NCCN GUIDELINES FOR PATIENTS®

2023

Melanoma

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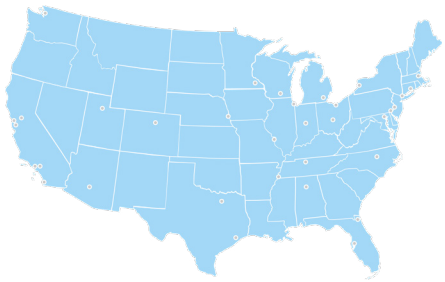
National Comprehensive Cancer Network®



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Cancer care is always changing. NCCN develops evidence-based cancer care recommendations used by health care providers worldwide. These frequently updated recommendations are the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®). The NCCN Guidelines for Patients plainly explain these expert recommendations for people with cancer and caregivers.

These NCCN Guidelines for Patients are based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Melanoma: Cutaneous: Version 2.2023 – March 10, 2023

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The **Melanoma Research Foundation (MRF)** is the largest independent organization devoted to melanoma. Committed to the support of medical research in finding effective treatments and eventually a cure for melanoma, the MRF also educates patients and physicians about prevention, diagnosis, and the treatment of melanoma. The MRF is an active advocate for the melanoma community, helping to raise awareness of this disease and the need for a cure. The MRF's website is the premier source for melanoma information seekers. melanoma.org

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NCCN Foundation seeks to support the millions of patients and their families affected by a cancer diagnosis by funding and distributing NCCN Guidelines for Patients. NCCN Foundation is also committed to advancing cancer treatment by funding the nation's promising doctors at the center of innovation in cancer research. For more details and the full library of patient and caregiver resources, visit NCCN.org/patients.

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1
Melanoma basics

Cutaneous (skin) melanoma is a serious form of skin cancer. However, it is curable, especially if caught early. While there is no clear cause of melanoma, there are several risk factors. Frequent exposure to ultraviolet (UV) radiation from things like sunlight or tanning devices may increase your risk.

Skin basics

Your skin is the largest organ of your body. It covers about 20 square feet. Skin protects you from invaders (such as bacteria, fungi, and viruses), helps control body temperature, and allows the sensations of touch, heat, and cold.

Skin has 3 layers:

- **Epidermis** – The outermost layer of skin provides a waterproof barrier and creates skin color.
- **Dermis** – This layer contains tough connective tissue, blood vessels, hair follicles, and sweat glands.
- **Hypodermis** – This deep skin tissue is made of subcutaneous fat, connective tissue, and lymphatic channels.

Melanin

Melanin is the pigment (chemical) in skin that gives it color. In addition, melanin also protects skin from harmful ultraviolet (UV) rays. Melanin is produced in cells called melanocytes. Melanocytes are mainly located in the skin at the base of the epidermis. They also determine the color in both your eyes and hair. Melanocytes are found in other areas of the body, but the focus of this book is cancer of skin melanocytes.

Melanin levels are typically determined by genetics (genes passed down from your parents). However, other factors affect melanin creation. They include:

- UV radiation exposure (from the sun or a tanning device)
- Hormones
- Age
- Skin pigment disorders

“Knowing there is treatment available gave me hope at diagnosis and for the future.”

Melanoma

Melanoma is one of the most serious types of skin cancer because it spreads beyond the skin more often than most other skin cancers. However, if discovered early, it is curable with the right treatment.

Melanoma occurs when something goes wrong in your melanocytes (the pigment cells that produce melanin). When skin cells are damaged, new cells may grow out of control and can form a mass of cancerous cells.

Diagnosing and treating melanoma early can help produce more positive outcomes. Melanoma often occurs in people over 50 years of age. It can also occur in people of younger age and even in children.

Causes

It is unclear how damage to cells leads to melanoma, but your genes, your health, and environmental risk factors can all contribute.

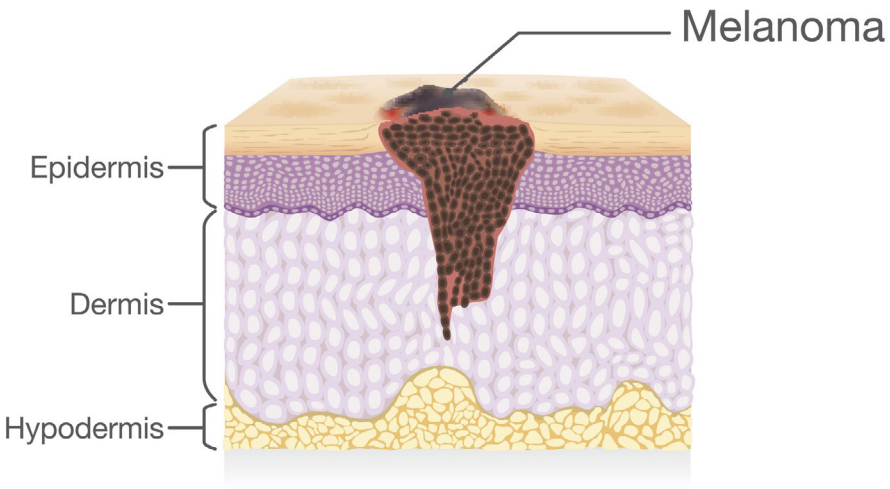
The clearest link is between exposure to UV radiation from the sun or tanning devices. Exposure to UV radiation causes changes to the DNA (genetic material) of pigment cells and increases the risk of melanoma. It is important to note that UV radiation does not cause all melanomas, especially in areas of your body that are not often exposed to sunlight.

Signs and symptoms

Melanoma can be found anywhere on your body. Most often, it is found in areas of periodic or constant sun exposure such as the back, legs, arms, and face. Sometimes, melanoma can be found in areas that get little or no sun exposure, such as the soles of your feet, palms of your hands, and underneath your fingernails (called acral lentiginous

Melanoma in the skin

Melanoma is the most serious type of skin cancer. Regularly look for new, changing, or unusual spots on both exposed and non-exposed skin.



melanomas). People with darker skin are more likely to develop melanoma in areas that are less exposed to the sun.

Melanoma can also occur in the nail bed, on internal mucosal surfaces such as in the mouth, on the tongue, or in the intestines (mucosal melanoma); in the genital areas; and in the eyes (ocular melanoma).

When you or your health care provider examine your skin, attention should be paid to the following:

- A change in an existing mole (its size, shape, or color)
- A new spot on the skin
- Ugly duckling sign (a spot that looks different from other spots on your skin)

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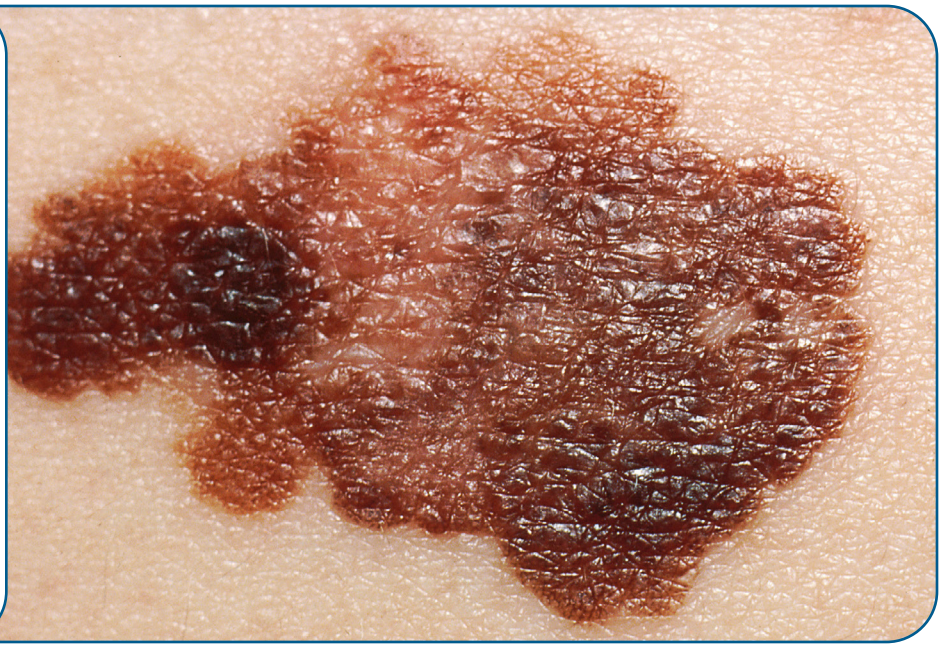
Melanoma skin cancer

Melanoma has an irregular shape and different colors.



The ABCDE rule

Using the ABCDE rule is also a good way to help detect the signs of melanoma:

- **Asymmetry** – One half of a mole or spot does not match the other half.
- **Border** – The edges of a spot seem irregular and are difficult to define.
- **Color** – The color of the spot is not the same throughout (may be brown, black, or sometimes with patches of pink, red, white, or blue).
- **Diameter** – The spot is larger than 6 millimeters across (about the size of a pencil eraser).
- **Evolving** – The spot or mole changes its size, shape, or color.

Risk factors

The exact cause of melanoma is unknown. But there are many risk factors. A risk factor is anything that increases your chance of developing a disease. Some risk factors are passed down through genes (from parent to child). Others are associated with activities that people do.

Having one or more risk factors does not mean you will develop melanoma. Key risk factors for melanoma are listed in **Guide 1.**

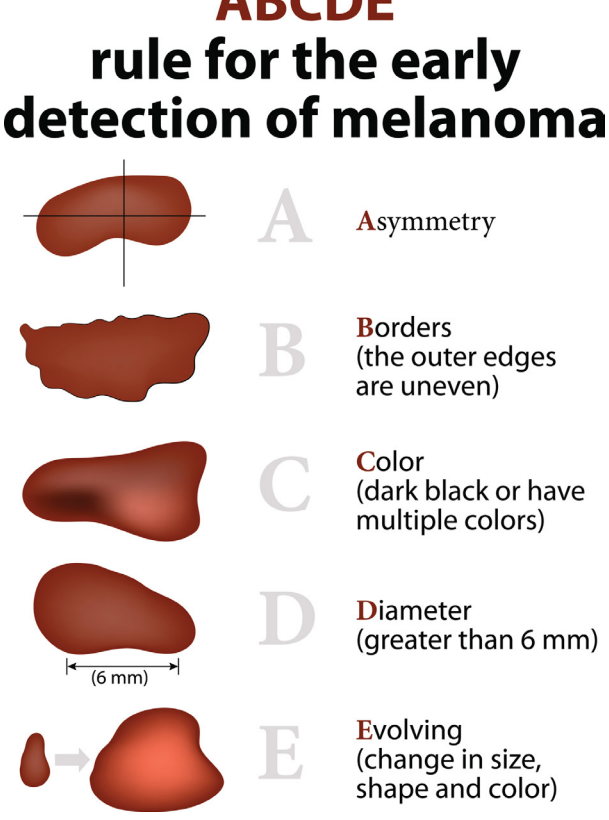
Genetic physical factors

Certain genetic physical factors can increase a person's chances of developing skin cancer. They include:

- **Lighter skin** — less melanin (pigment) in your skin means less protection from UV radiation, which makes you more likely to develop melanoma
- **Lighter hair and eyes** — you are also more likely to develop melanoma if you have blond or red hair, light-colored eyes, and freckles
- **A tendency to sunburn** — if you tend to sunburn easily or have a history of chronic sunburns, especially if you

Early detection of melanoma

For skin self-exams, always follow the ABCDE rule to detect unusual moles.



develop redness and blistering, you have a higher risk of developing melanoma

- **Many or unusual moles** — if you have more than 50 moles on your body, or moles that are unusual sizes or shapes, this increases your risk of melanoma

Guide 1
Risk factors for developing melanoma

If you are	• Male gender assigned at birth • Over 50 years of age
Physical factors	• Having very light and/or freckled skin, red hair, or light eyes (eg, blue or green) • Having a tendency to sunburn • Having atypical moles (moles that are flat, large, or have uneven borders or different colors) • Having a lot of moles (particularly large ones)
Environmental factors	• Using tanning devices • Living in a sunny climate/latitude near the equator • Having regular sun exposure (on the head, neck, or arms) or intense sun exposure (on the torso or legs)
Personal medical history factors	• Having multiple and/or blistering sunburns • Having precancerous conditions such as actinic keratosis, other non-melanoma skin cancers (for example, basal cell or squamous cell), or childhood cancers • Having a weakened immune system due to an organ transplant, cell transplantation, or having HIV or AIDS • Having a rare skin condition (for example, xeroderma pigmentosum)

Family history/ genetic factors	• Having gene changes (mutations) that could lead to developing melanoma
	• Having a family history of:
	  • Cutaneous melanoma or uveal melanoma
	  • Other cancers such as pancreatic, renal, or breast cancer
	  • Astrocytoma (cancer of the brain or spinal cord)
	  • Mesothelioma (cancer of the tissue that covers internal organs)

Environmental factors

People often think tan, glowing skin is a sign of good health. However, too much sun can actually speed up the effects of aging and increase your risk of developing skin cancer.

The main cause of skin cancer is too much exposure to UV radiation that comes from:

- Excessive time spent tanning in the sun
- Using tanning devices
- Living in a sunnier climate
- Working outdoors

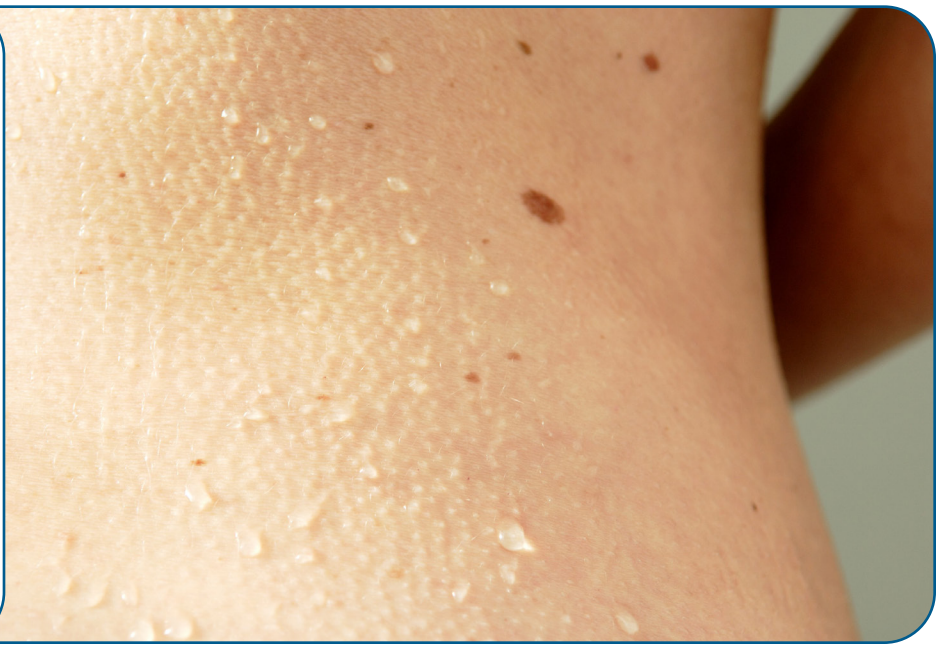
Personal history factors

There are medical and personal history factors that may cause people to develop melanoma, including:

- **Multiple or blistering sunburns** – if you have a history of severe sunburns and developing blisters after being exposed to the sun
- **Previous skin cancers** – if you have had conditions such as actinic keratosis, or other skin cancers (such as basal cell or squamous cell skin cancer)
- **Childhood cancers** – if you had cancer as a child, this could increase your risk of developing melanoma as you get older
- **Weakened or suppressed immune systems** – people with a weakened immune system or who take medicine that suppresses immune function are at higher risk of developing melanoma. This includes people who have had an organ transplant or who have HIV or AIDS
- **Rare inherited conditions** – if you have a skin condition such as xeroderma pigmentosum, or certain hereditary breast and ovarian syndromes, this can increase your risk of developing melanoma

Mole grouping, lower back

More than 50 moles on your body or an unusual type of mole increases the risk of melanoma.



Family history/genetic factors

Melanoma can run in families. About 1 in 10 people (10%) with melanoma have a family history of melanoma. Some families get melanoma because they share the same skin type or sun exposure. Other families share genes that put them at risk for melanoma.

Genes are the instructions in cells for making new cells and controlling how cells behave. An abnormal change in these instructions, called gene mutations, can cause cells to grow and divide out of control. Gene mutations could lead to genetic conditions like cancer.

Hereditary melanoma is sometimes called familial melanoma. Inherited genes that increase melanoma risk may also increase the risk of other cancers. You may have hereditary melanoma if you have a family history of:

- Skin (cutaneous) melanoma, especially among multiple blood relatives, or eye (uveal) melanoma
- Pancreatic, kidney, or breast cancer
- Astrocytoma (cancer of the brain or spinal cord)
- Mesothelioma (cancer of the tissue that covers internal organs)

There are several abnormal (mutated) genes related to hereditary melanoma. They include:

- A *CDKN2A* mutation, which is the most common gene mutation. It is also called p16INK4A or *MTS1*. It often means that many cases of melanoma that were found at an early age run in your family.
- The melanocortin-1 receptor (*MC1R*) gene, which helps determine your skin's color. *MC1R* can determine if you or your family members have red hair and/or fair skin, which increases your risk for developing melanoma.
- *BAP1* gene mutations, which can cause uveal and cutaneous melanoma.

Key points

- Your skin is the largest organ of your body.
- Skin protects you from invaders, helps control body temperature, and allows for the sensations of touch, heat, and cold.
- Melanin is the pigment (chemical) in skin that gives it color and protects it from harmful ultraviolet (UV) rays.
- Melanoma is a serious form of skin cancer, but it is also curable if found early.
- The main cause of skin cancer is exposure to UV radiation that comes mainly from excessive sun tanning and using tanning devices.
- Genetic physical factors that can increase the chances of developing skin cancer include having lighter skin, a tendency to sunburn, and many moles.
- Your medical history may play a role in developing melanoma, including frequent sunburns, blistering, previous skin cancers, and a weakened immune system.
- Some families share abnormal genes that put them at risk for melanoma. Your cancer care provider will assess if you have hereditary melanoma based on your history and your family's history of cancer.

2
Staging for melanoma

A cancer stage is a way to describe the extent of the cancer at the time you are first diagnosed. The American Joint Committee on Cancer (AJCC) created this process, called staging, to determine how much cancer is in your body, where it is located, and what subtype you have. Staging is needed to make treatment decisions.

TNM staging

The American Joint Committee on Cancer (AJCC) TNM staging system is widely used to stage melanoma. In this system, the letters T, N, and M describe different areas of cancer growth. Based on cancer test results, your doctor will assign a score or number to each letter. The higher the number, the larger the tumor or the more the cancer has spread. An example of this is T1, N0, or M0.

Tumor depth **(T)** – refers to the thickness of the primary tumor and whether the tumor has broken through the skin (this is called ulceration). This is measured in millimeters (mm).

Lymph node status **(N)** – refers to whether the cancer has spread nearby through small tubes called lymph vessels or to small bean-shaped structures called lymph nodes.

The thickness of a melanoma tumor is measured in millimeters (mm). The tip of a pencil is about 1 mm thick.

Metastasis **(M)** – describes whether the cancer has spread to parts of the body far away from the primary tumor and distant lymph nodes.

The TNM stages will be combined to assign the cancer stage group. There are 5 stages of melanoma. Often, doctors will write stages 1 through 4 as Roman numerals—stages I, II, III, and IV.

Stages 0 to 2

Stage 0, stage 1, and stage 2 melanoma are cancers in the skin that are not known to have spread elsewhere.

Stage 0 in situ

Stage 0 melanoma in situ refers to melanoma that is found only in the outermost layer of skin (epidermis). This early stage very likely has not yet spread to other parts of the body and is cured when it is completely removed.

Stage 1

Stage 1 melanoma has gone into the second layer of skin called the dermis. When melanoma reaches the dermis, it is described as invasive. Stage 1 is defined as a lesion (tumor) that is thinner than or equal to 2 mm (Breslow depth). Stage 1 melanoma may or may not show ulceration, though most do not.

Stage 2

Stage 2 refers to tumors that are 1 to 2 mm in thickness and have ulceration, or tumors that are thicker than 2 mm with or without ulceration. A person with stage 2 melanoma has a higher chance of cancer spreading beyond the primary tumor than a person with stage 1 melanoma.

Stage 3

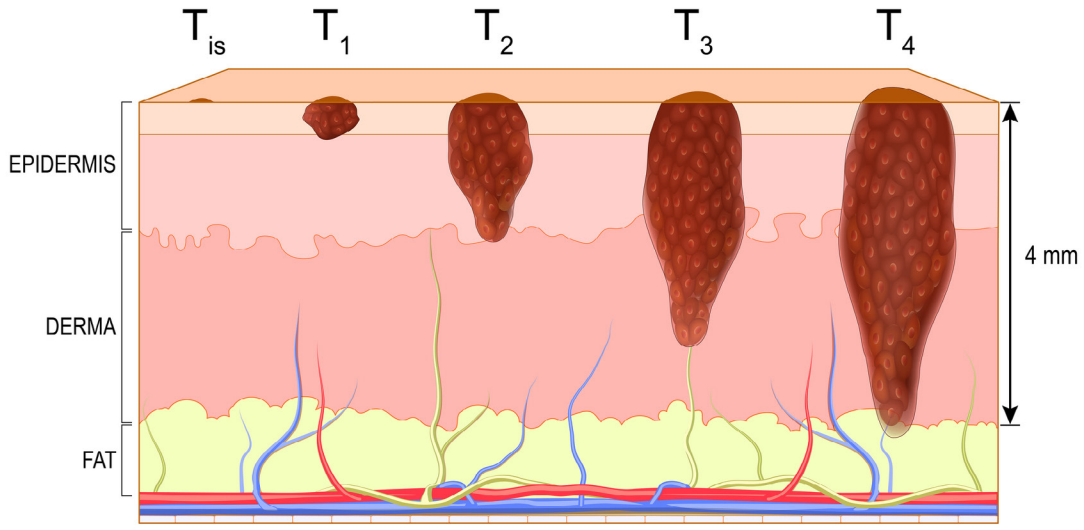
Stage 3 melanoma is known as regional melanoma. It is considered an advanced form of cancer. In this stage, the melanoma has spread to nearby lymph nodes or in the lymphatic vessels in the skin, called in-transit or satellite metastasis.

Stage 4

Stage 4 melanoma is determined when the cancer has spread from the primary tumor to distant areas of the body such as the lungs, liver, brain, bones, or gastrointestinal (GI) tract.

Stages of melanoma

(the TNM Classification of Malignant Tumors)



Key Points

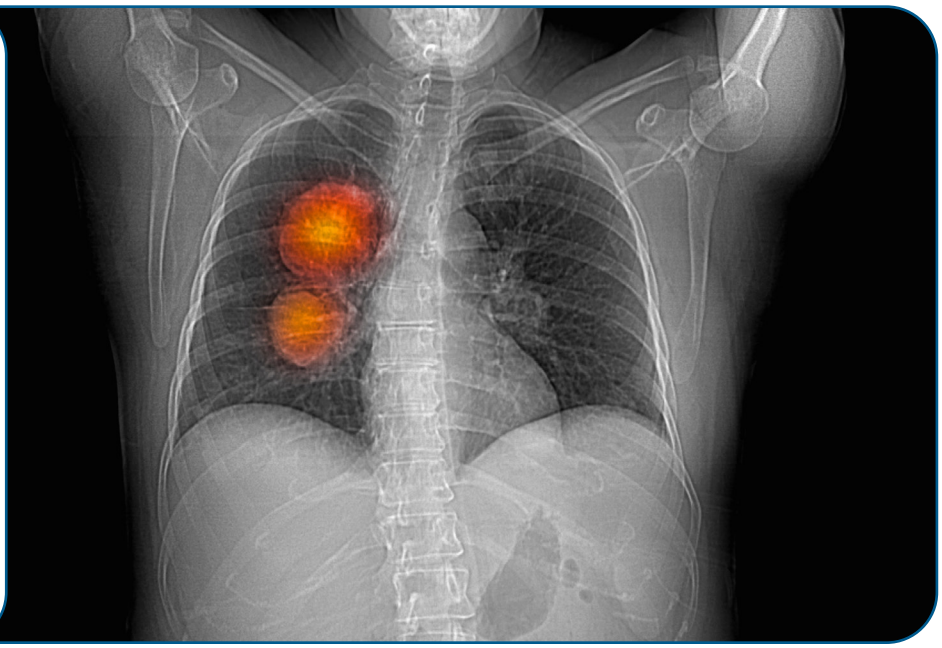
- Cancer stage is a way to describe the extent of the cancer at the time you are first diagnosed.
- Stage 0 melanoma in situ is found only in the top layer of skin (epidermis).
- Stage 1 melanoma is defined as a tumor that is thinner than 1 mm with or without ulceration (a break on the skin) or equal to 2 mm without ulceration.
- Stage 2 melanoma refers to tumors that are 1 to 2 mm in thickness with ulceration or deeper than 2 mm, with or without ulceration.
- Stage 3 melanoma is considered an advanced form of cancer. In this stage, the cancer has spread to regional lymph nodes or lymphatic vessels.

Melanoma staging can be complex. If you have any questions about your stage, ask your doctor to explain it in a way you can understand.

- Stage 4 melanoma refers to cancer that has moved to distant areas of the body such as the lungs, liver, brain, bones, or gastrointestinal (GI) tract.

Metastatic melanoma in the lungs

In this stage, cancer has spread through multiple layers of skin to distant areas of the body. It is pictured here in the lungs.



3
Testing for melanoma

Treatment planning starts with testing. Accurate testing is needed to correctly identify the type of cancer and assess how far it has spread. This chapter presents an overview of the tests you might receive and what to expect.

General health tests

Basic health tests help your doctor detect all diseases, including melanoma. They also help your care team assess the extent of the melanoma, which is called the cancer stage. You can read about melanoma cancer staging in more detail in *Part 2: Staging for melanoma.*

Medical history

A medical history is a record of all health issues and treatments you have had in your life. Your medical history will help determine which treatment is best for you.

Be prepared to list any illnesses or injuries and when they happened. Bring a list of old and new medicines and any over-the-counter medicines, vitamins, or herbal supplements you take. Tell your doctor about any medical conditions or allergies you have. You should also tell your doctor if you have had any severe sunburns or other severe scarring in the past.

Your medical history also includes if you have had other types of skin cancers, such as squamous cell skin cancer or basal cell skin cancer. These are often less serious types of skin cancer. Your doctor will consider how you were treated for these cancers before guiding your treatment for melanoma.

More information on squamous cell skin cancer is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

More information on basal cell skin cancer is available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

Family history

Your doctor will ask about the health history of family members who are blood relatives. This information is called a family history. Some cancers and other diseases can run in families. Ask family members about their health issues like heart disease, cancer, and diabetes, and at what age they were diagnosed.

Physical exam

During a physical exam, a health care provider may:

- Check your temperature, blood pressure, pulse, and breathing rate
- Weigh you and measure your height

- Listen to your lungs and heart
- Look in your eyes, ears, nose, and throat
- Feel and apply pressure to parts of your body to see if organs are of normal size, are soft or hard, or cause pain when touched
- Feel for small structures called lymph nodes in your neck, underarm, and groin to see if they are bigger than normal
- Conduct a complete skin exam

Skin exams

It's important to have an experienced health care provider, such as a dermatologist, give you a thorough skin exam. Skin exams are used for diagnosis, staging, and treatment planning. Expect a head-to-toe exam that includes a review of your:

- Head and scalp
- Face and mouth
- Eyes and eyelids
- Ears and earlobes
- Hands and fingers
- Feet, toes, and toenails
- Torso, arms, and legs

The doctor will make note of any spots that need monitoring or closer examination.

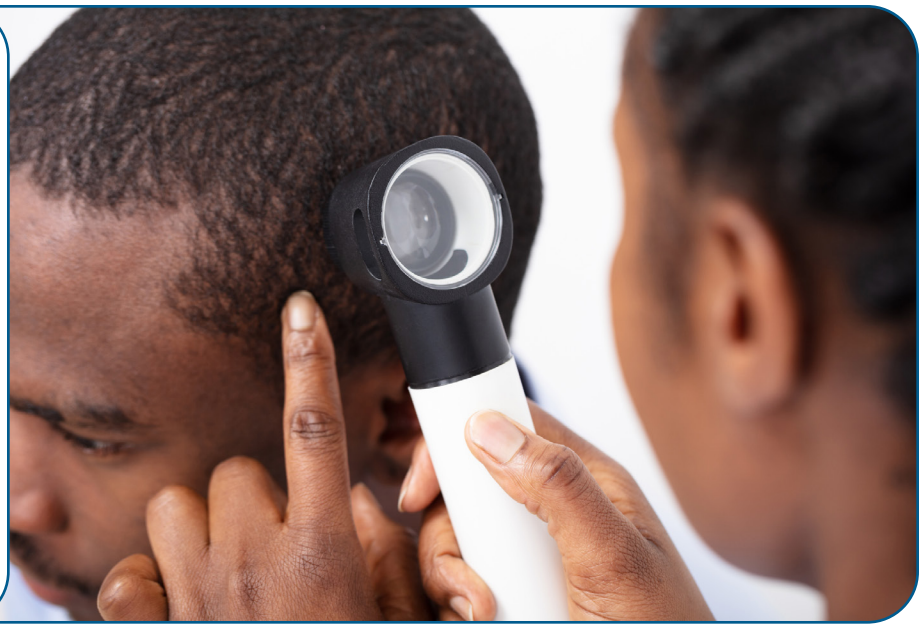
Not only does your skin protect your body, but it also tells doctors a lot about your health. Doctors take your pulse and blood pressure through your skin. They notice if the skin feels warm, hot, or cool to the touch.

Lesions

Your doctor will examine your skin for lesions. A skin lesion is defined as a change in skin color or texture. Skin lesions can appear anywhere on your body. Your doctor may use the ABCDE rule (mentioned in Part 1 of this book) to thoroughly review any marks or lesions on your skin.

Skin exam

A doctor uses a dermatoscope (a special magnifying lens and light source held near the skin) to see spots on the skin more clearly.



Skin color

Your skin color is mainly based on the amount of melanin in your skin.

You know your skin better than anyone. Tell your doctor about your normal skin color. Show your doctor any changes or differences where your skin might look abnormal or different to you.

Biopsy tests

If you are found to have a lesion of concern on the skin, part or all of it will be removed and sent to a lab to be looked at under a microscope. This is called a skin biopsy. A biopsy is needed to diagnose melanoma.

Skin biopsy types

Skin biopsies are done using a local anesthetic (numbing medicine), which is injected into the area with a very small needle. You will likely feel a small prick and a little stinging sensation as the medicine is injected, but you should not feel any pain during the biopsy.

You may also want to ask how the biopsy incision will be closed. There are a few options, including stitches or a special glue that can be used.

There are several ways to do a skin biopsy. The doctor will choose one based on the size of the affected area, where it is on your body, and other factors.

Any biopsy is likely to leave at least a small scar. Different methods can result in different types of scars. You can ask your doctor about the incision and the potential for scarring before you have the biopsy.

For the biopsy, a sample of your lesion will be removed and tested to confirm melanoma.

Ask questions and keep copies of your test results. Online patient portals are a great way to access test results.

A skin lesion biopsy can be incisional (does not completely remove the lesion) or excisional (completely removes the lesion).

An excisional or complete biopsy is preferred for finding melanoma, because it removes a larger area of skin than an incisional or partial biopsy. It can be done through an elliptical (full thickness) removal method, a punch method, or a deep shave removal method (also called a saucerization biopsy).

Elliptical biopsy

An elliptical excisional biopsy removes an area of skin usually in the shape of a fusiform (an oval “football” shape). A rim of normal-looking tissue that surrounds the lesion will be removed, too. This normal-looking tissue is called the margin. This method uses stitches.

Punch biopsy

For a punch biopsy, a small piece of skin and connective tissue are removed using a hand-held tool. Small stitches are then used to close the opening in the skin. One or more punch biopsies may be used on very large lesions, where a complete/excisional biopsy isn’t possible. This can help to avoid inaccurate pathology results.

Deep shave (saucerization) biopsy

A shave biopsy can be done either on the skin surface (superficial) or deeper. Superficial shave biopsies (also called broad or shallow biopsies) can be used when a lesion is likely not cancerous. They are generally not recommended when melanoma is suspected. Superficial shave biopsies may be useful for certain melanoma types that show as flat skin lesions.

Deep shave biopsies are used for most melanoma diagnoses to completely remove the suspicious skin lesion. This biopsy is also called a scoop biopsy or saucerization/shave removal. This type of biopsy removes the top layer of skin (epidermis) and part of the underlying layer (dermis) using a tool similar to a razor.

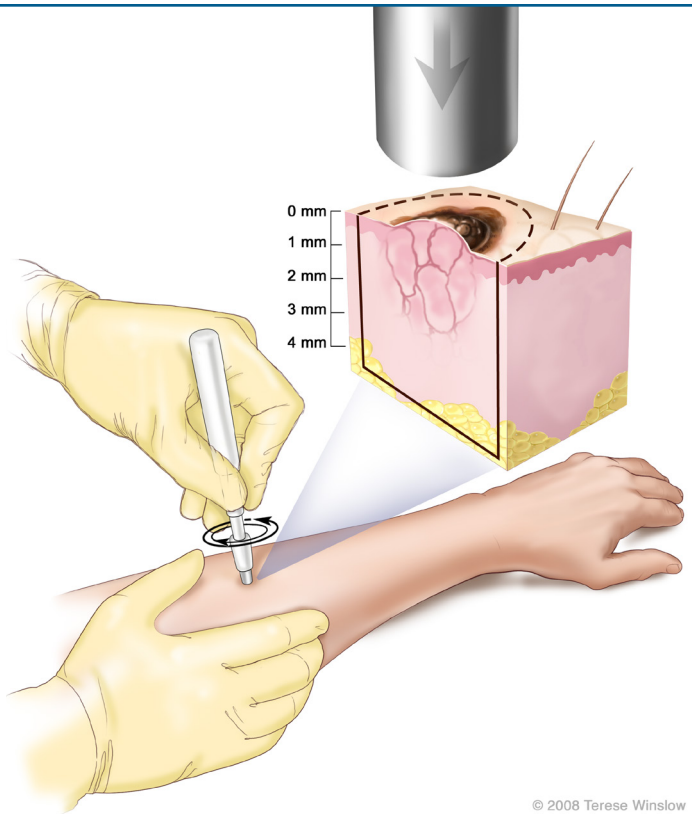
Lymph node biopsy

A lymph node might be biopsied if your care provider suspects it has cancer cells. Lymph nodes are usually too small to be seen or felt.

Lymph nodes may be cancerous if they feel swollen, enlarged, hard to the touch, or don't move when pushed (they are fixed or immobile). A lymph node biopsy can be done using a needle or as a small surgery to remove a lymph node.

Skin punch biopsy

A small piece of skin and connective tissue are removed using a hand-held tool.



Biopsy results

Your biopsy sample should be reviewed by a pathologist who is an expert in diagnosing melanocytic (skin) tumors, or preferably by a dermatopathologist, who is an expert in diagnosing skin disorders including melanoma. This review is called a histology or histopathology review. The pathologist will note the overall appearance and the size, shape, and type of your cells.

Breslow thickness

The Breslow thickness or depth is used to measure (in millimeters) how far the melanoma has gone into the deeper layers of the skin (dermis). This is a good predictor of how far melanoma has advanced and is used to determine treatment.

Ulceration status

Ulceration refers to a breakdown of skin on top of melanoma. An ulcerated melanoma is considered more serious because it has a greater risk of spreading.

Dermal mitotic rate

The dermal mitotic rate (MR) is a measure of how many cancer cells are growing and dividing in the dermis. The MR is measured by looking at the excised (surgically removed) tumor with a microscope. The number of cells that show mitosis (cells dividing) are counted. The mitotic rate should be measured as a specific number per square millimeter (mm) to provide the most helpful information.

The more the cells are dividing (higher mitotic count), the more likely they will invade the blood or lymphatic vessels and spread (metastasize) around the body.

Margin status (deep and peripheral)

The edge or border of the tissue removed in cancer surgery is called the margin. Margin status of a biopsy refers to whether the tumor is present at the deep or peripheral (lateral) margin.

The margin is described as negative or clean when the pathologist finds no cancer cells at the edge of the tissue, suggesting that all of the cancer has been removed.

Determining the surgical margin depends on how deep the melanoma is (the Breslow thickness). If needed, wider excision of the melanoma will follow the biopsy.

Expect your doctor to remove the melanoma as well as a small amount of normal-looking skin around it. This margin helps to increase the chance that all cancerous cells will be removed. Speak to your doctor about how much area around the tumor will be removed. They may draw it on your skin with a marker.

Microsatellitosis (present or absent)

Melanoma may metastasize (travel) through your lymphatic system to the skin, subcutaneous (situated or applied under the skin) tissues, and lymph nodes.

Microsatellitosis refers to tiny tumor deposits that have spread to lymphatic channels in the skin near the first melanoma tumor and can only be seen with a microscope.

Satellite lesions are found within 2 centimeters (cm) from the melanoma site or scar and show as a nodule or bump that can be seen or felt. Any bumps beyond 2 cm from the melanoma are referred to as in-transit metastases.

Pure desmoplasia (if present)

Desmoplastic melanoma (DM) is a rare type of melanoma that is found most often on the head, neck, and shoulders. It occurs in 1 out of 25 people (4%) with melanoma. It is divided into two categories: pure and mixed. Pure desmoplasia may be associated with a higher risk of local recurrence on the skin but has a lower risk of lymph node involvement.

Lymphovascular or angiolymphatic invasion

Lymphovascular or angiolymphatic invasion refers to melanoma that has grown into (invaded) lymph nodes or blood vessels and is more aggressive (spreads).

Neurotropism/perineural invasion

Neurotropism or perineural invasion refers to melanoma growing around nerves in the skin or within nerves (called intraneural invasion). It is most often seen in desmoplastic melanoma and has a higher tendency to recur on the skin.

For a list of what factors will be considered when analyzing biopsies, **see Guide 2.**

Your pathologist might also use immunostaining to help make a more accurate diagnosis. Immunostaining uses antibodies to detect markers on melanoma cells.

Guide 2
Biopsy result factors that can determine your cancer stage

Breslow thickness (how deep the melanoma tumor has grown into the skin)
Ulceration status (if there are breaks on the skin)
Dermal mitotic rate (a measure of how fast cancer cells grow)
Deep and peripheral margin status (if the area around the tumor is free from cancer)
Microsatellitosis (if there are small satellite lesions that aren't part of the primary lesion)
Pure desmoplasia (if there are adhesions or fibrous tissue within a tumor)
Lymphovascular or angiolymphatic invasion (if cancer is in lymph nodes or fluid)
Neurotropism (including peri-tumoral or intratumoral)/perineural invasion

Imaging tests

Imaging tests take pictures (images) of the inside of your body. These tests are sometimes used for cancer staging or to check a symptom. However, not everyone with melanoma needs imaging. A radiologist, an expert in interpreting test images, will write a report and send this report to your doctor. Your test results will be discussed with you.

For most of these testing scans, contrast materials will be used. Contrast materials are substances that help certain areas in the body stand out. They are used to make the pictures clearer. Contrast materials are not permanent and will leave the body in your urine. They will usually be given orally (by mouth) or intravenously (injected with a needle through the vein), which is called an IV contrast.

Most scans will be performed with IV contrast unless it is unsafe for you. This means it could cause a bad reaction if you have certain allergies or conditions or take certain medications.

It is important to tell your doctors if you have had an allergic reaction to contrast in the past. You might be given medicines, such as Benadryl and prednisone, for an allergy to contrast. Contrast might not be used if you have a serious allergy or if your kidneys aren't working well.

The general types of imaging tests include:

CT scan

A computed tomography (CT or CAT) scan uses x-rays and computer technology to take pictures of the inside of the body. It takes many x-rays of the same body part from different angles. All the images are combined to make one big picture.

MRI scan

A magnetic resonance imaging (MRI) scan uses radio waves and powerful magnets to take pictures of the inside of the body. It does not use x-rays.

CT machine

A CT 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.

PET-CT scan

A positron emission tomography (PET) scan uses a radioactive drug called a tracer. A tracer is injected into a vein (through an IV using a needle). The needle is most often inserted on the inside of your elbow.

The tracer travels through your blood and collects in organs and tissues. This helps the radiologist see certain areas more clearly. You may need to wait for the tracer to be absorbed by your body, which takes about 1 hour.

The tracer is attached to a substance that your cells and tissues use. Cancer cells use the substance differently than non-cancer cells. The radioactive part of the tracer lets your care team see how your cells are using the substance. This helps them find any usage that is not normal.

Cancer cells show up as bright spots on PET scans. Not all bright spots are cancer. It is normal for the brain, heart, kidneys, and bladder to be bright on a PET scan. When a PET scan is combined with CT, it is called a PET/CT scan, and they are almost always used together.

Create a medical binder

A medical binder or notebook is a great way to organize all of your records in one place.

- ✓ Make copies of blood tests, imaging results, and reports about your specific type of cancer. It will be helpful when getting a second opinion.
- ✓ Choose a binder that meets your needs. Consider a zipper pocket to include a pen, small calendar, and insurance cards.
- ✓ Create folders for insurance forms, test types (eg, blood, imaging, pathology, radiology, genetics), treatments, and procedures. Organize items in the folder by date.
- ✓ Use online patient portals to view your test results and other records. Download or print the records to add to your binder.
- ✓ Add a section for questions and to take notes.

Bring your medical binder to appointments. You never know when you might need it!

Biomarker tests

Biomarkers are specific features of cancer cells. Biomarkers can include proteins made in response to cancer and/or reflect changes (mutations) in the DNA of cancer cells. A mutation might cause a gene to create a protein and keep making it. This means certain cells get ongoing signals to keep dividing and no instructions on when to stop. This can lead to the development of a tumor.

Testing on biomarkers involves studying a piece of tumor tissue in a laboratory or testing a blood sample (also called a liquid biopsy). Other names for biomarker testing include molecular testing, tumor profiling, genomic testing, tumor gene testing, next-generation sequencing, and mutation testing.

Immunohistochemistry (IHC) is a common and quick lab test of biomarkers that involves adding a chemical marker to immune cells. The cells are then studied under a microscope. IHC might be used to see if cancer has spread, or to look for mutations such as *BRAF*, *KIT*, or *NRAS*, or PD-L1 proteins. It may also be used to help tell the difference between different types of cancer.

Biomarker testing is used to learn whether the cancer has any targetable changes to help guide your treatment. The results of the biomarker testing can also be used to determine whether you meet criteria for joining certain clinical trials.

Biomarker testing is usually done for stage 3 and stage 4 melanoma, but not everyone with melanoma will need testing.

Uses for biomarker testing

Biomarker or molecular testing can be used in the following instances:

- ✓ To help diagnose your cancer
- ✓ To help determine your prognosis or see how advanced your cancer is, especially the risk of metastasis (how likely it is to spread)
- ✓ To find genetic mutations that happen after birth that can be treated with a targeted therapy or an immune therapy
- ✓ To help you and your care team with treatment planning

BRAF mutations

BRAF is a human gene that encodes a protein called B-Raf. The B-Raf protein helps control cell growth. If a person has a mutation in their *BRAF* gene, it can cause a melanoma to grow more aggressively. *BRAF* mutation is found in at least half of people who have melanoma in the skin.

It is helpful if the *BRAF* gene mutation is found before treatment. Doctors can use targeted therapy to inhibit (stop) the *BRAF* gene mutation from continuing to grow the cancer.

If IHC detects a *BRAF* V600E mutation, targeted therapy or immunotherapy may be a treatment option if needed.

If IHC does not detect a *BRAF* V600E mutation, a more accurate test may be used or tests of other mutations may be done (*KIT*, *BRAF* non-V600).

See Part 4: Treatment for melanoma for more detailed information on treatment types.

Blood tests

Blood tests check for signs of disease and how well organs are working. They use a sample of your blood, which is removed through a needle placed into your vein.

Blood tests are not used to diagnose melanoma. However, they may be done before or during treatment, especially for more advanced melanomas.

Tests that may be requested include:

Lactate dehydrogenase (LDH) – Lactate dehydrogenase (LDH) or lactic acid dehydrogenase is a protein found in most cells. Dying cells release LDH into blood. A high LDH level is a sign that the melanoma may have spread to other parts of the body and may be harder to treat. This blood test may be done if your care provider suspects the cancer has spread to distant sites (stage 4).

Other blood tests – Other blood tests are not regularly done before starting treatment. They may be done to plan surgical treatment. These tests are done if you have advanced melanoma to define whether the bone marrow, liver, and kidneys are working before and during treatment. This may include a complete blood count (CBC) or comprehensive metabolic panel (CMP). A CMP measures your sugar (glucose) level, electrolyte and fluid balance, kidney function, and liver function.

Understanding test results

The results of your physical exam, skin biopsy, and possible imaging studies will determine your treatment plan. It's important you understand what these tests mean.

Keep these things in mind:

- Bring someone with you to your appointments, if possible.
- Write down questions before your appointments and take notes during clinic visits. Don't be afraid to ask your care team questions. Get to know your care team and let them get to know you.
- Get copies of blood tests, imaging results, and reports about the specific type of cancer you have.
- Organize your papers. Create files for insurance forms, medical records, and test results. You can do the same on your computer if you have one.
- Keep a list of contact information for everyone on your care team. Add it to your smartphone if you have one. Hang the list on your refrigerator or in an obvious place where someone can access it in an emergency.

Key points

- Basic health tests help your doctor and care team assess the extent of the melanoma, which is called the cancer stage.
- A medical history is a record of all health issues and treatments you have had in your life, including other cancers.
- A head-to-toe skin exam should include a review of the scalp, face, mouth, hands, feet, torso and extremities, eyes and eyelids, ears, fingers, toes, and toenails. This includes examining your skin for lesions.
- A melanoma diagnosis is primarily based on the results of a skin biopsy. If you have a suspicious lesion, it will be removed and sent to a lab to be examined.
- Imaging tests take pictures of the inside of your body, which are examined to look for cancer. Not everyone with melanoma needs imaging tests.
- Biomarker or molecular tests look for certain genes, proteins, or other molecules in a sample of tissue, blood, or other bodily fluid. These tests are sometimes used to help diagnose melanoma, and to stage and treat it.
- Blood tests are not used to diagnose melanoma and are not commonly done to plan treatment. However, they may be done if you have surgery or if your care provider suspects the cancer has spread. Blood tests are also routinely done if you are taking systemic treatment for melanoma.
- If possible, have someone come with you to doctor visits. Don’t be afraid to ask your care providers questions if you have them.
- Keep copies of your test results, medical records, insurance forms, care providers’ contact information, and other documents on hand in case questions or concerns arise.

4

Treatment for melanoma

This chapter briefly describes some examples of the kinds of treatments you may receive for melanoma. It's important to note that not everyone will receive the same treatment. Treatment for melanoma is based on its stage and location.

Treatment team

After being diagnosed, knowing what to do next can be confusing. Aside from your primary care provider (such as your family doctor), there are several medical professionals who will help you make decisions about your treatment and supportive care.

Depending on your diagnosis, your treatment team might include the following specialists:

Dermatologists are doctors who diagnose and treat skin conditions, including skin cancer. They can also do skin exams and help you learn how to do them on your own.

Surgical oncologists are doctors who are trained to diagnose and surgically treat and remove cancerous tumors.

Medical oncologists are doctors who specialize in prescribing cancer drugs. They are trained to diagnose and treat cancer using special medicines that may be taken by mouth or given through a vein.

Pathologists are doctors who are trained to study tissue and cells removed during a biopsy under a microscope to determine the stage of a tumor.

Plastic surgeons are doctors who reconstruct, restore, and repair body parts. They may be needed to close a wound after surgery, especially if it involves deeper tissue.

Head and neck surgeons are doctors who treat diseases (both cancerous and noncancerous) of the head and neck.

Radiation oncologists are doctors who are trained to use different types of radiation to destroy cancerous cells while keeping other cells healthy.

Pharmacists are medical professionals who are trained to prepare and give out medicine and teach about their proper use and any side effects. Some pharmacists specifically work with people with cancer.

Geneticists are medical specialists who study how traits are passed down from parents to children through genes. They are trained to diagnose and treat genetic disorders and counsel people and families at risk.

Oncology nurses are nurses who provide hands-on care, like giving systemic therapy, managing your care plan, answering questions, and helping you cope with side effects. Sometimes, these experts are called nurse navigators.

Nutritionists and dietitians are professionals who help guide you on what foods are most suitable for your diagnosis and treatment.

Palliative care nurses are professionals who help provide an extra layer of support with your cancer-related symptoms.

Psychologists and psychiatrists are mental health experts who can help you manage issues such as depression, anxiety, or other conditions that can affect how you feel during treatment.

Social workers are advocates who help people solve and cope with problems in their everyday lives while they have treatment.

Some members of your care team will be with you throughout your treatment, while others will only be there for parts of it.

You know your body better than anyone. Help other team members understand:

- How you feel
- What you need
- What is working and what is not
- Your goals for treatment

Keep a list of names and contact information for each member of your team. This will make it easier for you and anyone else who is involved in your care to know who to contact with questions or concerns.

Order of Treatments

Most people with melanoma will receive more than one type of treatment. This is an overview of the order of treatments and what they do.

Neoadjuvant (before) treatment is given to shrink the tumor before primary treatment (surgery). This might change a borderline resectable tumor into a resectable tumor.

Primary treatment is the main treatment given to rid the body of cancer. Surgery is usually the main treatment for resectable melanoma.

Adjuvant (after) treatment is given after primary treatment to rid the body of any cancer cells left behind from surgery. It is also used when the risk of cancer returning (recurrence) is felt to be high.

First-line treatment is the first set of treatments given.

Second-line treatment is the next set of treatments given if the first-line treatment hasn't worked.

Talk with your doctor about your treatment plan and what it means for your stage of melanoma.

Surgery

Surgery is an operation or procedure to remove cancer from the body. The type of surgery depends on the size, number, and location of the cancer. Surgery is the primary (first) treatment for almost all melanomas. A person diagnosed with melanoma should expect some surgery to follow the skin biopsy.

The goal of surgery is to remove all the cancer from your body. For melanomas that have a low risk of spread, surgery may be the only treatment needed. There are different types of surgery used for melanoma.

Wide excision

A wide excision surgery removes the melanoma tumor as well as some normal-looking tissue surrounding it (the surgical margin). The surgical margin is measured in centimeters (cm). The size to be removed depends on the thickness of the primary tumor **(see Guide 3)**.

A wide excision may be done in a doctor's office or in the hospital (operating room). You may receive local anesthesia before the surgery. Local anesthesia is a medicine that numbs a small area of the body to minimize pain during the surgery. Most stage 0 and stage 1 melanomas are treated under local anesthesia.

For deeper or more advanced melanomas that require lymph node biopsy or surgery, general anesthesia may be used. General anesthesia uses a breathing tube to help you breathe while you are fully asleep.

A wide excision is done even if the melanoma tumor was removed by biopsy. A wide excision will also remove lymphatic channels in the skin because there could be additional tumor cells and any nearby microsatellites. Lymphatic channels are thin-walled, tube-like vessels, like blood vessels, that carry a fluid called lymph.

A wide excision is often cut as an ellipse (football shape) to allow the wound to heal as a flat line. The surgical margin will be cut

Guide 3
Surgical margin guidelines for wide excision for melanoma

If your tumor thickness is:	The recommended surgical margin is:
In situ	0.5 to 1 centimeter
Less than 1.0 millimeters (mm)	1 centimeter (cm) -- category 1
Greater than 1.0 to 2.0 millimeters (mm)	1 to 2 centimeters (cm) -- category 1
Greater than 2.0 to 4.0 millimeters (mm)	2 centimeters (cm) -- category 1
Greater than 4.0 millimeters (mm)	2 centimeters (cm) -- category 1

based on the thickness of the melanoma tumor.

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.

Side effects of wide excision surgery may 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. Talk to your doctor if you are concerned about scars due to the surgery.

Following the surgery, a skin graft might be recommended to cover the wound. Skin grafting involves removing skin from one area of the body and moving it to a different area. Skin grafts are surgeries that can be performed in the clinic or hospital. Most larger skin grafts involve general anesthesia, which means you'll be asleep throughout the procedure and won't feel any pain.

Sometimes, rotational "flaps" of tissue may be used to plan for wound closure so you can avoid a skin graft. A skin flap is a type of wound closure that takes skin from an area close to a wound and layers it to fill the removal of a skin lesion. Talk to your doctor about your options and how you can expect to heal after wide excision surgery.

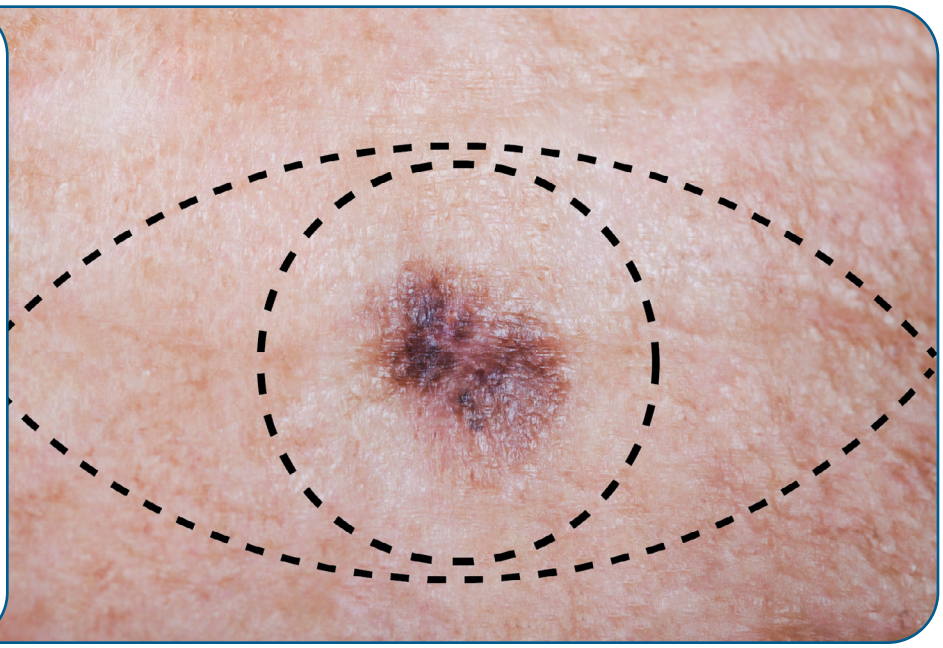
Sentinel lymph node biopsy

A sentinel lymph node is the first lymph node to which cancer cells most likely spread from a primary tumor. Sometimes, there is more than one sentinel lymph node.

A sentinel lymph node biopsy (SLNB) is a surgery that removes tissue samples to examine sentinel nodes. The lymph nodes will be checked for cancer cells by a pathologist in a lab. Many people with melanoma have an SLNB at the same time as the wide excision.

Wide excision

A wide excision surgery removes the melanoma tumor as well as some normal-looking tissue surrounding it.



The results will be used to stage the cancer and plan treatment.

To locate the sentinel lymph node(s), your surgeon will inject a radioactive substance (and in some cases, a blue-colored dye) into your skin near the tumor. The substance will drain into the sentinel lymph nodes. Your surgeon will identify the sentinel lymph nodes using a device and remove them through a small cut in your skin. This procedure is generally done under general anesthesia.

A negative result means the cancer has not yet spread to nearby lymph nodes or other organs. A positive result indicates that cancer is present in the sentinel lymph node, that other lymph nodes may be affected, and that more treatment called adjuvant therapy should be considered.

You could experience some side effects after an SLNB, including numbness, pain, or bruising. You could also develop a seroma, which is a collection of fluid in the lymph node basin. The lymph node basin is the group of lymph nodes where lymph from the tumor area drains.

A seroma usually goes away on its own but may need to be drained with a needle. If you develop a persistent seroma in the lymph node basin, your doctor may inject an irritant into the cavity that was formed by tissue removal. This procedure, called sclerotherapy, helps you heal by closing up the empty space.

Your doctor or care team should discuss with you the possible risks and benefits of an SLNB before you have the surgery *(see* **Guide 5** *in Part 5 of this book).*

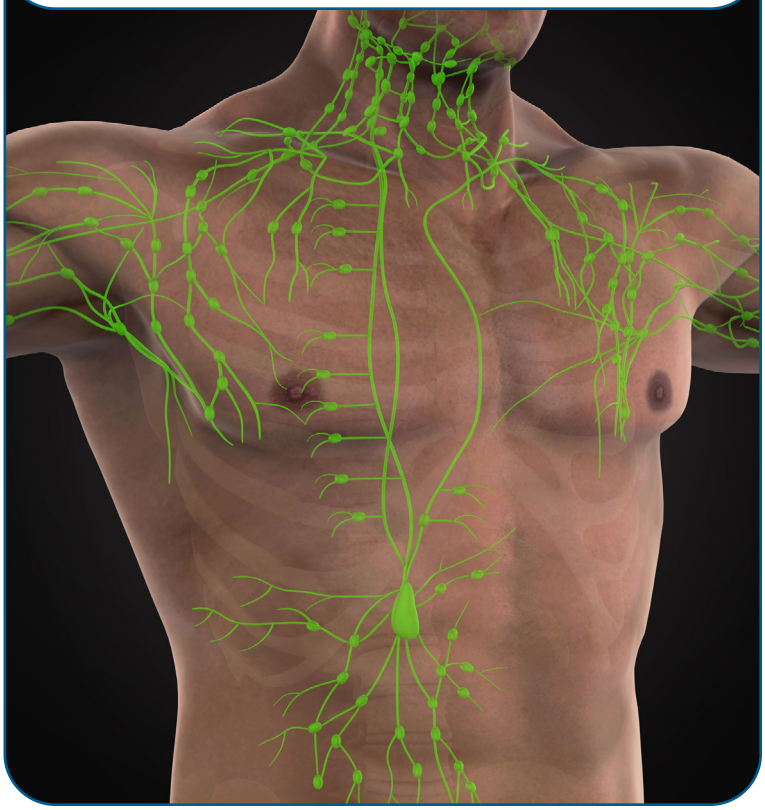
Lymph node dissection

A lymph node dissection may be done if the cancer has spread to the lymph node basin. This is not often done if you have a positive sentinel lymph node biopsy. A lymph node dissection removes the nodes to prevent disease from coming back or spreading elsewhere. This surgery is done under general anesthesia.

Lymph node dissection is generally reserved for advanced melanomas with nearby enlarged

Lymph nodes

There are hundreds of small bean-shaped structures throughout the human body called lymph nodes. Lymph nodes catch and filter out foreign particles and harmful cells, including cancer cells.



lymph nodes. Completion lymph node dissection refers to a dissection done after tiny amounts of cancer are found in the SLNB. It is not often performed after an SLNB, and nodal ultrasound or other imaging tools can be used instead to monitor the lymph nodes. Newer therapy options are lessening the need for this type of surgery for stage 3 melanoma.

Common side effects of this surgery include pain, numbness, limited movement (of arms or legs), and lymphedema. Lymphedema is the most serious side effect of lymph node surgery.

Lymphedema treatment

Lymphedema is swelling due to buildup of lymph fluid in the fatty tissue just under your skin near the surgery site. This buildup can often cause swelling and discomfort. It often happens in the arms or legs, but can also happen in the face, neck, trunk, abdomen (belly), or genital area.

Lymphedema can occur when the lymph system is damaged, which can prevent lymph fluid from returning to the blood. If you have a lymph node dissection, your care team should talk with you about the signs and symptoms of lymphedema.

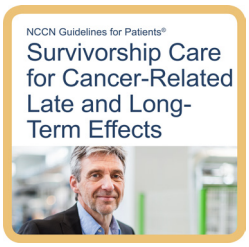
Fortunately, lymphedema is now less common after melanoma treatment since lymph node surgery is often not needed.

It's important to know that lymphedema can sometimes be serious and can become a long-term or chronic condition. Lymphedema can last for a short time or can continue throughout your life. There is no way to know if or when it will develop. It can happen just after surgery (most common) or even months or years later. This is why early and careful management is needed to help reduce symptoms and keep it from getting worse.

Steps you can take to prevent and reduce lymphedema symptoms include using compression garments and deep tissue massage.

If lymphedema symptoms continue, you might be referred to a vascular specialist or a certified lymphedema physical therapist. Joining a clinical trial for treatment for lymphedema is another option if one is available.

More information about managing lymphedema can be found in *NCCN Guidelines for Patients: Survivorship Care for Cancer-Related Late and Long-Term Effects,* available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.



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 and interfere with how those cancer cells grow.

Cancer growth inhibitors

Cancer growth inhibitors (or blockers) are a type of drug that stops cancer cells from growing. Our bodies make chemicals called growth factors that control cell growth.

Cancer growth blockers work by blocking the growth factors that trigger cancer cells to divide and grow. They are often taken orally (by mouth) and can be taken at home.

There are several types of cancer growth inhibitors, including:

- **BRAF inhibitors:** Mutations in the *BRAF* gene cause melanoma cells to produce proteins that help cancer cells grow. About half of melanoma skin cancers have a *BRAF* mutation. BRAF inhibitors include vemurafenib (Zelboraf), dabrafenib (Tafinlar), and encorafenib (Braftovi). These drugs attack the *BRAF* protein directly and can shrink or slow the growth of tumors in melanoma that has spread or can't be removed completely.
- **MEK inhibitors:** MEK inhibitors are often used with BRAF inhibitors. The MEK protein works with the *BRAF* gene. That means medications that target the MEK protein can also treat melanomas with *BRAF* mutations. They include trametinib (Mekinist), cobimetinib (Cotellic), and binimetinib (Mektovi).
- **KIT inhibitors:** Some rare melanomas, such as those that occur on the palms, soles, or under nail beds, have specific *KIT* gene mutations. KIT inhibitors include imatinib (Gleevec), dasatinib (Sprycel), and nilotinib (Tasigna).

In most cases, BRAF inhibitors and MEK inhibitors are combined to treat melanomas that have mutations in the *BRAF* genes, such as these combinations:

- Dabrafenib (Tafinlar) and trametinib (Mekinist)
- Vemurafenib (Zelboraf) and cobimetinib (Cotellic)
- Encorafenib (Braftovi) and binimetinib (Mektovi)

BRAF and MEK inhibitors can cause non-melanoma skin cell cancers, photosensitivity, other skin reactions, and many possible systemic side effects, including rash, nausea, diarrhea, loss of appetite, and fatigue. In some cases, side effects can be severe and even life-threatening, so tell your doctor if you have any of them.

If you develop a reaction on your skin (rash, itching, swelling) after you have any of the systemic therapies listed above, it is recommended that you see a dermatologist regularly for treatment.

See Part 3: Testing for melanoma for more information on BRAF mutations.

Immunotherapy

Immunotherapy is a treatment that uses the immune system to kill cancer cells. The body's defense against disease is called the immune system. T cells are a key part of this system. T cells that kill infected and cancer cells are called cytotoxic or killer T cells.

Your immune system can tell the difference between normal cells in the body and those it sees as "foreign," such as germs and cancer cells. This allows the immune system to attack the foreign cells while leaving normal cells alone.

Checkpoint inhibitors

Immune checkpoint inhibitors are a type of immunotherapy. They work by releasing the "brakes" on your body's T cells. Immunotherapy can be given alone or combined with other types of treatment.

The immune system has "brakes" that prevent or slow down an immune response. The brakes are called immune checkpoints. They protect the body's healthy cells. Proteins called CTLA-4 and PD-1 are two types of brakes on T cells.

The immune system does this by using "checkpoint" proteins on immune cells. The checkpoints act like switches that need to be turned on (or off) to start an immune response. In some cases, cancer cells find ways to use these checkpoints to avoid being attacked by the immune system.

Checkpoint inhibitors are injected into a vein (infusion). It may take up to 30 to 60 minutes to get the full dose. Infusions are usually given every few weeks. The number of weeks between treatments can depend on the type of inhibitor used.

Examples of checkpoint inhibitors that are used to treat melanoma include:

- Pembrolizumab (Keytruda)
- Nivolumab (Opdivo)
- Ipilimumab (Yervoy)
- Atezolizumab (Tecentriq)
- Nivolumab/Relatlimab-rmbw (Opdualag)

In some cases, a combination of targeted therapy and checkpoint inhibitors or combination immunotherapy is recommended for treatment. Some examples of these combination therapies are:

- Nivolumab + ipilimumab
- Nivolumab/relatlimab-rmbw
- Atezolizumab + vemurafenib & cobimetinib

Checkpoint inhibitors can cause immune-related side effects, including rash, diarrhea, shortness of breath, headache, and abnormal thyroid function. These side effects can occur during or after treatment.

Read about immune-related side effects at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

IL-2

Interleukin 2 (IL-2, Proleukin) is a type of immunotherapy that can be injected into the vein or directly into the cancer tumor. IL-2 is

a naturally occurring protein that is made by a specific type of white blood cell, called a T cell. It works by stimulating the immune system to target and kill cancer cells. This therapy can also be used with TIL (tumor-infiltrating lymphocytes) therapy.

Side effects of IL-2 can include fever, chills, muscle stiffness, diarrhea, dizziness, tiredness, headache, weight gain, nausea, vomiting, and loss of appetite.

T-VEC

Talimogene laherparepvec (T-VEC) (IMLYGIC) is a weakened form of the herpes virus made in a lab. T-VEC is a type of viral immunotherapy, which uses a genetically formed virus to stimulate the body's immune system. It is injected directly into a tumor. T-VEC destroys tumor cells and also helps your body find and attack nearby cancer cells.

Some side effects of T-VEC include fever, headaches, chills, muscle aches, and feeling tired and weak. About 9 out of 10 people (about 90%) who have T-VEC get flu-like symptoms, which usually get better after a few days.

Imiquimod

Imiquimod (Aldara) is a type of immune response modifier that has been used to treat early melanoma. It is usually a cream that is applied on the skin and works by activating your immune system to stop abnormal skin growth. It should be applied only to the area of skin that needs treatment.

Some side effects can happen from using imiquimod, such as redness, swelling, skin flaking, or itching. Using too much of it or using it for a long amount of time can also cause skin reactions such as redness or burning.

Are there vaccines that treat melanoma?

There are vaccines that can treat melanoma. But unlike vaccines for flu, pneumonia, and other illnesses, melanoma vaccines don't prevent melanoma. Instead, melanoma vaccines can be used to stop cancer from returning if you already had surgery to remove tumors. Vaccine therapies for melanoma are often tested in clinical trials. Vaccines for melanoma can be given either through **systemic** or **local** treatment.

Systemic treatment is usually given through drugs that release antigens through the bloodstream to boost the body's immune system so it can fight cancer. These drugs target the parts of melanoma cells that make them different from normal cells. They work differently from chemotherapy drugs, which attack both normal and cancer cells.

Local treatment directs antigens to a specific organ or area of the body, such as an abnormal growth on the skin. After surgery, these treatments could include forms of topical therapy (medicine in a lotion or cream that is applied directly to the skin).

Chemotherapy

Chemotherapy kills fast-growing cells throughout the body, including both cancer cells and normal cells. Chemotherapy drugs are usually given through injection into a vein or are taken through a pill (by mouth).

Types of chemotherapy drugs that can be used to treat melanoma include:

- Dacarbazine (also called DTIC)
- Temozolomide (Temodar)
- Nab-paclitaxel
- Paclitaxel
- Cisplatin
- Carboplatin

Chemotherapy doesn't work as well to treat melanoma as it does for other types of cancer. It's not used often, because immunotherapies and targeted therapies work well. Your care team will likely use immunotherapy or targeted therapy first to treat your melanoma. Chemotherapy may be an option for treatment if your disease does not respond to immunotherapy or targeted therapy, or if you have severe side effects.

If you are given chemotherapy, you may receive treatment for up to several months, depending on the stage of your cancer and how often you are able to come in for treatment. You might experience side effects, depending on your general health and the amount of chemotherapy drugs used. Side effects include feeling tired, nausea or vomiting, loss of appetite, diarrhea, nerve damage, and hair loss. These side effects often go away after you finish treatment.

Radiation therapy

Radiation therapy (RT) using photons, protons, or electrons can be used to kill cancer cells and shrink tumors.

RT can be given alone or with other treatments. Treatment may focus on individual tumors, a small area of the body, or a specific lymph node area. RT can also be used as palliative treatment to help ease pain or discomfort caused by cancer.

External beam radiation therapy (EBRT) is the most common method used. A large machine makes radiation beams that are directed at the tumor. The beams overlap at the site of the tumor or cancer cells to focus the high dose of radiation to that area. A much lower dose is given to nearby tissue. How often the treatment is given is based on the goal of your treatment and where the melanoma is located.

Intensity-modulated radiation therapy

Intensity-modulated radiation therapy (IMRT) uses many small beams of different strengths. This allows a high dose of radiation to be targeted at the tumor while limiting the amount of radiation to the surrounding normal tissue.

Image-guided radiation therapy

Image-guided RT (IGRT) uses imaging to deliver radiation to cancer. Imaging can confirm exactly where the tumor is in the body both before and during treatments.

Radiation therapy for distant disease

Other radiation techniques that can be used to treat distant metastatic disease are:

- Stereotactic radiosurgery (SRS) treats small tumors with very precise, high-dose x-ray beams and is usually finished in 1 session. It is preferred for brain metastases.
- Stereotactic radiotherapy (SRT) is a form of SRS and is finished in 1 to 5 sessions.

SRT used to treat tumors in the body, and not in the brain, is sometimes called stereotactic body radiation therapy (SBRT) or stereotactic ablative body radiotherapy (SABR).

If you have radiation therapy, you could experience some side effects, including:

- Sunburn-like skin problems
- Changes in skin color
- Hair loss in the area where the radiation enters the body
- Fatigue
- Nausea if aimed at the abdomen (belly)

Clinical trials

A clinical trial is a type of medical research study. After being developed and tested in a laboratory, potential new ways of fighting cancer need to be studied in people. If found to be safe and effective in a clinical trial, a drug, device, or treatment approach may be approved by the U.S. Food and Drug Administration (FDA).

Everyone with cancer should carefully consider all the treatment options available for their cancer type, including standard treatments and clinical trials. Talk to your doctor about whether a clinical trial may make sense for you.

Phases

Most cancer clinical trials focus on treatment. Treatment trials are done in phases.

- **Phase 1** trials study the dose, safety, and side effects of an investigational drug or treatment approach. They also look for early signs that the drug or approach is helpful.
- **Phase 2** trials study how well the drug or approach works against a specific type of cancer.
- **Phase 3** trials test the drug or approach against a standard treatment. If the results are good, it may be approved by the FDA.
- **Phase 4** trials study the long-term safety and benefit of an FDA-approved treatment.

Who can enroll?

Every clinical trial has rules for joining, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or

general health. These requirements ensure that participants are alike in specific ways and that the trial is as safe as possible for the participants.

Informed consent

Clinical trials are managed by a group of experts called a research team. The research team will review the study with you in detail, including its purpose and the risks and benefits of joining. All of this information is also provided in an informed consent form. Read the form carefully and ask questions before signing it. Take time to discuss it with family, friends, or others whom you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

Start the conversation

Don't wait for your doctor to bring up clinical trials. Start the conversation and learn about all your treatment options. If you find a study for which you may be eligible, ask your treatment team if you meet the requirements. If you have already started standard treatment, you may not be eligible for certain clinical trials. Try not to be discouraged if you cannot join. New clinical trials are always becoming available.

Frequently asked questions

There are many myths and misconceptions surrounding clinical trials. The possible benefits and risks are not well understood by many with cancer.

Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It is common to receive either a placebo with a standard treatment or a new drug with a standard treatment. You will be informed, verbally and in writing, if a placebo is part of a clinical trial before you enroll.

Are clinical trials free?

There is no fee to enroll in a clinical trial. The study sponsor pays for research-related costs,

Finding a clinical trial

In the United States

NCCN Cancer Centers
NCCN.org/cancercenters

The National Cancer Institute (NCI)
cancer.gov/about-cancer/treatment/clinical-trials/search

Worldwide

The U.S. National Library of Medicine (NLM)
clinicaltrials.gov

Need help finding a clinical trial?

NCI's Cancer Information Service (CIS)
1.800.4.CANCER (1.800.422.6237)
cancer.gov/contact

including the study drug. You may, however, have costs indirectly related to the trial, such as the cost of transportation or child care due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is billed to—and often covered by—insurance. You are responsible for copays and any costs for this care that are not covered by your insurance.

Key points

- Your treatment team will help you make decisions on how to approach care and treatment decisions.
- Treatment for melanoma is based on the stage and location.
- Surgery is usually the primary (first) treatment for melanoma that has not spread.
- A wide excision surgery removes the melanoma tumor as well as some normal-looking tissue surrounding it.
- A sentinel lymph node biopsy (SLNB) removes nodes that are the most likely to have cancer if the cancer has spread. They will be checked for cancer cells by a pathologist.
- A lymph node dissection may be done if nearby lymph nodes are larger than normal.
- Targeted therapy drugs target the activity of a specific or unique feature of melanoma cancer cells.
- Immunotherapy improves your body's ability to find and destroy cancer cells. It can be given alone or with other types of treatment.
- Chemotherapy is not often used as treatment for melanoma. But it may be an option for treatment if your disease does not respond to, or you are unable to tolerate, immunotherapy or targeted therapy.
- Radiation therapy uses radiation to kill cancer cells and shrink tumors. It may focus on individual tumors or on a specific lymph node area.
- A clinical trial is a type of medical research study. Talk to your doctor and care team about whether joining a clinical trial may make sense for you.

Speak to your doctor right away if you develop any side effects from treatments you have.

5
Stages 0 to 2: Skin only

This chapter explains the early stages of melanoma. It will provide an overview of what tests are recommended to identify the correct stage, and the best course of treatment.

Testing to identify early-stage melanoma will include a physical exam and medical history and may include imaging tests to check for specific signs or symptoms. Lab or imaging testing will likely not be recommended unless it is needed for possible surgery.

Stage 0 in situ

Stage 0 in situ refers to melanoma that is found only in the top layer of skin (epidermis). This stage is very unlikely to spread to other parts of the body.

Treatment

The standard treatment for Stage 0 in situ is wide excision surgery. Wide excision surgery removes the melanoma tumor as well as some normal-looking tissue surrounding it (the surgical margin).

See Part 4: Treatment for melanoma for more information on wide excision surgery.

There are some areas where it is harder to do surgery, such as on the face, ears, palms of the hands, and soles of the feet. In these cases, surgical techniques that can provide a closer look at the edge or border of the removed tissue (the histologic margin) may be considered.

The thickness of a melanoma tumor is measured in millimeters (mm). The tip of a pencil is about 1 mm thick.

In certain instances, topical treatment with imiquimod can also be considered for melanoma in situ, especially when complete removal by surgery is not feasible. One example is if the melanoma is considered lentigo maligna, which is a type of melanoma that looks like an irregular brown formation on sun-damaged skin, particularly on the head or neck.

Monitoring

Recommended steps after treatment for Stage 0 melanoma include a medical history review and skin exams at least once a year (annually). Imaging tests and regular blood tests aren't usually needed.

See Part 9: Follow-up care for more detailed information on monitoring.

Stage 1A

Stage 1 is divided into stage 1A and 1B. Stage 1A is defined as a lesion (tumor) that is less than 0.8 mm thick (Breslow thickness) and doesn't have a break on the skin (ulceration) under the microscope. It is considered still localized to the skin, but is invasive, which means that it has gone through the top layer of skin (epidermis) into the next layer of skin (dermis).

Treatment

Wide excision surgery is used to treat stage 1A melanoma. Sentinel lymph node biopsy is usually not recommended.

Monitoring

Recommended steps after treatment for stage 1A melanoma include a physical exam and medical history, with a focus on the skin and regional lymph nodes near the primary melanoma site, every 6 to 12 months for 5 years, and then every year afterwards. Imaging tests will be done only to check specific signs and symptoms (**see Guide 4**).

See Part 9: Follow-up care for more detailed information on monitoring.

Stage 1B or stage 2A

Stage 1B melanoma includes two types of tumors: a T1b tumor and a T2a tumor. A T1b tumor is an ulcerated tumor that is no more than 1 mm thick or a non-ulcerated tumor between 0.8- and 1-mm thickness. A T2a tumor is thicker than 1.0 mm but not thicker than 2 mm and isn't ulcerated. The primary tumor has moved into the lower layer of skin but is still curable.

Guide 4
Recommended follow-up for early-stage (stages 0 to 2) melanoma

For stage 0 in situ	• Physical exam • Medical history with a focus on the skin, at least 1 time a year (annually)
For stages 1A, 1B and 2A	• Physical exam • Medical history with a focus on the skin and lymph nodes, every 6 to 12 months for 5 years (1A) or for 5 years (1B and 2A), and then 1 time (annually) every year after • Imaging tests to check any concerning signs or symptoms
For stages 2B and 2C	• Physical exam • Medical history with a focus on the skin and lymph nodes, every 3 to 6 months for 2 years, and then every 3 to 12 months for 3 years • Imaging tests as needed to check any concerning signs or symptoms • Imaging tests every 3 to 12 months for 2 years, and then every 6 to 12 months for another 1 to 3 years, to watch for cancer return or spread

Stage 2A melanoma also includes two types of tumors: a T2b tumor and a T3a tumor. A T2b tumor is like a T2a tumor except it is ulcerated. A T3a tumor is thicker but not ulcerated (thicker than 2 mm but less than 4 mm).

Treatment

Primary treatment for stage 1B through stage 2A includes wide excision surgery. Your doctor may also consider a sentinel lymph node biopsy (SLNB), if your melanoma meets the criteria for this staging procedure, to find out whether cancer cells are found in one or more nearby lymph nodes.

A negative result means the cancer has not spread to nearby lymph nodes. However, a positive result indicates that cancer is present in the sentinel lymph nodes, and that other lymph nodes may be affected (**see Guide 5**).

Guide 5
Should you have a sentinel lymph node biopsy (SLNB)?

A sentinel lymph node is the first lymph node where cancer cells spread after leaving a tumor. An SLNB shows if cancer has spread from a tumor. It helps doctors tell the stage of your melanoma and can help you and your care team make treatment decisions.

You might need an SLNB if:

Your cancer is stage 1A and:	• the melanoma is less than 0.8 millimeters deep • the melanoma has no breakage (ulceration) or other features	**Recommendation: Your doctor likely will not consider an SLNB.**
Your cancer is stage 1B and:	• the melanoma is less than 0.8 millimeter deep and has ulceration • the melanoma is 0.8 to 1 millimeter deep with or without ulceration • the melanoma may have moved into your lymph nodes	**Recommendation: Your doctor might consider an SLNB.**
Your cancer is stage 1B or higher and:	• the melanoma has lesions less than 0.8 millimeter deep • the melanoma may have moved into your lymph nodes • you had a prior wide excision, rotational flap, or skin graft closure • you had an in-transit metastasis or local recurrence of a melanoma but no sign of regional or distant metastases	**Recommendation: Your doctor likely will consider an SLNB.**

Your care team will discuss with you whether an SLNB should be performed, based on any health conditions you have, your age and general health, and your personal preferences.

Your doctor may consider nodal basin ultrasound (US) testing before the SLNB, if results of the physical exam were unclear. A normal nodal basin US does not replace a biopsy of lymph nodes that may have cancer.

If the SLNB results find cancer in lymph nodes, the cancer will be upstaged to stage 3. The cancer will also be upstaged to stage 3 if very tiny tumors, called microscopic satellites, are found in the surgical margin.

If no cancer is found in lymph nodes, you may start follow-up care, which includes monitoring. For stage 2A melanoma, other options include clinical trials (if available) and adjuvant treatment with immunotherapy (pembrolizumab).

Monitoring

Recommended steps after treatment for stage 1B–2A melanoma include physical exams and medical history with a focus on the skin and regional lymph nodes, every 6 to 12 months for 5 years, and then every year afterwards. Imaging tests will be done only to evaluate for specific signs and symptoms to check to see if the cancer has returned (**see Guide 5**).

See Part 9: Follow-up care for more detailed information on monitoring.

Stage 2B or 2C

Stage 2B melanoma is defined as an ulcerated lesion (tumor) that is thicker than 2 mm but no thicker than 4 mm, or the melanoma is thicker than 4 mm and is not ulcerated.

Stage 2C means the melanoma is thicker than 4 mm, and the outermost layer of skin covering the tumor is broken (ulcerated) under the microscope.

Treatment

Primary treatment for stage 2B or 2C also includes wide excision surgery. An SLNB may be done for complete (pathologic) staging and is strongly recommended before adjuvant immunotherapy with pembrolizumab.

After surgery, some people start follow-up care, which includes monitoring. Other people receive adjuvant therapy in a clinical trial or with pembrolizumab. Though not used often, you may receive radiation therapy to areas where tumors are likely to return.

Adjuvant pembrolizumab can help reduce the chance of cancer returning. However, you could experience side effects. If you are being considered for adjuvant therapy, pretreatment imaging may also be recommended (**see Guide 5**).

Your doctor should discuss with you the pros and cons of pembrolizumab for treatment. Factors to consider, in addition to the stage of your disease, include your age, how active you are, your personal and family history of autoimmune disease, and your tolerance for risk.

Monitoring

Recommended steps after treatment for stage 2B and 2C include a physical exam and medical history, with a focus on the skin and lymph nodes, every 3 to 6 months for 2 years, and then every 3 to 12 months for 3 years. After frequent checkups for 5 years, you will see your health care provider once a year.

Imaging tests will be done to evaluate any concerning signs and symptoms. Your doctor may consider imaging tests every 3 to 12 months for 2 years, and then every 6 to 12 months for another 1 to 3 years to look for the return (recurrence) or spread (metastasis) of melanoma (**see Guide 5**).

“

In time you breathe a little easier, you have less scans, then less appointments and transition to survivorship.”

Key points

- The standard treatment for stage 0 in situ and stage 1A is wide excision surgery.
- A sentinel lymph node biopsy may be done in addition to a wide excision surgery for stage 1B and stage 2A melanoma.
- Stage 2B melanoma is defined as an ulcerated lesion (tumor) that is thicker than 2 mm but no thicker than 4 mm, or the melanoma is thicker than 4 mm and is not ulcerated.
- Stage 2C means the melanoma is thicker than 4 mm, and the outermost layer of skin covering the tumor looks broken (ulcerated) under the microscope.
- Primary treatment for stage 2B or 2C also includes wide excision surgery.
- Adjuvant therapy can help reduce the chance of cancer returning. If you are considered for adjuvant therapy, pretreatment imaging may be needed.
- Follow-up care for stages 1A to 2A melanoma includes a complete physical exam and medical history, as well as imaging tests (where appropriate) to check for specific signs or symptoms.
- Follow-up care for stages 2B and 2C melanoma will include more frequent skin and lymph node exams to look for melanoma returning (recurrence) or spread (metastasis).

6
Stage 3 melanoma

Stage 3 melanoma is considered an advanced form of cancer. In this stage, the melanoma has spread to the nearby lymph nodes, lymph vessels, or other parts of the skin.

About stage 3 melanoma

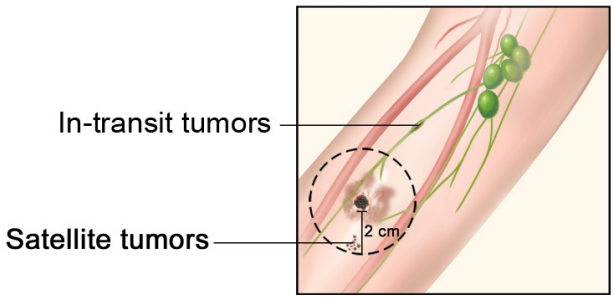
Stage 3 melanoma means the cancer has spread from the main skin tumor to nearby areas. It is called regional melanoma because the cancer has not spread far. Stage 3 melanoma is based on whether one or more of these four features is found:

- **Microscopic satellites** are tiny skin tumors that are next to or below the main skin tumor and can be seen only with a microscope.
- Lymph nodes are small structures that help fight disease. In stage 3 melanoma, nearby **lymph nodes with cancer** may be found. When distant nodes have cancer, the cancer is stage 4.
- **Satellite tumors** are deposits of melanoma in the lymph channels no more than 2 cm from the main tumor and are large enough to be seen or felt during a skin exam.
- **In-transit tumors** are lymph channel deposits that are farther than 2 cm from the main tumor but haven't reached the lymph nodes.

Satellite and in-transit tumors

Melanoma cells can spread from the main tumor through the lymph system. This system consists of small vessels and bean-shaped structures called lymph nodes (shown in green). Melanoma may form one or more satellite tumors, which are close to the main tumor. In-transit tumors are farther away but haven't reached nearby lymph nodes.

Have cancer cells spread near the primary tumor?



Microsatellite tumors (only seen with a microscope)

Know the N stage

It is important to know which stage 3 features, described above, define the melanoma. In this chapter, testing and treatment are based on these features and not by staging subgroups (stages 3A, 3B, 3C, 3D). Ask your care team to explain why the melanoma is stage 3. You may also be able to find this information in pathology reports.

The features of stage 3 melanoma are part of the N stage of the cancer. The TNM staging system was described in Part 2. Stage 3 melanoma can have any tumor stage (T1–T4) and the M stage is always M0. The N stages of melanoma are described in **Guide 6.**

Microscopic satellites

Microscopic satellites are so named because the tiny tumors can only be seen with a microscope. They are also called microsatellites. Microscopic satellites are found in either:

- A skin biopsy sample removed before treatment, or
- The tissue removed during surgery.

Early-stage melanoma is upstaged to stage 3 if microscopic satellites are found in surgical tissue.

This section explains the tests and treatments of stage 3 melanoma defined only by microsatellites (stage N1c). Note that the stage of the melanoma may change after more testing.

Tests

The tests for melanoma with microscopic satellites include:

- Imaging tests for staging
- Imaging tests to assess signs or symptoms of cancer
- *BRAF* mutation testing if you might have adjuvant therapy (described below) or enroll in a clinical trial

Once tests have been completed, your doctor may discuss having a sentinel lymph node biopsy (SLNB) if one wasn't already done. An SLNB will remove the tissue from the first lymph nodes where fluid from the tumor drains.

Treatment

Primary treatment will be wide excision surgery and possibly an SLNB. If you had a wide excision before, your care team may think it's best to forego an SLNB, which is ideally done at the same time as the wide excision.

After surgery, you may have more treatment called adjuvant therapy. Adjuvant therapy treats any cancer cells that may have been left behind. If you didn't have an SLNB or no cancer was found in lymph nodes, options include starting follow-up care, participation in a clinical trial, or adjuvant therapy with anti-PD-1 immunotherapy (pembrolizumab or nivolumab).

If the sentinel lymph nodes are involved with melanoma, the N stage will change from N1c to either N2c or N3c. See the section in this part called *Lymph nodes with cancer* for the next steps of care.

Guide 6
N stages for stage 3 melanoma (3A–3D)

N1	**Stage N1 is based on either one lymph node with cancer or nearby tumors**
N1a	One lymph node has cancer, which was found only after a pathologist examined nodal tissue
N1b	One lymph node has cancer, which was detected by physical exam or imaging and confirmed by pathology
N1c	There are microsatellite, satellite, or in-transit tumors but no cancer in lymph nodes
N2	**Stage N2 has more lymph nodes with cancer than stage N1**
N2a	Two or three lymph nodes have cancer, which was found only after the pathologist examined nodal tissue
N2b	Two or three lymph nodes have cancer, which was detected by physical exam or imaging and confirmed by pathology
N2c	There are microsatellite, satellite, or in-transit tumors and one lymph node has cancer
N3	**Stage N3 has more lymph nodes with cancer than stage N2, or lymph nodes are stuck together (matted) because of cancer growth**
N3a	Four or more lymph nodes have cancer, which was found only after the pathologist examined nodal tissue
N3b	Four or more lymph nodes have cancer, which was detected by physical exam or imaging and confirmed by pathology or Lymph nodes with cancer are stuck together
N3c	There are microsatellite, satellite, or in-transit tumors and two or more lymph nodes have cancer or There are microsatellite, satellite, or in-transit tumors and lymph nodes that are stuck together

Lymph nodes with cancer

Cancer in nearby lymph nodes is a common feature of stage 3 melanoma. There are two ways that cancer is found in these nodes:

- The pathologist found cancer in the SLNB (stages N1a, N2a, and N3a)
- The pathologist confirmed cancer in abnormal nodes that were detected by a physical exam or imaging and biopsied before treatment (stages N1b, N2b, and N3b)

Stages N1a, N2a, and N3a

Testing for stage 3 melanoma with cancer in sentinel lymph nodes depends on the number of nodes with cancer.

When only one sentinel node has cancer (N1a), your care team will consider imaging for staging. For stages N2a and N3b, imaging for staging is also recommended. If melanoma involves the lymph nodes or other parts of the body, *BRAF* testing is considered to determine whether targeted therapy may be used.

When sentinel lymph nodes have cancer, other nearby nodes may have cancer, too. Cancer care options include surveillance that involves a series of imaging to check nearby lymph nodes. Ultrasound is preferred over other types of imaging, such as computed tomography or magnetic resonance imaging (CT or MRI), though these can also be used. If signs of cancer appear, treatment can be received at that time.

Surveillance is preferred over surgery when the SLNB shows melanoma. Further lymph node removal with a surgery called a completion lymph node dissection (CLND) does not prolong life and can cause more harmful side effects such as lymphedema. It also involves more extensive surgery, recovery time, and hospitalization. For these reasons, CLND is not often performed after a positive SLNB.

Another care option is adjuvant therapy. During adjuvant therapy, imaging is used to check treatment results. Options for adjuvant therapy are listed below:

- Nivolumab
- Pembrolizumab
- Dabrafenib/trametinib or other BRAF or *MEK* inhibitors for people with *BRAF* V600-activating mutation

Before choosing one of the adjuvant systemic therapies listed above or observation, your care team should consider both your risk of cancer returning (recurrence) and how toxic the systemic therapies might be.

If your cancer is considered a very low-risk stage (N1a), for example, toxicity of adjuvant therapy may outweigh any potential benefit you might receive from the treatment, so it may not be recommended.

Stages N1b, N2b, and N3b

Your care team may have detected abnormal lymph nodes before starting treatment. Then a biopsy confirmed cancer in these nodes. Further recommended tests are:

- Imaging for staging and to assess signs or symptoms of cancer
- *BRAF* mutation testing

Your care team will discuss and decide if surgery can remove all the melanoma. **See Guide 7** for treatment options.

Before surgery, you may receive drug treatment to improve outcomes. This

treatment is called neoadjuvant therapy. Neoadjuvant therapy may consist of immunotherapy, targeted therapy, or both. Clinical trials have shown a benefit to receiving neoadjuvant therapy before surgery, although experts are still studying which drugs work best and how long treatment is needed.

Surgery consists of a wide excision of the skin tumor. Nearby lymph nodes are removed in what is called a therapeutic lymph node dissection (TLND). The number of lymph nodes removed depends on the involved lymph node basin. TLND may be performed if you had neoadjuvant therapy though it is becoming less common.

After surgery, your care team will decide if more treatment may help stop the cancer from returning. Treatment after surgery is called adjuvant therapy.

You may be treated with one of these drug options:

- Nivolumab
- Pembrolizumab
- Dabrafenib/trametinib or other BRAF or MEK inhibitors for people with *BRAF* V600-activating mutation

If the cancer is likely to return in the regional lymph node basin, you may receive adjuvant radiation therapy. This is not often recommended since it only treats the area where the lymph nodes were removed and not more places. It may be used alone, but its use has mostly been replaced by the cancer drugs listed above.

If surgery is not an option, the preferred treatment is systemic therapy (**see Guide 7**). Otherwise, you may get relief from radiation therapy, T-VEC injected into the cancer, or supportive care.

Guide 7
Treatment of melanoma with N stage of N1b, N2b, or N3b

If cancer can be treated with surgery	Treatment may include three phases: • Neoadjuvant therapy with immunotherapy, targeted therapy, or both may be received first • Surgery with a wide excision and therapeutic lymph node dissection (TLND) • Observation or adjuvant therapy with cancer drugs, radiation therapy, or both
If cancer can't be treated with surgery	There are four options: • Treatment for metastatic disease is the preferred option • Radiation therapy for symptom relief • T-VEC skin injection • Best supportive care

Satellite or in-transit tumors

Melanoma may spread and form nearby skin tumors called satellite or in-transit tumors. These tumors are seen or felt during the skin exam and then confirmed to be cancer by biopsy. Other recommended tests are:

- Imaging for staging and to assess signs or symptoms of cancer
- *BRAF* mutation testing

Treatment

Treatment depends on whether all of the cancer can be removed by surgery. Treatment can also include neoadjuvant therapy to shrink the tumor before surgery. When the cancer can be treated with surgery, it is called **resectable**. In turn, **unresectable** refers to cancer that cannot be treated with surgery. Treatment options for **resectable cancer** are listed next.

Surgery

The cancer will be removed with a complete excision. After surgery, your doctor will assess if it's likely that cancer cells remain in your body. If there are no signs of remaining cancer cells, you will be treated with systemic therapy listed in **Guide 8** or simply be observed for any new cancer signs or symptoms. If cancer cells remain, read the section below on unresectable disease for treatment options.

Adjuvant therapy is sometimes given in addition to primary treatments as a way to maximize their effectiveness.

Intralesional T-VEC or systemic therapy

Instead of upfront surgery, other treatment options are intralesional T-VEC (talimogene laherparepvec) injections, which is a type of immunotherapy, or systemic therapy. T-VEC is a virus that is injected into the skin tumor and triggers your body to find and attack nearby cancer cells.

Systemic therapy travels in your bloodstream to treat cancer anywhere in the body.

Guide 8
Systemic therapy options for resectable stage 3 melanoma with satellite or in-transit tumors

Nivolumab (Opdivo)
Pembrolizumab (Keytruda)
Dabrafenib (Tafinlar)/trametinib (Mekinist) or other BRAF or MEK inhibitors for people with *BRAF* V600-activating mutation

After treatment, your doctor will perform a skin exam and you will undergo imaging. The next treatment is based on test results:

- If there are no signs of cancer after T-VEC injections, you may start a systemic therapy listed in **Guide 8** or start observation; after systemic therapy, you may stay on the same type of treatment or start observation.
- If some cancer remains, you may have surgery.
- If the cancer worsened or too much remains, it will be treated as unresectable cancer.

Treatments for **unresectable cancer** are listed in **Guide 9**. The preferred treatment is systemic therapy that is listed in Part 8 for metastatic cancer. Options for systemic therapy are the same for unresectable and metastatic cancers. After treatment, your doctor will perform a skin exam and you will undergo imaging.

The next treatment is based on test results. If there are no signs of cancer after local or regional treatment, you may start systemic therapy as listed in **Guide 8** or start observation. After you have systemic therapy, you may stay on the same type of treatment or start observation.

If some cancer remains, you may have surgery. If the cancer worsens or too much remains, you may receive a different treatment for unresectable cancer.

Monitoring

Monitoring involves ongoing testing for new signs and symptoms of cancer. It is part of follow-up care, which is described in Part 9. Monitoring starts when there are no signs of cancer after treatment.

Guide 9
Primary treatment options for unresectable stage 3 melanoma with satellite or in-transit tumors

Systemic therapy (preferred)
Injections into the skin tumors with T-VEC (talimogene laherparepvec) or IL-2 (interleukin 2)
A prescribed topical skin cream called imiquimod
Radiation therapy
Relief of symptoms with a limited surgery or ablation of the tumors
Isolated limb infusion or isolated limb perfusion with melphalan (for melanoma in a wide area)

Recommended tests for stage 3 melanoma include:

- Physical exam and medical history with a focus on the skin and lymph nodes, every 3 to 6 months for 2 years, then every 3 to 12 months for 3 years, and every year thereafter
- Imaging tests as needed based on cancer signs and symptoms
- Routine imaging for 3 to 5 years to look for the return of cancer (recurrence) or metastatic melanoma

Systemic therapy decisions should be based on your specific goals and tolerance. How long you receive systemic therapy depends on the stage of your melanoma and how well your disease responds to treatment.

Key points

- Stage 3 melanoma has spread to nearby lymph nodes, lymph vessels, or skin areas. The N stage of melanoma is based on cancer spread to these nearby places.
- Tests for stage 3 melanoma include imaging and often *BRAF* mutation testing.
- Microscopic satellites are tiny tumors that can only be seen with a microscope.
- When cancer is found in sentinel lymph nodes, signs of cancer in other nodes may be assessed with ultrasound or other imaging, or more nodes may be removed. You may also receive adjuvant systemic therapy.
- Melanoma that is found in enlarged lymph nodes can often be treated with surgery.
- Neoadjuvant therapy is often recommended to shrink a tumor prior to surgery and can be followed by adjuvant therapy. People who have surgery often also receive systemic therapy.
- Melanoma may spread and form more skin tumors called satellite or in-transit tumors.
- To treat satellite or in-transit tumors, you may have surgery first, or have T-VEC injections or systemic therapy followed by surgery.
- If surgery isn't an option, systemic therapy is preferred, but you may have local or regional therapy instead. If some cancer remains after treatment, you may undergo surgery at this point.
- After initial treatment, the status of the cancer will be regularly monitored at appointments. You may have imaging tests on a routine basis or if cancer signs and symptoms appear.

7
Recurrence

When cancer comes back after treatment, it is called recurrent cancer. This chapter reviews the different types of melanoma recurrence, as well as testing and treatment options.

When melanoma recurs, it often does not look like the original melanoma. It often appears as lumps under the skin or in the lymph nodes. Early-stage melanoma is less likely to recur than advanced melanoma. Most recurrences occur within 3 years after treatment. If the recurrence is a distant metastasis, read Part 8 for options.

True scar recurrence

True scar recurrence is a tumor next to the scar tissue from the melanoma surgery. It occurs because not all of the melanoma was removed during surgery. This is known as persistent disease.

This tumor looks like the original melanoma. It is often found in the top layers of the skin (epidermis or superficial dermis).

Testing

Testing for true scar recurrence includes a skin biopsy to confirm it's cancer. The next tests you will receive are based on the stage and features of the recurrent melanoma. Ask your care team about any additional testing you may have.

Treatment

Treatment options for true scar recurrence include:

- Surgery to remove the tumor, with surgical margins based on the tumor depth (Breslow thickness)
- Sentinel lymph node biopsy (SLNB) based on lymphatic mapping (a procedure that finds the sentinel node) if the tumor grew near lymph vessels

Depending on how advanced the recurrence is, your care team might also recommend:

- Observation
- Clinical trial (for stage 2 if available)
- Pembrolizumab for pathologically staged 2B or 2C

Local satellite and in-transit recurrence

Local satellite recurrence and in-transit recurrence both mean the cancer has returned in the lymph channels.

Local satellite recurrence is usually found either within or surrounding the primary tumor scar. It can feel like a firm bump in or around the melanoma scar.

In-transit recurrence is usually found between the primary site and regional lymph nodes. It 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.

Testing

Testing for local satellite or in-transit recurrence includes these options:

- Core biopsy (the preferred option) or fine-needle aspiration (FNA), incisional/partial biopsy, or excisional biopsy
- Imaging for staging and to assess cancer signs or symptoms
- *BRAF* mutation testing (if not already done)

Treatment

Treatment of recurrent satellite or in-transit tumors is almost the same as when these tumors are found at diagnosis. See Part 6 for treatment at diagnosis. Treatment of recurrence depends on whether all of the cancer can be removed with surgery.

When cancer can be treated with surgery, your first treatment options may be surgery, T-VEC injection, or systemic therapy. After T-VEC or systemic therapy, you may have more surgery if there is still a tumor.

After surgery, you may receive systemic therapy. Systemic therapy used with surgery may consist of one of the following:

- Nivolumab
- Pembrolizumab
- Dabrafenib/trametinib or other BRAF or MEK inhibitors for people with *BRAF* V600-activating mutation
- Ipilimumab if prior treatment included PD-1 checkpoint inhibitors

When cancer can't be treated with surgery, there are many other options. The preferred treatment is systemic therapy as described in Part 8 for metastatic cancer.

Other options include:

Local therapy options, such as:

- Intralesional injection options (T-VEC or IL-2)
- Topical imiquimod for superficial dermal lesions
- Radiation therapy
- Symptom relief (palliation), which can include limited excision or local ablation therapy

Regional therapy options, such as isolated limb infusion/perfusion (ILI/ILP) with melphalan. This is a procedure where a high dose of drugs is injected directly into a tumor.

After initial treatment, your care team may use imaging tests to see if the disease responded to the treatment or if it spread. If there is no evidence of disease, your team may recommend observation or further systemic therapy.

Nodal recurrence

Nodal recurrence means the melanoma is found in your lymph nodes. It often appears as enlarged lymph nodes in the lymph node basin close to where the first melanoma was.

Testing

Testing for nodal recurrence can include:

- Core biopsy (the preferred option) or fine-needle aspiration (FNA), incisional/partial biopsy, or excisional biopsy
- Imaging to see how much the disease has spread and to check cancer signs or symptoms
- *BRAF* mutation testing (if not already done)

If tests find the melanoma has spread farther than nearby lymph nodes, see Part 8 to learn what treatment options are available.

Treatment for a recurrence only in lymph nodes depends on whether or not the cancer is removable by surgery (resectable) or not (unresectable).

Treatment for resectable cancer

Treatment of a resectable nodal recurrence may start with neoadjuvant therapy. Neoadjuvant therapy is used to reduce cancer before the main treatment. It may consist of systemic therapy, intralesional therapy, or both.

Receiving neoadjuvant therapy within a clinical trial is recommended since experts are still learning about its use for melanoma. It is standard treatment for other types of cancer.

The main treatment of a resectable nodal recurrence is surgery. Enlarged lymph nodes will be removed by excision. Other lymph nodes that may have cancer will be removed, too. This is called a therapeutic lymph node dissection (TLND). You may have already had a lymph node dissection, but more nodes may be removed if the prior dissection was incomplete.

Surgery may be followed by adjuvant therapy, such as:

- Nivolumab, pembrolizumab, or dabrafenib/trametinib or other BRAF or MEK inhibitors for people with *BRAF* V600-activating mutation (preferred regimens)
- Ipilimumab if you already had anti-PD-1 therapy
- Treatment within a clinical trial
- Radiation therapy to nodal basin if you have a higher risk of another recurrence

Treatment for unresectable cancer

The preferred treatment for unresectable nodal recurrence is systemic therapy. Options for systemic therapy are the same for unresectable and metastatic cancers.

There are also many clinical trials available for unresectable stage 3 and 4 melanoma. Ask your doctor about available clinical trials for your stage of disease.

See Part 8: Stage 4: Metastatic disease to learn which treatments are recommended.

Key points

- When cancer comes back after treatment, it is referred to as recurrent cancer.
- When melanoma recurs, it often appears as lumps under the skin or in the lymph nodes.
- True scar recurrence refers to skin tumors that formed from cancer cells that remained near the surgery scar.
- Treatment for true scar recurrence consists of surgery to remove the tumor and possibly lymph nodes. After surgery, you may receive adjuvant therapy.
- Local satellite recurrence and in-transit recurrence both mean the cancer has returned in the lymph channels.
- Treatment options for local satellite recurrence are based on whether surgery is an option. If there are no signs of cancer after treatment, you may receive more treatment to improve outcomes or start observation.
- Nodal recurrence means melanoma was found in your lymph nodes.
- Treatment for nodal recurrence depends on whether or not the cancer is removable by surgery. If surgery is not an option, the preferred treatment is systemic therapy.

I remember not being able to physically climb stairs, but today, after treatment, things are getting easier to navigate. One step at a time, one day at a time."

8

Stage 4: Metastatic disease

This chapter will review recommended tests and treatments for melanoma that has spread far away from the primary tumor. This is called metastatic melanoma.

Stage 4 cancer, also called metastatic cancer, is melanoma that has spread far from the skin. Metastatic melanoma most often spreads to distant lymph nodes, brain, bones, liver, or lungs.

It is important to note that stage 4 melanoma is treatable. Find a care team that is experienced in treating your type and stage of cancer and explore clinical trial options. This will ensure you have the best possible outcome.

Tests for metastatic cancer

Testing for stage 4 melanoma may involve one or more of the following:

- Core biopsy (the preferred option) or fine-needle aspiration (FNA), incisional/partial biopsy, or excisional biopsy
- Lactate dehydrogenase (LDH)
- Imaging to see how much the disease has spread and to check cancer signs or symptoms
- *BRAF* mutation testing if not already done

Limited metastases

When cancer has spread to only a few distant sites, it is called limited metastatic disease or oligometastases. Your care team will meet with you to discuss your options for primary treatment, which could include:

- Surgery (excision)
- Stereotactic ablative body radiotherapy (SABR)
- T-VEC injections into accessible tumors
- Systemic therapy, which is generally recommended after removal or treatment of oligometastatic melanoma (**See Guide 10**)

After surgery, radiation, or injections

Your team will assess if there are still signs of cancer. If there are **no cancer signs**, called no evidence of disease (NED), you may be treated with adjuvant systemic therapy or start follow-up care described in Part 9. Adjuvant therapy options are:

- Nivolumab (preferred)
- Pembrolizumab (preferred)
- Nivolumab/ipilimumab (preferred)
- Dabrafenib/trametinib
- Vemurafenib/cobimetinib
- Encorafenib/binimetinib
- Ipilimumab if you already had anti-PD-1 therapy

If **cancer remains in your body**, see the next section, *Widespread metastases*, for treatment options.

After systemic therapy for primary treatment

If you received systemic therapy, you will have imaging tests to assess whether the therapy worked.

- If the cancer grew during treatment, see treatment options for widespread metastases.
- If the cancer did not grow, you may have a resection. After surgery, you may receive adjuvant therapy if there are no signs of cancer.

Widespread metastases

Widespread metastases refers to cancer that has spread to many distant sites. It is unresectable, which means it cannot be completely removed with surgery.

Treatment of brain metastases

The first step in treating widespread metastases is to learn if the cancer has reached your brain. Brain metastases are often treated first to prevent serious health problems.

Your care team will meet to discuss treatment options. It is recommended that the team include a neurosurgeon, radiation oncologist, and medical oncologist. Treatment of brain metastases usually includes both systemic therapy listed in **Guide 10** and local treatment to the brain.

For local treatment, surgery is preferred if large brain metastases are causing symptoms or if there is a single metastasis. You may receive radiation therapy after surgery. When radiation therapy is used for treatment, stereotactic radiosurgery (SRS) is the preferred method.

Sometimes, brain metastases are treated with the goal to relieve symptoms. This is called palliative care. Palliative options include:

- Corticosteroids to relieve swelling
- Anticonvulsant therapy to control seizures
- Bevacizumab
- If SRS or stereotactic radiotherapy (SRT) are not options, whole brain RT (WBRT) may help

Treatment of body metastases

Treatment options for metastatic melanoma not in the brain include:

- Systemic therapy (this is the preferred treatment) and/or clinical trials
- Intralesional T-VEC injections to treat metastatic skin lesions
- Supportive care including palliative surgery, radiation therapy, or both

Metastatic melanoma may be treated with multiple lines of systemic therapy. The first treatment given is referred to as first-line therapy. Second-line therapy is the second treatment used. If more lines of therapy are needed, other second-line options may be tried. **See Guide 10** for systemic therapy of metastatic melanoma.

Preferred regimens work better, are safer, or cost less than other options. Your medical oncologist may not prescribe a preferred regimen. Ask why since there are different reasons for this decision.

Non-preferred regimens also have benefits for people with melanoma. They may extend life, delay cancer growth, or reduce symptoms.

Guide 10
Systemic therapy for metastatic melanoma

Regimens	First-line therapy	Second-line therapy
Nivolumab/ipilimumab	●	●
Nivolumab and relatlimab-rmbw	●	●
Pembrolizumab	●	●
Nivolumab	●	●
Dabrafenib/trametinib for *BRAF* V600 mutation	○	●
Vemurafenib/cobimetinib for *BRAF* V600 mutation	○	●
Encorafenib/binimetinib for *BRAF* V600 mutation	○	●
Pembrolizumab/low-dose ipilimumab	○	●
Ipilimumab		○
High-dose IL-2		○
Imatinib, dasatinib, nilotinib, or ripretinib for *KIT* mutations		○
Crizotinib or entrectinib for *ROS1* fusions		○
Larotrectinib or entrectinib for *NTRK* fusions		○
Trametinib for *BRAF* fusions		○
Binimetinib for *NRAS* mutation		○
Pembrolizumab/lenvatinib		○
Ipilimumab/intralesional T-VEC		○
Dabrafenib/trametinib plus pembrolizumab or vemurafenib/ cobimetinib plus atezolizumab		○
Chemotherapy		○

● preferred option ○ not a preferred option

Key points

- Stage 4 cancer, also referred to as metastatic cancer, is cancer that has spread from its origin to distant parts of the body. Metastatic melanoma is often treatable.
- When cancer has spread to only a few distant sites it is referred to as limited metastatic disease.
- Limited metastatic disease is considered resectable, which means it can be treated by surgery.
- Widespread metastatic disease refers to cancer that has spread to many distant sites.
- If there are brain metastases, they will likely be treated first with systemic therapy and/or local treatment.
- The preferred treatment for body metastases is systemic therapy and/or clinical trials.

Let us know what you think!

Please take a moment to complete an online survey about the NCCN Guidelines for Patients.

NCCN.org/patients/response

9
Follow-up care

After treatment for melanoma, your care team will check for any new skin cancers. They can also help you take good care of your skin and prevent melanoma from coming back. This chapter explains common care for everyone who's had melanoma.

Melanoma tests

Skin and lymph node exams

Your doctor may do exams on your skin and lymph nodes at least once a year depending on the melanoma stage. Your doctor should also explain how you can do self-exams of your skin and your lymph nodes at home. It's important to regularly look for any new, changing, or unusual spots on both exposed and non-exposed skin.

What you can do:

- **Examine your skin regularly** – If you spot anything that looks out of the ordinary or doesn't look normal, get it checked out as soon as possible.
- **See your health care provider annually for a skin exam** – Ask for a full-body skin exam by a health professional once a year. You may want to consider a skin exam more often if you are at higher risk for skin cancer.

Skin devices

Your care team might use medical tools to check for skin cancer, such as:

- dermoscopy (a hand-held device to improve accuracy of melanoma diagnosis at the bedside)
- total-body photography (to help with ongoing monitoring of moles on the skin)

This is especially important if you develop atypical-looking moles (moles that are called dysplastic under a microscope) or other suspicious skin surfaces. Though they are usually non-cancerous, they can put you at greater risk of developing future melanoma.

Imaging tests

If you had a past positive lymph node exam, your doctor might consider more imaging testing (for example, an ultrasound or CT scan). This could be followed by a more thorough imaging biopsy if your doctor feels it is needed.

How often you receive follow-up testing depends on how likely it is that your cancer will return, which can also depend on your family history of melanoma, if you have a high mole count, or if you have any signs of atypical-looking moles.

Genetic tests

Your clinical and family history might call for multigene testing, which can help doctors know if you have a higher genetic risk for developing melanoma and other cancers. This information can help guide recommendations for monitoring and early detection in both you and your family members.

You might be referred for genetic counseling and p16/*CDKN2A* testing if your history has three or more instances of diagnoses of invasive cutaneous melanomas, pancreatic cancer, and/or astrocytomas (cancers of the brain or spinal cord) that run in your family.

Multigene panel testing that includes *CDKN2A* may also be recommended if you have a relative diagnosed with pancreatic cancer. Testing for other genes that can harbor melanoma-predisposing mutations may also be needed.

See Part 1: Melanoma basics for more information on genetic testing.

Preventing melanoma

There are steps you can take to help stop melanoma cells from reforming. These are especially important if you have sun sensitivity or a lighter complexion:

- **Reduce UV radiation exposure** – This means reducing your exposure to the sun and avoiding the use of indoor tanning beds and other devices.
- **Prevent sun damage** – Limit your sun exposure between peak hours of 10:00 am and 4:00 pm.
- **Wear protective clothing** – This includes a wide-brim hat, clothes made with UV-protective fabric, and sunglasses.
- **Use sunscreen** – Choose a broad-spectrum sunscreen with a sun protection factor (SPF) of at least 30 and reapply at least once every 2 hours. Sunscreen should be applied 15 minutes before going outside.
- **Examine your skin regularly** – This includes self-examinations and skin exams by a health care provider.

Sunbathing at the beach

Use caution when spending time outdoors. Reduce your risk of skin cancer by limiting sun exposure, wearing protective clothing, and using sunscreen.

Key points

- Your doctor may do exams on your skin and lymph nodes at least once a year.
- Your doctor should also explain how you can do self-exams of your skin and your lymph nodes.
- Your care team might use devices to help detect new melanomas early.
- If you had a past positive lymph node exam, your doctor might consider more imaging testing.
- You might be referred for genetic counseling if genetic tests show 3 or more instances of diagnoses of cancers that run in your family.
- You can take several steps to help stop melanoma cells from reforming, especially if you have sun sensitivity.

We want your feedback!

Our goal is to provide helpful and easy-to-understand information on cancer.

Take our survey to let us know what we got right and what we could do better.

NCCN.org/patients/feedback

10
Making treatment decisions

It's important to be comfortable with the cancer treatment you choose. This choice starts with having an open and honest conversation with your care team.

It's your choice

In shared decision-making, you and your doctors share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your doctor.

Treatment decisions are very personal. What is important to you may not be important to someone else.

Some things that may play a role in your decision-making:

- What you want and how that might differ from what others want
- Your religious and spiritual beliefs
- Your feelings about certain treatments
- Your feelings about pain or side effects
- Cost of treatment, travel to treatment centers, and time away from school or work
- Quality of life and length of life
- How active you are and the activities that are important to you

Think about what you want from treatment. Discuss openly the risks and benefits of specific treatments and procedures. Weigh options and share concerns with your doctor.

If you take the time to build a relationship with your doctor, it will help you feel supported when considering options and making treatment decisions.

Second opinion

It is normal to want to start treatment as soon as possible. While cancer can't be ignored, there is time to have another doctor review your test results and suggest a treatment plan. This is called getting a second opinion, and it's a normal part of cancer care. Even doctors get second opinions!

Things you can do to prepare:

- Check with your insurance company about its rules on second opinions. There may be out-of-pocket costs to see doctors who are not part of your insurance plan.
- Make plans to have copies of all your records sent to the doctor you will see for your second opinion.

Support groups

Many people diagnosed with cancer find support groups to be helpful. Support groups often include people at different stages of treatment. Some people may be newly diagnosed, while others may be finished with treatment. If your hospital or community doesn't have support groups for people with cancer, check out the websites listed in this book.

Questions to ask

Possible questions to ask your doctors are listed on the following pages. Feel free to use these questions or come up with your own. Be clear about your goals for treatment and find out what to expect from treatment.

Questions about cancer testing

1. What tests will I have?
2. Do the tests have any risks?
3. Will my insurance pay for all of the tests you are recommending?
4. Do I need to do anything to prepare for testing?
5. Should I bring someone with me to the appointments?
6. Where do I go for testing, and how long will it take?
7. If any of the tests will hurt, what will you do to make me comfortable?
8. How soon will I know the results and who will explain them to me?
9. How can I get a copy of the pathology report and other test results?
10. Is there an online portal with my test results?

Questions about treatment options

1. What is my cancer stage?
2. What are my treatment options?
3. Is a clinical trial an option for me?
4. What will happen if I do nothing?
5. Are you suggesting options other than what NCCN recommends? If yes, why?
6. How do my age, sex, overall health, and other factors affect my options?
7. What if I am pregnant, or planning to become pregnant?
8. Does any option offer a cure or long-term cancer control?
9. What are the side effects of the treatments?
10. How do I get a second opinion?
11. How long do I have to decide about treatment, and is there a social worker or someone who can help me decide?

Questions about what to expect

1. Does this hospital or cancer center offer the best treatment for me?
2. Do I have a choice of when to begin treatment?
3. How long will treatment last?
4. Will my insurance cover the treatment you're recommending?
5. Are there any programs to help pay for treatment?
6. What supportive care and services are available to me and my caregivers?
7. Whom should I contact with questions or concerns if the office is closed?
8. How will you know if treatment is working?
9. What are the chances of the cancer worsening or returning?
10. What follow-up care is needed after treatment?

Questions about side effects

1. What are the possible complications and side effects of treatment?
2. Does the cancer itself cause any side effects?
3. Which side effects are most common and how long do they usually last?
4. Which side effects are serious or life-threatening?
5. Are there any long-term or permanent side effects?
6. What symptoms should I report right away, and whom do I contact?
7. What can I do to prevent or relieve the side effects of treatment?
8. Do any medications worsen side effects?
9. Do any side effects lessen or worsen in severity over time?
10. Will you stop or change treatment if there are serious side effects?

Questions about clinical trials

1. Do you recommend that I consider a clinical trial for treatment?
2. How do I find clinical trials that I can participate in?
3. What are the treatments used in the clinical trial?
4. Has the treatment been used for other types of cancer?
5. What are the risks and benefits of this treatment?
6. What side effects should I expect and how will they be managed?
7. How long will I be in the clinical trial?
8. Will I be able to get other treatment if this doesn't work?
9. How will you know if the treatment is working?
10. Will the clinical trial cost me anything?

Questions about your care team's experience

1. Are you board certified? If yes, in what area?
2. What is your experience as well as your team's experience with treating the type of cancer I have?
3. How many patients like me (of the same age, gender, race, or ancestry) have you treated?
4. Will you be consulting with experts to discuss my care? Whom will you consult?
5. Is this treatment (or procedure) a major part of your practice? How often have you done this treatment (or procedure) in the last year?
6. How many of your patients have had complications? What were the complications?

Questions about supportive care and services

1. Where can I get information about getting health insurance or more affordable health insurance?
2. Where can I get help with child care while I receive treatment?
3. Are there tools I can use to help me learn what foods to eat and what foods to avoid?
4. Are there ways to help me get more affordable food and other grocery items?
5. Are there resources that can help me with paying my utilities and household needs?
6. Where can I find help if I need legal services or guidance?
7. Are there resources I can use to find help for tasks like shopping, home maintenance, scheduling appointments, etc.?
8. Are there places I can go to if my home environment feels unsafe?
9. Are there tools I can use to help me cope with stress and anxiety?

Resources

AIM at Melanoma Foundation
aimatmelanoma.org

Cancer Hope Network
cancerhopenetwork.org

Melanoma Research Alliance
curemelanoma.org

Melanoma Research Foundation
melanoma.org

Save Your Skin Foundation
saveyourskin.ca

The Skin Cancer Foundation
skincancer.org

Triage Cancer
Triagecancer.org

Words to know

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

adjuvant treatment
Treatment (usually medicine or radiation) that is given after the main (primary) treatment.

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

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

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

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

best supportive care
Treatment given to prevent, control, or relieve side effects and improve comfort and quality of life.

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

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

***BRAF* mutations**
BRAF mutations can cause normal cells to become cancerous. They are most commonly found in melanomas but can occur in other forms of cancer.

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.

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

chromosomes
Chromosomes contain most of the genetic information in a cell.

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.

completion lymph node dissection (CLND)
A procedure to remove the lymph nodes.

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

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

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

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

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

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

deoxyribonucleic acid (DNA)
A long molecule that contains our unique genetic code.

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.

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).

general anesthesia
A controlled loss of wakefulness from drugs.

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

in-transit metastases
Skin cancer spreads through a lymph vessel.

lymph node basin
Lymph nodes drain from a particular part of the body.

neoadjuvant treatment
Treatment (usually medicine) that is given before the main (primary) treatment, usually surgery.

palliative care
Specialized medical care aimed at increasing quality of life and reducing pain and discomfort for people with serious, complex illness.

resectable
Able to be removed (resected) by surgery.

sentinel lymph node biopsy (SLNB)
Surgery to find and remove a sentinel lymph node to see if it contains cancer cells.

stereotactic ablative body radiotherapy (SABR)
A treatment that gives a high dose of radiation concentrated on a tumor, while limiting the dose to surrounding organs.

sun protection factor (SPF)
A number that indicates how well the sunscreen protects skin against sunburn.

talimogene laherparepvec (T-VEC)
Treatment that uses a virus to infect and kill cancer cells while avoiding normal, healthy cells.

ulceration
A break in the skin.

unresectable
Not capable of being surgically removed.

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This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Melanoma: Cutaneous Version 2.2023. It was adapted, reviewed, and published with help from the following people:

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NCCN Cancer Centers

Abramson Cancer Center
at the University of Pennsylvania
Philadelphia, Pennsylvania
800.789.7366 • pennmedicine.org/cancer

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer Center and
Cleveland Clinic Taussig Cancer Institute
Cleveland, Ohio
UH Seidman Cancer Center
800.641.2422 • uhhospitals.org/services/cancer-services
CC Taussig Cancer Institute
866.223.8100 • my.clevelandclinic.org/departments/cancer
Case CCC
216.844.8797 • case.edu/cancer

City of Hope National Medical Center
Duarte, California
800.826.4673 • cityofhope.org

Dana-Farber/Brigham and Women's Cancer Center |
Massachusetts General Hospital Cancer Center
Boston, Massachusetts
617.732.5500 • youhaveus.org
617.726.5130 • massgeneral.org/cancer-center

Duke Cancer Institute
Durham, North Carolina
888.275.3853 • dukecancerinstitute.org

Fox Chase Cancer Center
Philadelphia, Pennsylvania
888.369.2427 • foxchase.org

Fred & Pamela Buffett Cancer Center
Omaha, Nebraska
402.559.5600 • unmc.edu/cancercenter

Fred Hutchinson Cancer Center
Seattle, Washington
206.667.5000 • fredhutch.org

Huntsman Cancer Institute at the University of Utah
Salt Lake City, Utah
800.824.2073 • huntsmancancer.org

Indiana University Melvin and Bren Simon
Comprehensive Cancer Center
Indianapolis, Indiana
888.600.4822 • www.cancer.iu.edu

Mayo Clinic Comprehensive Cancer Center
Phoenix/Scottsdale, Arizona
Jacksonville, Florida
Rochester, Minnesota
480.301.8000 • Arizona
904.953.0853 • Florida
507.538.3270 • Minnesota
mayoclinic.org/cancercenter

Memorial Sloan Kettering Cancer Center
New York, New York
800.525.2225 • mskcc.org

Moffitt Cancer Center
Tampa, Florida
888.663.3488 • moffitt.org

O'Neal Comprehensive Cancer Center at UAB
Birmingham, Alabama
800.822.0933 • uab.edu/onealcancercenter

Robert H. Lurie Comprehensive Cancer
Center of Northwestern University
Chicago, Illinois
866.587.4322 • cancer.northwestern.edu

Roswell Park Comprehensive Cancer Center
Buffalo, New York
877.275.7724 • roswellpark.org

Siteman Cancer Center at Barnes-Jewish Hospital
and Washington University School of Medicine
St. Louis, Missouri
800.600.3606 • siteman.wustl.edu

St. Jude Children's Research Hospital/
The University of Tennessee Health Science Center
Memphis, Tennessee
866.278.5833 • stjude.org
901.448.5500 • uthsc.edu

Stanford Cancer Institute
Stanford, California
877.668.7535 • cancer.stanford.edu

The Ohio State University Comprehensive Cancer Center -
James Cancer Hospital and Solove Research Institute
Columbus, Ohio
800.293.5066 • cancer.osu.edu

The Sidney Kimmel Comprehensive
Cancer Center at Johns Hopkins
Baltimore, Maryland
410.955.8964
www.hopkinskimmelcancercenter.org

The UChicago Medicine Comprehensive Cancer Center
Chicago, Illinois
773.702.1000 • uchicagomedicine.org/cancer

The University of Texas MD Anderson Cancer Center
Houston, Texas
844.269.5922 • mdanderson.org

UC Davis Comprehensive Cancer Center
Sacramento, California
916.734.5959 • 800.770.9261
health.ucdavis.edu/cancer

UC San Diego Moores Cancer Center
La Jolla, California
858.822.6100 • cancer.ucsd.edu

UCLA Jonsson Comprehensive Cancer Center
Los Angeles, California
310.825.5268 • cancer.ucla.edu

UCSF Helen Diller Family
Comprehensive Cancer Center
San Francisco, California
800.689.8273 • cancer.ucsf.edu

University of Colorado Cancer Center
Aurora, Colorado
720.848.0300 • coloradocancercenter.org

University of Michigan Rogel Cancer Center
Ann Arbor, Michigan
800.865.1125 • rogelcancercenter.org

University of Wisconsin Carbone Cancer Center
Madison, Wisconsin
608.265.1700 • uwhealth.org/cancer

UT Southwestern Simmons
Comprehensive Cancer Center
Dallas, Texas
214.648.3111 • utsouthwestern.edu/simmons

Vanderbilt-Ingram Cancer Center
Nashville, Tennessee
877.936.8422 • vicc.org

Yale Cancer Center/Smilow Cancer Hospital
New Haven, Connecticut
855.4.SMILOW • yalecancercenter.org

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