NCCN GUIDELINES FOR PATIENTS®

2024

# Melanoma

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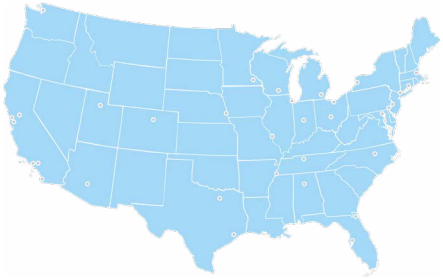
# About the NCCN Guidelines for Patients®

National Comprehensive Cancer Network®



Did you know that top cancer centers across the United States work together to improve cancer care? This alliance of leading cancer centers is called the National Comprehensive Cancer Network® (NCCN®).

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 2.2024 – April 3, 2024.**

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# 1
# Melanoma basics

**Melanoma is a serious form of skin cancer. But it is curable, especially if caught early.**

**While there is no clear cause of melanoma, there are several risk factors described ahead. This patient guideline provides the latest information on melanoma testing, staging, and treatment to help you make informed decisions with your doctor. First, it's important to know what exactly melanoma is and where it starts.**

## Skin basics

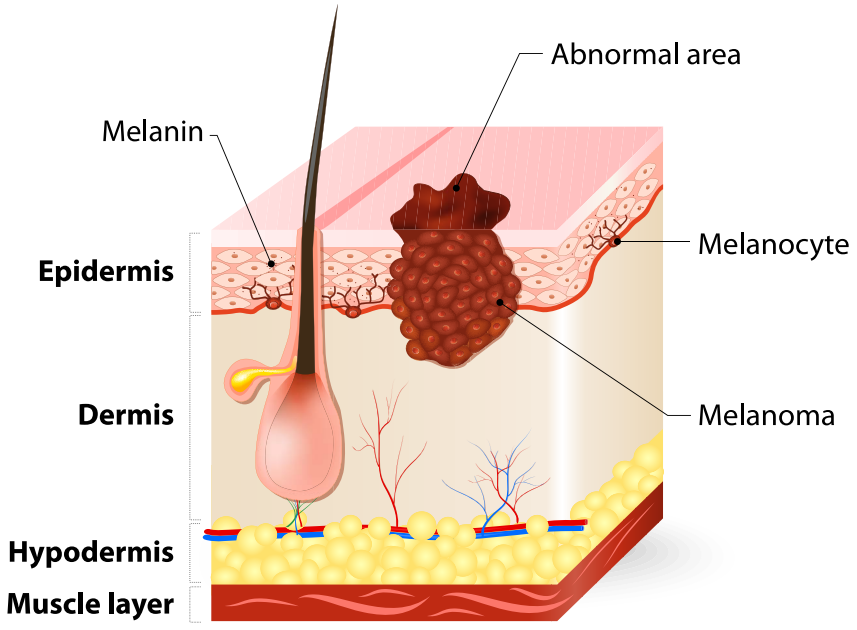
Your skin is the largest organ of your body. It covers about 20 square feet. Skin protects you from invaders (such as bacteria, fungi, and viruses), helps control body temperature, and allows the sensations of touch, heat, and cold.

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 lymph vessels.

### 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.**



# Melanin

Melanin is the pigment (chemical) in skin that gives it color. In addition, melanin also protects skin from harmful ultraviolet (UV) rays from the sun. 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, called melanoma.

Melanin levels are typically determined by your skin type and 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

# Melanoma

Melanoma is one of the most serious types of skin cancer because it spreads beyond the skin more often than many other skin cancers. However, if discovered early, it is curable with the right treatment. Most melanomas (77%) are found in the early stages — before they have spread — and when they're easier to treat.

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.

**Most melanomas are found in the early stages when they're easier to treat.**

Diagnosing and treating melanoma early can help ensure more positive outcomes. Also encouraging is that more treatments have become available for melanoma that has spread, especially in the past decade.

Important to note: While melanoma often occurs in people over 50 years of age, it can occur in people of younger age — 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, especially in people with lighter skin tones. It is important to note that UV radiation does not cause all melanomas. Some melanomas can occur 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 high intensity sun exposure such as the trunk, legs, arms, and head.

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 or toenails (called acral melanomas).

People with darker skin are more likely to develop melanoma in areas that are less exposed to the sun. Melanoma can also occur 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 or uveal melanoma).

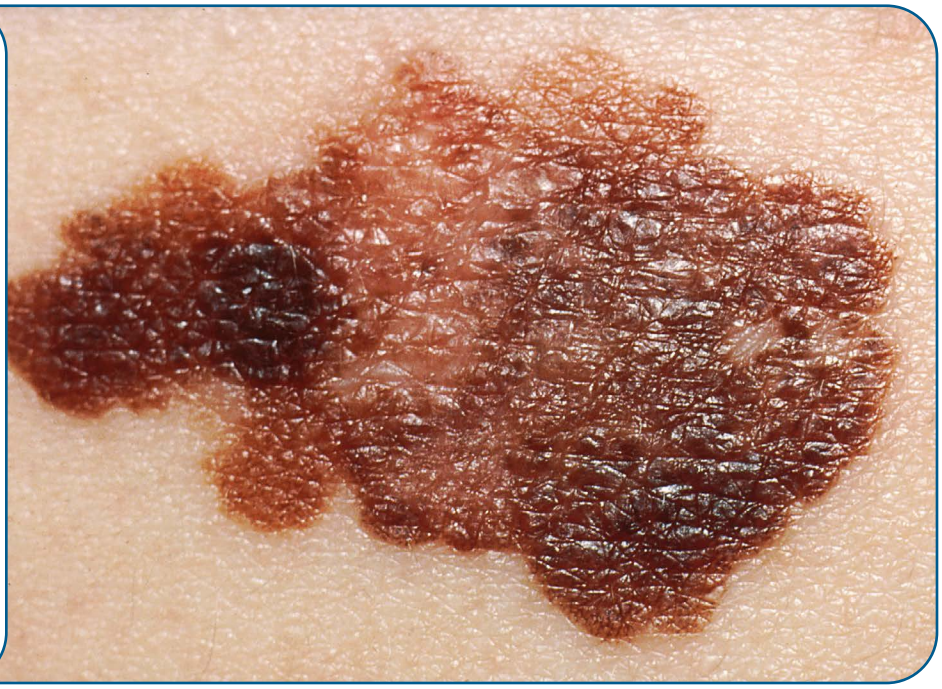
Although rare, melanoma can also show as a bump or a nodule that lacks dark pigment (usually pink or light brown in color), called amelanotic melanoma.

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

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

**Melanoma skin cancer**

**Melanoma has an irregular shape and different colors.**



## The ABCDE rule

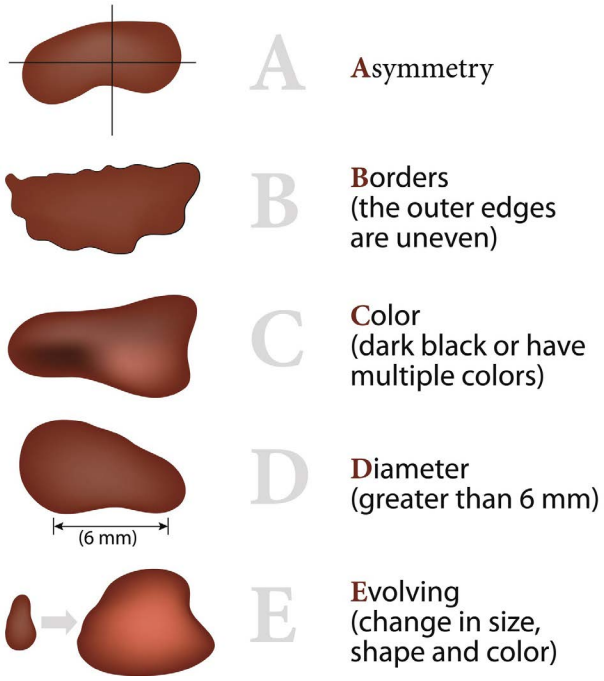
Following the ABCDE rule is also a good way to help detect the signs of melanoma:

- **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 (mm) across (about the size of a pencil eraser).
- **Evolving** – The spot or mole changes its size, shape, or color.

> **Knowing there is treatment available gave me hope at diagnosis and for the future."**

### Early detection of melanoma: ABCDE rule

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



# 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.

## Genetic physical factors

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

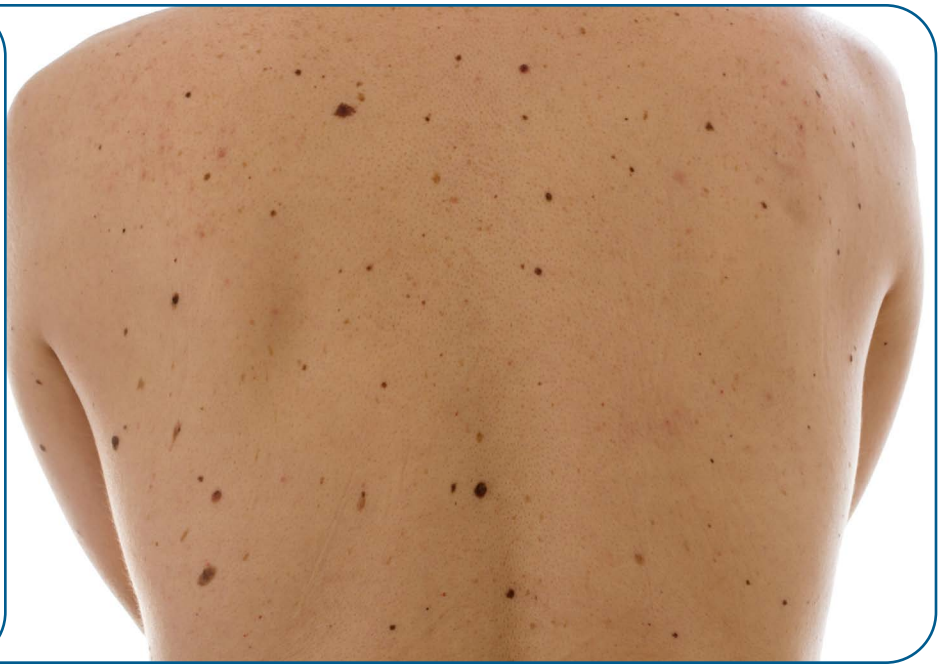
- **Lighter skin** — less melanin (pigment) in your skin means less protection from UV radiation, which makes you more likely to develop melanoma
- **Lighter hair and eyes** — you are also more likely to develop melanoma if you have blond or red hair, light-colored eyes, and freckles
- **A tendency to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

## Environmental factors

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

### Pay attention to moles

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



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

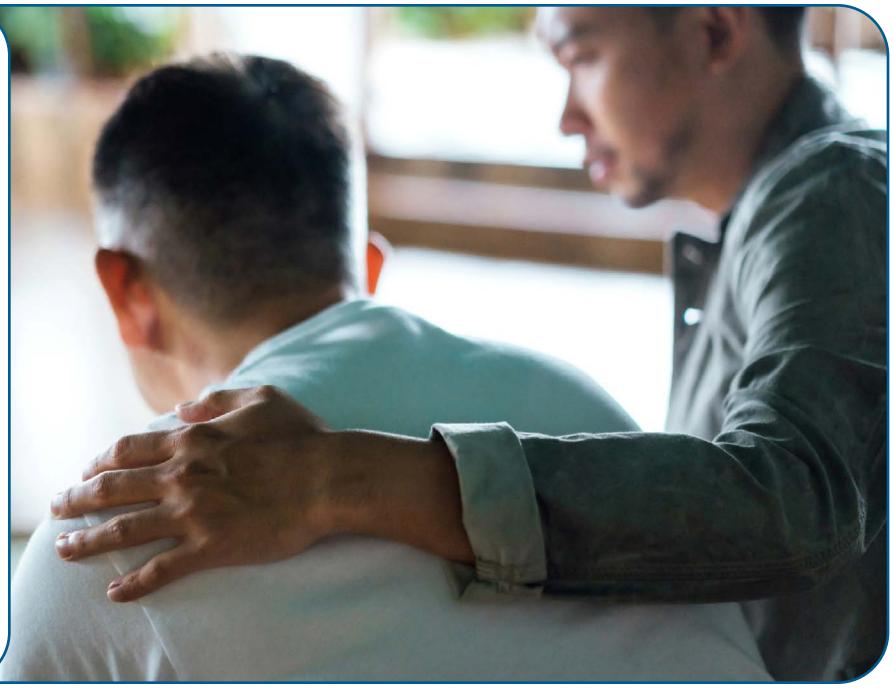
- Excessive time spent tanning in the sun
- Using tanning devices
- Living in a sunnier climate
- Working outdoors

## 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

**While a diagnosis of melanoma can be scary, many advances in treatment have been made in the past decade.**



### Family history 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 history of 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 light skin, which increases your risk for developing melanoma.
- BAP1 gene mutations, which can cause uveal and, less often, 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 curable if found early.
- The main cause of skin cancer is exposure to UV radiation from the sun and 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.

# 2
# Testing for melanoma

**Treatment planning starts with testing. Accurate testing is needed to correctly identify the type of cancer and assess if it has spread and how far. This chapter presents an overview of the tests you might receive and what to expect. Depending on your melanoma stage (see Chapter 3), you may not receive all these tests, especially imaging 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 the next chapter, *Chapter 3: Staging*.

## 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.

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

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.

More information on squamous cell skin cancer and 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

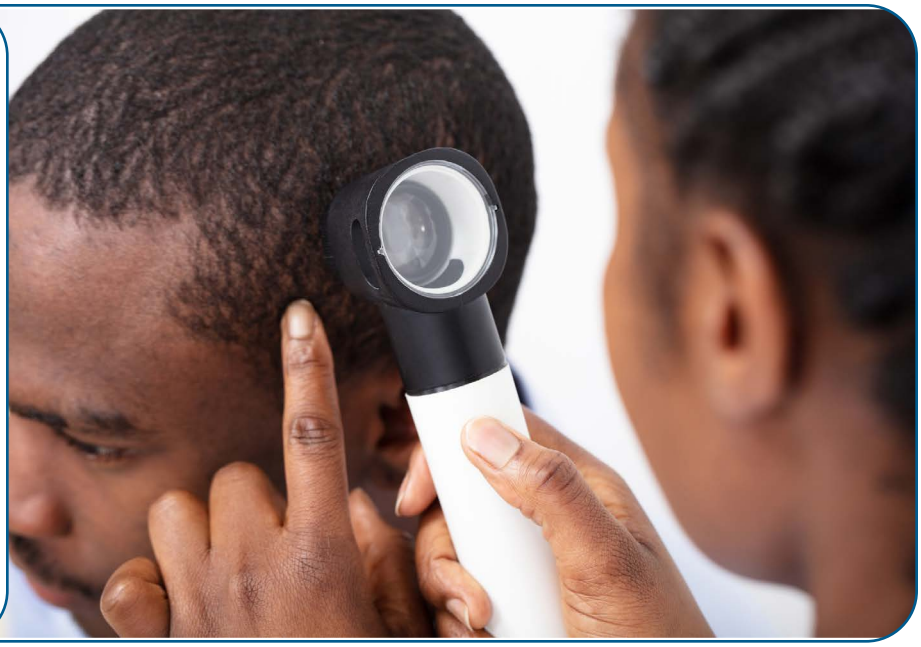
It's important to have an experienced health care provider, such as a dermatologist, give you a thorough skin exam. Skin exams are used for diagnosis, staging, and treatment planning. Expect a head-to-toe exam that includes a review of your:

- 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.

### 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.**



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 ugly duckling or the ABCDE rule (mentioned in Chapter 1 of this book) to thoroughly review any marks or lesions on your skin. When melanoma is diagnosed, it is considered a cancerous tumor and will be referred that way throughout this book.

### 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. Usually it will be closed with stitches. 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.

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.

For the biopsy, all of your lesion or a sample of it will be removed and tested to confirm melanoma under the microscope.

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 (also known as skin punch biopsy), a small piece of skin and underlying connective tissue are removed using a hand-held tool. A few 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 but may be useful for certain melanoma types (mainly, lentigo maligna) that are flat skin lesions.

Deeper 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.

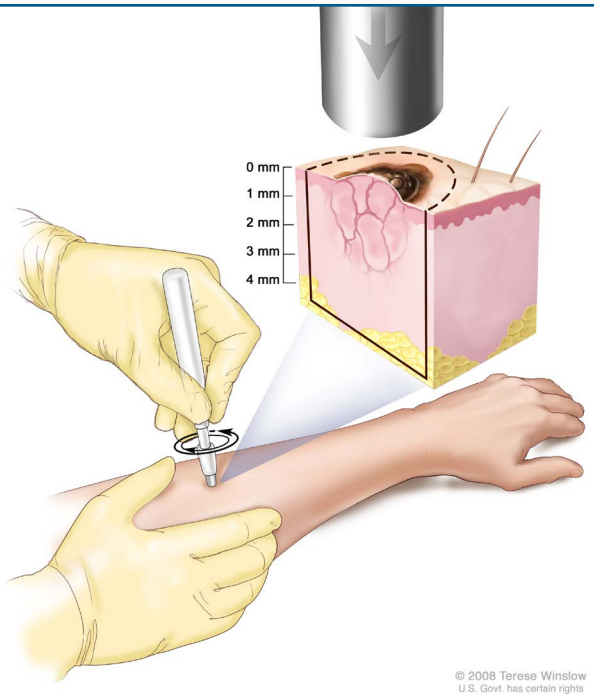
## Lymph node biopsy

A lymph node might be biopsied if your doctor 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. You will be given a stage based on this information and other factors. See the next chapter for more details on staging.

## Breslow thickness

The Breslow thickness or depth is used to measure in millimeters (mm) 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, like an open sore. An ulcerated melanoma is considered more serious because it has a greater risk of spreading.

## Dermal mitotic rate

The dermal mitotic rate or 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 lymph vessels and spread (metastasize) to other sites of 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 or excision specimen 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.

The extent of the final surgical margin depends on how deep the melanoma is (the Breslow thickness). A wider excision of the melanoma is typically done after the initial 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 (spread or travel) through your lymphatic system to the skin, subcutaneous (under the skin) tissues, and lymph nodes.

Microsatellitosis (having microsatellite tumors) refers to tiny tumor deposits that have spread to lymph vessels in the skin near the first melanoma tumor and can only be seen with a microscope.

Satellite tumors 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 vessels or blood vessels and is more aggressive (more likely to spread).

## 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 or nearby.

For a list of what factors will be considered when pathologists analyze biopsies, **see Guide 3.**

Your pathologist might also use immunostaining to help make a more accurate

**Guide 3**
**Factors that can determine your cancer stage from the biopsy**

| |
|---|
| 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 (invasion in, around, and through peripheral nerves) |

diagnosis. Immunostaining uses antibodies to detect markers on melanoma cells.

## Imaging (radiology) tests

Imaging tests take pictures (images) of the inside of your body. These tests are sometimes used for cancer staging or to check symptoms. 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.

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.

**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.**

### 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.

### 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 for energy or food. Cancer cells use more of this substance 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 since they require a lot of food or energy. When a PET scan is combined with CT, it is called a PET/CT scan, and they are almost always used together.

## 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.

### *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

**Biomarker testing is usually done in advanced stages (stage 3 and stage 4) of melanoma. But not everyone with melanoma in those stages will need this type of 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

more aggressively. A *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 of advanced disease. 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 specialized test like polymerase chain reaction (PCR) or next generation sequencing (NGS) may be used. These tests may also detect other mutations like *BRAF* V600K, *NRAS*, and *KIT*.

# 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 or monitor early melanomas. However, they may be done before or during treatment, especially for more advanced melanomas.

Tests that may be requested include:

**Lactate dehydrogenase** – 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 (called stage 4 or metastatic cancer).

**Other blood tests** – Other blood tests are not regularly done before starting treatment. But 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.

### Positive vs. Negative Results
### The truth of what they mean

It might seem confusing and the opposite of what you'd think at first. But it's important to know that when you hear of a **positive** result in cancer testing, it means that the **cancer was found**. When you hear of a **negative** result, that means the **cancer was not found**.

- 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 (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 may be done if you have surgery, if your care provider suspects the cancer has spread, or if you are taking systemic treatment for melanoma.

**You can only control what you can control. Let go of anything that is not serving you well and stay present in the moment."**

# 3
# Staging for melanoma

**A cancer stage is a way to describe the extent of the cancer at the time you are first diagnosed. Staging is needed to make treatment decisions and it happens twice with melanoma: after biopsy and after surgery. Understanding your melanoma stage is very important so don't hesitate to ask your care team questions.**

# TNM staging

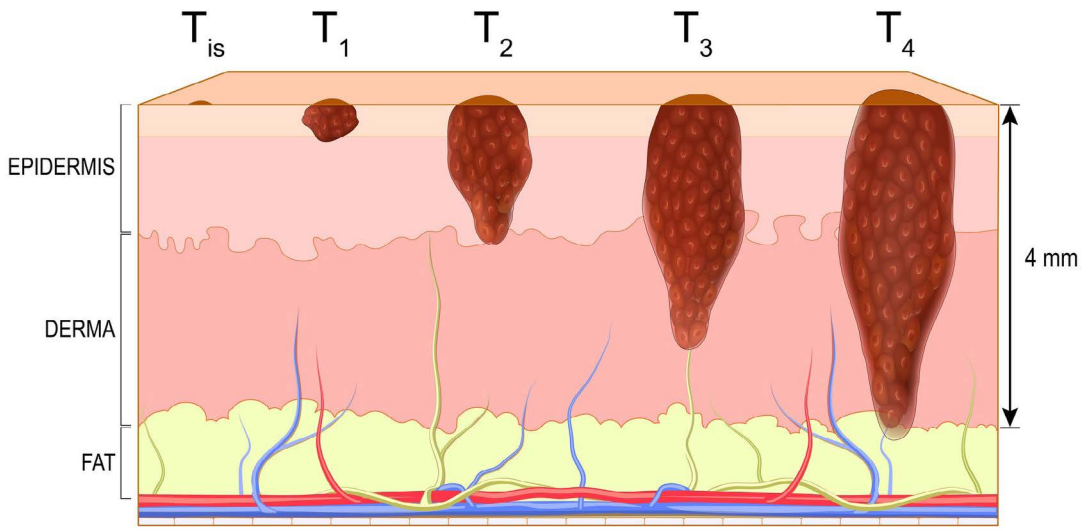
The American Joint Committee on Cancer (AJCC) TNM staging system is widely used to stage melanoma. In this system, the letters T (tumor), N (node or lymph node status), and M (metastasis) describe different areas of cancer growth. The TNM stages will be combined to assign the cancer stage group.

There are 5 stages of melanoma, including stage 0. Doctors may write the later stages (1 through 4) as Roman numerals — stages I, II, III, and IV.

Based on cancer test results described in Chapter 2, your doctor will assign a melanoma stage (0,1,2,3, or 4). Many times that stage will be accompanied by a letter (A,B,C, or D).

**Stages of melanoma**

**The TNM classification of malignant tumors**



The higher the stage, the thicker the tumor or the more the cancer has spread. An example of this is T1a, N0, M0, which indicates a stage 1A melanoma.

- **Tumor depth (T)** – refers to the thickness of the primary tumor and whether the tumor has broken through the skin like an open sore (this is called ulceration). This is measured in millimeters (mm).
- **Lymph node status (N)** – refers to whether the cancer has spread nearby (regionally) through small tubes called lymph vessels or to small bean-shaped structures (in the neck, armpits, or groin) called lymph nodes.
- **Metastasis (M)** – describes whether the cancer has spread to parts of the body far away from the primary tumor, like internal organs and distant lymph nodes.

**See Guide 1** and **Guide 2** for a breakdown of the 5 stages of melanoma.

The following information details the features of melanoma that help determine its stage.

## Tumor depth (T)

The tumor part of staging describes the characteristics of the original melanoma in thickness and ulceration. The following is a breakdown of what each type of T means.

**Tis** – (also called melanoma in situ) means the melanoma tumor is only on the top layer (epidermis) of the skin.

**T1** – the tumor is less than 1 mm and has unknown or unspecified ulceration

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

- T1a – less than 0.8 mm without ulceration
- T1b – less than 0.8 mm with ulceration or between 0.8 and 1 mm with or without ulceration

**T2** – the tumor is between 1 mm and 2 mm with unknown or unspecified ulceration

- T2a – between 1 mm and 2 mm without ulceration
- T2b – between 1 mm and 2 mm with ulceration

**T3** – the tumor is between 2 mm and 4 mm with unknown or unspecified ulceration

- T3a – between 2 mm and 4 mm without ulceration
- T3b – between 2 mm and 4 mm with ulceration

**T4** –the tumor is greater than 4 mm

- T4a – greater than 4 mm without ulceration
- T4b – greater than 4 mm with ulceration

## Lymph node status (N)

The node part of staging describes cancer in nearby lymph nodes. It also includes in-

transit, satellite, and/or microsatellite tumors. The following is a breakdown of what each type of N means. For more information on in-transit, satellite, and microsatellite tumors, see *Chapter 6: Treatment for stage 3.*

**N0** – there are no regional metastases (in lymph nodes) detected

**N1** – involves one tumor-involved node or in-transit, satellite, and/or microsatellite metastases with no tumor-involved nodes

- N1a – one node detected by sentinel lymph node biopsy (SLNB)
- N1b – one node clinically detected (felt during physical examination)
- N1c – no regional lymph node disease

**N2** – means 2 or 3 tumor-involved nodes or in-transit, satellite, and/or microsatellite metastases with one tumor-involved node

- N2a – 2 or 3 detected by SLNB
- N2b – 2 or 3 nodes, at least one of which was clinically detected
- N2c – 2 nodes found by SLNB or clinically detected

**N3** – means 4 or more tumor-involved nodes or in-transit, satellite, and/or microsatellite metastases with 2 or more tumor involved nodes, or any number of matted nodes without or with in-transit, satellite, and/or microsatellite metastases

- N3a – 4 or more tumors detected by SLNB
- N3b – 4 or more tumors, at least one of which was clinically detected, or presence of any number of matted nodes
- N3c – 2 or more detected by SLNB or clinically detected and/or presence of any number of matted nodes.

### Breslow thickness: What is it?

In your pathology report, you might see Breslow depth or thickness mentioned. This is the measurement in millimeters (mm) of how deep or thick the melanoma tumor is.

## Metastasis (M)

The metastasis part of staging describes whether the cancer has spread to a distant part of the body, which tends to be lungs, liver, bones, brain, and gastrointestinal (GI) tract. There are only two descriptors for metastasis: either the cancer has spread to distant areas or it has not.

**M0** – no evidence of distant metastasis

**M1** – evidence of distant metastasis

# Clinical vs. pathological

With melanoma, you will be staged twice. The first time is called clinical staging **(see Guide 1)**, which happens after your biopsy. This is when you find out you are diagnosed with melanoma and your doctor gives you the stage.

The second time is called pathological (or surgical) staging. The pathological staging **(see Guide 2)** happens after you have surgery to remove the tumor and surrounding area (and nearby lymph nodes, if needed) to see how advanced the cancer is. From the clinical stage, your cancer may have changed or the additional information from the surgery might alter your stage. This is especially true when a sentinel lymph node biopsy is done and finds melanoma microscopically in nearby lymph nodes.

**Guide 1**
**After biopsy: Clinical staging (cTNM)**

| | |
|---|---|
| **Stage 0** | • Tis, N0, M0 |
| **Stage 1A** | • T1a, N0, M0 |
| **Stage 1B** | • T1b, N0, M0<br>• T2a, N0, M0 |
| **Stage 2A** | • T2b, N0, M0<br>• T3a, N0, M0 |
| **Stage 2B** | • T3b, N0, M0<br>• T4a, N0, M0 |
| **Stage 2C** | • T4b, N0, M0<br>• Any T, N0, M0 |
| **Stage 3** | • Any T, Tis, greater than or equal to N1, M0 |
| **Stage 4** | • Any T, Any N, M1 |

**Guide 2**
**After surgery: Pathological staging (pTNM)**

| | |
|---|---|
| **Stage 0** | • Tis, N0, M0 |
| **Stage 1A** | • T1a, N0, M0<br>• T1b, N0, M0 |
| **Stage 1B** | • T2a, N0, M0 |
| **Stage 2A** | • T2b, N0, M0<br>• T3a, N0, M0 |
| **Stage 2B** | • T3b, N0, M0<br>• T4a, N0, M0 |
| **Stage 2C** | • T4b, N0, M0 |
| **Stage 3A** | • T1a/b,T2a, N1a, N2a |
| **Stage 3B** | • T0, N1b, N1c, M0<br>• T1a/b, T2a, N1b/c, N2b, M0<br>• T2b, T3a, N1a/b/c, N2a/b, M0 |
| **Stage 3C** | • T0, N2b/c, N3b/c, M0<br>• T1a/b,T2a/b,T3a, N2c, N3a/b/c<br>• T3b, T4a, Any N greater than or equal to N1, M0<br>• T4b, N1a/b/c, N2a/b/c, M0 |
| **Stage 3D** | • T4b, N3a/b/c, M0 |
| **Stage 4** | • Any T, Tis, Any N, M1 |

While the clinical stage helps guide treatment, the pathological stage is more accurate and specific. The pathological stage involves more information from the surgery to make your diagnosis and further treatment.

## A snapshot of stages

Because it might be challenging at first glance to follow the clinical and pathological stages, they are described in more detail in the stage-specific chapters.

In general, **stage 0, stage 1, and stage 2** melanoma are early cancers in the skin that are not known to have spread elsewhere. Stage 0 through stage 2 are almost the same in the clinical and pathological stages. For more detailed information on early stage melanoma, see *Chapter 5: Treatment for stages 0 to 2*.

**Stage 3** melanoma has spread but is considered regional. Once the tumor is considered stage 3, it involves the lymph nodes and lymphatic vessels and after surgery, it is broken down into four pathological stages (3A, 3B, 3C, 3D). For more detailed information on stage 3 melanoma, see *Chapter 6: Treatment for stage 3*.

**Stage 4** melanoma is cancer that has spread (metastasized) to distant areas of the body such as the lungs, liver, brain, bones or gastrointestinal (GI) tract. For more detailed information on stage 4 melanoma, see *Chapter 8: Treatment for stage 4.*

If you have any questions, be sure to ask your doctor to explain your melanoma in a way that you can best understand it. Also, be sure to check out the stage-specific chapter in this book that pertains to your stage of melanoma.

## Key points

- Staging for melanoma is needed to make appropriate treatment choices.
- Staging helps describe the depth of the tumor, whether any lymph nodes are involved, and whether or not the melanoma has spread (metastasized).
- You will be staged for cancer twice: after biopsy (clinical stage) and after surgery (pathological stage).
- The clinical stage helps guide treatment but the pathological stage is more accurate.
- Stage 0 through stage 2 are considered early stage cancer.
- Stage 3 melanoma has spread but is called regional.
- Stage 4 melanoma refers to cancer that has spread (metastasized) to distant areas of the body.

# 4
# Treatment overview

**This chapter 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. For more specific information on your stage, follow the stage-specific chapters.**

# Care team

After being diagnosed, knowing what to do next can be overwhelming and confusing. But you have a care team to help. 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.

## Doctors who treat cancer

**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. Some dermatologists do surgery.

**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.

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

**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.

## Other health professionals

**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.

**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.

**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 make surgery possible for some challenging melanoma tumors.

**Primary treatment** is the main treatment given to rid the body of cancer. Surgery is usually the main treatment when the tumor can be removed, often in early stage 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 cancer drugs given.

**Second-line treatment** is the next set of cancer drugs 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 for a primary melanoma tumor 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 4).**

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 (described below) or more extensive surgery, general anesthesia may be used. While you are fully asleep, you will inhale the anesthesia through a breathing tube.

A wide excision is done even if the melanoma tumor was removed by biopsy. A wide excision will also remove lymph vessels in the skin

**Guide 4**
**Surgical margin guidelines for wide excision for melanoma**

| If your tumor thickness is: | The recommended surgical margin is: |
|---|---|
| **In situ** | 0.5 to 1 cm |
| **Less than 1 mm** | 1 cm |
| **Greater than 1 to 2 mm** | 1 to 2 cm |
| **Greater than 2 to 4 mm** | 2 cm |
| **Greater than 4 mm** | 2 cm |

because there could be additional tumor cells and any nearby microsatellites. Lymph vessels are thin-walled and tube-like — similar to blood vessels — that carry a fluid called lymph. Microsatellites are tiny tumor deposits that have spread to lymph vessels in the skin near the first melanoma tumor and can only be seen with a microscope.

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 based on the thickness of the melanoma tumor.

## Side effects of wide excision

Side effects of wide excision surgery may include pain, swelling, numbness and/or 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.

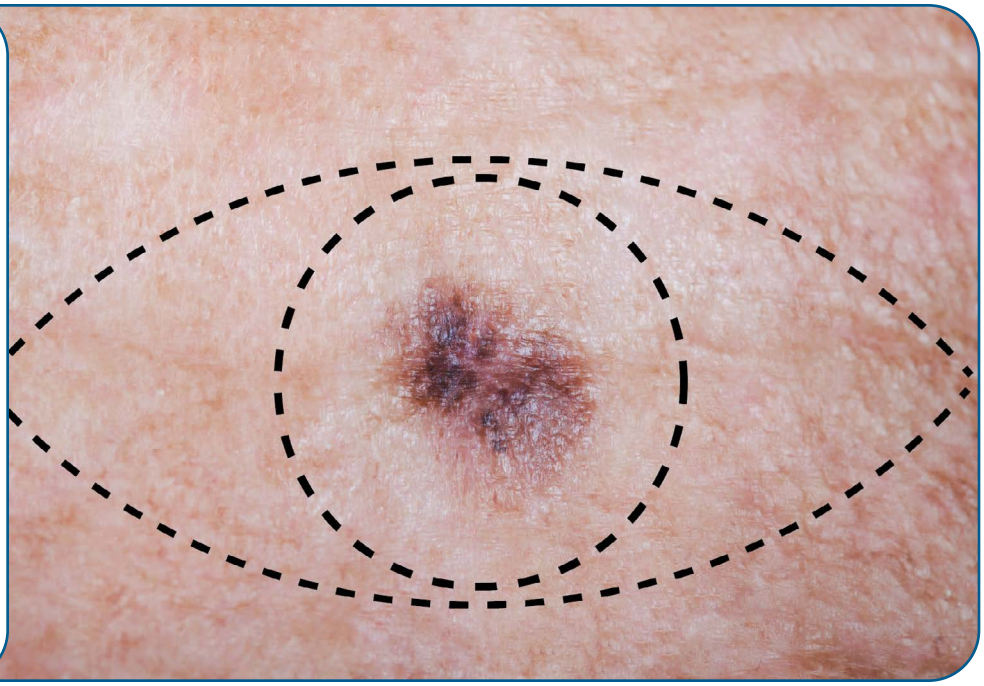
Following the surgery, a skin graft might be recommended to cover the wound. Skin grafting involves removing skin from one area of the body and moving it to a different area.

Skin grafts are surgeries that can be performed in the clinic or hospital. Most larger skin grafts involve sedation (giving medicine to help relax you) or 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.

### Wide excision

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



## Sentinel lymph node biopsy

A sentinel lymph node is the first lymph node where 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 a lymph node to examine if any cancer cells have spread to the local lymph nodes. These 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.

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

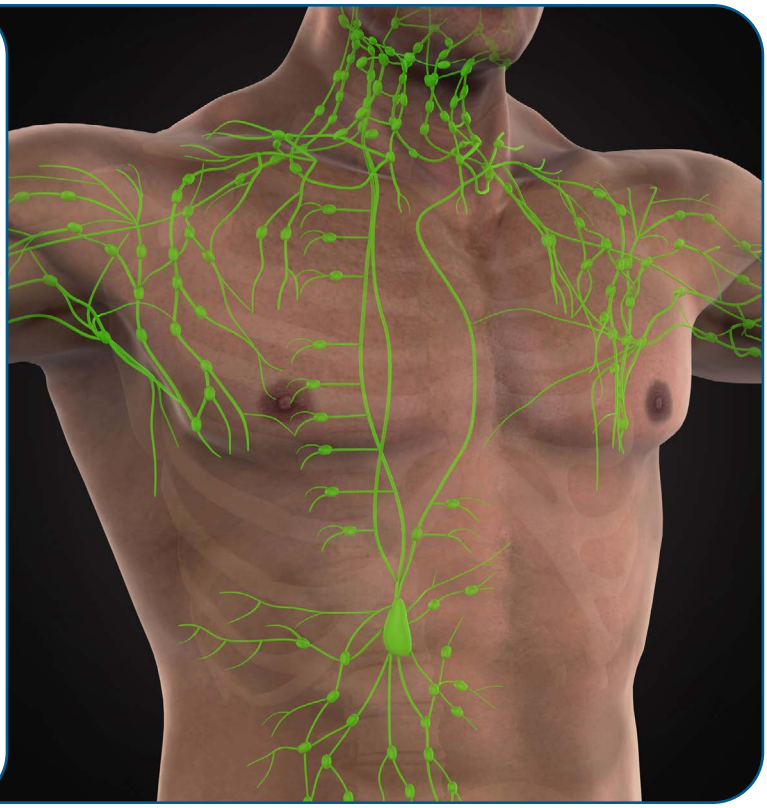
To locate the sentinel lymph node(s), your surgeon or the radiology team will inject a radioactive substance (and in some cases, a blue-colored dye) into your skin near the tumor. The substance will drain into the sentinel lymph nodes. Your surgeon will identify the sentinel lymph nodes using a device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

## Side effects of SLNB

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.

### 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.**



A seroma (pocket of clear fluid) may form and usually goes away on its own but sometimes may need to be drained with a needle.

Your doctor or care team should discuss with you the possible risks and benefits of an SLNB before you have the surgery.

## 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 there is cancer only in sentinel lymph nodes. A lymph node dissection removes nodes to prevent disease from coming back or spreading elsewhere. This surgery is done under general anesthesia.

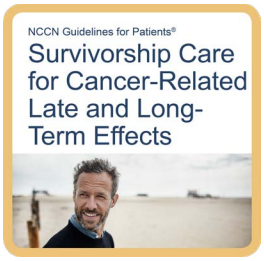
Lymph node dissection is generally reserved for advanced melanomas with nearby enlarged lymph nodes. Or it's done for nodes that have grown over time and are shown to contain melanoma.

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 SLNB for most patients, and nodal ultrasound or other imaging tools can be used instead to monitor the lymph nodes. Newer systemic therapy options are lessening the need for this type of surgery for SLNB-positive stage 3 melanoma.

However, for more extensive node disease found on exam or on imaging, full therapeutic lymph node dissection is still the most common approach. But it may be combined with systemic drug therapy before or after surgery.

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 because it causes swelling and discomfort in body parts, most commonly in the arms or legs and is treated with compression therapy and/or physical therapy.

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.




**From the time of diagnosis, ask your doctor about participating in a clinical trial of a melanoma treatment. Clinical trials can be an option at any stage of disease.**

# 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 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.

# 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 easing 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

### 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).

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, combination therapy including immunotherapy and/or targeted therapy is recommended for treatment. Two examples of combination therapies are:

- Nivolumab + ipilimumab
- Nivolumab/relatlimab-rmbw

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 and be lifelong.

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, decrease in blood pressure, muscle stiffness, diarrhea, dizziness, tiredness, headache, weight gain, nausea, vomiting, and loss of appetite.

## TIL

Tumor-infiltrating lymphocyte (TIL) therapy is an immune cell treatment that uses the patient's T cells or TILs. These T cells are collected from a patient's own tumor in a laboratory. Once isolated from the tumor sample, the TILs are expanded into the billions and infused back into the patient.

Side effects are common and include anemia, high fevers, and drops in levels of platelets and certain white blood cells. Most of the time, they resolve within a couple of weeks.

## T-VEC

Talimogene laherparepvec (T-VEC) (IMLYGIC) is a modified 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 (90%) who have T-VEC get flu-like symptoms, which usually get better after a few days.

### 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).

Because chemotherapy doesn't work as well to treat melanoma as immunotherapies and targeted therapies, your care team will likely use those therapies first to treat your melanoma.

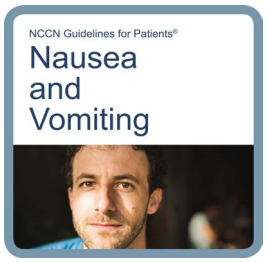
But if your disease does not respond to immunotherapy or targeted therapy, or if you have severe side effects, chemotherapy may be an option.

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

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

If you are given chemotherapy, you may receive treatment for up to several months. 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.

Read more about help for nausea and vomiting at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.




## 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)

**It is important to find a support network that understands your cancer type and the journey you are taking. Learning from others and having a safe place to ask questions is a huge benefit."**

# 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 of 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 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 of your treatment options. If you find a study that you may be eligible for, 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, 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.

## 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

## Key points

- 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.

# 5

# Treatment for stages 0 to 2: Early stage

**This chapter explains the early stages of melanoma — when most melanomas are diagnosed. It will provide an overview of the best course of treatment and follow-up care.**

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. Stage 0 has no subgroup but Stage 1 and Stage 2 are further broken down into subgroups described below and in *Chapter 3: Staging*.

## 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. It is cured when completely removed.

### 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).

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 of the removed tissue (called the histologic margin) may be considered.

***In situ* means "in place" in Latin. With melanoma, it means the cancer hasn't spread.**

### Follow up

Recommended steps after treatment for Stage 0 melanoma include a medical history and skin exams at least once a year, which may help detect other skin cancers. You won't need imaging tests and blood tests.

## Stage 1

Stage 1 melanoma has moved 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 or thickness). Stage 1 melanoma may or may not be ulcerated, though most are not. Stage 1 melanoma is broken down into two subgroups: 1A and 1B.

### Stage 1A

This stage is defined as a tumor that is less than 0.8 mm thick 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 into the next layer of skin.

## Treatment

Wide excision surgery is used to treat stage 1A melanoma. Sentinel lymph node biopsy (SLNB) is usually not recommended at this stage.

## Follow up

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 afterward. Imaging tests will be done only to check specific signs and symptoms.

### Guide 5
### When you might 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 mm deep<br>• The melanoma has no breakage (ulceration) or other features | **Recommendation: Your doctor will not likely discuss an SLNB.** |
| **Your cancer is stage 1B and:** | • The melanoma is less than 0.8 mm deep and has ulceration<br>• The melanoma is 0.8 to 1 mm deep with or without ulceration<br>• The melanoma may have moved into your lymph nodes | **Recommendation: Your doctor might discuss and consider SLNB.** |
| **Your cancer is stage 1B or higher and:** | • The melanoma is less than 0.8 mm deep<br>• The melanoma may have moved into your lymph nodes<br>• You had a prior wide excision, rotational flap, or skin graft closure<br>• You had an in-transit metastasis or local recurrence of a melanoma but no sign of regional or distant metastases | **Recommendation: Your doctor will likely discuss and recommend an SLNB.** |

### Stage 1B

Stage 1B melanoma includes tumors that are less than 0.8 mm thick with ulceration (broken skin) and tumors that are between 0.8 mm and 1 mm with or without ulceration; or a tumor without ulceration that is more than 1 mm thick but not thicker than 2 mm. The primary tumor has moved into the lower layer of skin but is still curable.

Keep reading for treatment as stage 1B is treated the same as stage 2A.

## Stage 2

Stage 2 refers to tumors that are 1 to 2 mm in thickness and are ulcerated, 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 2 melanoma is broken down into three subgroups: 2A, 2B, and 2C.

### Stage 2A

Stage 2A melanoma also includes two types of tumors: One that is between 1 mm and 2 mm that with ulceration or one that is between 2 mm and 4 mm without ulceration.

### Treatment

Primary treatment for stage 1B through stage 2A is the same and includes wide excision surgery. Your doctor may also discuss an SLNB. If your melanoma meets the criteria for this staging procedure, an SLNB will find out whether cancer cells are in one or more nearby lymph nodes **(see Guide 5)**.

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 you hear you have a negative result, it 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.

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. For more information on stage 3 melanoma treatment, see *Chapter 6: Treatment for stage 3.*

If no cancer is found in lymph nodes, you may start follow-up care.

### Follow up

Recommended steps after treatment for stage 1B to 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 afterward as needed. Imaging tests will be done only to evaluate for specific signs and

symptoms to check to see if the cancer has returned.

## Stage 2B or stage 2C

Stage 2B melanoma is defined as a lesion (tumor) that is thicker than 2 mm but no thicker than 4 mm with ulceration, or the melanoma is thicker than 4 mm without ulceration.

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

## Treatment

Primary treatment for stage 2B or 2C is the same and involves wide excision surgery. An SLNB may be done for complete (pathological also known as surgical) staging and is strongly recommended before adjuvant immunotherapy with pembrolizumab or nivolumab.

Following surgery and if no cancer is found in sentinel lymph nodes, close follow-up care is recommended and may include imaging studies to help detect melanoma recurrence. After talking with a medical oncologist, some people choose to receive adjuvant therapy with pembrolizumab or nivolumab. Though not used often, you may receive radiation therapy to areas where tumors are likely to return.

Adjuvant pembrolizumab or nivolumab can help reduce the chance of cancer returning. However, you could experience long-term immunotherapy-related side effects. If you are being considered for adjuvant therapy, pretreatment imaging is generally recommended.

Your doctor should discuss with you the pros and cons of pembrolizumab or nivolumab 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 how toxic systemic therapies might be for you.

If cancer is found in the SLNB, your cancer will be upstaged to stage 3. For more information on stage 3 treatment options, see *Chapter 6: Treatment for stage 3*.

## Follow up

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, then yearly after that point.

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. Imaging tests are generally done when a person receives adjuvant therapy.

# Key points

- Stage 0 through stage 2 melanoma is considered early-stage cancer. It is highly treatable.
- The standard treatment for stage 0 *in situ* and stage 1A is wide excision surgery.
- A sentinel lymph node biopsy (SLNB) may be done in addition to wide excision surgery for stage 1B and stage 2 melanoma.
- If cancer is found in the SLNB, you will be upstaged to stage 3 melanoma.
- Adjuvant therapy may be used for stage 2 melanoma. It can help reduce the chance of cancer returning.
- If you are considered for adjuvant therapy, pretreatment imaging may be needed.
- Depending on your signs and symptoms, you may undergo monitoring of your skin and lymph nodes for up to 3 years.

**Knowledge is power. Do not settle if your questions and concerns are not properly addressed. Advocate for yourself and your needs."**

# 6

# Treatment for stage 3: Regional

**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 but has not spread further than that. There are many treatment options depending on the features of the melanoma.**

## Stage 3 features

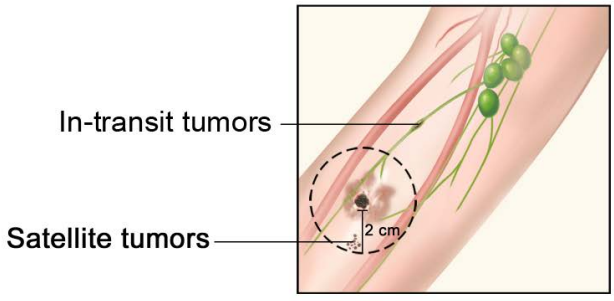
Stage 3 melanoma means the cancer has spread from the main skin tumor to nearby areas. It is called regional melanoma because the cancer has spread but not far. Stage 3 melanoma is based on whether one or more of these 4 features is found:

- **Nearby lymph nodes with cancer** may be found. Lymph nodes are small bean-shaped structures that help fight disease. When distant nodes have cancer, the cancer is stage 4.
- **Microscopic satellites** (microsatellites) are tiny skin tumors that are next to or below the main skin tumor and can be seen only with a microscope.
- **Satellite tumors** are deposits of melanoma in the lymph vessels no more than 2 cm from the main tumor. They are large enough to be seen or felt during a skin exam.
- **In-transit tumors** are lymph vessel deposits that are farther than 2 cm from

**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)

the main tumor but haven't reached the lymph nodes.

It is important to know which stage 3 features, outlined above, define the melanoma. Stage 3 melanoma involves the lymph node (N) stage and can have any tumor stage (T1–T4) and the metastasis (M) stage is always M0, because there is no distant spread.

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

## Features and subgroups

Stage 3 cancer is further broken down into 4 subgroups: 3A, 3B, 3C, and 3D. Each subgroup describes the extent of stage 3 melanoma. Stage 3A is less advanced melanoma while stage 3D is more advanced.

The way stage 3 is treated depends on its features, which help determine the subgroup. For more information on staging and the TNM staging system, see *Chapter 3: Staging.*

## Stage 3A

Stage 3A melanoma means the tumor is 1 mm thick or less with or without ulceration or 2 mm thick or less without ulceration. Between 1 to 3 lymph nodes have cancer detected microscopically after a sentinel lymph node biopsy (SLNB).

## Stage 3B

Stage 3B indicates the tumor can be less than 1 mm thick or up to 4 mm thick with or without ulceration; involves anywhere from 1 to 3 lymph nodes found by physical exam or imaging tests; and/or it has microsatellite tumors, satellite tumors, or in-transit metastases on or under the skin.

## Stage 3C

In stage 3C, the tumor can measure anywhere from less than 2 mm thick to more than 4 mm thick with or without ulceration; it can involve anywhere from 1 to 4 lymph nodes found by physical exam or imaging tests; and/or any number of lymph nodes matted together; and/or it involves microsatellite tumors, satellite, tumors, or in-transit metastases on or under the skin.

## Stage 3D

Stage 3D indicates the tumor is more than 4 mm thick with ulceration; cancer is found in 4 or more lymph nodes, or any number of lymph nodes matted together; or involves 2 or more lymph nodes and/or any number of lymph nodes matted together with microsatellite tumors, satellite tumors, and/or in-transit metastases on or under the skin.

Ask your care team to explain why the melanoma is stage 3. You may also be able to find this information in pathology reports.

All follow-up care is the same for stage 3 and mentioned at the end of this chapter.

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

- The pathologist confirmed cancer in abnormal nodes that were detected by a physical exam or imaging and biopsied before treatment
- The pathologist found cancer in the sentinel lymph node biopsy (SLNB)

# Cancer in the sentinel nodes

A sentinel lymph node is the first lymph node where cancer cells most likely spread from a primary tumor. When cancer is found in sentinel lymph nodes, it is called sentinel node positive. Testing and treatment depends on the number of nodes with cancer.

## Tests

For stage 3A, your care team may consider imaging for staging. For stages 3B, 3C, or 3D that have cancer in sentinel nodes, imaging for staging is recommended. If melanoma involves the lymph nodes or other parts of the body, *BRAF* V600 mutation testing is considered to determine whether targeted therapy is an option.

When sentinel lymph nodes have cancer, other nearby nodes may have cancer, too. Cancer care options include surveillance that involves a series of imaging tests to check nearby lymph nodes (called the nodal basin).

Active nodal basin ultrasound or other types of imaging (CT, PET-CT, or MRI) are the preferred treatment without further lymph node removal, called completion lymph node dissection (CLND). CLND should only be used with certain patients and circumstances because of its side effects like lymphedema (swelling due to buildup of lymph fluid in the fatty tissue just under your skin near the surgery site), as well as extensive surgery, longer recovery time, and hospitalization. If signs of cancer appear, adjuvant (after surgery) treatment can be received at that time.

## Treatment

After imaging surveillance, the next step is adjuvant treatment. Before choosing one of the adjuvant systemic therapies or observation (also referred to as active surveillance), your care team should consider both your risk of cancer returning (recurrence) and how toxic the systemic therapies might be for you.

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

But if your doctor recommends adjuvant therapy, options are:

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

As mentioned above, another option is undergoing observation. Observation means active surveillance and includes clinical skin

and lymph node exams, attention to any concerning signs and symptoms, and/or imaging surveillance, when needed.

# Cancer in the lymph nodes

Your care team may have detected abnormal lymph nodes before starting treatment, possibly during a physical exam or through imaging. Then a biopsy confirmed cancer in these nodes, which is referred to as clinically positive lymph nodes. Cancer at this stage could be 3B, 3C, or 3D.

## Tests

Further recommended tests are:

- Imaging for staging and to assess signs or symptoms of cancer
- *BRAF* V600 mutation testing

Your care team will discuss and decide if surgery can remove all the melanoma (meaning it's resectable). **See Guide 6** for treatment options.

## Treatment

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. But experts are still studying which drugs work best, in which patients, and how long treatment is needed.

**Guide 6**
**Treatment of melanoma with clinically positive nodes**

| | |
|---|---|
| **If cancer can be treated with surgery (resectable)** | Treatment may include three phases:<br>• Neoadjuvant therapy with immunotherapy, targeted therapy, or both<br>• Surgery with a wide excision and therapeutic lymph node dissection (TLND)<br>• Adjuvant therapy with systemic drugs, radiation therapy, or observation |
| **If cancer can't be treated with surgery (unresectable)** | • Systemic therapy is the preferred option<br>• Radiation therapy (palliative) for symptom relief<br>• T-VEC skin injection<br>• Best supportive care |

You may be treated with one of these preferred drug options as part of neoadjuvant therapy:

- Pembrolizumab
- Nivolumab/ipilimumab

Other recommended options include:

- Nivolumab
- Nivolumab and relatlimab

Used in some cases:

- Dabrafenib/trametinib (if *BRAF* V600 mutation positive)

Another option is to have surgery, which consists of a wide excision of the tumor while removing nearby lymph nodes. This is called a therapeutic lymph node dissection (TLND). The number of lymph nodes removed depends on the involved lymph node basin.

TLND will be performed if you had neoadjuvant therapy first or can be done without neoadjuvant therapy.

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

If the cancer is likely to return in the regional lymph node basin, you may receive adjuvant systemic (preferred) therapy that includes these options:

- Nivolumab
- Pembrolizumab
- Dabrafenib/trametinib (if *BRAF* V600 mutation positive)

**Adjuvant therapy is sometimes used in addition to primary treatments to boost their effectiveness.**

And you may receive adjuvant radiation therapy. This is not often recommended since it only treats the region where the lymph nodes were removed and not other areas. It may be used alone, but its use has mostly been replaced by the cancer drugs listed above.

One other option is observation and is based on your care team's decision of the risk of the melanoma's recurrence and the risk of treatment toxicity (side effects of treatment).

Observation means active surveillance and includes clinical skin and lymph node exams, attention to any concerning signs and symptoms, and/or imaging surveillance, when needed.

But if surgery is not an option (considered unresectable), the preferred treatment is systemic therapy *(*see *Chapter 8:Treatment for stage 4,* **Guide 8**) for therapies.

Otherwise, you may get relief from palliative radiation therapy, T-VEC (virus that is injected into the skin tumor and triggers your body to find and attack nearby cancer cells), or best supportive care or a combination of these treatments.

# Microsatellites

Stage 3 melanoma may involve microscopic satellites (microsatellites) so named because these tiny tumors can only be seen with a microscope. Stage 3A does not involve microsatellites. But if microsatellites are found in the biopsy, the melanoma can be upstaged to a pathological stage 3B. For all stages, microsatellites are found in either:

- A skin biopsy sample removed before treatment

or

- The tissue removed during surgery

**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.**

## 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) to see if the cancer has spread to the lymph nodes. 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 you had one and no cancer was found in lymph nodes, options include participation in a clinical trial or systemic therapy with:

- Nivolumab
- Pembrolizumab
- Dabrafenib/trametinib (but only if *BRAF* V600 mutation positive)

Observation is also an option. Observation means active surveillance and includes clinical skin and lymph node exams, attention to any concerning signs and symptoms, and/or imaging surveillance, when needed.

# 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.

### Tests

Other recommended tests to determine if surgery is necessary include:

- Imaging for staging and to assess signs or symptoms of cancer
- *BRAF* mutation testing if not already done

When the cancer can be removed with surgery, it is called resectable. Cancer that cannot be treated with surgery is called unresectable. Sometimes satellite/in-transit tumors can be considered either limited resectable or unresectable/borderline resectable. This means the tumor is on the border (outside limit) of what surgery might be able to accomplish or the tumor could be resectable if treatment shrinks the tumor first.

## Treatment: Limited resectable disease

There are four options in initial treatment for limited resectable cancer:

- Neoadjuvant systemic therapy **(see Guide 7)**
- Surgery (complete excision) to clear margins
- Talimogene laherparepvec (T-VEC/ intralesional therapy)
- Systemic therapy (see *Chapter 8: Treatment for stage 4*, **Guide 8** for options)

If you received neoadjuvant systemic therapy, the next step is surgery. The cancer will be removed with complete excision to clear margins. After surgery, your options might include adjuvant systemic therapy: nivolumab,

**Guide 7**
**Neoadjuvant (before surgery) systemic therapy options**

| | |
|---|---|
| **Preferred options** | • Pembrolizumab<br>• Nivolumab/ipilimumab |
| **Other recommended options** | • Nivolumab<br>• Nivolumab and relatlimab |
| **Used in some cases** | • Dabrafenib/trametinib if *BRAF* V600 mutation positive |

pembrolizumab or dabrafenib/trametinib if *BRAF* V600 mutation positive. Or your doctor might just observe you with clinical exams and imaging studies for any new cancer signs or symptoms.

If you received a complete excision to clear margins as initial treatment and there are no signs of remaining cancer cells, you might receive adjuvant systemic treatment options or observation.

If cancer cells remain, read the section below on unresectable/borderline resectable disease for treatment options.

## Treatment: Unresectable/ borderline resectable disease

Instead of upfront surgery because it's considered unresectable/borderline resectable, initial treatment options include systemic therapy, which is preferred (see *Chapter 8: Treatment for stage 4,* **Guide 8**). Or you could have local therapy options that include:

- Intralesional injection options:
  - T-VEC (talimogene laherparepvec), which is preferred
  - Interleukin-2 (IL-2), which is a type of immunotherapy and only helpful in some cases
- Palliative (limited) surgery or local ablation (minimally invasive) therapy

Regional chemotherapy is another option for local satellite/in-transit melanoma that's confined to an arm or leg. The treatment is called isolated limb infusion or isolated limb perfusion (ILI/ILP) with melphalan and treats just the limb involved with the melanoma.

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

- If some cancer remains and appears to be unresectable, you may have the same treatment as in the initial treatment section.
- If there is some resectable melanoma remaining, you will have the same treatment as the limited resectable disease, mentioned previously.
- If there are no signs of cancer after local or regional therapy, you may start adjuvant systemic therapy (nivolumab, pembrolizumab or dabrafenib/trametinib if *BRAF* V600 mutation positive) or start observation with periodic surveillance imaging.
- If no cancer remains after systemic therapy, you will move to observation.

## Follow up for stage 3

For all of stage 3, follow up care involves ongoing testing for new signs and symptoms of cancer, also known as observation. It is described in *Chapter 9: Follow-up care.* Follow up starts when there are no signs of cancer after treatment.

Recommended follow-up 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 as needed.
- Imaging tests as needed based on cancer signs and symptoms. Imaging might occur

every 3 to 12 months for 2 years, then every 6 to 12 months for another 3 years.

- After 3 to 5 years, routine imaging is not recommended to look for the return of cancer (recurrence) or metastatic melanoma.

## Key points

- Stage 3 melanoma has spread to nearby lymph nodes, lymph vessels, or skin areas.
- 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.
- 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.
- Melanoma may spread and form more skin tumors called satellite or in-transit tumors.

**Come armed to each and every appointment with all of your questions and concerns and do not leave until you get them all answered!"**

# 7
# Treatment for 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. Many times, the melanoma appears as lumps under the skin or in the lymph nodes. Early-stage melanoma is less likely to recur than advanced melanoma. Most recurrences happen within 3 years after treatment. If the recurrence is a distant metastasis, read *Chapter 8: Treatment for stage 4* for options.

# True scar recurrence

True scar recurrence, also known as persistent disease, is a tumor next to the scar tissue from the melanoma surgery. It occurs because not all of the melanoma was removed during surgery despite best efforts. 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).

## Tests

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 and could include lymphatic mapping (the use of dyes and radioactive substances to identify cancer in lymph nodes) or sentinel lymph node biopsy (SLNB). 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)
- SLNB based on lymphatic mapping if the tumor grew near lymph vessels

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

- Clinical trial (for stage 2, if available)
- Observation with or without surveillance imaging
- Pembrolizumab or nivolumab for pathologically staged 2B or 2C
- Primary tumor site radiation therapy

# Local satellite and in-transit recurrence

Local satellite recurrence and in-transit recurrence both mean the cancer has returned in the lymph vessels. It is usually found either within or surrounding the primary melanoma scar. Local satellite recurrence can feel like a firm bump in or around that area.

In-transit recurrence is usually found between the primary site and regional lymph nodes. It means the cancer has returned and formed tumors in the lymph vessels between the melanoma scar site and the regional lymph nodes, but not in the lymph nodes themselves.

These two types of recurrence are tested and treated the same way.

## Tests

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 to assess cancer signs or symptoms
- *BRAF* mutation testing, if not already done

Treatment of recurrent satellite or in-transit tumors is almost the same as when these tumors are found at diagnosis. For treatment at diagnosis see *Chapter 6*: *Treatment for stage 3*. Treatment of recurrence depends on if the cancer can be removed with surgery (limited resectable disease).

**Palliative options mean they're intended to ease the suffering from cancer symptoms.**

## Treatment: Limited Resectable

When cancer has limited resectable disease, your first treatment options may be neoadjuvant systemic therapy **(see Guide 7),** or complete excision to clear margins, T-VEC injection, or systemic therapy (**see Guide 8** in *Chapter 8:Treatment for stage 4*). After T-VEC or systemic therapy, you may have more surgery if cancer remains.

After surgery, you may receive adjuvant systemic therapy. It may consist of one of the following:

- Nivolumab
- Pembrolizumab
- Dabrafenib/trametinib or other BRAF or MEK inhibitors for people with *BRAF* V600 mutation
- In some cases, ipilimumab might be used if prior treatment included PD-1 checkpoint inhibitors

Observation with surveillance imaging is another option.

## Treatment: Unresectable/ borderline resectable

When cancer can't be treated with surgery (unresectable/borderline resectable disease), there are many other options. The preferred

initial treatment is systemic therapy as described in *Chapter 8: Treatment for stage 4* (**see Guide 8**) for metastatic cancer.

Other treatment includes local therapy options, such as:

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

Regional therapy, such as isolated limb infusion/perfusion (ILI/ILP) with melphalan, is another option for unresectable/borderline resectable recurrent disease. This is a procedure where a high dose of drugs is injected directly into a tumor in an arm or a leg.

After initial treatment, your care team will examine you and may use imaging tests to see if the disease responded to the treatment or if it spread. The next treatment is based on test results:

- If some cancer remains and appears to be unresectable, you may have the same treatment as mentioned in the initial treatment section.
- If there is some resectable melanoma remaining, you will have the same treatment as the limited resectable disease, mentioned previously.
- If there are no signs of cancer after local or regional therapy, you may start adjuvant systemic therapy that could include:
  - Nivolumab
  - Pembrolizumab
  - Dabrafenib/trametinib if BRAF V600 mutation positive--preferred)
  - If you had anti-PD-1 therapy, you might have ipilimumab
- If no cancer remains after systemic therapy, you move to follow-up care.

For more information on follow-up care, see *Chapter 9: Follow-up care.*

**Guide 7**
**Neoadjuvant (before surgery) systemic therapy options**

| | |
|---|---|
| **Preferred options** | • Pembrolizumab<br>• Nivolumab/ipilimumab |
| **Other recommended options** | • Nivolumab<br>• Nivolumab and relatlimab |
| **Used in some cases** | • Dabrafenib/trametinib if *BRAF* V600 mutation positive |

# Nodal recurrence

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

## Tests

Testing for nodal recurrence can include:

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

Results from these tests will determine if the cancer is limited to the lymph nodes or if has spread, known as metastatic disease.

If tests find the melanoma has spread farther than nearby lymph nodes, see *Chapter 8: Treatment for stage 4* to learn what treatment options are available for metastatic disease.

If you have disease limited to the lymph nodes, then the nodes are either removable by surgery (resectable) or not (unresectable).

## Treatment: Resectable

The main treatment of a resectable nodal recurrence is surgery (called excision) but first may start with neoadjuvant therapy options like pembrolizumab and nivolumab/ipilimumab (preferred). Other recommended neoadjuvant regimens include nivolumab, nivolumab and relatlimab; in some cases, dabrafenib/trametinib will be used if you are *BRAF* V600 mutation-positive.

**Neoadjuvant therapy is used to reduce cancer before the main treatment.**

Your neoadjuvant therapy might be followed by excision, which will remove enlarged lymph nodes. Other lymph nodes that may have cancer will be removed, too. This is called a therapeutic lymph node dissection (TLND).

Or you might not have neoadjuvant therapy and instead just have the excision and TLND.

After the surgery, you may receive adjuvant therapy, such as:

- Nivolumab, pembrolizumab, or dabrafenib/trametinib or other BRAF or MEK inhibitors for people with *BRAF* V600 mutation (preferred regimens)
- Ipilimumab if you already had anti-PD-1 therapy, in some cases

and/or

- Locoregional radiation therapy to nodal basin if you have a higher risk of another recurrence

or

- Move to follow up care

For more information on follow-up care, see *Chapter 9: Follow-up care.*

### Treatment: Unresectable cancer

If you have disease limited to lymph nodes and the cancer is unresectable, the preferred treatment is systemic therapy see **Guide 8** *in Chapter 8: Treatment for stage 4*. Other options include palliative radiation therapy and/or intralesional T-VEC and/or best supportive care.

For more information about palliative care, see *NCCN Guidelines for Patients®: Palliative Care* at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.


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.

To learn which treatments are recommended, see *Chapter 8: Treatment for stage 4*.

## Key points

- 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 vessels.
- 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.

# 8

# Treatment for stage 4: Metastatic disease

**Stage 4 cancer, also called metastatic cancer, is melanoma that has spread far from where it started. Metastatic melanoma most often spreads to distant lymph nodes, brain, bones, liver, lungs or gastrointestinal (GI) tract.**

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. Always ask questions. This will ensure you have the best possible outcome.

## Tests

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 on a metastatic tumor

## Limited metastases

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

- Surgery (resection)
- Stereotactic radiation therapy, which uses special equipment to position the patient and precisely deliver radiation to a tumor
- T-VEC injections into accessible tumors

or

- Systemic therapy, which is generally recommended after removal or treatment of oligometastatic melanoma (**see Guide 8**)

### 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 Chapter 9. Adjuvant therapy options that are preferred are:

- Nivolumab
- Pembrolizumab
- Nivolumab/ipilimumab

Other recommended therapy, if *BRAF* V600 mutation-positive:

- Dabrafenib/trametinib
- Vemurafenib/cobimetinib
- Encorafenib/binimetinib

In some cases, ipilimumab might be used if you already had anti-PD-1 therapy, or you might undergo observation (clinical exams and surveillance imaging) with your doctor.

If cancer remains in your body (called residual disease), see the next section on widely disseminated (spread), for treatment options.

### After systemic therapy for primary treatment

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

- If the cancer remains after treatment, see treatment options for widely disseminated metastases.
- If the cancer stayed the same, you may have a resection. After the surgery, you may receive the same adjuvant therapy mentioned above, if there are no signs of cancer.

## Widely disseminated

Widely disseminated 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 widely disseminated 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 8** 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. This is an external beam radiation therapy that uses a high dose of radiation directly into the tumor.

Sometimes, brain metastases are treated with the goal of relieving 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 be considered

## Guide 8
## Systemic therapy for metastatic melanoma

| Regimens | First-line therapy | Second-line therapy |
|---|---|---|
| Nivolumab/ipilimumab | ● | ● |
| Nivolumab and relatlimab-rmbw | ● | ● |
| Pembrolizumab | ● | ● |
| Nivolumab | ● | ● |
| Dabrafenib/trametinib or vemurafenib/cobimetinib or encorafenib/binimetinib for *BRAF* V600 mutation | ○ | ● |
| Pembrolizumab/low-dose ipilimumab | ○ | ● |
| Lifileucel (tumor-infiltrating lymphocyte therapy-TIL) | | ● |
| 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 and non-V600 mutations | | ○ |
| Binimetinib for *NRAS* mutation | | ○ |
| Pembrolizumab/lenvatinib | | ○ |
| Ipilimumab/intralesional T-VEC | | ○ |
| Dabrafenib/trametinib plus pembrolizumab or vemurafenib/cobimetinib plus atezolizumab for *BRAF* V600 mutation | | ○ |
| Chemotherapy | | ○ |

● preferred option ○ not a preferred option

## Treatment of body metastases

Treatment options for metastatic melanoma not in the brain include:

- Systemic therapy (this is the preferred treatment)
- Palliative resection and/or radiation therapy
- Intralesional T-VEC injections to treat metastatic skin lesions
- Best supportive care

For more information about palliative care, see *NCCN Guidelines for Patients: Palliative Care* available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.


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 8** for systemic therapy options for 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 because 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.

Be sure to ask your care team if you have questions about any of your options.

**Stage 4 melanoma has many treatment options.**

# 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 treatable and has many options.
- 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.
- Widely disseminated metastatic disease refers to cancer that has spread to many distant sites.
- If brain metastases occur, they will likely be treated first with systemic therapy and/or local treatment.
- The preferred treatment for body metastases is systemic therapy.

**“There are always options. You know your body best and must advocate for what would best meet your needs. Second and third opinions should always be encouraged and if something doesn't feel right, speak up and take action.”**

# 9
# Follow-up care

**After treatment for melanoma, your care team will check for any new skin cancers often called follow up or monitoring. They can also help you take the best care of your skin and help 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 provide a closer look at suspicious lesions)
- 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 3 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.

## Preventing melanoma

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

- **Reduce UV (ultraviolet) 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.

### Limit time in the sun

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

- **Examine your skin regularly** – This includes self-examinations and skin exams by a health care provider.

## Key points

- Your doctor may do exams on your skin and lymph nodes at least once a year.
- How often you receive follow-up testing depends on how likely it is that your cancer will return.
- 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 cancer diagnoses that run in your family.
- You can take several steps to help stop melanoma cells from reforming, especially if you have sun sensitivity.

**“I was lucky. I had melanoma twice: once on my leg and once on my back. If it weren't for my doctor doing the skin exam, I would not have known about the one on my back.”**

# 10
# Making treatment decisions

**It is 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 care team share information, discuss the options, and agree on a treatment plan. It starts with an open and honest conversation between you and your team.

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 care team. If you take the time to build a relationship with your team, 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 should not be ignored, there is time to have another care provider 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 care team are listed on the following pages. Feel free to use these 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 this test?
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 your care team's experience

1. What is your experience treating melanoma? What else do you treat?
2. What is the experience of those on your team?
3. How many people like me have you treated?
4. Will you be consulting with experts to discuss my care? Whom will you consult?
5. How many procedures like the one you're suggesting have you done?
6. Is this treatment a major part of your practice?
7. How many of your patients have had complications? What were the complications?
8. Who will manage my day-to-day care?
9. I would like a second opinion. Is there someone you can recommend?

# Questions about treatment options

1. What are my treatment options?
2. Is a clinical trial an option for me?
3. What will happen if I do nothing?
4. How do my age, sex, overall health, and other factors affect my options?
5. What if I am pregnant, or planning to become pregnant?
6. Does any option offer a cure or long-term cancer control?
7. What are the side effects of the treatments?
8. How do I get a second opinion?
9. 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. Who 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 who 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 resources and support

1. Who can I talk to about help with housing, food, and other basic needs?
2. What assistance is available for transportation, childcare, and home care?
3. How much will I have to pay for treatment?
4. What help is available to pay for medicines and other treatment?
5. What other services are available to me and my caregivers?
6. How can I connect with others and build a support system?
7. How can I find in-person or online support?
8. Who can help me with my concerns about missing work or school?
9. Who can I talk to if I don't feel safe at home, at work, or in my neighborhood?
10. How can I get help to stop smoking or vaping?

# Resources

**AIM at Melanoma Foundation**
aimatmelanoma.org

**AIM at Skin Cancer Foundation**
AIMatSkinCancer.org

**Cancer*Care***
Cancercare.org

**Cancer Hope Network**
cancerhopenetwork.org

**Imerman Angels**
Imermanangels.org

**Melanoma Research Alliance**
curemelanoma.org

**National Coalition for Cancer Survivorship**
canceradvocacy.org

**Save Your Skin Foundation**
saveyourskin.ca

**The Skin Cancer Foundation**
skincancer.org

**Triage Cancer**
Triagecancer.org


**Take our survey and help make the NCCN Guidelines for Patients better for everyone!**

**NCCN.org/patients/comments**

# 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.

**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.

***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.

**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.

**completion lymph node dissection (CLND)**
A procedure to remove the lymph nodes after a positive sentinel lymph node biopsy.

**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.

**dermal mitotic rate**
A measure of how many cancer cells are growing and dividing in the dermis.

**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.

**DNA (deoxyribonucleic acid)**
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.

**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.

**imaging**
A test that makes pictures (images) of the insides of the body.

**immunotherapy**
Treatment that uses the immune system to kill cancer cells.

**infusion**
A method of putting fluids, including drugs, into the bloodstream.

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

**lymphedema**
Swelling due to buildup of lymph fluid in the fatty tissue just under the skin near the surgery site.

**lymph node**
A small bean-shaped structure that is part of the body's immune system.

**lymph node basin**
A group of lymph nodes that receives and filters lymph that flows from a certain area of the body.

**lymph vessels**
Similar to blood vessels, lymph vessels are thin-walled and tube-like but carry a fluid called lymph.

**metastasis**
The spread of cancer cells from the first (primary) tumor to a new site.

**microsatellites**
Tiny tumor deposits that have spread to lymph vessels in the skin near the first melanoma tumor and can only be seen with a microscope.

**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.

**radiation therapy (RT)**
A cancer treatment that uses high-energy rays.

**recurrence**
The return of cancer after a cancer-free period.

**resectable**
Cancer 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 radiosurgery (SRS)**
A treatment that gives a single large 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.

**tumor-infiltrating lymphocyte (TIL) therapy**
Treatment where tumor-infiltrating lymphocytes are removed from the patient's tumor, grown in a laboratory, and given to the patient by infusion.

**ulceration**
A break in the skin like an open sore.

**unresectable**
Cancer that is not able to be surgically removed.

## 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**

# NCCN Contributors

This patient guide is based on the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Melanoma: Cutaneous, Version 2.2024. 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 |
Mass General Cancer Center
*Boston, Massachusetts*
*877.442.3324 • 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 • healthcare.utah.edu/huntsmancancerinstitute*

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 • uclahealth.org/cancer*

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

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