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NCCN Guidelines for Patients®

Version 1.2016

Melanoma



Available online at NCCN.org/patients





Melanoma

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 cancer tests and treatments are recommended by experts in melanoma.

The National Comprehensive Cancer Network® (NCCN®) is a not-for-profit alliance of 27 of the world's 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 related **NCCN Quick Guide™**. NCCN also offers patient resources on kidney cancer, ovarian cancer, breast cancer, and other cancer types. Visit **NCCN.org/patients** for the full library of patient books, summaries, and other patient and caregiver resources.

Credits

NCCN aims to improve the care given to patients with cancer. NCCN staff work with experts to create helpful programs and resources for many stakeholders. Stakeholders include health providers, patients, businesses, and others. One resource is the series of books for patients called the NCCN Guidelines for Patients®. Each book presents the best practice for a type of cancer. The patient books are based on clinical practice guidelines written for cancer doctors. These guidelines are called the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). Clinical practice guidelines list the best health care options for groups of patients. Many doctors use them to help plan cancer treatment for their patients.

Panels of experts create the NCCN Guidelines®. Most of the experts are from NCCN Member Institutions. Panelists may include surgeons, radiation oncologists, medical oncologists, and patient advocates. 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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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 is 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.

www.aimatmelanoma.org

MELANOMA RESEARCH FOUNDATION

The Melanoma Research Foundation is very pleased to endorse the NCCN patient 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. In a time when the treatment landscape is changing rapidly, this information is critical to ensuring that melanoma patients live as long and as well as possible.

www.melanoma.org

Supported by NCCN Foundation®

NCCN Foundation supports the mission of the National Comprehensive Cancer Network® (NCCN®) to improve the care of patients with cancer. One of its aims is to raise funds to create a library of books for patients. Learn more about the NCCN Foundation at NCCN.org/foundation.

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Melanoma

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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.

Where should I start reading?

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 the whole book apply to me?

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.

Making sense of medical terms

In this book, many medical words are included. These are words that 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. Be sure 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. Words in the Dictionary are underlined when first used on a page. Acronyms are defined in the text when first used and are also defined in the Glossary. Acronyms are words formed from the first letters of other words. One example is CBC for **complete blood count**.

Melanoma basics



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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.

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.

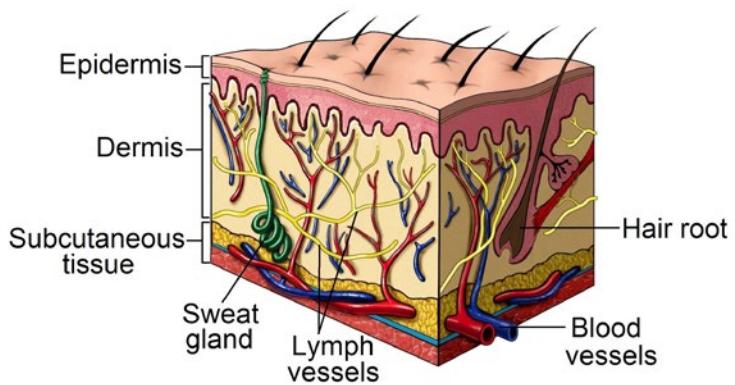


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How does melanoma start?

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.

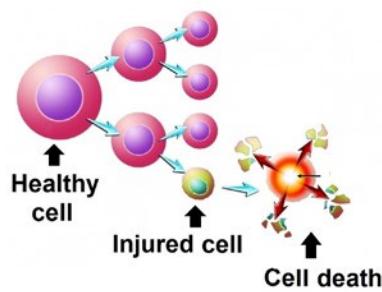
Normal cells divide to make new cells. New cells are made as the body needs them to replace injured or dying cells. Normal cells stay in one place and do not spread to other parts of the body. When normal cells grow old or get damaged, they die.

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 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.

Normal cell growth



Cancer cell growth

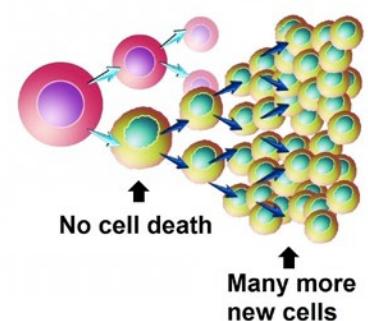


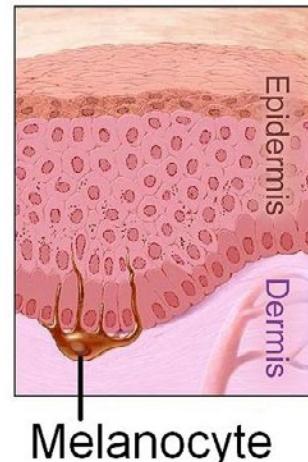
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Melanoma skin tumors are made of abnormal pigment cells (melanocytes) that have become cancer cells. **See Figure 3.** These tumors are usually brown or black in color because the cells still make melanin. Melanoma is more dangerous than most other common skin cancers because it is more likely to spread if it isn't found early. However, most melanomas—about 90 out of 100—are found early before they have spread.

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. (See page 10 for details of how cancer spreads.) This is why finding melanoma as early as possible is so important. Most people can be cured if melanoma is found and treated early.

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>

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.

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 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.

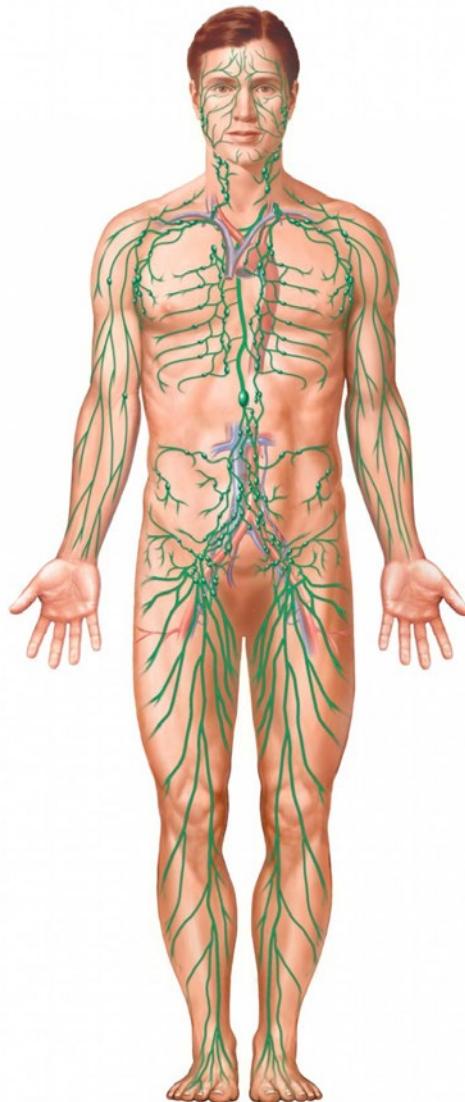


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Types of melanoma

There are four major types of melanoma skin cancer. The unique features of each can help you to recognize features that 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 light (such as from tanning beds), including the trunk and legs.

Nodular melanoma

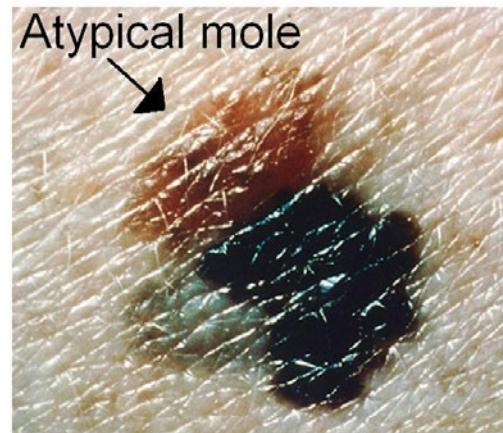
Nodular melanoma grows more quickly into the dermis than other types of melanoma. It tends to be deeper than other types of melanoma at the time it is found. The dermis is the second layer of skin, located under the epidermis. Once in the dermis, it can spread to other tissues. Nodular melanoma looks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

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>

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 of melanoma

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. **See Figure 6.** Normal moles tend to have an even tan, brown, or black color. Most normal moles are less than $\frac{1}{4}$ inch in size—about the width of a pencil eraser. However, normal moles may be larger than $\frac{1}{4}$ inch and some melanomas are smaller than $\frac{1}{4}$ 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.

Figure 6.
ABCDE rule: Skin lesions 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.

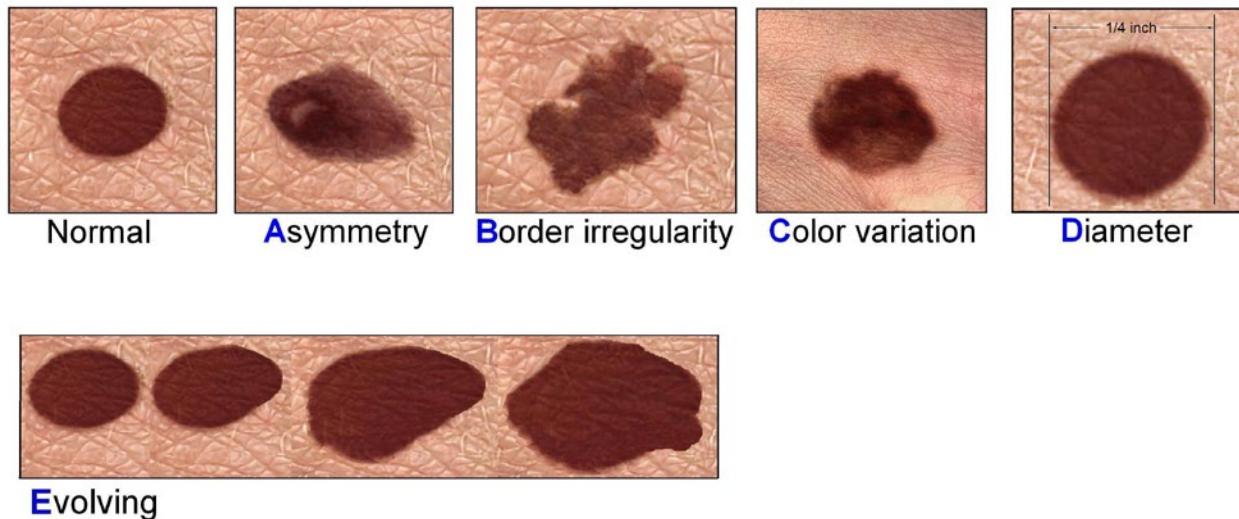


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In contrast, melanoma often presents as a spot that does not "match" a person's other moles. Or, it may cause an existing mole to change size, shape, or color. Itching, scaling, oozing, bleeding, redness, swelling, and tenderness are also possible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

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 $\frac{1}{4}$ inch—the size of the top of a pencil eraser. However, doctors have found melanomas as small as $\frac{1}{8}$ inch.

Evolving: The lesion has changed in size, shape, color, or texture over the past few weeks or months.

Melanoma risks and prevention

Risk factors

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 (ultraviolet) energy. UV energy is an invisible light energy. The main source of UV energy or rays is sunlight. Tanning beds also expose skin to UV rays.

Both UVA (ultraviolet-A) and UVB (ultraviolet-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.

Xeroderma pigmentosum

Xeroderma pigmentosum is a 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 50. But, melanoma is one of the most common cancers in people younger than age 30. This may stem from more use of tanning beds in this age group. 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. 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.

- **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 (sun protection factor) 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. 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.

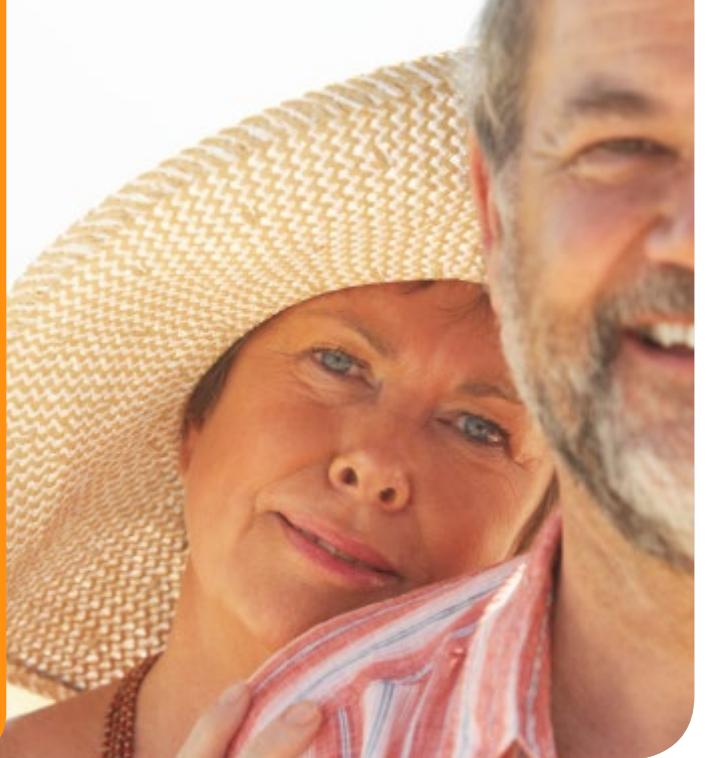
- Your risk for melanoma is higher if your skin is fair, freckled, or has many moles.
- Lower your cancer risk by using sun protection and by not using tanning beds.
- Learn what skin cancer looks like so you can check your skin often.

Testing for melanoma



2 Testing for melanoma

- 19 General health tests
- 20 Tumor tissue tests
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- 24 Blood tests
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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 14 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 or 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

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 (millimeter) 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 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

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.

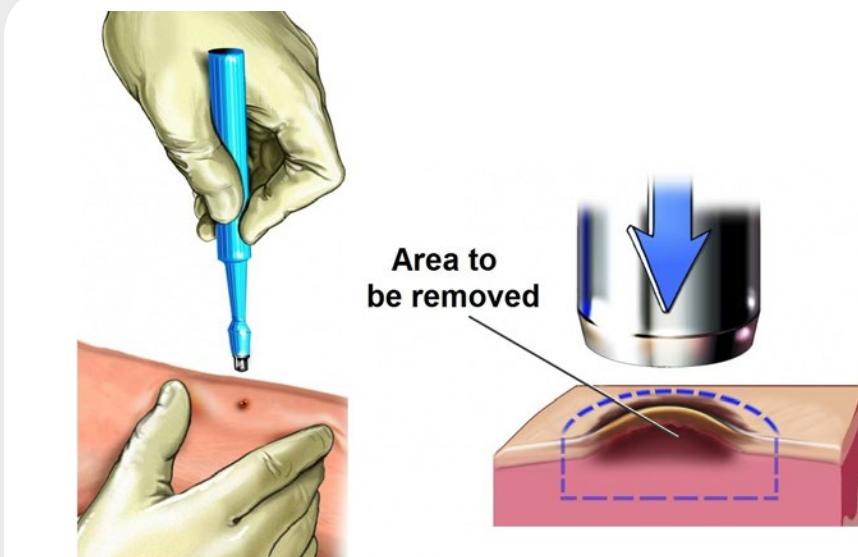


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place where it can't be easily removed such as your face, ear, palm of your hand, or sole of your foot.

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 is commonly used to remove the entire lesion and, therefore, is a type of excisional biopsy. 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 (see page 22). 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.

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 the results to your doctor often 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. Type of melanoma found, 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.

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

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. A decrease in the size of the tumor.

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 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.

Types of lymph node biopsies

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.

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 (computed tomography) scan to guide the needle into the lymph node. (Read page 24 for details on CT scans.)

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 (lactate dehydrogenase) level, but only in the setting of advanced melanoma at the outset. 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 (computed tomography) 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.** 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 (magnetic resonance imaging) 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.

Like a CT scan, a contrast dye may be used. MRI may be used along with other imaging tests or if you are concerned about radiation exposure from other tests.

PET/CT scan

PET/CT (positron emission tomography/computed tomography) 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.

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.

Ultrasound

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 situations. 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.

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.



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.

Melanoma staging



3 Melanoma staging

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- 30 TNM scores
- 32 Stages of melanoma
- 34 Review



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.

What is 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 TNM 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 (millimeters). **See Figure 9.** The sharp point of a pencil is about 1 mm.

For T1 to T4 melanomas, subcategories are given based on two important factors. The first factor is the ulceration status—whether or not the tumor's top skin layer is present and intact (not ulcerated) or is broken or missing (ulcerated). The second factor is the dermal mitotic rate—a measure of how many melanoma cells are dividing per mm^2 (millimeter squared) of melanoma tissue.

- Tis means there are abnormal cells in the epidermis only.
- T1 tumors are ≤ 1 mm thick.
 - T1a tumors have a mitotic rate of $<1/\text{mm}^2$ and no ulceration.
 - T1b tumors have a mitotic rate of $\geq 1/\text{mm}^2$ or have ulceration or both.

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.

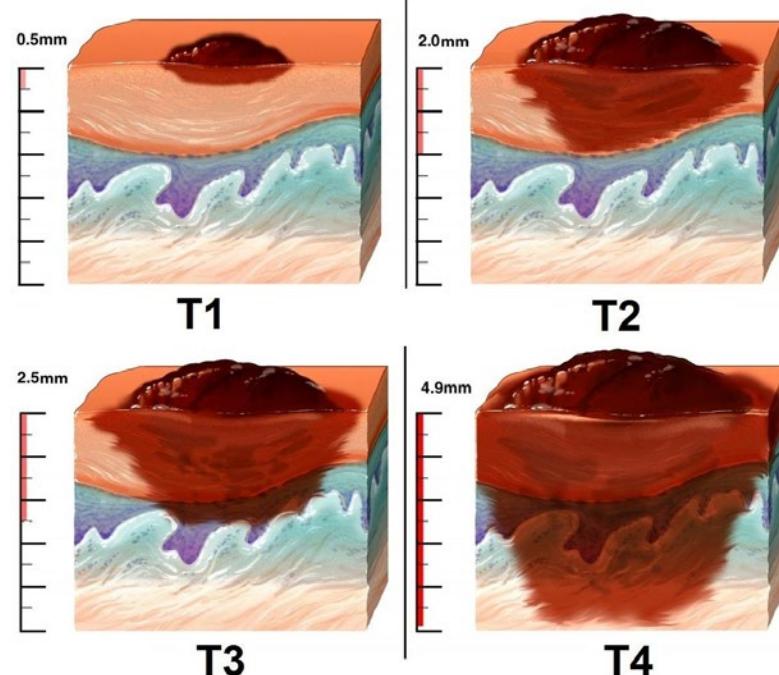


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- T2 tumors are 1.01 to 2.0 mm thick.
 - T2a tumors do not have ulceration.
 - T2b tumors have ulceration.
- T3 tumors are 2.01 to 4.0 mm thick.
 - T3a tumors do not have ulceration.
 - T3b tumors have ulceration.
- T4 tumors are >4.0 mm thick.
 - T4a tumors do not have ulceration.
 - T4b tumors have ulceration.

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 and N2 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.

- N0 means there is no cancer in nearby lymph nodes.
- N1 means that cancer cells have spread to only 1 lymph node.
 - N1a means that lymph node metastases were found only by the pathologist because they were very small.
 - N1b means that the lymph node metastases were found during a physical exam or by imaging tests and then were confirmed by the pathologist.
- N2 means that cancer cells have spread to 2 to 3 lymph nodes, the lymph vessels, or nearby skin.
 - N2a means that the lymph node metastases were found only by the pathologist because they were very small.

- N2b means that the lymph node metastases were found during a physical exam or by imaging tests and then were confirmed by the pathologist.
- N2c means that cancer cells have spread to small areas of nearby skin (called a satellite metastasis) or to nearby lymph vessels (called an in-transit metastasis) but not to the regional lymph nodes.
- 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.

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 whether LDH levels are normal or high.

- 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, with normal LDH levels.
 - M1b means the cancer has spread to the lungs, with normal LDH levels.
 - M1c means the cancer has spread to internal organs with normal LDH levels or it has spread to any site with high LDH levels.

Stages of melanoma

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

Most melanomas—about 85 out of 100—are found early, before they have spread beyond the primary tumor. Most melanomas that are found and removed early 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 a higher dermal mitotic rate or have ulceration, or they are a bit thicker (1.2 to 2 mm) without ulceration. In stage I, there is no cancer in the lymph vessels, lymph nodes, or distant organs.

Stage II

This stage is divided into three 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 3 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. Stage IV includes all the subcategories (a, b, and c).

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.

Chart 1. Melanoma stages**Anatomic Stage/Prognostic Groups**

Clinical staging*				Pathologic staging**			
Stage 0	Tis	N0	M0	Stage 0	Tis	N0	M0
Stage IA	T1a	N0	M0	Stage IA	T1a	N0	M0
Stage IB	T1b	N0	M0	Stage IB	T1b	N0	M0
	T2a	N0	M0		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	≥N1	M0	Stage IIIA	T1–4a	N1a	M0
					T1–4a	N2a	M0
				Stage IIIB	T1–4b	N1a	M0
					T1–4b	N2a	M0
					T1–4a	N1b	M0
					T1–4a	N2b	M0
					T1–4a	N2c	M0w
				Stage IIIC	T1–4b	N1b	M0
					T1–4b	N2b	M0
					T1–4b	N2c	M0
					Any T	N3	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 evaluation for metastases. By convention, it should be used after complete excision of the primary melanoma with clinical assessment for regional and distant metastases.

** Pathologic staging includes microstaging of the primary melanoma and pathologic information about the regional lymph nodes after partial or complete lymphadenectomy. Pathologic Stage 0 or Stage IA patients are the exception; they do not require pathologic evaluation of their lymph nodes.

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Review

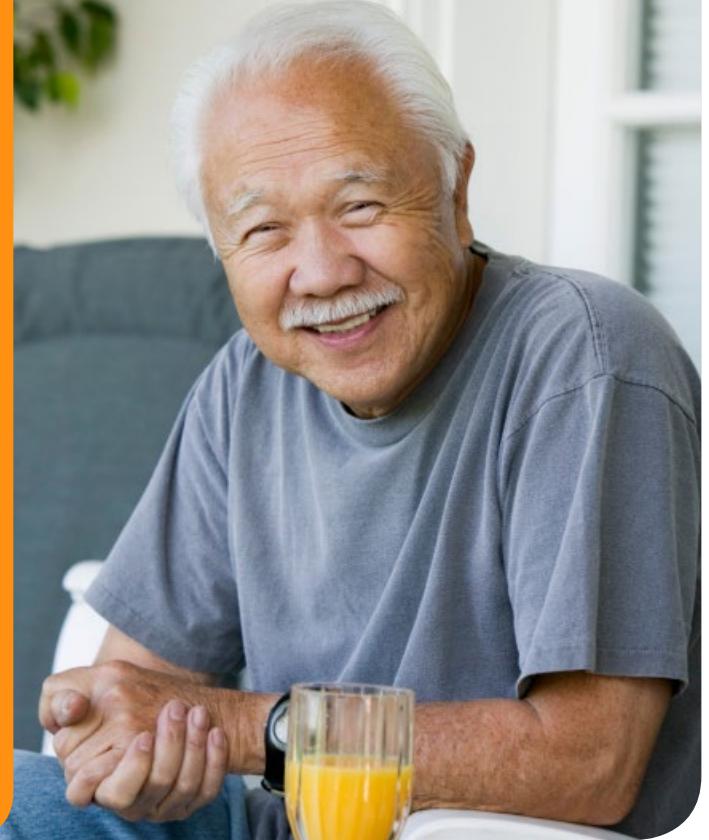
- Cancer staging is how doctors rate and describe the extent of cancer in the body.
- Melanoma is grouped into stages to help plan treatment.
- Cancer stages are based on the growth and spread of the first tumor.
- Cancer staging is often done two times—before and after lymph node surgery.

Overview of melanoma treatments



4 Overview of melanoma treatments

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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 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. **See Figure 10.** The normal-looking tissue is called the surgical margin. The size of the surgical margin, measured in cm (centimeters), depends mostly on the thickness of the tumor. **See Chart 2.**

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.

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.



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Chart 2. Surgical margins for melanoma

T	Tumor thickness	Surgical margin
Tis	In situ	0.5–1.0 cm
T1	≤1.0 mm	1.0 cm
T2	1.01–2.0 mm	1.0–2.0 cm
T3	2.01–4.0 mm	2.0 cm
T4	>4 mm	2.0 cm

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.

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.

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.

Sentinel lymph node biopsy: Possible side effects may include numbness, pain, bruising, and fluid buildup near the biopsy site. 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.

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.

Neoadjuvant treatment

Treatment given to shrink the tumor before surgery. This may be used for metastatic melanoma to shrink the tumor before surgery.



Primary treatment

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



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. **Chart 3** lists the immunotherapy drugs used as systemic therapy for melanoma. **Chart 4** lists the immunotherapy drugs that are used as local therapy for melanoma.

Interferon alfa and IL-2

Two common immunotherapy drugs used as systemic therapy for melanoma are interferon alfa and IL-2 (interleukin-2). They 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.

Ipilimumab

Ipilimumab is a newer 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

Chart 3. Immunotherapy drugs as systemic therapy for melanoma

Generic name	Brand name (sold as)	Route given
IL-2 (interleukin-2)	Proleukin	Liquid injected into a vein
Interferon alfa	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

Chart 4. Immunotherapy drugs as local therapy for melanoma

Generic name	Brand name (sold as)	Route given
BCG (Bacillus Calmette-Guérin)	n/a	Liquid injected into the tumor
Interferon alfa	Intron-A	Liquid injected into the tumor
Imiquimod	Aldara, Zyclara	Cream that is spread onto the tumor
IL-2 (interleukin-2)	Proleukin	Liquid injected into the tumor
T-VEC (talimogene laherparepvec)	Imlygic	Liquid injected into the tumor

blocker." This boosts the immune system's response against melanoma cells in the body.

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. See Principles of systemic therapy on page 90 for details.

BCG and imiquimod cream

BCG (Bacillus Calmette-Guérin) 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.

T-VEC

T-VEC (talimogene laherparepvec) 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.

Pembrolizumab and nivolumab

Pembrolizumab and nivolumab are two other newer immunotherapy drugs approved for melanoma. They are a type of immunotherapy called PD-1 inhibitors. 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 kill melanoma cells. Pembrolizumab and nivolumab are used as systemic therapy for melanoma. They are given every few weeks as a liquid that is injected into a vein.

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.

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. **Chart 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 five years, the FDA (U.S. Food and Drug Administration) has approved four new targeted therapy drugs for melanoma: vemurafenib, dabrafenib, trametinib, and cobimetinib. All four 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 is the newest targeted drug for melanoma—it 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.

Imatinib (Gleevec) 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.

Chart 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	Gleevec	Pill that is swallowed
Trametinib	Mekinist	Pill that is swallowed
Vemurafenib	Zelboraf	Pill that is swallowed

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.
(Read 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. 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. **Chart 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 dosage, schedule, and length of treatment.

Chart 6. Chemotherapy drugs for melanoma

Generic name	Brand name (sold as)	Route given
Carboplatin	n/a	Liquid injected into a vein
Cisplatin	Platinol	Liquid injected into a vein
Dacarbazine	DTIC-Dome	Liquid injected into a vein
Melphalan	Alkerlan	Isolated limb infusion/perfusion
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	Velban, Velsar	Liquid injected into a vein

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.

Radiation therapy

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 external beam radiation therapy.

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 to relieve symptoms such as pain caused by the cancer, especially when it has spread to the bones.

SRS (stereotactic radiosurgery) is a type of external beam radiation therapy that may be used for melanoma. This type of radiation therapy is most often used to treat melanoma that has spread to the brain—called brain metastases. SRS delivers a high dose of radiation to a very specific, small area of the body.

Side effects of radiation therapy

A side effect is an unhealthy or unpleasant physical or emotional condition caused by treatment. Side effects of radiation therapy depend on the dose and the area of skin 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. Common 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.

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 (risk evaluation and mitigation strategy) 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. Examples include:

- Wearing elastic stockings or sleeves to help prevent or control lymphedema,
- Medications to relieve pain, and
- 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.

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.

New tests and treatments go through a series of clinical trials to make sure they're safe and work. 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. 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.

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.

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.

Treatment guide



5 Treatment guide

54 Tests for melanoma

Initial tests needed to confirm (diagnose) melanoma and plan treatment.

58 In situ and local melanoma

Tests and treatment options for melanoma tumors that have not spread beyond the skin. This includes stage 0 (in situ), stage I, and stage II.

64 Regional melanoma

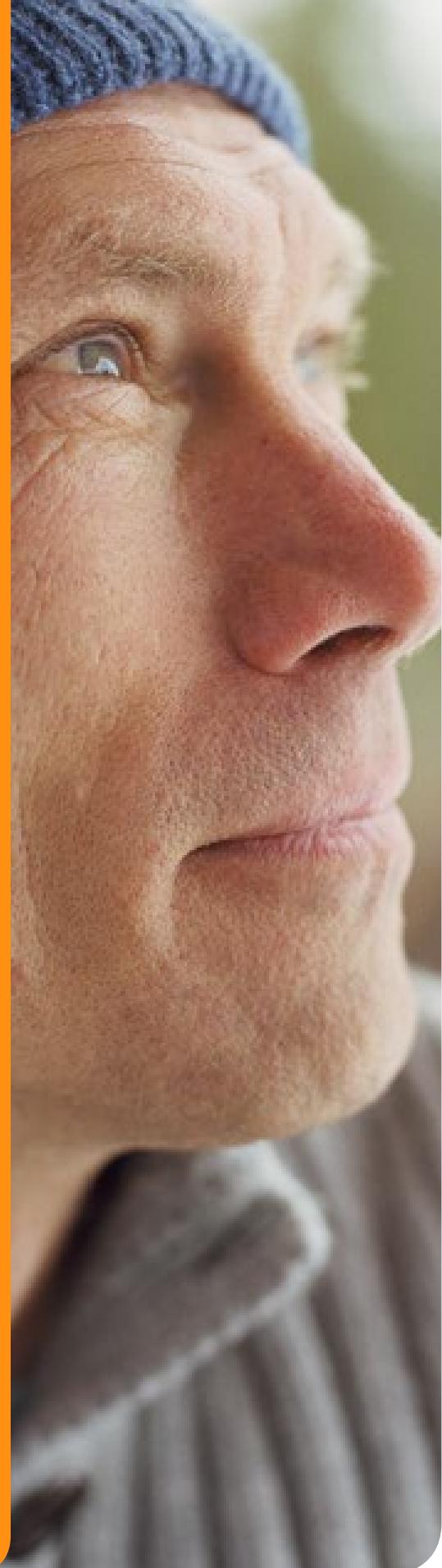
Tests and treatment options for melanoma that has spread from the first tumor to nearby skin, lymph vessels, and/or lymph nodes—stage III melanoma.

71 Persistent melanoma and nonmetastatic recurrence

Treatment options for melanoma that did not go away or came back after treatment but has not spread beyond the area near the first tumor.

80 Metastatic melanoma

Treatment options for melanoma that has spread to parts of the body far away from the first tumor—stage IV melanoma.



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.

Much effort has been made to make this guide easy to read. The treatment options in Part 5 are grouped by the extent (stage) of the cancer. Guides list the treatment options and map the steps through the treatment process. The text along with each guide explains the information shown in the guide.

There are many treatment options for melanoma. The type of treatment that is best for you depends on a number of factors. But, supportive care is an important part of the overall treatment for all patients.

Tests for melanoma

Guide 1. Skin biopsy

Symptoms	Skin biopsy	Pathology report
Area of skin that's a darker color, or doesn't look normal	Excisional biopsy (preferred) Incisional biopsy Punch biopsy Shave biopsy	<ul style="list-style-type: none">• Breslow thickness,• Ulceration status,• Dermal mitotic rate,• Surgical margin status,• Clark level for lesions ≤ 1 mm,• Microsatellitosis (present or absent),• Pure desmoplasia if present

Guide 1 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. (Read Part 2 on page 20 for skin biopsy details.)

An excisional biopsy can be done with an elliptical, deep shave, or punch technique. (See page 20 for details.) Narrow surgical margins (1 to 3 mm) are preferred 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.

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.

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 of the first biopsy are unclear, your doctor may perform another biopsy. Or, the pathologist may do other tests on the tissue sample.

Next steps:  See Guide 2 on page 56 for tests that are needed after the biopsy.

Guide 2. Medical history and physical exams

Exams

- Medical history,
- Physical exam with focus on nearby lymph nodes and organs,
- Complete skin exam, and
- Assess for risk factors for melanoma

Guide 2 shows the tests recommended after your doctor has confirmed that you have melanoma. For your medical history, your doctor will ask about general health symptoms, 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 before.

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 the 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 3 on page 58. For stage III melanoma, see Guide 6 on page 64. For stage IV melanoma, see Guide 13 on page 80.

In situ and local melanoma

Guide 3. Tests for in situ and local melanoma

Clinical stage	Tests
Stage 0 (in situ) Stage IA or IB (≤0.75 mm thick, any features)	<ul style="list-style-type: none">• Medical history• Physical exam• Imaging tests (CT, PET/CT, MRI) for specific signs or symptoms only
Stage IA (0.76–1 mm thick, no ulceration, mitotic rate 0 per mm ²) Stage IB (0.76–1 mm thick with ulceration or mitotic rate ≥1 per mm ²) Stage IB or Stage II (>1 mm thick, any features, no cancer in lymph nodes)	<ul style="list-style-type: none">• Medical history• Physical exam• Imaging tests (CT, PET/CT, MRI) for specific signs or symptoms only• Possible sentinel lymph node biopsy

Guide 3 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. (See Part 3 on page 28 for more details on the stages of melanoma.)

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 24 for imaging test details.) Routine imaging and blood tests are not recommended in the absence of specific signs or symptoms.

For stage II and some thicker stage IA and 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. (Read page 23 for details.)

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.

Next steps:  See Guide 4 on page 60 for treatment options for stages 0, I, and II melanoma.

Guide 4. Primary and adjuvant treatment

Clinical stage	Primary treatment options	Adjuvant treatment options
Stage 0 Stage IA or IB (≤0.75 mm thick, any features)	Wide excision	Observation
Stage IA (0.76–1 mm thick, no ulceration, mitotic rate 0 per mm ²)	Wide excision ± SLN biopsy	No SLN biopsy or SLN negative → Observation SLN positive → See Next steps
Stage IB (0.76–1 mm thick) Stage IB (>1 mm thick, any features) Stage IIA	Wide excision ± SLN biopsy	No SLN biopsy or SLN negative → Clinical trial No SLN biopsy or SLN negative → Observation SLN positive → See Next steps
Stage IIB or IIC	Wide excision ± SLN biopsy	No SLN biopsy or SLN negative → Clinical trial No SLN biopsy or SLN negative → Observation No SLN biopsy or SLN negative → Interferon alfa SLN positive → See Next steps

Guide 4 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.

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. (See page 37 for more details about surgical margins for melanoma.) 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 imiquimod cream and radiation therapy. (See Part 4 on page 36 for details on each treatment type.)

For thicker melanomas, you may also have a sentinel lymph node biopsy during surgery to remove the tumor. An SLN (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 SLN 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 28 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 observation—a period of scheduled follow-up testing to watch for cancer spread (metastasis) or return (recurrence). While most people with stage IB and IIA melanoma are also watched closely for recurrence, a second option is to receive adjuvant treatment within a clinical trial. A clinical trial is a type of research that studies a treatment to assess how safe it is and how well it works.

For patients with stage IIB or IIIC melanoma, the options described above are still options. Most people with stage IIB or IIIC are also watched closely for recurrence—including possible use of imaging tests for surveillance. In addition, a third option for these patients is to receive interferon alfa.

Next steps:  For stage 0, I, or II melanoma, see Guide 5 on page 62 for follow-up tests. For melanoma that was upstaged to pathologic stage III based on the SLN biopsy, see Guide 6 on page 64.

Guide 5. In situ and local melanoma follow-up testing

Stage	Follow-up tests
All stages	<ul style="list-style-type: none">• Complete skin exam every year for life,• Regular self-exam of skin and lymph nodes,• Imaging tests as needed to check specific signs and symptoms, and• Possible regional lymph node ultrasound
Stage IA Stage IB Stage IIA	<ul style="list-style-type: none">• Tests listed above for <i>all stages</i>, and• Medical history and physical exam with focus on skin and lymph nodes<ul style="list-style-type: none">◦ Every 6 to 12 months for 5 years, then◦ Every year as needed
Stage IIB Stage IIC	<ul style="list-style-type: none">• Tests listed above for <i>all stages</i>, and• Medical history and physical exam with focus on skin and lymph nodes<ul style="list-style-type: none">◦ 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

Guide 5 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. A recurrence is when cancer comes back (recurs) after a period of time. The tests and frequency of follow-up described in the chart are based on the risk of recurrence for each stage.

Four 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. (Read Part 2 on page 18 for more test details.) 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 history check-ups and physical exams. Your doctor will look carefully at your lymph nodes and skin during the physical exam. The chart to the left 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

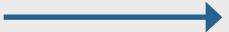
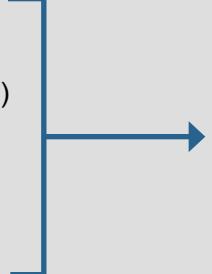
a disease when there are no signs or symptoms present. Imaging tests for screening may be done every 3 to 12 months. This may include a CT scan of your chest, abdomen, and pelvis; MRI of your brain; and/or a PET/CT scan. Your doctor may also consider doing an x-ray of your chest to watch for cancer spread in your lungs. 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), treatment options will depend on the type of recurrence. 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. Metastatic melanoma is cancer that has spread to parts of the body apart from or far from the first tumor.

Next steps:  For persistent melanoma or nonmetastatic recurrence, see Guide 9 on page 72 for treatment options. For metastatic melanoma, see Guide 13 on page 80.

Regional melanoma

Guide 6. Regional melanoma tests

Stage	Tests
Clinical stage I or II upstaged to pathologic stage III (Cancer in lymph nodes found by sentinel node biopsy)	 <ul style="list-style-type: none">Possible imaging tests for baseline stagingImaging tests to check out specific signs or symptoms
Clinical stage III (Enlarged lymph nodes found by physical exam or imaging tests) Stage III in-transit (Cancer cells found in lymph vessels but not in lymph nodes)	 <ul style="list-style-type: none">FNA biopsy preferred, if feasible, or core, incisional, or excisional biopsy of enlarged lymph nodesImaging tests for baseline staging and to check out specific signs or symptoms

Guide 6 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. (See Part 3 on page 28 for details on melanoma stages.)

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. The pathologic stage is based on the clinical stage as well as tests of lymph nodes and other tissue removed during surgical treatment.

Clinical stage I or II melanoma is upstaged to pathologic stage III if the sentinel lymph node biopsy finds 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. A baseline is a starting point to which future test results are compared. (Read Part 2 on page 24 for more details on imaging tests.)

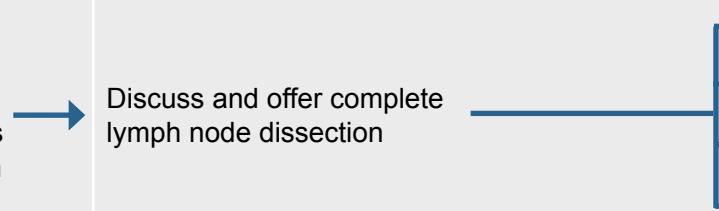
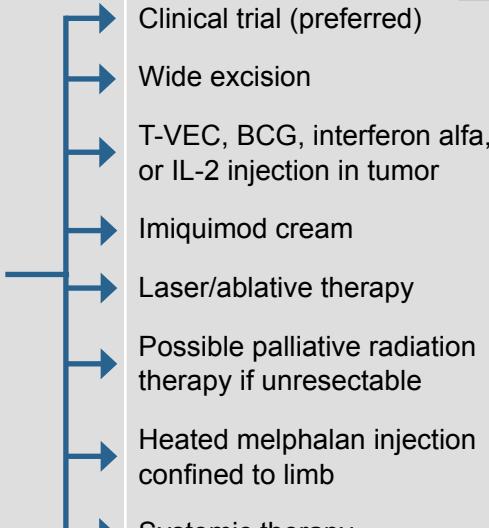
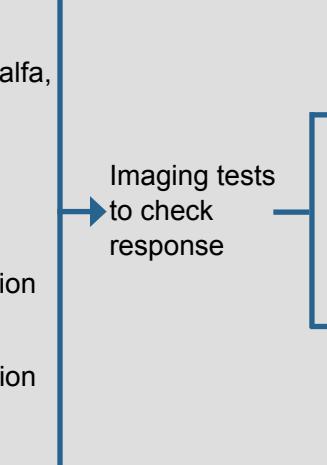
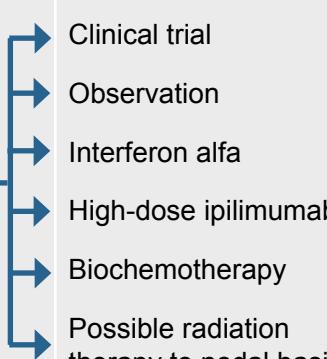
Clinical stage III melanoma is when your doctor feels enlarged lymph nodes during the physical exam or sees them with imaging tests. Stage III in-transit melanoma is when cancer cells have spread into lymph vessels near the first tumor, but not into nearby lymph nodes.

For clinical stage III and stage III 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 are also options.

(Read page 20 and page 23 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 7 on page 66 for treatment options for stage III melanoma.

Guide 7. Primary and adjuvant treatment

Stage	Primary treatment options	Adjuvant treatment
Pathologic stage III upstaged from clinical stage I or II (Cancer in lymph nodes found by sentinel lymph node biopsy)	Discuss and offer complete lymph node dissection	 Clinical trial Observation Interferon alfa High-dose ipilimumab
Stage III in-transit (Cancer cells found in lymph vessels but not in lymph nodes)	 Clinical trial (preferred) Wide excision T-VEC, BCG, interferon alfa, or IL-2 injection in tumor Imiquimod cream Laser/ablative therapy Possible palliative radiation therapy if unresectable Heated melphalan injection confined to limb Systemic therapy	 <p>If free of disease by surgery:</p> <ul style="list-style-type: none"> • Clinical trial, • Observation, or • Interferon alfa <p>If free of disease by other treatments:</p> <ul style="list-style-type: none"> • Clinical trial, or • Observation
Clinical stage III (Enlarged lymph nodes found by physical exam or imaging tests)	Wide excision of primary tumor + complete therapeutic lymph node dissection	 Clinical trial Observation Interferon alfa High-dose ipilimumab Biochemotherapy Possible radiation therapy to nodal basin

Guide 7 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). Read Part 4 on page 36 for details on each type of treatment listed in the chart.

For pathologic stage III melanoma that was upstaged based on the sentinel lymph node biopsy, the tumor has already been removed. Therefore, the only primary treatment option is to discuss and offer a complete lymph node dissection.

After primary treatment, there are four options for adjuvant treatment. You can join a clinical trial, begin observation, receive interferon alfa, or receive high-dose ipilimumab. Observation is a period of scheduled follow-up testing to watch for cancer spread (metastasis) or return (recurrence).

For stage III in-transit melanoma, primary treatment within a clinical trial is preferred if one is available. If possible, the preferred treatment 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 consider doing a sentinel lymph node biopsy during surgery since it is likely that the cancer has spread. (See page 23 for biopsy details.) 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 only a few in-transit metastases. Laser/ablative therapy is also a local therapy option. 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. This may be a good option if you have several in-transit metastases in one arm or leg. Another treatment option is systemic therapy. If you will receive systemic therapy, see *Next steps* at the end of this section.

After primary treatment for stage III in-transit melanoma, your doctor will give imaging tests to check how well treatment worked. An outcome or improvement caused by treatment is caused 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 three options for adjuvant treatment. You can join a clinical trial, begin observation, or receive interferon alfa. Observation is a period of scheduled follow-up testing to watch for cancer metastasis or recurrence. (See Part 4 on page 36 for details on each type of treatment.)

If you had treatment other than surgery as primary treatment and there are no signs of cancer, then you have two options for adjuvant treatment. One option is to join a clinical trial. The other option is to begin observation with follow-up tests.

For clinical stage III melanoma, the primary treatment option is a wide excision of the melanoma with a complete lymph node dissection of all affected nearby lymph nodes. After the tumor and lymph node surgery, there are six options for adjuvant treatment.

Continued on page 68

For adjuvant treatment, the options are to join a clinical trial, begin observation, or receive interferon alfa, high-dose ipilimumab or biochemotherapy. Biochemotherapy is generally only used as adjuvant treatment for melanoma that has a high chance (risk) of recurrence. In such cases, biochemotherapy consists of dacarbazine, cisplatin, vinblastine, IL-2, and interferon alfa. See *Principles of systemic therapy* on page 90 for more details about biochemotherapy.

In selected patients, radiation therapy to the area near the tumor where the group of lymph nodes was removed (nodal basin) may be considered for adjuvant treatment. For more information, read *Principles of radiation therapy* on page 91.

Next steps:  If you will receive systemic therapy, see *Guide 16* on page 86 for options. For follow-up tests that are recommended during observation and after treatment for regional melanoma, see *Guide 15* on page 84.

Guide 8. Regional melanoma follow-up testing

Stage	Follow-up tests
Stage III 	<ul style="list-style-type: none">• Complete skin exam every year for life,• Regular self-exam of skin and lymph nodes,• Medical history and physical exam with focus on skin and lymph nodes<ul style="list-style-type: none">◦ Every 3 to 6 months for 2 years, then◦ Every 3 to 12 months for 3 years, then◦ Every year as needed• Possible regional lymph node ultrasound,• Imaging tests as needed to check specific signs and symptoms, and• Possible imaging tests every 3 to 12 months to screen for recurrence or metastases

Guide 8 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 history check-ups and physical exams. During the physical exam, your doctor will carefully examine your lymph nodes and skin. The chart to the left lists the recommended exam schedule.

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

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 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.

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 recurrence is cancer that came back after treatment but hasn't spread beyond the area near the first tumor. Metastatic melanoma is cancer that has spread to parts of the body far from the first tumor.

Next steps:  For persistent melanoma or nonmetastatic recurrence, see Guide 9 on page 72 for the next options. For metastatic melanoma, see Guide 13 on page 80 for the next options.

Persistent melanoma and nonmetastatic recurrence

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 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 recurrence

means the cancer returned in the surgical scar where the primary tumor was removed. 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.

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. These recurrences are called "node-negative" because there is no cancer in the lymph nodes.

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 13 for recommended tests.

Guide 9. Tests for persistent melanoma and nonmetastatic recurrence

Stage	Tests
Persistent melanoma or true local scar recurrence	 <ul style="list-style-type: none">• Skin biopsy to confirm• Other tests based on the features and stage of the primary tumor
Local, satellite, and/or in-transit recurrence	 <ul style="list-style-type: none">• FNA preferred, if feasible, or core, incisional, or excisional biopsy• Possible imaging tests for baseline staging• Imaging tests to check out specific signs or symptoms
Regional lymph node recurrence	 <ul style="list-style-type: none">• FNA (preferred) or core, incisional, or excisional biopsy of enlarged lymph nodes• Imaging tests for baseline staging and to check out specific signs or symptoms

Guide 9 shows the tests that are needed for cancer that came back after treatment and is at or near the site of the first (primary) melanoma. Read Part 2 on page 18 for more details on the tests listed in the chart.

For persistent melanoma or true local scar recurrence, 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, the first recommended test is a biopsy to confirm the diagnosis. An FNA biopsy is preferred, but an incisional biopsy, excisional biopsy, or core biopsy are other options. During the biopsy, your doctor may remove another tissue sample for genetic testing if you might join a clinical trial of 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.

For regional lymph node recurrence, the first recommended test is a biopsy of the enlarged lymph nodes to confirm the diagnosis. An FNA biopsy of the enlarged lymph node(s) is preferred. But, an excisional, incisional, or core biopsy are other options. Imaging tests may be done for baseline staging and to check out specific signs and symptoms. Possible imaging tests are the same as those described above for local, satellite, and/or in-transit recurrence.

Next steps:  For persistent melanoma or true local scar recurrence, see Guide 3 on page 58 for the next tests that are needed.

For node-negative recurrence (satellite or in-transit recurrence), see Guide 10 on page 74 for the next options. For regional lymph node recurrence, see Guide 11 on page 76 for the next options.

Guide 10. Node-negative recurrence treatment

Stage	Initial treatment options for recurrence	Adjuvant treatment
Persistent melanoma or true local scar recurrence	Wide excision of the tumor site with possible sentinel lymph node biopsy	Options based on the pathologic stage of the recurrence
Local, satellite, and/or in-transit recurrence	<p>Clinical trial (preferred)</p> <p>Wide excision</p> <p>T-VEC, BCG, interferon alfa, or IL-2 injection in tumor</p> <p>Imiquimod cream</p> <p>Laser/ablative therapy</p> <p>Possible palliative radiation therapy if unresectable</p> <p>Heated melphalan injection confined to limb</p> <p>Systemic therapy</p>	<p>If free of disease by surgery:</p> <ul style="list-style-type: none"> • Clinical trial, • Observation, or • Interferon alfa <p>If free of disease by other treatments:</p> <ul style="list-style-type: none"> • Clinical trial, or • Observation

Guide 10 shows the treatment options for cancer that came back in or near the site of the first melanoma. Node-negative means that there are no cancer cells in the lymph nodes. See page 71 for recurrence definitions.

The initial or main treatment is called the primary treatment. Adjuvant treatment is additional treatment given after the main one to try to kill any remaining cancer cells and lower the chance of recurrence. Read Part 4 on page 36 for details on each type of treatment listed in the chart.

For persistent melanoma, or true local scar recurrence, a wide excision is recommended. A wide excision is surgery to remove the whole tumor along with 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 as shown in Chart 2 on page 37.

You may also have a sentinel lymph node biopsy during surgery to remove the tumor if microscopic features meet criteria for this staging procedure. Any additional treatment recommendations will be based on the pathologic stage of the recurrence as described in Guide 4 on page 60.

For local, satellite, and/or in-transit recurrence, treatment within a clinical trial is preferred in all cases if one is available. A wide excision with negative margins is recommended if all of the cancer can be removed. 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 consider doing a sentinel lymph node biopsy during the surgery. (See page 23 for biopsy details.)

If surgery isn't possible, local therapy options include T-VEC, BCG, interferon alfa, or IL-2 injections into the tumor, imiquimod cream rubbed onto the tumor, and laser/ablative therapy. 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.

Another option is to receive systemic therapy. If you will receive systemic therapy, see *Next steps* at the end of this section.

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 caused a treatment response. Based on these tests, you may have adjuvant treatment if there are no signs of cancer.

If you had surgery as initial treatment and there are no signs of cancer, then you have three options for adjuvant treatment. You can join a clinical trial, begin observation, or receive interferon alfa. Interferon alfa is a type of immunotherapy. Observation is a period of scheduled follow-up testing to watch for cancer metastasis or recurrence.

If you had treatment other than surgery as primary treatment and there are no signs of cancer, then you have two options for adjuvant treatment. One option is to join a clinical trial. The other option is to begin observation with follow-up tests.

Next steps:  If you will receive systemic therapy, see Guide 16 on page 86.

Recommended follow-up tests during observation and after treatment are based on the cancer stage. For stage 0, I, or II, see Guide 5 on page 62. For stage III, see Guide 8 on page 68. For metastatic melanoma, see Guide 13 on page 80 for the next options.

Guide 11. Regional lymph node recurrence treatment

Previous treatment	Initial treatment options for 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	Tumor excision + complete lymph node dissection if incomplete before, then adjuvant treatment
Had lymph node dissection and you aren't able to have surgery or cancer is widespread	<ul style="list-style-type: none">→ Systemic therapy (preferred)→ Clinical trial→ Palliative radiation therapy→ T-VEC injection into tumor→ Best supportive care

Guide 11 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 initial or main treatment is called primary treatment. Adjuvant treatment is additional treatment given after the main one to try to kill any remaining cancer cells and lower the chance of recurrence.

The treatment options for regional lymph node recurrence depend on whether or not you had a lymph node dissection with treatment before. 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 36 for details on each treatment.

If you didn't have a lymph node dissection before, then a therapeutic complete lymph node dissection is recommended to remove all of the cancer. After surgery, you may have adjuvant treatment. Your doctor will discuss the use of systemic treatment or clinical trials as adjuvant treatment options. See *Next steps* at the end of this section.

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 systemic treatment or clinical trials as adjuvant treatment options. See *Next steps* at the end of this section.

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. For systemic therapy options, see *Next steps* at the end of this section. The second option is to receive

treatment within a clinical trial. The third option is to receive palliative radiation therapy. (For more details, read *Principles of radiation therapy* on page 91.) The fourth 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 47 to read more about supportive care. (See Part 4 on page 36 for more details about each type of treatment.)

Next steps:  After tumor excision and/or lymph node dissection, see Guide 12 on page 78 for adjuvant treatment options. For systemic therapy options, see Guide 16 on page 86.

Guide 12. Lymph node recurrence next treatment

Initial treatment results	Next treatment options
All cancer was removed with complete lymph node dissection and/or tumor excision	<ul style="list-style-type: none">→ Clinical trial→ Observation→ Interferon alfa→ High-dose ipilimumab→ Biochemotherapy→ Possible radiation therapy to nodal basin
All of the cancer was not removed	<ul style="list-style-type: none">→ Systemic therapy (preferred)→ Clinical trial→ Palliative radiation therapy→ T-VEC injection into tumor→ Best supportive care

Guide 12 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. Read Part 4 on page 36 for more details on each treatment listed in the chart.

If all of the cancer was removed with surgery, then you have several adjuvant treatment options. You can join a clinical trial—a type of research that studies a test or treatment to assess its safety or how well it works. You can begin observation—a period of scheduled follow-up tests to watch for cancer metastases or recurrence. A third option is to receive interferon alfa if you haven't had it before. High-dose ipilimumab is also an option if you haven't had it before. Both are types of immunotherapy drugs.

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 or temozolamide, and cisplatin or carboplatin, with or without vinblastine or nitrosourea, and IL-2 and interferon alfa. For more details about biochemotherapy read *Principles of systemic therapy* on page 90.

Your doctor may also 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 X](#) or read *Principles of radiation therapy* on page 91.

If all of the cancer wasn't removed with surgery, then you also have several adjuvant treatment options. The first and preferred option is to receive systemic therapy. For systemic therapy options, see *Next steps* at the end of this section.

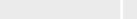
The second option is to receive treatment within a clinical trial. The third option is to receive palliative radiation therapy to relieve the symptoms of melanoma. (For details, read *Principles of radiation therapy* on page 91.)

The fourth option is to receive the immunotherapy drug T-VEC as 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:  For systemic therapy options, see Guide 16 on page 86.

Metastatic melanoma

Guide 13. Metastatic melanoma tests

Stage	Tests
Stage IV 	<ul style="list-style-type: none">• FNA or biopsy (core, incisional, or excisional) of distant tumor<ul style="list-style-type: none">◦ FNA is preferred if initial resection is planned◦ Biopsy is preferred if initial treatment with systemic therapy is planned• LDH• Imaging tests for baseline staging and to check out specific signs or symptoms

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 13 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 or biopsy (excisional, incisional, or core) may be used. FNA is preferred if initial treatment with surgery (resection) is planned. Biopsy is preferred if your initial treatment will be with systemic therapy. (Read page 23 for details on FNA and page 20 for details on each type of biopsy.)

Your doctor may remove another tissue sample for genetic testing if you're thinking about entering a clinical trial of targeted therapy. In this case, an excisional biopsy is preferred.

A blood test to measure your LDH levels is recommended. This test will give information about your prognosis—the likely course or outcome of a disease. Your doctor may also order other blood tests.

Imaging tests are recommended for baseline staging and to check out 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.

Next steps:  See Guide 14 on page 82 for treatment options for metastatic melanoma.

Guide 14. Metastatic melanoma treatment

Stage	Treatment options	Next options
Limited stage IV (Resectable - cancer can be removed with surgery)	<p>Surgery to remove cancer</p> <p>Observe or systemic therapy, then imaging tests to check response</p>	<p>All cancer removed → Clinical trial All cancer not removed → Treat as widespread</p> <p>No other cancer → Treat with surgery, shown above</p> <p>Other cancer → Treat as widespread, shown below</p>
Widespread stage IV (Unresectable - cancer can't be removed with surgery)	If cancer in brain: May have palliative surgery and/or radiation therapy for brain metastases	<p>Systemic therapy (preferred)</p> <p>Clinical trial</p> <p>T-VEC injection into tumor</p> <p>Possible palliative surgery and/or radiation therapy for symptoms</p> <p>Best supportive care</p>

Guide 14 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 many distant sites. It is unresectable, which means it can't be treated with surgery.

For limited metastatic disease, there are two treatment options to choose from. The preferred treatment option is surgery to remove the whole tumor if possible. The other options are to begin observation with follow-up tests or receive systemic therapy. This may help your doctor decide if surgery is a good option for you.

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 you have surgery, then 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 receive additional (adjuvant) treatment, possibly within a clinical trial. Or, you can begin observation with follow-up tests. 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.)

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 five main options for treating widespread metastatic disease. The first and preferred option is to receive systemic therapy. For systemic therapy options, see *Next steps* at the end of this section. The second option is to receive treatment within a clinical trial.

The third option is to receive the immunotherapy drug T-VEC as an injection into the tumor. The fourth option is to consider palliative surgery or radiation therapy to relieve the symptoms caused by the cancer. Palliative treatment can be given alone or in addition to the other options. (For more details, read *Principles of radiation therapy* on page 91.) The fifth option is to receive best supportive care only. For more about supportive care, see page 47.

Next steps:  For systemic therapy options, see Guide 16 on page 86. See Guide 15 on page 84 for follow-up tests after completing treatment for metastatic melanoma.

Guide 15. Metastatic melanoma follow-up testing

Stage	Follow-up tests
Stage IV →	<ul style="list-style-type: none">• Complete skin exam every year for life,• Regular self-exam of skin and lymph nodes,• Medical history and physical exam with focus on skin and lymph nodes<ul style="list-style-type: none">◦ Every 3 to 6 months for 2 years, then◦ Every 3 to 12 months for 3 years, then◦ Every year as needed• Possible regional lymph node ultrasound,• Imaging tests as needed to check specific signs and symptoms, and• Possible imaging tests every 3 to 12 months to screen for recurrence or metastases

Guide 15 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. The chart to the left lists the recommended exam schedule.

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.

You may have imaging tests for screening 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.

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 16. Initial systemic therapy for metastatic or unresectable melanoma

First-line treatment options	Treatment results
<ul style="list-style-type: none">• Immunotherapy:<ul style="list-style-type: none">◦ Pembrolizumab◦ Nivolumab◦ Nivolumab/ipilimumab• Targeted therapy if <i>BRAF</i> mutated:<ul style="list-style-type: none">◦ Combination therapy (preferred)<ul style="list-style-type: none">- Dabrafenib/trametinib- Vemurafenib/cobimetinib◦ Single-agent therapy<ul style="list-style-type: none">- Vemurafenib- Dabrafenib• Clinical trial	<p>Disease progression, or</p> <p>Maximum clinical benefit from targeted therapy</p>

Guide 16 shows the initial 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 treatment given for a disease. There are several first-line treatment options to choose from. One option is to receive treatment with only one immunotherapy drug—called a single agent—such as pembrolizumab or nivolumab. Or, you may receive both nivolumab and ipilimumab together—called a combination regimen. Immunotherapy may be a good option for patients with low-volume metastatic melanoma that isn't causing symptoms.

If you have melanoma with a mutated BRAF gene, then a second option is to receive targeted therapy. Targeted therapy is preferred if it is needed for an early treatment response. Treatment responses to immunotherapy can take longer. 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.

A third option is to receive treatment within a clinical trial. A clinical trial is research on a test or treatment to see how safe it is and how well it works.

For more details about each treatment, see Part 4 on page 36. Also, read *Principles of systemic therapy* on page 90.

Treatment results

After starting systemic therapy, your doctor will give follow-up tests to check how well it is working. Progression 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 other treatment options. See *Next steps* at the end of this section.

Next steps:  See Guide 17 on page 88 for the next systemic treatment options.

Guide 17. Next systemic therapy for metastatic or unresectable melanoma

Performance status	Second-line or later treatment options
Performance status 0-2 	<ul style="list-style-type: none"> • Immunotherapy: <ul style="list-style-type: none"> ◦ Pembrolizumab ◦ Nivolumab ◦ Nivolumab/ipilimumab ◦ Ipilimumab ◦ High-dose IL-2 • Targeted therapy for <i>BRAF</i> mutated tumors: <ul style="list-style-type: none"> ◦ Combination therapy (preferred) <ul style="list-style-type: none"> - Dabrafenib/trametinib - Vemurafenib/cobimetinib ◦ Single-agent therapy <ul style="list-style-type: none"> - Vemurafenib - Dabrafenib • Biochemotherapy: <ul style="list-style-type: none"> ◦ Dacarbazine or temozolomide, and cisplatin or carboplatin, with or without vinblastine or nitrosourea, and IL-2 and interferon alfa • Other systemic chemotherapy: <ul style="list-style-type: none"> ◦ Dacarbazine ◦ Temozolomide ◦ Paclitaxel ◦ Nab-paclitaxel ◦ Carboplatin/paclitaxel • Imatinib for <i>c-kit</i> mutated tumors • Clinical trial
Performance status 3-4	<ul style="list-style-type: none"> • Consider best supportive care

Guide 17 shows the next systemic therapy options that are recommended for metastatic or unresectable melanoma. These options are recommended if melanoma that progressed or stopped responding to first-line treatment. To help decide which option is best for you, your doctor will rate your overall health, cancer symptoms, and your ability to do daily activities. This rating is called your performance status.

The ECOG (Eastern Cooperative Oncology Group) Performance Scale is a common scoring scale for performance status. This scale consists of scores from 0 to 4. Lower scores mean you can do more activities.

A performance status score of 0 to 2 or 0-2 means your overall health is pretty good, you are able to take care of yourself, and you are able to do your daily activities, but maybe not too much physical work. A performance status score of 3 to 4 or 3-4 means your overall health is somewhat poor, you may not be able to do all of your daily activities, and you can't do much physical work.

Treatment options

If you have a performance status score of 0 to 2 or 0-2, then there are several treatment options to choose from. One option is to receive treatment with an immunotherapy drug. Most of the immunotherapy drugs are given alone—called a single agent. But, nivolumab and ipilimumab may be given together—called a combination regimen. See Part 4 on page 40 for more details about each of the immunotherapy drugs listed in the chart.

If you have melanoma that has a mutated *BRAF* gene, then a second option is to receive targeted therapy. Combination therapy is preferred over treatment with a single agent. There are two combination therapy options: dabrafenib and

trametinib or vemurafenib and cobimetinib. The single agent options are vemurafenib alone or dabrafenib alone.

A third option is to receive biochemotherapy. Biochemotherapy is combination treatment with immunotherapy and chemotherapy. For metastatic melanoma, biochemotherapy consists of dacarbazine or temozolomide; cisplatin or carboplatin, with or without vinblastine or nitrosourea; and IL-2 and interferon alfa. This is very strong treatment that can cause very bad side effects. See *Principles of systemic therapy* on page 90 for more details.

A fourth option is to receive other systemic chemotherapy. The 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 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 42 for details on imatinib.) The last option—and a very important option—is to receive treatment within a clinical trial. A clinical trial is research on test or treatment to assess its safety and how well it works.

If you have a performance status score of 3 to 4 or 3-4, then you may receive best supportive care. 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. See page 47 for more details about supportive care.

Principles of systemic therapy

Ipilimumab is an immunotherapy drug used as systemic therapy for advanced and metastatic melanoma. Immunotherapy is treatment that activates the body's natural defense against disease (immune system) to fight cancer cells. However, ipilimumab can cause serious side effects involving the immune system.

You should take part in your treatment center's REMS program while taking ipilimumab. A REMS program is a system for tracking and treating side effects. Ipilimumab should be used with extreme caution, if at all, if you have a serious autoimmune disorder—a health condition that causes the immune system to attack healthy tissue in the body. Examples of autoimmune disorders include ulcerative colitis and active rheumatoid arthritis.

Vemurafenib, dabrafenib, and trametinib are targeted therapy drugs used as systemic therapy for certain advanced and metastatic melanomas. Targeted therapy drugs are designed to specifically target cancer cells. These three targeted therapies treat melanoma tumors that have a damaged BRAF gene.

Vemurafenib can cause serious side effects such as non-melanoma skin cancer, extreme sensitivity to sunlight, and joint pain and swelling. You should have regularly scheduled skin exams with your doctor while taking vemurafenib. You should also see a

dermatologist if you have any symptoms. A dermatologist is a doctor who's an expert in diseases of the skin.

Dabrafenib can also cause serious side effects such as non-melanoma skin cancer and severe fevers. Therefore, you should have regularly scheduled skin exams with your doctor while taking dabrafenib and see a dermatologist if you have any skin symptoms. For severe or frequent fevers, you should briefly stop treatment with dabrafenib and take medicine to lower the fever. You can take acetaminophen (Tylenol) or a nonsteroidal anti-inflammatory drug such as ibuprofen (Motrin).

Biochemotherapy is combination treatment with immunotherapy and chemotherapy. You and your doctor may consider biochemotherapy to control symptoms or so that you can receive other treatment. However, a special warning is needed when treatment with high-dose IL-2 or biochemotherapy is being considered because each can cause serious side effects.

You should not take high-dose IL-2 if your organs aren't working well, your overall health isn't good, or you have untreated or active brain metastases. Biochemotherapy and high-dose IL-2 should be given by medical staff experienced with these treatments.

Principles of radiation therapy

Radiation therapy is the use of high-energy rays to destroy cancer cells. For melanoma, radiation therapy is most commonly used as palliative treatment or to treat brain metastases. Stereotactic radiosurgery is a type of radiation often used for brain metastases. (Read Part 4 on page 46 for details.)

Palliative treatment is treatment given to relieve the symptoms caused by cancer. Palliative radiation therapy may 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.

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 desmoplastic melanoma removed with narrow surgical margins, local recurrence, or extensive neurotropism. 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.

Adjuvant radiation may reduce the risk of lymph node recurrence in the treated lymph node basin. However, it can cause serious long-term side effects that may have a negative impact on quality of life. It is important to fully understand these risks and weigh them against the benefits when considering this treatment.

My notes

Making treatment decisions



6 Making treatment decisions

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Having cancer can feel very stressful. While absorbing the fact that you have cancer, you must also learn about tests and treatments. And, the time you have to decide on a treatment plan may feel short. Parts 1 through 5 described the test and treatment options recommended by NCCN experts. These options are based on science and agreement among NCCN experts. Part 6 aims to help you make decisions that are in line with your beliefs, wishes, and values.

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 may not know much about cancer. You may have 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. However, 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, you still have to agree by signing a consent form.

On the other hand, you may want to take the lead or share in decision-making. Most patients do. In shared decision-making, you and your doctors share information, weigh 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 are likely to get a higher quality of care and be more satisfied. You'll likely get the treatment you want, at the place you want, and by the doctors you want.

Questions to ask your doctors

You will likely meet with experts from different fields of medicine. Strive to have helpful talks with each person. Prepare questions before your visit and ask questions if the person isn't clear. You can also record your talks and get copies of your medical records. It may be helpful to have your spouse, partner, or a friend with you at these visits. A patient advocate or navigator might also be able to come. They can help to ask questions and remember what was said. Some suggested questions to ask your doctors are listed on the next pages.

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. Are you suggesting options other than what NCCN recommends? If yes, why?
5. Do your suggested options include clinical trials? Please explain why.
6. How do my age, health, and other factors affect my options?
7. Which option is proven to work best?
8. Which options lack scientific proof?
9. What are the benefits of each option? Does any option offer a cure? Are my chances any better for one option than another? Less time-consuming? Less expensive?
10. What are the risks of each option? What are possible complications? What are the rare and common side effects? Short-lived and long-lasting side effects? Serious or mild side effects? Other risks?
11. What can be done to prevent or relieve the side effects of treatment?
12. 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. Will the treatment hurt?
6. How much will the treatment cost me? What does my insurance cover?
7. Will I miss work or school? Will I be able to drive?
8. Is home care after treatment needed? If yes, what type?
9. How soon will I be able to manage my own health?
10. 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?

Weighing your 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.

2nd opinion

The time around a cancer diagnosis can be very stressful. People with cancer often want to start treatment as soon as possible. They want to make the cancer go away before it spreads farther. While cancer can't be ignored, there is time to think about and choose which option is best for you.

You may wish to have another doctor review your test results and suggest a treatment plan. This is called getting a 2nd opinion. You may completely trust your doctor, but a 2nd opinion on which option is best can help.

Copies of all of the test results need to be sent to the doctor giving the 2nd opinion. Some people feel uneasy asking for copies from their doctors. However, a 2nd opinion is a normal part of cancer care.

When doctors have cancer, most will talk with more than one doctor before choosing their treatment. What's more, some health plans require a 2nd opinion. If your health plan doesn't cover the cost of a 2nd opinion, you have the choice of paying for it yourself.

If the two opinions are the same, you may feel more at peace about the treatment you accept to have. If the two opinions differ, think about getting a 3rd opinion. A 3rd opinion may help you decide between your options. Choosing your cancer treatment is a

very important decision. It can affect your length and quality of life.

Support groups

Besides talking to health experts, it may help to talk to patients who have walked in your shoes. Support groups often consist of 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. They will understand how you feel, and it is quite likely you will find someone whose case was once similar to your present situation.

Compare benefits and downsides

Every option has benefits and downsides. Consider these when deciding which option is best for you. Talking to others can help identify benefits and downsides you haven't thought of. Scoring each factor from 0 to 10 can also help since some factors may be more important to you than others.

My notes

Websites and resources

American Cancer Society

www.cancer.org/cancer/skincancer-melanoma/

[www.cancer.org/Treatment/
FindingandPayingforTreatment/index](http://www.cancer.org/Treatment/FindingandPayingforTreatment/index)

National Cancer Institute

www.cancer.gov/types/skin/patient/melanoma-treatment-pdq

Melanoma Research Foundation

www.melanoma.org

Aim at Melanoma Foundation

www.aimatmelanoma.org

National Coalition for Cancer Survivorship

www.canceradvocacy.org/toolbox

NCCN

www.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 informed decisions.
- Getting a 2nd opinion, attending support groups, and comparing benefits and downsides may help you decide which treatment is best for you.

Glossary

Dictionary Acronyms

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.

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.

in situ

In its original place.

incisional biopsy

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

interferon alfa

A drug used to activate the body's natural defense against disease (immune system) to fight cancer cells.

interleukin-2 (IL-2)

A drug used to activate the body's natural defense against disease (immune system) to fight cancer cells.

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).

ipilimumab

A drug used to activate the body's natural defense against disease (immune system) to fight cancer 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.

laser/ablative therapy

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

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.

lymphedema

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

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.

peginterferon alfa-2b

A long-acting type of interferon—a drug used to activate the body's natural defense against 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.

vemurafenib

A drug that treats melanoma by targeting a certain abnormal change in the instructions in cells for making and controlling cells.

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

BCG

Bacillus Calmette-Guerin

cm

centimeter

CT

computed tomography

ECOG

Eastern Cooperative Oncology Group

FDA

U.S. Food and Drug Administration

FNA

fine-needle aspiration

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

NCCN Abbreviations and Acronyms

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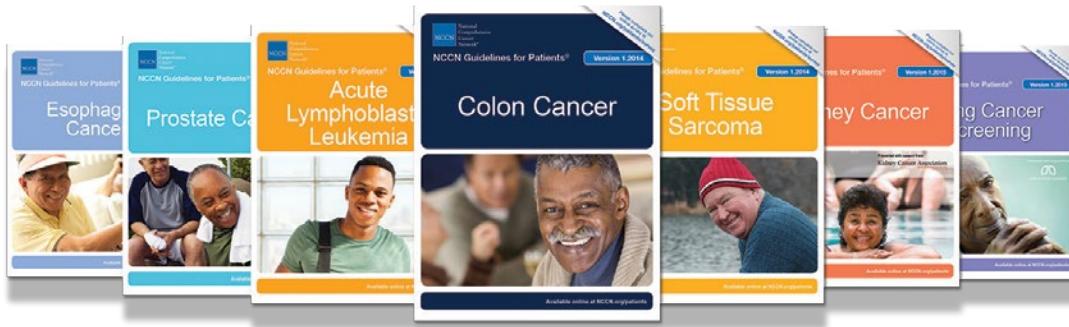
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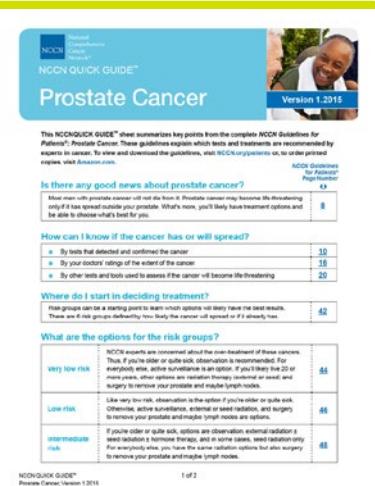
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