**	Tis	N0	M0
Stage IA	T1a	N0	M0	**Stage IA**	T1a	N0	M0
					T1b	N0	M0
	T2a	N0	M0	**Stage IB**	T2a	N0	M0
Stage IIA	T2b	N0	M0	**Stage IIA**	T2b	N0	M0
	T3a	N0	M0		T3a	N0	M0
Stage IIB	T3b	N0	M0	**Stage IIB**	T3b	N0	M0
	T4a	N0	M0		T4a	N0	M0
Stage IIC	T4b	N0	M0	**Stage IIC**	T4b	N0	M0
Stage III	Any T, Tis	≥N1	M0	**Stage IIIA**	T1a/b, T2a	N1a, N2a	M0
				Stage IIIB	T0	N1b, N1c	M0
					T1a/b, T2a	N1b/c, N2b	M0
					T2b, T3a	N1a/b/c, N2a/b	M0
				Stage IIIC	T0	N2b/c, N3b/c	M0
					T1a/b, T2a/b, T3a	N2c, N3a/b/c	M0
					T3b, T4a	Any N ≥N1	M0
					T4b	N1a/b/c, N2a/b/c	M0
				Stage IIID	T4b	N3a/b/c	M0
Stage IV	Any T	Any N	M1	**Stage IV**	Any T	Any N	M1

Clinical staging includes microstaging of the primary melanoma and clinical/radiologic/biopsy evaluation for metastases. By convention, clinical staging should be used after biopsy of the primary melanoma, with clinical assessment for regional and distant metastases. Note that pathological assessment of the primary melanoma is used for both clinical and pathological classification. Diagnostic biopsies to evaluate possible regional and/or distant metastasis also are included. Note there is only one stage group for clinical Stage III melanoma

*Pathological staging includes microstaging of the primary melanoma, including any additional staging information from the wide-excision (surgical) specimen that constitutes primary tumor surgical treatment and pathological information about the regional lymph nodes after SLN biopsy or therapeutic lymph node dissection for clinically evident regional lymph node disease.

* Pathological Stage 0 (melanoma in situ) and T1 do not require pathological evaluation of lymph nodes to complete pathological staging; use cN information to assign their pathological stage

The five stages of melanoma are also grouped into three broad categories—local melanoma, regional melanoma, and metastatic melanoma.

- **Local melanoma** is when the cancer cells haven't spread beyond the primary tumor. This includes stage I and stage II melanomas, when the tumor is in the outer layer of skin (epidermis) and the second layer of skin (dermis). This group also includes stage 0 (in situ melanoma), when melanoma cells are only in epidermis.

- **Regional melanoma** is when cancer cells have spread from the primary tumor into lymph nodes and/or lymph vessels in the nearby (regional) area. Stage III is considered regional metastatic melanoma.

- **Distant metastatic melanoma** is when the cancer has spread to other organs and parts of the body far away from the primary tumor. Stage IV is distant metastatic melanoma.

Once your doctors know more about your diagnosis and stage of melanoma, they can talk to you about your next steps of care. Talking with your doctor about the cancer stage can help with treatment planning. Shared decision-making is a process in which you and your doctors plan treatment together. Shared-decision making is an important part of your care plan.

Your care plan:

- ✓ Keep a list of contact information of all of your health care providers.
- ✓ Use a calendar or ask a caregiver to make note of your treatment schedule and follow-up appointments.

Review

- Cancer staging is how doctors rate and describe the extent of cancer in the body.
- Melanoma is grouped into stages to help plan treatment.
- Cancer stages are based on the growth and spread of the first tumor.
- Cancer staging is often done two times—before and after lymph node surgery.

4
Overview of melanoma treatments

Part 4 describes the main treatments for melanoma. Knowing what a treatment is will help you understand your treatment options listed in the *Treatment guide* in Part 5. There is more than one treatment for melanoma. Not every person with melanoma will receive every treatment listed in this chapter.

Surgery

Surgery is an operation to remove or repair a body part. Generally, surgery is the main or primary (first) treatment for melanoma skin cancer. Thus, almost all patients with melanoma will have surgery after the skin biopsy.

The goal of surgery is to remove all of the cancer from your body. For melanomas that are deemed by your doctor to have a low risk of spread, surgery to remove the primary tumor on the skin may be the only treatment needed. There are different types of surgery that may be used for melanoma. The two main types of surgery used are a wide excision and a lymph node dissection.

Wide excision

A wide excision is surgery that removes the entire melanoma tumor on the skin along with some normal-looking tissue around its edge. Even if the melanoma is removed on the initial diagnostic biopsy, a wider excision is performed to remove nearby lymphatic channels in the skin, where there could be additional tumor cells. **See Figure 10**. The normal-looking tissue is called the surgical margin. The size of the surgical margin, measured in cm (**c**enti**m**eters), depends mostly on the thickness of the tumor. See Guide 2.

Guide 2. Surgical margins for melanoma

Tumor thickness	Surgical margin
In situ	0.5–0.1 cm
≤1.0 mm	1.0 cm
>1.0–2.0 mm	1.0–2.0 cm
>2.0–4.0 mm	2.0 cm
>4.0 mm	2.0 cm

Depending on the size of the surgical margin and the location of the melanoma, a wide excision may be done using local anesthesia that is injected into the area to numb it before the surgery. Local anesthesia is medicine that results in a temporary loss of feeling in a small area of the body to prevent pain during the procedure.

When wider margins are removed, or when wide excision is combined with lymph node surgery, general anesthesia is often needed. General anesthesia is medicine that causes a temporary loss of feeling and a complete loss of awareness that feels like a very deep sleep. For lentigo maligna melanoma, particularly on the face, different types of surgery may be recommended to very carefully examine the surgical margins.

A pathologist will examine the removed tissue with a microscope to see if there is any cancer in the surgical margins. If the margins have cancer, you may need more surgery. A positive margin means there is cancer in the surgical margin. A negative margin means there is no cancer in the surgical margin.

Sentinel lymph node biopsy

Based on the features of the primary melanoma tumor, there may be an increased risk of microscopic spread of melanoma cells to nearby (regional) lymph nodes. These lymph nodes are often found in nodal basins. Nodal basins are groups or clusters of lymph nodes found in certain parts of the body, such as the neck, armpit, and groin area.

Microscopic spread to a lymph node cannot be detected by touch or by imaging tests. If the risk is high enough, your doctor may recommend a sentinel lymph node biopsy. This surgery involves injecting a special dye into the skin near the primary tumor.

The dye follows the path lymph takes when it leaves the area of tumor and where cancer cells may invade nearby (regional) lymph vessels and lymph nodes. Your doctor will measure movement of the dye to find the sentinel lymph node—the first lymph node to which lymph, and possibly a cancer cell, travels.

The sentinel lymph node will then be removed through a small surgical cut in the skin so a pathologist can test it for melanoma cells.

Lymph node dissection

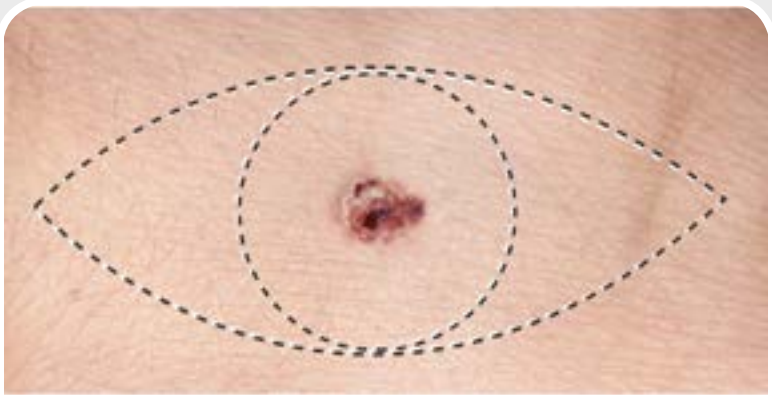
Your doctor may perform a complete lymph node dissection if the sentinel lymph node biopsy or other tests show that cancer cells have spread to a lymph node basin. A lymph node dissection is surgery that removes all the lymph nodes in the nodal basin. This surgery is done with general anesthesia. Studies are being done around the world to determine if this more extensive surgery is helpful to patients who have had a positive sentinel lymph node biopsy.

Side effects of surgery

A side effect is an unhealthy or unpleasant physical or emotional condition caused by treatment. Each treatment for melanoma can cause side effects. The risk and severity of side effects from surgery for melanoma depend on many factors. This includes the type of surgery, extent of surgery, and the size of the melanoma tumor.

Figure 10
Area of wide excision with a 1.5 cm margin

A wide excision is surgery that removes the entire melanoma tumor along with some normal-looking tissue around its edge. The normal-looking tissue is called the surgical margin. The curved cut taken around the circle is needed to close the surgical wound in a flat line.



Wide excision: Side effects of this surgery include pain, swelling, and scarring. Pain and swelling are usually temporary and should only last for a few weeks after surgery. Scars can be a lasting result of surgery.

Sentinel lymph node biopsy: Possible side effects may include numbness, pain, bruising, and lymph fluid buildup near the biopsy site, which is called a seroma. Serious side effects such as lymphedema are rare.

Lymph node dissection: Common side effects of this surgery include pain, numbness, limited arm or leg movement, and lymphedema—swelling due to buildup of lymph fluid in a limb. Normally, lymph flows in one direction toward the heart. Lymph node surgery can disrupt the normal flow of lymph and cause it to build up in the limb (arm or leg).

The buildup of lymph causes the arm or leg to swell. This is called lymphedema and it is the most serious side effect of lymph node surgery. Lymphedema may be temporary or permanent. There is no way to know who will develop it or when it will develop. It can happen just after surgery (most common) or months to years later.

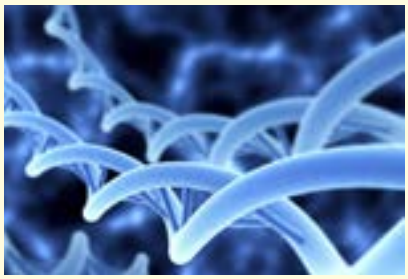
My dermatologist recommended immediate excision until we got clear margins.

- Suzanne, current age 53
  first diagnosed at age 49

Order of treatments

Most people with melanoma will receive more than one type of treatment. When and why treatments are given can be hard to understand. Part 5 gives full details. Here, the terms that describe the order of treatments are explained.

1



Neoadjuvant treatment

Treatment given to shrink the tumor before surgery. This may be used for metastatic melanoma to shrink the tumor before surgery. This treatment is mostly given in clinical trials.

2

Primary treatment

The main treatment given to rid the body of cancer. Surgery is most often used as the primary treatment for melanoma.

3

Adjuvant treatment

Treatment given after primary treatment to kill any remaining cancer cells.

Immunotherapy

The immune system is the body's natural defense against infection and disease. The immune system has many chemicals and proteins that are made naturally in the body. These substances can also be made in a lab to use as immunotherapy.

Immunotherapy (also called biological therapy) is treatment that increases the activity of your immune system. By doing so, immunotherapy drugs improve your body's ability to find and destroy cancer cells. Immunotherapy may be used as adjuvant treatment after surgery. Or, it may be used as primary treatment for melanomas that can't be removed by surgery.

Depending on how the drugs are given, immunotherapy can be used as local therapy or as systemic therapy. Guide 3 lists the immunotherapy drugs used as systemic therapy for melanoma. Guide 4 lists the immunotherapy drugs that are used as local therapy for melanoma.

Pembrolizumab and nivolumab

Pembrolizumab and nivolumab are two newer immunotherapy drugs approved for melanoma. They are a type of immunotherapy called PD-1 (**p**rogrammed **d**eath receptor-1) inhibitor. PD-1 is a protein found on immune system cells called T cells. PD-1 normally helps keep T cells from attacking other cells in the body.

These drugs block the PD-1 protein and boost the immune system response against the melanoma cells. This helps the immune system find, attack, and kills melanoma cells. Pembrolizumab and nivolumab are used as systemic therapy for melanoma. Adjuvant treatment with PD-1 inhibitors may prevent recurrence following surgery in patients with lymph node involvement. They are given every few weeks as a liquid that is injected into a vein.

Receiving treatment with drugs

Cancer doctors use drugs to treat melanoma in different ways. Sometimes drugs are given to treat melanoma in a specific, small area of the body, such as the tumor and nearby area. This is called local therapy or regional therapy.

Drugs can also be given to treat melanoma throughout the body. This is called systemic therapy. Doctors use systemic drugs to treat cancer cells that may have spread beyond the skin to distant sites. The types of drugs used for melanoma include immunotherapy, targeted therapy, vaccine therapy, and chemotherapy.

Guide 3. Immunotherapy drugs as systemic therapy for melanoma

Generic name	Brand name (sold as)	Route given
Aldesleukin; IL-2 (**i**nter**l**eukin-2)	Proleukin®	Liquid injected into a vein
Interferon alfa-2b	Intron® A	Liquid injected into a vein or under the skin
Ipilimumab	Yervoy®	Liquid injected into a vein
Nivolumab	Opdivo®	Liquid injected into a vein
Peginterferon alfa-2b	Sylatron™	Liquid injected under the skin
Pembrolizumab	Keytruda®	Liquid injected into a vein

Guide 4. Immunotherapy drugs as local therapy for melanoma

Generic name	Brand name (sold as)	Route given
BCG (**B**acillus **C**almette-**G**uérin) Live	TICE® BCG	Liquid injected into the tumor
Imiquimod	Aldara®	Cream that is spread onto the tumor
Interferon alfa-2b	Intron® A	Liquid injected into the tumor
IL-2; Aldesleukin	Proleukin®	Liquid injected into the tumor
T-VEC (**t**alimogene laherparep**vec**)	Imlygic™	Liquid injected into the tumor

Side effects of pembrolizumab and nivolumab
The most common side effects of these drugs are diarrhea, skin rash, itchy skin, fatigue, nausea, vomiting, diarrhea, and bone, joint, and/or muscle pain. Some of these side effects are more common for one drug than the other. Not all side effects are listed here. Be sure to discuss this with your doctor.

Ipilimumab

Ipilimumab is an immunotherapy drug used as systemic therapy for melanoma. It is a monoclonal antibody—a type of immune system protein made in a lab. It works by removing the “brakes” on the immune system and is often called an "immune checkpoint locker." This boosts the immune system’s response against melanoma cells in the body.

Ipilimumab is a liquid that is injected into a vein. It may be given at high doses for adjuvant treatment of melanoma in the lymph nodes that has been surgically removed. Adjuvant treatment is additional treatment given after surgical removal of the tumor to kill any remaining cancer cells elsewhere in the body.

Ipilimumab can also be given in lower doses to treat melanoma that can't be removed by surgery or has spread to distant sites and is also combined with anti-PD1 therapy to improve immune responses in patients with advanced melanoma.

Side effects of ipilimumab
The most common side effects of ipilimumab are fatigue, diarrhea, skin rash, and itching. Ipilimumab can also cause serious side effects such as severe inflammation and problems in the intestines, liver, nerves, skin, eyes, and hormone glands.

Interferon alfa and IL-2

Two older immunotherapy drugs used as systemic therapy for melanoma are interferon alfa and IL-2 (**i**nter**l**eukin-**2**). Another name for IL-2 is aldesleukin. Interferon alpha and IL-2 are molecules called cytokines that stimulate immune cells.

Cytokines exist naturally in your body as part of the immune system—the body's natural defense against infection and disease. They can also be made in the lab and be used as drugs to treat melanoma. When used as a treatment, cytokines are given in much higher amounts than what the body naturally makes.

High doses of these drugs may cause severe side effects. A side effect is an unplanned or unwanted physical or emotional condition caused by treatment. Doctors don't completely agree about using interferon alfa as adjuvant treatment. This is because its benefits may not clearly outweigh the side effects. Talk with your doctor if you have any concerns about taking interferon alfa.

Interferon alfa and IL-2 can also be used as local therapy. In this case, the drugs are injected directly into the tumor with a needle.

Side effects of interferon alfa and IL-2
A side effect is an unhealthy or unpleasant physical or emotional condition caused by treatment. The side effects of immunotherapy depend on the drug, how it is given, the amount taken, the length of treatment, and the person. When given in high doses, some immunotherapy drugs can cause very serious side effects.

Flu-like symptoms are a very common side effect of interferon alfa and IL-2. Such symptoms include fever, chills, tiredness, headache, and body aches. Some of the other most common side effects of interferon alfa are nausea, vomiting, not feeling hungry, depression, hair thinning, and liver damage.

Other common side effects of IL-2 are low blood pressure, nausea, vomiting, shortness of breath, confusion, fluid buildup, heart damage, skin rash, and abnormal bloods tests suggesting liver or kidney problems.

Not all side effects of immunotherapy drugs are listed here. Be sure to ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better. There are also ways to prevent some side effects.

T-VEC

T-VEC (**t**alimogene laherparep**vec**) is one of the newer immunotherapy drugs approved for melanoma. It is a type of virus made in a lab to infect and kill mainly cancer cells. T-VEC is used as local therapy and is given as an injection into metastatic, but not primary, melanoma tumors. In addition to killing the cancer cells directly, T-VEC also triggers the immune system to find and attack the cancer cells nearby and sometimes elsewhere in the body.

Side effects of T-VEC
The most common side effects of T-VEC are fatigue, chills, fever, nausea, vomiting, and pain at the injection site. Flu-like symptoms are also a common side effect of T-VEC. Such symptoms include fever, chills, tiredness, headache, and body aches.

Because T-VEC is derived from a herpes virus, it is generally given in a controlled hospital or clinic setting.

BCG and imiquimod cream

BCG (**B**acillus **C**almette-**G**uérin) is a germ that activates the immune system to attack melanoma cells. It is used as a local therapy for some melanomas and is injected directly into the tumor. Imiquimod cream is another immunotherapy drug that is used as local topical therapy for melanoma. The cream is rubbed onto the surface of the tumor and causes local skin inflammation.

Targeted therapy

Targeted therapy drugs are designed to specifically target cancer cells. For melanoma, these drugs target the activity of a specific or unique feature of melanoma cancer cells. Genes are the instructions in cells for making new cells and controlling how cells behave. An abnormal change in these instructions—called a gene mutation—can cause cells to grow and divide out of control.

Some targeted therapy drugs target a specific gene that is associated with cancer. Guide 5 lists the targeted therapy drugs used for melanoma. These drugs are used as systemic therapy. They are given as a pill that is swallowed.

In the past six years, the FDA (U.S. **F**ood and **D**rug **A**dministration) has approved 4 new targeted therapy drugs for metastatic melanoma that cannot be surgically removed: vemurafenib, dabrafenib, trametinib, and cobimetinib. All 4 of these drugs target tumors that have a damaged *BRAF* gene, so they will only help if you have this type of melanoma. Vemurafenib was the first to be approved, in 2011. Then, dabrafenib and trametinib were each approved in 2013. Cobimetinib, another targeted therapy drug for melanoma, was approved in 2015. These drugs are all given as a pill that is swallowed. The combination of BRAF inhibitors (vemurafenib or dabrafenib) and MEK inhibitors (trametinib or cobimetinib) is more effective than a single drug, and so a BRAF and MEK inhibitor are usually used together. The adjuvant use of dabrafenib and trametinib may prevent recurrence following surgery in patients with lymph node involvement.

Guide 5. Targeted therapy drugs as systemic therapy for melanoma

Generic name	Brand name (sold as)	Route given
Cobimetinib	Cotellic®	Pill that is swallowed
Dabrafenib	Tafinlar®	Pill that is swallowed
Imatinib mesylate	Gleevec®	Pill that is swallowed
Trametinib	Mekinist®	Pill that is swallowed
Vemurafenib	Zelboraf®	Pill that is swallowed

Imatinib mesylate is a targeted therapy drug that may be used for certain melanoma tumors. It targets tumors that have a damaged *c-kit* gene, but this mutation is less common than a *BRAF* mutation in melanoma. Imatinib is also given as a pill that is swallowed. Cancer tissue may be removed from your body to be tested for specific gene mutations before you begin treatment with a targeted therapy drug.

Side effects of targeted therapy

A side effect is an unhealthy or unpleasant physical or emotional condition caused by treatment. Each treatment for melanoma can cause side effects. The reactions to treatment differ between people. Some people have many side effects. Others have few. Some side effects can be very serious while others can be unpleasant but not serious. Most side effects appear soon after treatment starts and will go away after treatment ends. But, other side effects are long-term and may appear years later.

The side effects of targeted therapy depend on the drug and dose. Some of the side effects listed are caused by only one targeted drug. Others are caused by many targeted drugs but differ in how likely they are to occur.

Some common side effects of targeted therapy drugs used for melanoma are tiredness, joint pain, muscle pain, swelling, headache, fever, nausea or vomiting, and diarrhea. These drugs may also cause low blood cell counts. Other common side effects are skin rash or itching, sun sensitivity, other skin cancer (not melanoma), and hair loss. Because so many of the side effects occur on the skin, most patients on targeted therapy are also followed by a dermatologist or provider experienced in the management of skin side effects of these drugs.

Not all side effects of targeted therapy drugs are listed here. Be sure to ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better. There are also ways to prevent some side effects.

Vaccine therapy

This type of treatment is being tested in clinical trials for melanoma. A clinical trial is a type of research that studies the safety and effectiveness of a test or treatment. Vaccine therapy for melanoma is similar to vaccines used to prevent other diseases, such as polio, measles, and mumps. These vaccines have a weak or dead virus that can't cause disease but that activates the immune system. Since it is unknown how well vaccine therapies work for melanoma, they are only recommended as part of a clinical trial. (See page 48 for more details on clinical trials.)

Chemotherapy

Chemotherapy is a type of drug commonly used to treat cancer. Many people refer to this treatment as "chemo." Chemotherapy drugs kill fast-growing cells, including cancer cells and normal cells.

When only one drug is used, it is called a single agent. However, different types of chemotherapy drugs attack cancer cells in different ways. Therefore, more than one drug is often used. A combination regimen is the use of two or more chemotherapy drugs.

Chemotherapy can be used as systemic therapy or regional therapy for melanoma, although it is not as effective as newer immunotherapies or targeted therapies. Thus, it is used less often. Chemotherapy may be given as a palliative treatment. The goal of palliative treatment would be to shrink or stabilize tumors when other treatment options are no longer working.

For systemic therapy, the drug can be given as a pill that is swallowed. Or, it can be given as a liquid that is injected into a vein or under the skin with a needle. When given as systemic therapy, the drugs travel in the bloodstream to treat cancer throughout the body.

For regional therapy, the drug is given as an injection into a limb (arm or leg) in a way that it does not reach or affect the rest of the body. This is called isolated limb infusion/perfusion. The chemotherapy drug melphalan is given this way for melanoma. Guide 6 lists the chemotherapy drugs used for melanoma. Except for melphalan, all of the chemotherapy drugs listed in the chart are used as systemic therapy.

Chemotherapy is given in cycles of treatment days followed by days of rest. These cycles vary in length depending on which drugs are used. Usually, the cycles are 14, 21, or 28 days long. These cycles give the body a chance to recover before the next treatment. Thus, a regimen of 3 to 6 months has rest periods between treatments. A regimen is a treatment plan that specifies the dose, schedule, and length of treatment

Side effects of chemotherapy

Like targeted therapy, the side effects of chemotherapy depend on many factors. This includes the drug, the dose, and the person. In general, side effects are caused by the death of fast-growing cells, which are found in the intestines, mouth, and blood.

Thus, common side effects of chemotherapy are nausea, vomiting, mouth sores, not feeling hungry, hair loss, low blood cell counts, fever, infections, and easy bruising or bleeding. Feeling very tired (fatigue) or weak is also common.

Not all side effects of chemotherapy are listed here. Be sure to ask your treatment team for a complete list of common and rare side effects. If a side effect bothers you, tell your treatment team. There may be ways to help you feel better. There are also ways to prevent some side effects.

Guide 6. Chemotherapy drugs for melanoma

Generic name	Brand name (sold as)	Route given
Carboplatin	--	Liquid injected into a vein
Cisplatin	Platinol®	Liquid injected into a vein
Dacarbazine	--	Liquid injected into a vein
Melphalan	Alkerlan®	Liquid is infused into the arm or leg during a surgical procedure
Nab-paclitaxel	Abraxane®	Liquid injected into a vein
Paclitaxel	Taxol®	Liquid injected into a vein
Temozolomide	Temodar®	Pill that is swallowed or liquid injected into a vein
Vinblastine sulfate	--	Liquid injected into a vein

Radiation therapy

Radiation therapy uses a beam of high-energy rays to kill cancer cells. The rays damage a cell's instructions for making and controlling cells. This either kills the cancer cells or stops new cancer cells from being made. For melanoma, radiation is often given using a machine outside the body. This method is called EBRT (**e**xternal **b**eam **r**adiation **t**herapy).

Radiation therapy is almost never used to treat the first (primary) melanoma tumor. Radiation therapy may help to prevent local recurrence after surgical removal of enlarged lymph nodes. But, this is less common with the advent of newer, more effective drugs for advanced melanoma. A more common use of radiation therapy for melanoma is as palliative treatment to relieve symptoms such as pain caused by the cancer, especially when it has spread to the bones.

Palliative radiation therapy may also be used to treat the symptoms caused by metastatic melanoma. Palliative radiation therapy may also be used for lymph node, satellite, or in-transit metastases that can't be treated with surgery. A wide range of radiation doses and schedules are effective.

For melanoma, radiation therapy is most commonly used as palliative treatment or to treat brain metastases. Stereotactic radiosurgery or whole brain radiation therapy may be given for brain metastases.

SRS (**s**tereotactic **r**adio**s**urgery) is a type of external beam radiation therapy. SRS delivers a high dose of radiation to a very specific, small area of the body. Whole brain radiation therapy is EBRT aimed at treating the whole brain. Both types may be given as primary (first) treatment or adjuvant therapy for brain metastases.

In selected patients with desmoplastic melanoma, adjuvant radiation therapy may be used to treat the tissue around the first (primary) melanoma tumor after wide excision based on certain factors. These factors include thicker desmoplastic melanoma removed with narrow surgical margins, local recurrence, or extensive neurotropism, also called perineural invasion. Neurotropism is when the melanoma cells surround and might invade nerves.

Adjuvant radiation therapy may also sometimes be used for regional melanoma if it's likely that the cancer will return in the area where nearby (regional) lymph nodes were removed. This area is called the nodal basin. Adjuvant radiation may be considered for selected patients after lymph node surgery based on certain features of the lymph node metastases.

Side effects of radiation therapy

Radiation therapy or any kind may have side effects. Side effects may occur during or after treatment (late side effects). It is important to talk with your doctor and fully understand the side effects when considering this treatment.

Side effects of radiation therapy depend on the dose and the area being treated. Some of the physical side effects are temporary. For example, some skin changes may go away within 6 to 12 months after completing treatment. Some side effects of radiation therapy for melanoma are swelling, aches, heaviness in the treated area, sunburn-like skin changes, fatigue, and second cancer.

Supportive care and symptom control

The focus of this book is on cancer treatments. However, controlling treatment side effects is important for your quality of life. It is important that you are aware of and understand the possible side effects of each treatment you receive. Don't wait to tell your treatment team about side effects. If you don't tell your treatment team, they may not know how you are feeling.

Supportive care is treatment given to relieve the symptoms caused by cancer and side effects of cancer treatment. It doesn't treat the cancer itself. The goal of supportive care is to improve quality of life and relieve any discomfort you may have. Treating the side effects of cancer treatment, including those on the skin, may help a person to continue treatment and improve quality of life.

Supportive care is an important part of the overall treatment for patients with cancer. It can address many needs. One example is treatment for physical and emotional symptoms. It can also help with treatment decisions and coordination between health care providers.

You should also consider taking part in your hospital's system for tracking and treating symptoms if available. This tracking system is called a REMS (**r**isk **e**valuation and **m**itigation **s**trategy) program. Taking part in the REMS program is strongly recommended if you receive the immunotherapy drug ipilimumab.

There are many ways to limit the problems caused by cancer treatment. However, listing all the ways is beyond the scope of this booklet. In general, changes in behavior, diet, or medications may help. Some examples include:

- Wearing elastic stockings or sleeves to help prevent or control lymphedema
- Medications to relieve pain
- Exercise to help reduce fatigue

Clinical trials

New tests and treatments aren't offered to the public as soon as they're made. They first need to be studied. A clinical trial is a type of research that studies a test or treatment. NCCN experts consider clinical trials to be the best treatment option for people with cancer.

Clinical trials study how safe and helpful tests and treatments are. When found to be safe and helpful, they may become tomorrow's standard of care. Because of clinical trials, the tests and treatments in this book are now widely used to help people with melanoma. Future tests and treatments that may have better results than today's treatments will depend on clinical trials.

Without clinical trials, there is no way to know if a test or treatment is safe or helpful. Clinical trials are done in four steps, called phases. Some examples of the four phases of clinical trials for treatment are:

- **Phase I** trials aim to find the best dose and way to give a new drug with the fewest side effects.
- **Phase II** trials assess if a drug works to treat a specific type of cancer.
- **Phase III** trials compare a new drug to the standard treatment.
- **Phase IV** trials test new drugs approved by the FDA in many patients with different types of cancer.

Joining a clinical trial has benefits and is strongly encouraged.

- First, you'll have access to the most current cancer care.
- Second, you will receive the best management of care.
- Third, the results of your treatment—both good and bad—will be carefully tracked.
- Fourth, you may help other people who will have cancer in the future.

Clinical trials have risks, too. Like any other test or treatment, there may be side effects. Also, new tests or treatments may not help. Another downside may be that paperwork or more trips to the hospital are needed.

To join a clinical trial, you must meet the conditions of the study. Patients in a clinical trial often have a similar cancer type and general health. This is to know that any progress is because of the treatment and not because of differences between patients.

To join, you'll need to review and sign a paper called an informed consent form. This form describes the study in detail. The study's risks and benefits should be described and may include others than those described above.

Next steps

Ask your treatment team if there is an open clinical trial that you can join. There may be clinical trials where you are getting treatment or at other treatment centers nearby. You can also find clinical trials through the websites listed in Part 6.

Complementary and alternative medicine

CAM (**c**omplementary and **a**lternative **m**edicine) is a group of treatments sometimes used by people with cancer. Many CAMs are being studied to see if they are truly helpful.

- Complementary medicines are meant to be used alongside standard therapies, most often for relaxation, improving your health, or to prevent or reduce side effects.
- Alternative medicine is treatment or techniques that are used instead of standard treatments such as chemotherapy or radiation. Some are sold as cures even though they haven't been proven to work in clinical trials.

Many cancer centers or local hospitals have complementary therapy programs that offer acupuncture, yoga, and other types of therapy.

It's important to tell your treatment team if you are using any complementary medicines, especially supplements, vitamins, or herbs. Some of these can interfere with your cancer treatment. For example, some supplements or herbs can increase or decrease levels of immunotherapy or chemotherapy drugs in your body. This may cause more side effects or make the treatment not work as well.

For more information about CAM, ask your doctor and visit the websites in Part 6.

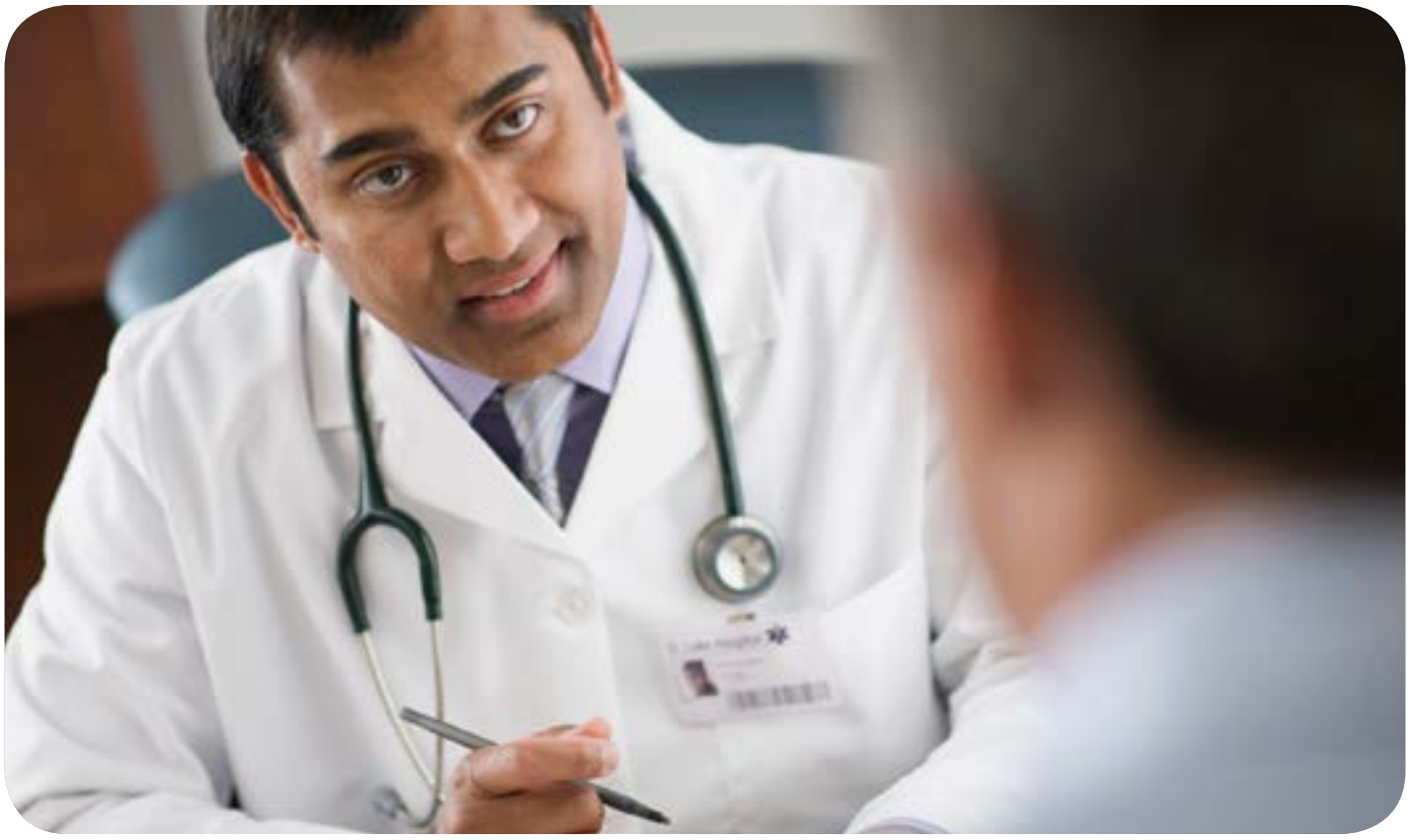
Review

- Surgery to remove tumors is often used to treat melanoma.
- Drugs can be given to treat melanoma in one area or throughout the body.
- Chemotherapy drugs kill fast-growing cells.
- Immunotherapy drugs help the immune system fight off cancer cells.
- Targeted therapy drugs specifically target cancer cells.
- Radiation therapy kills cancer cells or stops new cancer cells from forming.
- A clinical trial studies a test or treatment to see how safe it is and how well it works.

After 18 months of immunotherapy, my body still offers an occasional, unwelcome, surprising symptom. But the remarkable thing to me has been to participate in a life-extending therapy regimen that still allows me to continue and advance my career, be present with my family, and live a largely typical lifestyle all while receiving treatment.

- John, current age 41
  first diagnosed at age 35

5
Treatment guide



Part 5 is a guide through the treatment options for people with melanoma. This information is taken from the treatment guidelines written by NCCN experts of melanoma. These treatment guidelines list options for people with melanoma in general. Thus, your doctors may suggest other treatment for you based on your health and personal wishes. Fully discuss your treatment options with your doctor.

Melanoma testing

Guide 7 shows the initial tests that are recommended when your doctor thinks you might have melanoma skin cancer. These tests help your doctor to confirm (diagnose) melanoma and plan treatment.

Your doctor may test you for melanoma if an area of your skin is darker in color and doesn't look normal. The abnormal-looking area—called a lesion—may be a mole, blemish, or spot. To confirm if you have melanoma, all or part of the skin lesion must be removed and tested for cancer cells. This is called a skin biopsy. (See Part 2 on page 18 for skin biopsy details.)

An excisional biopsy can be done with an elliptical, deep shave/saucerization, or punch technique. (See page 20 for details.) Narrow surgical margins (1–3 mm) are preferred in order to remove the entire skin tumor for diagnosis. An excisional biopsy removes the entire lesion along with a small amount of normal-looking skin around its edge. The normal-looking skin removed is called the surgical margin. This type of biopsy is preferred for a diagnosis of melanoma.

The direction and width of the surgical cut should be done in a way that it won't affect future treatment. If this can't be done, your doctor may perform an incisional biopsy or partial biopsy instead. This type of biopsy only removes part of the lesion. A partial biopsy may be used for a very large lesion or for a lesion that's on a part of the body where it can't be easily removed.

Guide 7. Skin biopsy

Signs or symptoms		Skin biopsy		Pathology report
• Area of skin that doesn't look normal • Assess melanoma-related risk factors	→	Excisional biopsy Incisional biopsy Punch biopsy Shave biopsy	→	• Breslow thickness • Ulceration status (present or absent) • Dermal mitotic rate • Surgical margin status • Microsatellitosis (present or absent) • Pure desmoplasia if present

Superficial shave biopsies are not recommended to confirm (diagnose) melanoma since they may not go deep enough to measure the full thickness of the lesion. The exception is in the setting of the lentigo maligna type of melanoma in situ, where a broad shave biopsy may help to accurately diagnose the lesion under the microscope.

After the skin biopsy, the tissue sample will be sent to a pathologist to be tested for cancer cells. A pathologist who has experience with skin lesions should examine the biopsy sample. A pathology report is a document with information about tissue removed from your body during a biopsy or surgery. The pathology report should include a number of important results from the biopsy examination. Read page 22 for details on what should be included in the pathology report. If test results from the first biopsy are unclear, your doctor may perform another biopsy. Or, the pathologist may do other tests on the tissue sample.

Medical history and physical exams

After your doctor has confirmed that you have melanoma, he or she will talk with you about the diagnosis and may order more tests. Your doctor will ask about your medical history, including your general health, changes in the look and size of the tumor, and any lifetime medical conditions.

Your doctor will also assess your risk for melanoma. A risk factor is anything that increases the chance of getting a disease. Your risk is higher if you have many moles or atypical-appearing moles, fair skin, prior sunburns, red hair and very fair complexion, prior tanning bed use, or if you or any of your family members have had melanoma.

During the physical exam, your doctor will note the current size, shape, color, and texture of the melanoma tumor. Any bleeding will be recorded. Your doctor will feel your lymph nodes and organs near the lesion to check if they are normal in size and firmness. A complete skin exam will be done to check for other unusual spots or moles.

Based on the biopsy test results, pathology report, and physical exam, your doctor will determine the clinical stage of melanoma. The clinical stage is a rating of the extent of melanoma in your body based on tests done before surgery. Which tests and treatments you will have next depends on the clinical stage of melanoma. (Read Part 3 on page 28 for more details on melanoma stages.)

Next steps

For stages 0, I, and II melanoma, see Guide 8 on page 54. For stage III melanoma, see Guide 11 on page 58. For stage IV melanoma, see Guide 20 on page 71.

Guide 8 shows the tests that are recommended for in situ and local melanoma. The clinical stage is a rating of the extent of melanoma in your body based on tests done before surgery.

In situ melanoma—stage 0—is when melanoma cells are only in the outer layer of the skin (epidermis). Local melanoma includes stages I and II. Local melanoma tumors have grown into both skin layers—the epidermis and dermis, the second layer of skin. But, these melanomas haven't spread anywhere beyond the skin.

A few tests are recommended for all in situ and local melanoma tumors. These include a medical history and physical exam. Imaging tests take pictures of the inside of the body. They are only recommended if you have a concerning sign or symptom that your doctor needs to check. (Read page 25 for imaging test details.) Routine imaging and blood tests are not recommended without specific signs or symptoms.

For stage II and some thicker stage IB melanoma tumors, it may be more likely that cancer cells have spread to lymph nodes based on certain risk factors. Therefore, your doctor may talk to you about having a surgical test called a sentinel lymph node biopsy.

Lymph nodes are groups of special disease-fighting cells located throughout the body. The sentinel lymph node is the first lymph node to which cancer cells are likely to spread from the primary tumor. A sentinel lymph node biopsy is a surgery that removes the sentinel lymph node(s) to test for cancer cells.

If cancer cells are found in the sentinel lymph node, it may be more likely that cancer has spread to other nearby lymph nodes or tissue. If needed, your doctor will likely perform the sentinel lymph node biopsy during treatment with surgery to remove the tumor.

Guide 8. Tests for in situ and local melanoma

Clinical stage		Tests
• Stage 0 (in situ) • Stage IA (<0.8 mm thick, no ulceration)	→	• Medical history • Physical exam • Imaging tests (CT, PET/CT, MRI) for specific signs or symptoms only
• Stage IB (T1b [<0.8 mm thick with ulceration or 0.8–1.0 mm thick ± ulcertaion]) • Stage IB (T2a [>1.0–2.0 mm without ulceration]) • Stage II (>1.0 mm thick, any feature, N0)	→	• Medical history • Physical exam • Imaging tests (CT, PET/CT, MRI) for specific signs or symptoms only • Possible SLN (**s**entinel **l**ymph **n**ode) biopsy

In situ and local melanoma

Guide 9 shows the primary treatment options for stage 0, I, and II melanomas. Primary treatment is the main treatment used to rid the body of cancer. Adjuvant treatment is additional treatment given after the main one to try to kill any remaining cancer cells and lower the chance that the cancer will come back. The return of cancer after a period of improvement is called a recurrence.

For local melanomas of stage 0 or IA, the chance of metastasis or recurrence is low. Thus, surgery to remove the primary tumor is the only treatment needed. However, some local melanomas may have certain features that increase the chance of metastasis or recurrence. For these melanomas, additional staging and treatments may be needed.

Guide 9. Primary treatment and next steps of care

Clinical stage	Primary treatment			Next steps
• Stage 0 (in situ) • Stage IA (<0.8 mm thick, no ulceration)	• Wide excision			• Follow-up care (See Guide 11)
• Stage IB (T1b [<0.8 mm thick with ulceration or 0.8–1.0 mm thick ± ulcertaion])	• Wide excision			• Follow-up care (See Guide 11)
	• Wide excision with SLN biopsy		• SLN negative	• Follow-up care (See Guide 11)
			• SLN positive	• See Guide 12
• Stage IB (T2a) • Stage II (>1.0 mm thick, any feature, N0)	• Wide excision		• SLN negative	If Stage IB, IIA: • Observe If Stage IIB, IIC: • Observe • Interferon alfa
	• Wide excision with SLN biopsy		• SLN positive	• See Guide 12

Primary treatment

For stage 0, I, and II melanomas, the primary treatment is a wide excision. A wide excision is a surgery to remove the whole tumor and some normal-looking tissue around its edge. The normal-looking tissue is called the surgical margin. The size of the surgical margin depends on the thickness of the tumor. For lentigo maligna melanoma, different types of surgery may be used and wider margins may be needed, particularly on the face where tissue-sparing surgery is important.

Under certain circumstances, surgery may not be possible for melanoma in situ, particularly lentigo maligna type on the face. In such cases, your doctor may discuss other treatment options. These may include topical imiquimod cream and local radiation therapy. (See Part 4 on page 35 for where to find each treatment type.)

For thicker melanomas, you may also have a sentinel lymph node biopsy during surgery to remove the tumor. A sentinel lymph node biopsy removes the sentinel lymph node to test for cancer cells. The sentinel lymph node is the first lymph node to which cancer cells will likely spread from the primary tumor. If the sentinel lymph node biopsy finds cancer in the sentinel lymph node, the melanoma stage will be moved up (upstaged) to pathologic stage III. In this case, you will be treated for stage III melanoma instead of stage I or II. See *Next steps* at the end of this section. (Read Part 3 on page 29 for details and criteria of melanoma stages.)

Adjuvant treatment

For stage 0, IA, IB, and IIA tumors, adjuvant treatment after surgery isn't needed. Instead, you will begin follow-up care or observation. During observation, scheduled follow-up testing will allow your doctor to watch you closely for cancer spread (metastasis) or return (recurrence).

Most people with stage IIB or IIC are also watched closely for recurrence—including possible use of imaging tests for surveillance. In addition, another option for certain patients is to receive interferon alfa. It may be given at a high dose for one year as adjuvant treatment.

Next steps

For stage 0, I, or II melanoma, see Guide 10 on the next page for follow-up tests. For stage III, see Guide 11 on page 58 for follow-up tests.

Guide 10 shows the follow-up tests and schedule that is recommended after completing treatment for stage 0, I, or II melanoma. Follow-up tests are used to monitor you after treatment to check for signs of recurrence or metastasis. A recurrence is when cancer comes back (recurs) after a period of time. Metastasis is when cancer spreads from the original (primary) tumor to other sites in the body. The tests and frequency of follow-up described in the chart are based on the risk of recurrence for each stage.

Main follow-up tests are used for all stages of melanoma. First, you should have a complete skin exam by your doctor every year for life. You should also examine your own skin on a regular basis. And, you should check your lymph nodes during the self-exam of your skin. Imaging tests such as a CT, PET/CT, or MRI scan are only suggested if you have specific signs or symptoms of cancer that your doctor needs to check out.

An ultrasound of nearby (regional) lymph nodes may be used for follow-up in certain situations. One is when the physical lymph node exam findings are unclear. The second is if you did not undergo the sentinel lymph node biopsy that was offered at the time melanoma was found (diagnosed). The third is if you did not have a complete lymph node dissection after the sentinel lymph node biopsy found cancer.

Routine blood tests to check for recurrence are not recommended. No other follow-up tests, apart from ongoing skin exams, are recommended for stage 0 (in situ) melanoma.

For stage I and II melanomas, you should also have regular medical check-ups and physical exams. Your doctor will examine your lymph nodes and look carefully at your skin during the physical exam. The guide below lists the recommended exam schedule.

For stage IIB and IIC melanomas, you may have imaging tests to screen for cancer recurrence or metastases. Screening means testing to detect a disease when there are no signs or symptoms present. Imaging tests for screening may be done every 3 to 12 months. This may include a CT scan of your chest, abdomen, and pelvis; MRI of your brain; and/or a PET/CT scan. Your doctor may also consider doing an x-ray of your chest to watch for cancer spread in your lungs or CT of your neck. These tests may be done for up to 3 to 5 years after treatment has ended. Routine imaging tests are not recommended after 3 to 5 years if there has been no recurrence and you don't have any symptoms.

If follow-up tests show that the cancer has come back (recurred) or spread (metastasis), treatment options will depend on the type of recurrence or metastasis. Persistent melanoma is when cancer cells remain in the skin after surgery or other treatments and does not represent a metastatic type of local recurrence. A nonmetastatic recurrence is cancer that has come back after treatment but hasn't spread beyond the area near the first tumor.

Guide 10. In situ and local melanoma follow-up

Clinical stage (no evidence of disease)		Follow-up tests
All stages	→	• Complete skin exam at least once a year for life • Regular self-exam of skin and lymph nodes • Imaging tests as needed for specific signs and symptoms • Possible regional lymph node ultrasound • Genetic counseling/testing if 3 or more invasive melanomas, or personal or family history of melanoma and certain cancers
Stage IA to IIA	→	• Tests listed above for all stages • Medical history and physical exam with focus on skin and lymph nodes ◦ Every 6 to 12 months for 5 years, then ◦ Every year as needed
Stage IIB to IIC	→	• Tests listed above for all stages • Medical history and physical exam with focus on skin and lymph nodes ◦ Every 3 to 6 months for 2 years, then ◦ Every 3 to 12 months for 3 years, then ◦ Every year as needed • Possible imaging tests every 3 to 12 months to screen for recurrence or metastases

Metastatic melanoma is cancer that has spread from the original (primary) tumor to other parts of the body.

Next steps

For persistent melanoma or nonmetastatic recurrence, see Guide 15 on page 65 for treatment options. For metastatic melanoma, see Guide 20 on page 71.

Guide 11 shows the tests that are recommended for stage III (regional) melanoma. Regional melanoma has spread beyond the first (primary) tumor to nearby lymph nodes, lymph vessels, or both.

Lymph nodes are small groups of special disease-fighting cells located throughout the body. Lymph vessels are tiny tubes that connect lymph nodes to each other. Lymph vessels also carry a clear fluid (lymph) containing white blood cells throughout the body. Regional melanoma has not spread to parts of the body far away from the primary tumor.

The pathologic stage is based on the clinical stage as well as tests of lymph nodes and other tissue removed during surgical treatment. The clinical stage is a rating of the extent of melanoma in your body based on the physical exam and biopsy of the primary tumor.

For pathologic stage IIIA, IIIB, and IIIC the sentinel lymph node biopsy found cancer in the sentinel lymph node. In this case, your doctor may use imaging tests for baseline staging and to check out specific signs or symptoms of cancer.

Guide 11. Regional melanoma tests

Stage	Tests
Stage IIIA (Cancer in lymph nodes found by sentinel node biopsy)	• Possible imaging tests for baseline staging • Imaging tests to check out specific signs or symptoms
Stage IIIB/C (Cancer in lymph nodes found by sentinel node biopsy)	• Imaging tests for baseline staging and to check out specific signs or symptoms
Clinical stage III (Enlarged lymph nodes found by physical exam or imaging tests) and Stage III clinical satellite or in-transit (Cancer cells found in lymph vessels but not in lymph nodes)	• FNA biopsy preferred, or core, incisional, or excisional biopsy of enlarged lymph nodes • Imaging tests for baseline staging and to check out specific signs or symptoms

He or she may consider a baseline MRI scan of your brain if you have stage IIIC and have no symptoms. A baseline is a starting point to which future test results are compared.

For clinical stage III and stage III clinical satellite or in-transit melanoma, your doctor will perform a biopsy on the enlarged lymph nodes to test them for cancer cells. An FNA biopsy is the preferred method, but an excisional, incisional, or core biopsy is also an option. (Read page 20 and 24 for details on each type of biopsy.) You may also have imaging tests for baseline staging and to check out specific signs or symptoms of cancer. For example, you may have a CT scan of your pelvis if your doctor feels enlarged lymph nodes in your groin.

Next steps

See Guide 12 on page 61 for treatment options for stage III melanoma.

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For the past six years I have felt very involved in every surgery plan, every radiation plan, every chemical plan. I have worked with three surgeons, my oncologist and all of their great support team members. We have made joint decisions throughout the process.

- Marty, current age 55
  diagnosed at age 49

Regional melanoma

Guide 12 shows the treatment options for stage III melanoma, also called regional melanoma. Primary treatment is the main treatment used to rid your body of cancer. Adjuvant treatment is additional treatment given after the main one to try to kill any remaining cancer cells and lower the chance of cancer recurrence (return). See Part 4 on page 35 to get details on each type of treatment listed in the chart.

For pathologic stage IIIA, IIIB, and IIIC melanoma that was upstaged based on the sentinel lymph node biopsy, the tumor has already been removed. Therefore, the primary treatment options are to closely watch the active lymph node basin (usually with ultrasound studies) or have a complete lymph node dissection, although additional lymph node surgery has not been shown to improve overall survival.

After primary treatment, there are five options that may be considered for adjuvant treatment. You can begin observation; receive nivolumab if stage IIIB or IIIC (preferred adjuvant immunotherapy); receive dabrafenib and trametinib if you have a *BRAF* V600–activating mutation and sentinel lymph node metastasis >1 mm; receive high-dose ipilimumab for sentinel lymph node metastasis >1 mm; or receive interferon alfa (either 1 year of high-dose interferon or up to 5 years of the pegylated form of interferon). Observation without systemic therapy but with imaging surveillance is an option for surgically removed melanoma in the lymph nodes. With or without adjuvant treatment, all patients are observed for a period of scheduled follow-up testing to watch for cancer spread (metastasis) or return (recurrence).

For clinical stage III melanoma, primary treatment with wide excision of the primary tumor and complete therapeutic lymph node dissection is an option.

Adjuvant therapy includes local treatment using radiation. This is only for certain patients that are at high risk of the cancer spreading further into the lymph nodes.

For systemic treatment, you can begin observation, receive nivolumab (preferred adjuvant immunotherapy), receive dabrafenib and trametinib if you have a *BRAF* V600–activating mutation, or receive high-dose ipilimumab, interferon alfa, or biochemotherapy. Biochemotherapy is combination treatment with chemotherapy and immunotherapy. It is a very strong treatment and may not be a good option for everyone. Observation is another option.

For stage III clinical satellite or in-transit melanoma, primary treatment includes many options, including clinical trials. The first is systemic therapy for metastatic or unresectable melanoma. The next option is surgery to remove the tumor(s) with negative margins. Negative margins means there are no cancer cells in the normal-looking tissue around the edge of the tumor removed during surgery.

Your doctor may also consider doing a sentinel lymph node biopsy during surgery since it is likely that the cancer has spread. If the entire tumor can't be removed with surgery, there are other treatment options.

Local therapy options include T-VEC, BCG, interferon alfa, or IL-2 injections into the tumor or imiquimod cream rubbed onto the tumor. These are immunotherapy drugs and may be good options if you have clinical satellite or in-transit metastases. Your doctor may consider palliative radiation to relieve symptoms if the cancer can't be removed by surgery.

A regional therapy option is isolated limb infusion/perfusion with the chemotherapy drug melphalan. The drug is infused into the arm or leg during a surgical procedure. This may be a good option if you have several in-transit metastases in one arm or leg.

Next steps

If you will receive systemic therapy, see Guide 23 on page 74. For follow-up tests that are recommended during observation and after treatment for regional melanoma, see Guide 14 on page 63.

Guide 12. Primary and adjuvant treatment

Stage	Primary treatment	Adjuvant treatment
Stage IIIA/B/C (Cancer in lymph nodes found by sentinel node biopsy)	• Active lymph node basin surveillance • Complete lymph node dissection	• Observation • Nivolumab (IIIB/C) • Dabrafenib/trametinib • High-dose ipilimumab • Interferon alfa
Clinical stage III (Enlarged lymph nodes found by physical exam or imaging tests)	• Wide excision of primary tumor + complete therapeutic lymph node dissection	• Radiation therapy to lymph node basin for certain high-risk patients • Observation • Nivolumab • Dabrafenib/trametinib • High-dose ipilimumab • Interferon alfa • Biochemotherapy
Stage III clinical satellite or in-transit (Cancer in the skin near the first tumor or cells found in lymph vessels but not in lymph nodes)	• Systemic therapy • Local therapy: ◦ Complete surgical excision to clear margins if possible ◦ T-VEC, BCG, interferon alfa, or IL-2 injection in tumor ◦ Imiquimod cream ◦ Consider radiation therapy if can't be removed by surgery • Regional therapy: ◦ Isolated limb infusion/perfusion with melphalan	• See Guide 13

Guide 13 shows the response assessment and next treatment options for stage III clinical satellite or in-transit melanoma. After primary treatment, your doctor will give imaging tests to check how well treatment worked. An outcome or improvement caused by treatment is called a treatment response. Based on these tests, you may have adjuvant treatment if there are no signs of cancer.

If you had surgery as primary treatment and there are no signs of cancer, then you have several options for adjuvant treatment. You can begin observation; receive nivolumab, dabrafenib, and trametinib if you have a *BRAF* V600–activating mutation, or you can receive interferon alfa. Interferon alpha would be given at a high dose for one year or at smaller doses for up to 5 years. Observation is a period of scheduled follow-up testing to watch for cancer metastasis or recurrence. (See Part 4 on page 35 for details on each type of treatment.)

If you had surgery but the cancer was not able to be fully resected, you have second-line treatments as an option. They include systemic therapy, local therapy options with T-VEC, BCG, interferon alfa, or IL-2 injections into the tumor or imiquimod cream rubbed onto the tumor. These are immunotherapy drugs and may be good options if you have clinical satellite or in-transit metastases. Your doctor may consider palliative radiation to relieve symptoms if the cancer can't be removed by surgery. A regional therapy option is isolated limb infusion/perfusion with the chemotherapy drug melphalan. The drug is infused into the arm or leg during a surgical procedure.

If you had treatment other than surgery as your primary treatment and the disease is progressing or responding to treatment, you would have the same options as you would for disease that couldn't be fully removed by surgery. If you had other treatment besides surgery and there are no signs of cancer, then you will be observed by your doctor. He or she will begin follow-up tests and will watch you closely for any signs or symptoms of disease.

Next steps

If you will receive systemic therapy, see Guide 23 on page 74. For stage III follow-up tests, see Guide 14 on the next page.

Guide 14 shows the follow-up tests that are needed after completing primary treatment or adjuvant treatment for stage III regional melanoma. Follow-up tests are used to monitor you after treatment and check for signs of recurrence or metastasis.

A recurrence is when cancer comes back (recurs) after a period of time. Metastasis is when cancer spreads from the first (primary) tumor to other sites in the body. Your doctor may suggest more or less frequent follow-up testing based on your risk for recurrence.

A complete skin exam by your doctor is recommended every year for life. In addition, you should examine your own skin and lymph nodes on a regular basis. You should also have regular medical check-ups and physical exams. During the physical exam, your doctor will carefully examine your lymph nodes and skin.

Imaging tests are recommended to check out specific signs or symptoms of cancer. You may also have imaging tests to screen for cancer recurrence or metastases. Screening means testing to detect a disease when there are no signs or symptoms present.

The type and frequency of imaging tests varies based on your risk of cancer recurrence or spread (metastasis). You may have imaging tests for screening every 3 to 12 months. This may include a CT scan of your chest, abdomen, and pelvis; a PET/CT scan; and/or an MRI of your brain.

Your doctor may also order a CT scan of your neck. He or she may also want an x-ray of your chest. This is done to asses for cancer spread in your lungs.

These tests may be done for up to 3 to 5 years after treatment has ended. Routine imaging tests are not recommended after 3 to 5 years if there has been no recurrence and you don't have any symptoms.

Guide 13. Response assesment and next treatment

Stage III clinical satellite or in-transit

Response assessment	Second-line treatment	Next treatment
After surgery: • No evidence of disease	→	• Adjuvant treatment: ◦ Observation ◦ Nivolumab ◦ Dabrafenib/trametinib ◦ Interferon alfa
After surgery: • Less than complete resection	• Systemic therapy • Local therapy: ◦ T-VEC, BCG, interferon alfa, or IL-2 injection in tumor ◦ Local ablation therapy ◦ Imiquimod cream ◦ Consider radiation therapy if unresectable • Regional therapy: ◦ Isolated limb infusion/perfusion with melphalan	
Clinical assessment ± imaging: • Disease remains or is progressing	→	• Treatment options are based on response to second-line treatment
Clinical assessment ± imaging: • No evidence of disease	→	• Observation

Guide 14. Regional melanoma follow-up

Stage (no evidence of disease)	Follow-up tests
Stage III	• Regular self-exam of skin and lymph nodes • Medical history and physical exam with focus on skin and lymph nodes ◦ Every 3 to 6 months for 2 years, then ◦ Every 3 to 12 months for 3 years, then ◦ Every year as needed • Imaging tests as needed to check specific signs and symptoms • Possible imaging tests every 3 to 12 months to screen for recurrence or metastase • See Guide 10, *All stages* for more information on follow-up care

Routine blood tests to check for recurrence are not recommended.

If follow-up tests show that the cancer has come back (recurred), treatment options will depend on the type of recurrence. Persistent melanoma is when cancer cells remain after surgery or other treatments. A nonmetastatic local recurrence at the initial melanoma scar site means that cancer came back in the skin after treatment but hasn't spread beyond the area near the first tumor. This is generally treated with additional surgery at the scar site. Metastatic melanoma is cancer that has spread to parts of the body far from the first tumor.

The next set of Guides describe the recommended tests and treatments for melanoma that came back after treatment at or near the site of the first (primary) melanoma.

Persistent melanoma or recurrence

Persistent melanoma, or true local scar recurrence refers to cancer cells that remain after surgery or to cancer cells not destroyed by other treatments. Persistent melanoma is found in or around the scar from the surgery to remove the primary melanoma. It is defined by the presence of melanoma in the most superficial layers of the skin (epidermis or superficial dermis). This usually presents as a return of color (pigment) in or around the melanoma scar.

Local (metastatic) recurrence means the cancer returned in the surgical scar where the primary tumor was removed due to involvement of underlying lymph channels (intralymphatic metastasis). However, as opposed to persistent disease, the cancer cells are found in the scar tissue within the deep tissue of the dermis or subcutaneous fat. This usually presents as a firm bump in or around the melanoma scar. This can occur in the scar (called "satellite" recurrence) or between the scar and the regional lymph node basin.

Satellite recurrence is a type of local recurrence. It means the cancer has come back and formed tumors in lymph vessels in the skin, deep within the scar, or just outside of the scar site.

In-transit recurrence means the cancer has come back and formed tumors in the lymph vessels between the melanoma scar site and the regional lymph nodes, but not in the lymph nodes themselves.

Regional lymph node recurrence means the cancer has come back in the lymph nodes near the first melanoma. This is also referred to as a "node-positive" recurrence.

Distant recurrence means the cancer has come back in tissues or organs far beyond the first melanoma and regional lymph nodes. For distant metastatic recurrence, see Guide 21 on page 72 for recommended tests.

Guide 15 shows the tests that are needed for cancer that has come back after treatment and is at or near the site of the first (primary) melanoma.

For true local scar recurrence (persistent disease), the first recommended test is a skin biopsy to confirm the diagnosis. A biopsy is the removal of small amounts of tissue from your body to test for disease. The next tests you will receive are based on the stage and features of the recurrent melanoma tumor in the skin.

For local, satellite, and/or in-transit recurrence, and regional lymph node recurrence the first recommended test is a biopsy to confirm the

diagnosis. This may include an FNA, incisional biopsy, excisional biopsy, or core biopsy. During the biopsy, your doctor may remove another tissue sample for genetic testing if you might join a clinical trial or receive targeted therapy.

Imaging tests may be done for baseline staging and to check out specific signs or symptoms. A baseline is a starting point to which future test results are compared. Such imaging tests may include a CT scan of your chest, abdomen, and pelvis; an MRI of your brain; and/or a PET/CT scan.

Next steps

For a true local scar recurrence and a node-negative recurrence (satellite or in-transit recurrence) treatment, see Guide 16 on the next page. For regional lymph node recurrence treatment, see Guide 18 on page 68 for the next options.

Guide 16 shows the treatment options for cancer that came back (recurred) in or near the site of the first melanoma. Node-negative means that there are no cancer cells in the lymph nodes.

For true local scar recurrence (persistent disease), more tissue may be removed from the tumor site. This would be the normal-looking tissue that was around the primary tumor. This is called the surgical margin. Your doctor would decide how much would be removed.

You may also have lymph node mapping and sentinel lymph node biopsy based on the features of the recurrence. The mapping will allow your doctor to locate the sentinel node for biopsy. Any adjuvant treatment will be based on the pathologic stage of the recurrence as described in Guide 4 on page 41.

For local, satellite, and/or in-transit recurrence, systemic therapy is an option. Local therapies may also be offered. This includes a complete resection if all of the cancer can be removed. If the margins are clear this means there are no cancer cells in the normal-looking tissue around the edge of the tumor removed during surgery.

Guide 15. Tests for persistent melanoma and nonmetastatic recurrence

Stage		Tests
True local scar recurrence (persistent disease)	→	• Skin biopsy to confirm • Other tests based on the features and stage of the primary tumor
Local, satellite, and/or in-transit recurrence	→	• Biopsy to confirm • Imaging tests to assess the extent of disease, and to check out specific signs or symptoms
Regional lymph node recurrence	→	

If surgery isn't possible, other local therapy options include T-VEC, BCG, interferon alfa, or IL-2 injections into the tumor, imiquimod cream rubbed onto the tumor, and ablative therapy. Your doctor may consider palliative radiation to relieve symptoms if the cancer can't be removed by surgery or local ablative therapy. A regional therapy option is isolated limb infusion/perfusion with the chemotherapy drug melphalan.

Next steps

For local, satellite, and/or in-transit recurrence treatment response and next treatment options, see Guide 17 on page 67. If you will receive systemic therapy, see Guide 23 on page 74. Recommended follow-up tests during observation and after treatment are based on the cancer stage. For stage 0, I, or II, see Guide 10 on page 57. For stage III, see Guide 14 on page 63. For metastatic melanoma tests, see Guide 20 on page 71.

Guide 16. Node-negative recurrence treatment

Stage		Treatment of recurrence		Adjuvant treatment
True local scar recurrence (persistent disease)	→	• Remove more tissue from the tumor site (for clear margins) • Possible lymph node mapping and SLN biopsy	→	• Options based on the pathologic stage of the recurrence
Local, satellite, and/or in-transit recurrence	→	• Systemic therapy • Local therapy: ◦ Complete excision to clear margins, if possible ◦ T-VEC, BCG, interferon alfa, or IL-2 injection in tumor ◦ Local ablation therapy ◦ Imiquimod cream ◦ Consider radiation therapy can't be removed by surgery • Regional therapy: ◦ Isolated limb infusion/perfusion with melphalan	→	• See Guide 17

Guide 17 shows treatment response and further treatment options for a local, satellite, and/or in-transit recurrence. After initial treatment for the recurrence, your doctor will give imaging tests to check how well treatment worked.

An outcome or improvement caused by treatment is called a treatment response. Based on these tests, you may have further treatment.

Guide 17. Node-negative recurrence response and next treatment

Stage	Response	Second-line treatment	Next treatment
Local, satellite, and/or in-transit recurrence	→ After surgery: • No evidence of disease	→	• Adjuvant treatment: ◦ Observation ◦ Nivolumab ◦ Dabrafenib/ trametinib ◦ Interferon alfa
	→ After surgery: • Less than complete resection	→ • Systemic therapy • Local therapy: ◦ T-VEC, BCG, interferon alfa, or IL-2 injection in tumor ◦ Local ablation therapy ◦ Imiquimod cream ◦ Consider radiation therapy if not given before • Regional therapy: ◦ Isolated limb infusion/perfusion with melphalan	• Treatment options are based on response to second-line treatment
	→ After other treatment, not surgery: • Clinical assessment ± imaging shows disease remains or is progressing	→	
	→ After other treatment, not surgery: • Clinical assessment ± imaging shows no evidence of disease	→	• Observation

If you had surgery as the primary treatment and there are no signs of cancer, your next options for adjuvant treatment are to begin observation, receive nivolumab, receive dabrafenib and trametinib if you have a *BRAF* V600–activating mutation, or receive interferon alfa. Observation is a period of scheduled follow-up testing to watch for cancer metastasis or recurrence.

If you had treatment other than surgery and the cancer remains or is progressing, then you have the same options as listed for cancer that remains after surgery. If you had treatment other than surgery as the primary treatment and there are no signs of cancer, then you may begin observation.

Next steps

If you will receive systemic therapy, see Guide 23 on page 74.

Guide 18 shows the treatment options for cancer that came back in the lymph nodes near the first (primary) melanoma. This is called regional lymph node recurrence.

The treatment options for regional lymph node recurrence depend on whether or not you already had a lymph node dissection. A lymph node dissection is surgery to remove some or all of the lymph nodes in the area near the tumor. Read Part 4 on page 35 for details on each treatment.

If you didn't have a lymph node dissection before, then a complete lymph node dissection is recommended to remove all of the cancer. After surgery, you may receive adjuvant treatment, and the available systemic options have increased. Your doctor will discuss the use of local and systemic treatment as adjuvant treatment options.

Guide 18. Regional lymph node recurrence treatment

Stage		Treatment of recurrence
No prior lymph node dissection	→	• Complete lymph node dissection to remove all of the cancer, then adjuvant treatment
Had lymph node dissection and you're able to have surgery	→	• Remove lymph node recurrence + complete lymph node dissection if incomplete before, then adjuvant treatment
Had lymph node dissection and you aren't able to have surgery	→	• Systemic therapy (preferred) • Palliative radiation therapy • T-VEC injection into tumor • Best supportive care

If you already had a lymph node dissection and you are able to have surgery, then surgery to remove the cancer (tumor excision) with negative margins is recommended. All of the lymph nodes in the affected area should also be removed if you didn't have a "complete" lymph node dissection before. After surgery, you may have adjuvant treatment. Your doctor will discuss the use of local and systemic treatment as adjuvant treatment options.

If you already had a lymph node dissection and you are unable to have surgery or the cancer is widespread, you have several options. The first and preferred option is to receive systemic therapy. The second option is to receive palliative radiation therapy. The third option is to receive the immunotherapy drug T-VEC as an injection into the tumor.

Another option is to receive best supportive care. Supportive care is treatment to relieve the symptoms caused by cancer and side effects of cancer treatment. See page to read more about supportive care.

Next steps

If you will receive systemic therapy, see Guide 23 on page 74.

Guide 19 shows the options for adjuvant treatment after surgery for regional lymph node recurrence. Adjuvant treatment is additional treatment given after the main one to try to kill any remaining cancer cells and lower the chance of recurrence.

Guide 19. Regional lymph node recurrence adjuvant treatment

Treatment of recurrence		Adjuvant treatment
All cancer was removed	→	• Local therapy: ◦ Possible radiation therapy to nodal basin in certain high-risk patients • Systemic therapy: ◦ Observation ◦ Nivolumab ◦ Dabrafenib/trametinib ◦ High-dose ipilimumab ◦ Interferon alpha ◦ Biochemotherapy
All of the cancer was not removed	→	• Systemic therapy (preferred) • Palliative radiation therapy • T-VEC injection into tumor • Best supportive care

If all of the cancer was removed with surgery, then you have several adjuvant treatment options. Your doctor may consider radiation therapy to the nodal basin—the area near the tumor where the group of lymph nodes was removed—to help prevent recurrence in the nodal basin. For more details, read about radiation therapy on page 46.

You may begin observation at this time. Another option is to receive nivolumab, dabrafenib and trametinib for patients with *BRAF* V600 activating mutation, high-dose ipilimumab, or interferon alfa.

Another option is to receive biochemotherapy. Biochemotherapy is combination treatment with chemotherapy and immunotherapy. It is a very strong treatment and may not be a good option for everyone. For metastatic melanoma, biochemotherapy consists of dacarbazine, cisplatin, vinblastine, IL-2, or interferon alfai.

If all of the cancer wasn't removed with surgery, then you also have several adjuvant treatment options. The preferred option is to receive systemic therapy. The second option is to receive palliative radiation therapy to relieve the symptoms of melanoma.

Another option is to receive the immunotherapy drug T-VEC as an injection into the tumor. Another option is to receive best supportive care. Supportive care is treatment to relieve the symptoms caused by the cancer or side effects of cancer treatment.

Next steps

If you will receive systemic therapy, see Guide 23 on page 74.

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At my local hospital, the initial treatment proposal was radical surgery. I sought a second opinion at a cancer center and researched the standard of care, and concluded with help that immunotherapy and participation in a clinical drug trial were the best options for me.

- John, current age 35
  diagnosed at age 41

Metastatic melanoma

This section explains the recommended tests and treatments for melanoma that has spread far away from the first (primary) tumor. This is called metastatic melanoma. Melanoma with distant metastases when first found (diagnosed) is stage IV cancer. However, cancer may come back in a distant site after previous melanoma treatment. This is called a distant metastatic recurrence. The recommended tests and treatments are the same for an initial diagnosis of metastatic melanoma and for metastatic recurrence.

Guide 20 shows the tests that are needed for metastatic melanoma. The first step is to confirm the metastatic cancer with a biopsy of one of the distant tumors. An FNA, core, incisional, or excisional biopsy may be used. Your doctor may remove another tissue sample for genetic testing if you're thinking about entering a clinical trial or getting targeted therapy.

A blood test to measure your LDH level is recommended. This test will give information about your prognosis—the likely course or outcome of the disease. Your doctor may also order other blood tests. For example, your doctor may test for *BRAF* and other genetic changes as well.

Imaging tests are recommended for baseline staging and to evaluate specific signs and symptoms. A baseline is a starting point to which future test results are compared. This may include a CT scan of your chest, abdomen, and pelvis; a PET/CT scan; and/or an MRI of your brain.

Guide 21 shows the treatment options for metastatic melanoma. The treatment options depend on whether or not all of the cancer can be removed by surgery. Limited metastatic disease is when cancer has spread to only one or a few distant sites. It is resectable, which means it can be treated with surgery. Widespread metastatic disease is when cancer has spread to too many distant sites. It is unresectable, which means it can't be treated with surgery.

For limited metastatic disease, one of the first treatment options is surgery to remove the whole tumor if possible. The next options depend on whether or not disease remains. If there is no evidence of disease, you can begin observation or receive nivolumab. If surgery is not possible, you may receive systemic therapy.

Guide 20. Metastatic melanoma tests

Stage		Tests
Stage IV	→	• Biopsy (FNA, core, incisional, or excisional) of distant tumor • LDH • Imaging tests for baseline staging and to check out specific signs or symptoms

After a period of observation or systemic therapy, your doctor will repeat imaging tests to show if there are any other metastatic cancer sites. If the imaging tests don't show any other cancer, then you may have surgery to remove the metastatic tumor. If they do show other cancer, then you will have treatment for widespread metastatic disease.

If the tests are negative for other disease after systemic therapy, you may have surgery. The next treatment options depend on whether or not all of the cancer was removed. If all of the cancer was removed by surgery, then you may begin observation or receive nivolumab. If all of the cancer wasn't removed by surgery, then you will receive treatment for widespread metastatic disease, which is described next.

For widespread metastatic disease, the first step is to assess for metastases in your brain. If you have brain metastases, then you will likely receive treatment for the cancer in your brain first to try to prevent other serious medical conditions. This may include surgery and/or radiation therapy. (For more information on treating cancer in the brain and spinal cord, see the *NCCN Guidelines for Central Nervous System Cancers*. These guidelines are online at www.NCCN.org. They were written for your doctor, so he or she will likely be able to answer your questions about treatment.)

Guide 21. Metastatic melanoma treatment

Stage	Treatment for metastatic disease	Next treamtent
Limited stage IV (Resectable - cancer can be removed with surgery)	→ • Surgery to remove cancer	→ • If no evidence of disease, observe or nivolumab • If disease remains, treat as widespread
	→ • Systemic therapy, then imaging tests to check response or for disease progression	→ • If negative for disease, resect and if no disease observe or nivolumab, or if disease remains, treat as widespread • If postive for disease, treat as widespread
Widespread stage IV (Unresectable - cancer can't be removed with surgery)	→ • If no cancer in the brain, see next treatment options	→ • Systemic therapy • T-VEC injection into tumor • Possible palliative surgery and/or radiation therapy for symptoms • Best supportive or palliative care
	→ • If cancer in the brain, possible radiation therapy or palliative surgery ± radiation therapy for brain metastases	→

After treating the brain metastases, you can move on to the main treatment options for widespread metastatic disease. These options are the same regardless of brain metastases.

There are four options for treating widespread metastatic disease. The first option is to receive systemic therapy. The second option is to receive the immunotherapy drug T-VEC as an injection into the tumor. The third option is to consider palliative surgery and/or radiation therapy to relieve the symptoms caused by the cancer. Palliative treatment can be given alone or in addition to the other options. The fourth option is to receive best supportive or palliative care. For more about supportive care, see page 47.

Next steps

For systemic therapy options, see Guide 23 on page 74. See Guide 22 on page 73 for follow-up tests after completing treatment for metastatic melanoma.

Guide 22 shows the follow-up tests that are needed after completing treatment for metastatic melanoma. Follow-up tests are used to monitor you after treatment to check for cancer return (recurrence) or spread (metastasis). These tests are important if you were treated for stage IV melanoma and have no current signs of cancer.

A complete skin exam by your doctor is recommended every year for life. In addition, you should also examine your own skin and lymph nodes on a regular basis. You should also have regular medical history check-ups and physical exams. During the physical exam, your doctor will carefully examine your lymph nodes and skin.

Imaging tests are recommended to check out specific signs or symptoms of cancer. You may also have imaging tests to screen for cancer recurrence or metastases. Screening means testing to detect a disease when there are no signs or symptoms present.

Depending on the stage of your initial melanoma or extent of recurrent disease, you may undergo imaging tests for screening every 3 to 12 months.

Guide 22. Metastatic melanoma follow-up testing

Stage (no evidence of disease)		Follow-up tests
Stage IV	→	• Regular self-exam of skin and lymph nodes • Medical history and physical exam with focus on skin and lymph nodes ◦ Every 3 to 6 months for 2 years, then ◦ Every 3 to 12 months for 3 years, then ◦ Every year as needed • Imaging tests as needed to check specific signs and symptoms • Possible imaging tests every 3 to 12 months to screen for recurrence or metastases • See Guide 10, *All stages* for more follow-up care

This may include a CT scan of your chest, abdomen, and pelvis; MRI of your brain; and/or a PET/CT scan. Your doctor may also consider doing an x-ray of your chest to watch for cancer spread in your lungs.

These tests may be done for up to 3 to 5 years after treatment has ended. Routine imaging tests are not recommended after 3 to 5 years if there has been no recurrence and you don't have any symptoms. Routine blood tests to check for recurrence are not recommended.

Guide 23 shows the first-line and second-line systemic therapy options that are recommended for metastatic or unresectable melanoma. Metastatic melanoma is when the cancer has spread to other organs and parts of the body far away from the primary tumor. Unresectable means all of the cancer can't be removed by surgery (resection).

First-line treatment options

First-line treatment is the first treatment or set of treatments given for a disease. There are several first-line treatment options to choose from. One option is to receive treatment with one immunotherapy drug—called a single agent—such as pembrolizumab or nivolumab, which are anti-PD1 inhibitors. Or, you may receive both nivolumab and ipilimumab together—called a combination regimen.

If you have melanoma with a mutated *BRAF* gene, then another option is to receive targeted therapy.

Guide 23. Systemic therapy for metastatic or unresectable melanoma

First-line therapy	Second-line therapy
• Immunotherapy: ◦ Pembrolizumab ◦ Nivolumab ◦ Nivolumab/ipilimumab	• Immunotherapy: ◦ Pembrolizumab ◦ Nivolumab ◦ Nivolumab/ipilimumab
• Targeted therapy if *BRAF* mutated: ◦ Dabrafenib/trametinib ◦ Vemurafenib/cobimetinib	• Targeted therapy if *BRAF* mutated: ◦ Dabrafenib/trametinib ◦ Vemurafenib/cobimetinib
	• Ipilimumab
	• High-dose IL-2
	• Cytoxic agents: ◦ Dacarbazine ◦ Temozolomide ◦ Paclitaxel ◦ Albumin-bound paclitaxel ◦ Carboplatin/paclitaxel
	• Imatinib for tumors with activating mutations of *KIT*
	• Consider best supportive care for poor perfomance status

Targeted therapy may be preferred if it is needed for an early treatment response. Treatment responses to single-agent immunotherapy can take longer in some cases. Thus, targeted therapy may be preferred if melanoma is causing symptoms or progressing quickly or if your overall health is getting much worse.

The immunotherapy drugs and targeted therapy drugs cause different side effects. Thus, your doctor will look at a number of factors to decide which treatment option is best for you. Such factors include your overall health, medical history, other current health problems, other current medicines, and your ability to take your medicine exactly as prescribed.

Treatment results

After starting systemic therapy, your doctor will give follow-up tests to check how well it is working. Progression is when the cancer grows, spreads, or gets worse. Maximum response is when the cancer is no longer shrinking or getting better in response to treatment. At this point, your doctor will consider second-line treatment options.

Second-line treatment options

The next systemic therapy options or second-line treatment options are recommended if the melanoma has progressed or stopped responding to first-line treatment. Your doctor will consider how well the first-line treatment is working. Second-line treatment will follow first-line treatment that did not work or cancer that progressed after completing first-line treatment. If disease progresses soon after, you may receive treatment with a different type of drug. If the disease comes back 3 months after the completing the first-line treatment, the same type of drug you got the first time may be given again.

You may receive an immunotherapy drug—as a single agent—such as pembrolizumab or nivolumab which are anti-PD1 inhibitors. Other single agent immunotherapy options may include ipilimumab or high-dose IL-2. Or, you may receive both nivolumab and ipilimumab together—called a combination regimen.

If you have melanoma that has a mutated *BRAF* gene, you may receive a targeted therapy. There are two combination therapy options: dabrafenib and trametinib or vemurafenib and cobimetinib. If you have melanoma that has a mutation of the *c-kit* gene, then another option is to receive imatinib. Imatinib is a type of targeted therapy. (See page 43 for details on imatinib.)

Other systemic chemotherapy options are dacarbazine, temozolomide, paclitaxel, nab-paclitaxel, and carboplatin/paclitaxel. Most of these drugs are given alone—called single agents. But, carboplatin and paclitaxel may be given together—called a combination regimen.

If your overall health is somewhat poor, and you can't do all of your daily activities or much physical work, best supportive care may be recommended. Supportive care is treatment given to relieve symptoms caused by cancer or side effects of cancer treatment. It does not treat the cancer itself, but aims to improve your well-being and quality of life.

NCCN experts also recommend participating in a clinical trial at any stage of disease. A clinical trial type of research that studies the safety and effectiveness of a test or treatment. See page 48 for more information on clinical trials or refer to the websites listed in Part 6.

6
Making treatment decisions

It's your choice

The role patients want in choosing their treatment differs. You may feel uneasy about making treatment decisions. This may be due to a high level of stress. It may be hard to hear or know what others are saying. Stress, pain, and drugs can limit your ability to make good decisions. You may feel uneasy because you don't know much about cancer. You've never heard the words used to describe cancer, tests, or treatments. Likewise, you may think that your judgment isn't any better than your doctors'.

Letting others decide which option is best may make you feel more at ease. But, whom do you want to make the decisions? You may rely on your doctors alone to make the right decisions. But, your doctors may not tell you which to choose if you have multiple good options. You can also have loved ones help. They can gather information, speak on your behalf, and share in decision-making with your doctors. Even if others decide which treatment you will receive, your treatment team may still ask that you sign a consent form.

On the other hand, you may want to take the lead or share in decision-making. In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. Your doctors know the science behind your plan but you know your concerns and goals. By working together, you can decide on a plan that works best for you when it comes to your personal and health needs.

Questions to ask

You will likely meet with experts from different fields of medicine. It is helpful to talk with each person. Prepare questions before your visit and ask questions if the information isn't clear. You can get copies of your medical records. It may be helpful to have a family member or friend with you at these visits to listen carefully and even take notes. A patient advocate or navigator might also be able to come. They can help you ask questions and remember what was said.

The questions below are suggestions for information you read about in this book. Feel free to use these questions or come up with your own personal questions to ask your doctor and other members of your treatment team.

What's my diagnosis and prognosis?

It's important to know that there are different types of cancer. Cancer can greatly differ even when people have a tumor in the same organ. Based on your test results, your doctors can tell you which type of cancer you have. He or she can also give a prognosis. A prognosis is a prediction of the pattern and outcome of a disease. Knowing the prognosis may affect what you decide about treatment.

1. Where did the cancer start? In what type of cell?
2. Is this cancer common?
3. What is the cancer stage? Does this stage mean the cancer has spread far?
4. What other tests results are important to know?
5. How often are these tests wrong?
6. Would you give me a copy of the pathology report and other test results?
7. Can the cancer be cured? If not, how well can treatment stop the cancer from growing?

What are my options?

There is no single treatment practice that is best for all patients. There is often more than one treatment option along with clinical trial options. Your doctor will review your test results and recommend treatment options.

1. What will happen if I do nothing?
2. Can I just carefully monitor the cancer?
3. Do you consult NCCN recommendations when considering options?
4. Do your options include clinical trials?
5. How do my age, health, and other factors affect my options?
6. Which option is proven to work best?
7. Which options lack scientific proof?
8. What are the side effects of each treatment?
9. What can be done to prevent or relieve the side effects of treatment?
10. How quickly must I make these treatment decisions?

What does each option require of me?

Many patients consider how each option will practically affect their lives. This information may be important because you have family, jobs, and other duties to take care of. You also may be concerned about getting the help you need. If you have more than one option, choosing the option that is the least taxing may be important to you.

1. Will I have to go to the hospital or elsewhere? How often? How long is each visit?
2. Do I have a choice of when to begin treatment? Can I choose the days and times of treatment?
3. How do I prepare for treatment? Do I have to stop taking any of my medicines? Are there foods I will have to avoid?
4. Should I bring someone with me when I get treated?
5. How much will the treatment cost me? What does my insurance cover?
6. Will I miss work or school? Will I be able to drive?
7. Is home care after treatment needed? If yes, what type?
8. How soon will I be able to manage my own health?
9. When will I be able to return to my normal activities?

What is your experience?

More and more research is finding that patients treated by more experienced doctors have better results. It is important to learn if a doctor is an expert in the cancer treatment he or she is offering.

1. Are you board certified? If yes, in what area?
2. How many patients like me have you treated?
3. How many procedures like the one you're suggesting have you done?
4. Is this treatment a major part of your practice?
5. How many of your patients have had complications?

Deciding between options

Deciding which option is best can be hard. Doctors from different fields of medicine may have different opinions on which option is best for you. This can be very confusing. Your spouse or partner may disagree with which option you want. This can be stressful. In some cases, one option hasn't been shown to work better than another, so science isn't helpful. Some ways to decide on treatment are discussed next.

Getting a 2nd opinion

Even if you like and trust your doctor, it is helpful to get a 2nd opinion. You will want to have another doctor review your test results. He or she can suggest a treatment plan or check the one you already heard about.

Things you can do to prepare:

- Check with your insurance company about its rules on 2nd opinions. You want to know about out-of-pocket costs for doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your 2nd opinion. Do this well before your appointment. If you run into trouble having records sent, pick them up and bring them with you.

If the new doctor offers other advice, make an appointment with your first doctor to talk about the differences. Do whatever you need to feel confident about your diagnosis and treatment plan.

Getting support

Support groups often include people at different stages of treatment. Some may be in the process of deciding while others may be finished with treatment. At support groups, you can ask questions and hear about the experiences of other people with melanoma. If your hospital or community doesn't have support groups for people with melanoma, check out the websites on the next page.

You can also reach out to a social worker or psychologist. They can help you find ways to cope or refer you to support services. These services may also be available to your family, friends, and to those with children, so they can connect and get support.

Keep in mind...

- ✓ Every treatment option has benefits and risks. Consider these when deciding which option is best for you.
- ✓ Talking to others may help learn about benefits and risks you haven't thought of.

Websites

AIM at Melanoma
aimatmelanoma.org

American Cancer Society
cancer.org/cancer/skincancer-melanoma/

www.cancer.org/Treatment/FindingandPayingforTreatment/index

Melanoma Research Alliance
curemelanoma.org

Melanoma Research Foundation
melanoma.org

National Cancer Institute
cancer.gov/types/skin/patient/melanoma-treatment-pdq

National Coalition for Cancer Survivorship
canceradvocacy.org/toolbox

NCCN Patient and Caregiver Resources
nccn.org/patients

Review

- Shared decision-making is a process in which you and your doctors plan treatment together.
- Asking your doctors questions is vital to getting the information you need to make decisions.
- Getting a 2nd opinion, attending support groups, and comparing benefits and risks may help you decide which treatment is best for you.

“

I am Blessed. I live in a small, rural town and have had unbelievable support from several churches and numerous friends. My family has always been very positive as well. The medical staff has shown great empathy for my situation and we have laughed about it for six years now. Not that cancer is funny, but laughter at the ridiculous situation I found myself in. For me, laughter was the best medicine.

- Marty, current age 55
  diagnosed at age 49

Dictionary

ABCDE rule
A memory device for characteristics of moles or skin lesions that might be cancer.

abdomen
The belly area between the chest and pelvis.

ablative therapy
Use of intense, narrow beams of light or carbon dioxide to cut into the surface of the skin and kill cancer cells.

abnormal
Not normal.

acral lentiginous melanoma
An uncommon type of melanoma that looks like a bruise on the palms of the hands or soles of the feet or like a dark stripe in a nail.

adjuvant treatment
Treatment given after the main (primary) treatment.

advanced melanoma
Cancer that has spread beyond the area near the main tumor.

anesthesia
A controlled loss of feeling with or without loss of wakefulness.

anesthetic
A drug or other substance that causes a controlled loss of feeling or awareness with or without loss of wakefulness.

angiolymphatic invasion
Melanoma has grown into (invaded) lymph or blood vessels.

asymmetry
One half or side of the mole does not match the other half or side.

atypical mole
A mole that looks different from a normal or common mole.

autoimmune disorder
A condition in which the body's natural defense against infection and disease (immune system) attacks healthy tissue in the body.

Bacillus Calmette-Guérin (BCG)
A germ similar to the one that causes tuberculosis that is given to activate the body's natural defense against disease.

baseline
A starting point to which future test results are compared.

biochemotherapy
Combination treatment with immunotherapy (drugs that boost the body's natural response to fight disease) and chemotherapy (drugs that kill fast-growing cells).

biological therapy
Treatment that boosts the body's natural defense against disease.

biopsy
Removal of small amounts of tissue from your body to test for disease.

blood test
A test that checks for signs of disease in the blood.

blood thinner
A medication given to prevent or treat blood clots.

blood vessel
A tube that carries blood throughout the body.

border irregularity
The edges (border) of the mole are ragged or notched.

Breslow thickness
A measure of how deep the melanoma tumor has grown into the skin.

broad-spectrum sunscreen
A substance that protects the skin from the sun by blocking 2 types of harmful ultraviolet (UV) rays—UVA and UVB.

cancer stage
Rating or description of the growth and spread of cancer in the body.

cells
The "building blocks" of tissues in the body.

central nervous system (CNS)
The brain and spinal cord.

chemotherapy
Drugs that kill fast-growing cells, including normal cells and cancer cells.

Clark level
A scale of tumor depth with 5 scores based on which layer of skin the tumor has grown into.

clinical stage
A rating of the extent of melanoma in the body based on the physical exam and biopsy of the first (primary) tumor.

clinical trial
Research on a test or treatment to assess its safety or how well it works.

combination regimen
The use of two or more drugs.

computed tomography (CT) scan
A test that uses x-rays from many angles to make a picture of the inside of the body.

connective tissue
Supporting and binding tissue that surrounds other tissues and organs.

contrast dye
A dye put into your body to make clearer pictures during tests that take pictures of the inside of the body.

cytokines
Substances made in the body that boost or activate the immune system (the body's natural defense against disease). Cytokines can also be made in a lab.

deep margin status
Presence or absence of cancer cells in the normal-looking tissue under a tumor removed during surgery.

dermal mitotic rate
A measure of how many cancer cells are actually growing and dividing.

dermatologist
A doctor who's an expert in diseases of the skin.

dermatopathologist
A doctor who's an expert in testing skin cells and tissues for disease.

dermis
The second layer of skin that is beneath the top layer (epidermis).

desmoplastic melanoma
A melanoma tumor with dense connective tissue.

diagnosis
Identification of a disease.

distant metastasis
Cancer cells have spread to a part of the body far away from the first (primary) melanoma tumor.

epidermis
The outer layer of skin.

excision
Removal by surgery.

excisional biopsy
Surgery that removes the entire skin tumor or abnormal-looking area (lesion) to test for cancer cells.

excisional lymph node biopsy
Surgery that removes the entire enlarged lymph node(s) through a surgical cut in the skin to test for cancer cells.

external beam radiation therapy
Radiation therapy (use of high-energy rays to destroy cancer cells) received from a machine outside the body.

fatigue
Severe tiredness despite getting enough sleep that limits one's ability to function.

fine-needle aspiration (FNA) biopsy
Use of a thin needle to remove fluid or tissue from the body to be tested for disease.

follow-up tests
Tests done after treatment to check for signs of cancer return (recurrence) or spread (metastasis).

genes
A set of coded instructions in cells for making new cells and controlling how cells behave.

general anesthesia
A controlled loss of wakefulness from drugs.

genetic test
Tests of the instructions in cells for making and controlling cells.

gland
An organ that makes fluids or chemicals the body needs.

groin
The area of the body where the thigh meets the lower belly area (abdomen).

histologic subtype
Grouping of cancer types based on cancer cell qualities.

hormones
Chemicals in the body that activate cells or organs.

imaging tests
Tests that make pictures (images) of the inside of the body.

imiquimod cream
A drug made as a cream that boosts the immune system (the body's natural defense against disease) response against skin cancer cells.

immune cells
Cells that are part of the body's natural defense against infection and disease.

immune system
The body's natural defense against infection and disease.

immunotherapy
Treatment that activates or boosts the body's natural defense against disease (immune system) to fight cancer.

incisional biopsy
Surgery that removes part of the skin tumor or abnormal-looking area (lesion) to test for cancer cells.

in situ
In its original place.

intestine
The organ that eaten food passes through after leaving the stomach.

in-transit metastases
Cancer that has spread into lymph vessels near the first tumor but not into lymph nodes (groups of special disease-fighting cells).

in-transit recurrence
Cancer that has come back after treatment in lymph vessels near the first tumor but not in lymph nodes (groups of special disease-fighting cells).

isolated limb infusion/perfusion
Anticancer drugs are given directly into an arm or leg in a way that they don't reach or affect the rest of the body.

kidneys
A pair of organs that filter blood and remove waste from the body through urine.

lactate dehydrogenase (LDH)
A substance found in the blood that is involved in energy production in cells.

lentigo maligna melanoma
The slowest growing type of melanoma; it starts in sun-exposed skin and is commonly mistaken for a sunspot.

lesion
An area of abnormal tissue that has been damaged by disease or injury.

limited metastatic disease
Cancer that has spread to one or a few distant sites.

liver
An organ that removes waste from the blood.

local anesthesia
Medicine that results in a temporary loss of feeling in a small area of the body to prevent pain in that area during a test or procedure.

local melanoma
Cancer cells haven't spread beyond the skin near the first (primary) tumor.

local metastasis
The spread of cancer cells from the first tumor to a nearby site.

local recurrence
Cancer that has come back after treatment in or near the same place as the first tumor. A satellite recurrence is a type of local recurrence.

local therapy
Treatment that affects cells in one small, specific part of the body only, such as the tumor and nearby area.

long-term side effect
An unplanned or unwanted physical or emotional response to treatment that continues for months or years after finishing treatment.

lymph
A clear fluid containing white blood cells that fight infection and disease.

lymphedema
Swelling due to buildup of a clear fluid containing white blood cells (lymph).

lymph node
Small groups of special disease-fighting cells located throughout the body.

lymph node biopsy
Removal of all or part of a lymph node (groups of special disease-fighting cells located throughout the body) to test for disease.

lymph node dissection
Surgery to remove some or all lymph nodes (groups of special disease-fighting cells) from the area near the tumor.

lymph node recurrence
Cancer that has come back after treatment and has spread to lymph nodes (groups of special disease-fighting cells).

lymph vessels
Tubes that carry lymph—a clear fluid containing white blood cells that fight disease and infection—throughout the body and connect lymph nodes to one another. Also called lymphatic channels.

magnetic resonance imaging (MRI) scan
A test that uses radio waves and powerful magnets to make pictures of the inside of the body showing the shape and function of body parts.

medical history
All health events and medications taken to date.

medical skin exam
A careful examination of your skin by a doctor to check for any areas that look abnormal.

melanin
A substance that gives color to the skin.

melanocytes
Cells that are located in the lower part of the top layer of the skin (epidermis) and make a substance that gives skin its color.

melanoma
Cancer that starts in melanocytes—cells that give skin its color and are located in the top layer of the skin (epidermis).

melanoma in situ
Cancer cells are only in the outer layer of the skin (epidermis).

metastases
Tumors formed by cancer cells that have spread from the first tumor to other parts of the body.

metastasis
The spread of cancer cells from the first tumor to another body part.

metastatic
Containing cancer cells that have spread from the first tumor.

microsatellitosis
Tiny tumors (satellites) that have spread to skin near the first melanoma tumor and can only be seen with a microscope.

microscope
A tool that uses lenses to see things the eyes can't.

microscopic
Something so small it can't be seen by the naked eye.

mole
A spot on the skin formed by a cluster of cells that make melanin (substance that gives skin its color).

monoclonal antibody
A type of immune system protein made in a lab that can attach to substances in the body such as cancer cells.

negative margins
There are no cancer cells in the normal-looking tissue around the edge of the tumor removed during surgery.

neoadjuvant treatment
Treatment given before the main or primary treatment.

neurotropism
Melanoma cells are able to grow into (invade) nerves.

nodal basin
A group or cluster of lymph nodes (groups of special disease-fighting cells) located close to one another in a certain area of the body such as near a tumor.

node-negative
Cancer cells are not found in lymph nodes (groups of special disease-fighting cells located throughout the body).

node-positive
Cancer cells are found in lymph nodes (groups of special disease-fighting cells located throughout the body).

nodular melanoma
A type of melanoma that has a dome shape and may grow more quickly into the second layer of skin (dermis) than other melanomas.

non-melanoma skin cancer
Cancer of the skin that starts in cells other than melanocytes (cells that give skin its color).

nonmetastatic recurrence
Cancer that has come back after treatment but has not spread to parts of the body far away from the first tumor.

observation
A period of scheduled follow-up testing to watch for signs of cancer spread (metastasis) or return (recurrence).

palliative treatment
Treatment given to relieve symptoms caused by cancer or side effects caused by cancer treatment. Also called supportive care.

pathologic stage
A rating of the extent of melanoma in the body based on tests of lymph nodes and other tissue removed during surgical treatment.

pathologist
A doctor who's an expert in testing cells and tissue to find disease.

pathology report
A document with information about cancer cells and tissue that were removed from the body and examined with a microscope for disease.

pelvis
The body area between the hipbones.

peripheral margin status
Presence or absence of cancer cells in the normal-looking tissue around the sides of a tumor removed during surgery.

persistent melanoma
Cancer not completely removed or destroyed by treatment; persistent melanoma is found in or right next to the surgical scar where the first melanoma was removed. Also called true local scar recurrence.

physical exam
A review of the body by a health expert for signs of disease.

positive margins
There are cancer cells in the normal-looking tissue around the edge of the tumor removed during surgery.

positron emission tomography (PET) scan
A test that uses radioactive material to see the shape and function of organs and tissues inside the body.

primary treatment
The main treatment used to rid the body of cancer.

primary tumor
The first mass of cancer cells in the body.

prognosis
The likely or expected course and outcome of a disease.

protein
A chain of chemical compounds important to every cell in the body.

punch biopsy
Removal of tissue using a sharp, hollow, round-shaped knife in order to test it for disease.

radiation therapy
Use of high-energy rays to destroy cancer cells.

radiotracer
Matter with energy that is put into the body to make pictures clearer.

recurrence
The return of cancer after treatment.

regimen
A treatment plan that specifies the dosage, schedule, and duration of treatment.

regional lymph node recurrence
Cancer that has come back after treatment in lymph nodes (groups of special disease-fighting cells) near the first melanoma.

regional lymph nodes
Groups of special disease-fighting cells located near the tumor.

regional melanoma
Cancer cells have spread from the first tumor to nearby lymph vessels, lymph nodes (groups of special disease-fighting cells), and/or nearby skin.

regional therapy
Treatment with cancer-killing drugs directed to a specific area of the body such as an arm or leg.

rheumatoid arthritis
An autoimmune disorder that causes pain, swelling, and stiffness in the joints.

risk evaluation and mitigation strategy (REMS) program
A program to monitor and manage serious side effects (unplanned physical or emotional effects) of cancer treatments.

risk factor
Something that increases the chance of getting a disease.

satellite metastases
Small melanoma tumors (satellites) in the skin near the first (primary) tumor.

satellite recurrence
Cancer that came back after treatment and formed small melanoma tumors in lymphatic channels in the skin deep within the scar site or just outside of the surgical scar of the first tumor.

scar
A permanent mark on the skin after an injury or surgery.

self-exam of skin
A careful review of your own skin for abnormal-looking spots that may be signs of skin cancer.

sentinel lymph node
The first lymph node (groups of special disease-fighting cells) to which lymph, and possibly a cancer cell, travels after leaving the first (primary) tumor.

sentinel lymph node biopsy
Surgery to remove the first lymph node to which lymph, and possibly a cancer cell, travels after leaving the first (primary) tumor.

shave biopsy
Surgery that removes a thin tissue sample from the top of a tumor to test for cancer cells.

side effect
An unplanned or unwanted physical or emotional condition caused by treatment.

single agent
The use of one drug.

skin biopsy
Removal of a sample of tissue from the skin to test for disease.

skin exam
A careful review of the skin to check for abnormal-looking spots that may be signs of skin cancer.

spleen
An organ to the left of the stomach that helps protect the body against disease.

staging
The process of rating and describing the extent of cancer in the body.

stereotactic radiosurgery (SRS)
A type of radiation therapy that delivers a high dose of radiation to a small, specific area.

subcutaneous
Below the skin.

sun protection factor (SPF)
A rating of the level of protection sunscreen products provide against the UV rays from the sun.

superficial
At, on, or near the top or surface.

superficial spreading melanoma
The most common type of melanoma; it grows slowly and spreads from a mole.

supportive care
Treatment given to relieve the symptoms caused by cancer or side effects caused by cancer treatment. Also called palliative treatment.

surgery
An operation to remove or repair a part of the body.

surgical margin
The normal-looking tissue around the edge of a tumor removed during surgery.

systemic therapy
Drugs used to treat cancer cells throughout the body.

targeted therapy
Drugs that specifically target and kill cancer cells.

treatment response
An outcome or improvement caused by treatment.

true local scar recurrence
Cancer not completely removed or destroyed by treatment, with cancer cells found in or right next to the surgical scar where the first melanoma was removed. Also called persistent melanoma.

tumor
An overgrowth of cells.

tumor regression
A decrease in the size of the tumor.

ulceration
The tumor's top skin layer is broken or missing.

ulceration status
Whether or not the tumor's top skin layer is present and intact (not ulcerated) or is broken or missing (ulcerated).

ulcerative colitis
Long-lasting inflammation that causes tears (ulcers) in the lining of the colon (organ that changes eaten food from liquid to solid).

ultrasound
A test that uses sound waves to take pictures of the inside of the body.

ultraviolet (UV) energy or rays
Invisible light energy that comes from the sun and tanning beds. UV energy has a wavelength shorter than visible light but longer than x-rays.

ultraviolet-A (UVA) energy or rays
Long-wave invisible light energy that comes from the sun and tanning beds.

ultraviolet-B (UVB) energy or rays
Short-wave invisible light energy that comes from the sun and in small amounts from tanning beds.

upstage
Changing the rating of the extent of cancer in the body—the cancer stage—from a lower, less extensive stage to a higher, more extensive stage.

vaccine therapy
A treatment used to help the immune system (the body's natural defense against disease) prevent a disease.

vertical growth phase
Direction of tumor growth is down into the skin.

white blood cells
A type of blood cell that fights disease and infection.

wide excision
Surgical treatment that removes the whole tumor and some normal-looking tissue around its edge.

widespread metastatic disease
Cancer that has spread from the first tumor to many distant sites in the body.

x-ray
Use of small amounts of radiation to make pictures of organs and structures inside the body.

Acronyms

ABCDE rule
Asymmetry, Border irregularity, Color, Diameter, Evolving

AJCC
American Joint Committee on Cancer

BCG
Bacillus Calmette-Guerin

CAM
complementary and alternative medicine

cm
centimeter

CNS
central nervous system

CT
computed tomography

EBRT
external beam radiation therapy

ECOG
Eastern Cooperative Oncology Group

FDA
U.S. Food and Drug Administration

FNA
fine-needle aspiration

GI
gastrointestinal

IL-2
interleukin-2

LDH
lactate dehydrogenase

mm
millimeter

MRI
magnetic resonance imaging

PET
positron emission tomography

PET/CT
positron emission tomography/computed tomography

REMS
risk evaluation and mitigation strategy

SLN
sentinel lymph node

SPF
sun protection factor

SRS
stereotactic radiosurgery

TNM
Tumor, Node, Metastasis

T-VEC
talimogene laherparepvec

UV
ultraviolet

UVA
ultraviolet-A

UVB
ultraviolet-B

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Index

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Melanoma

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