National Comprehensive Cancer Network®

2026

# NCCN Guidelines for Patients®

Cancer care recommendations from leading experts at the National Comprehensive Cancer Network® (NCCN®)

# Melanoma



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# NCCN Guidelines for Patients®

The essential guide for people facing cancer.

Based on care recommendations from leading cancer experts.

Explains high-quality cancer care provided at state-of-the-art cancer centers.

Reviewed and revised every year.

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®).

Because cancer care is always evolving, NCCN develops and frequently updates evidence-based cancer care recommendations used by health care providers worldwide. These recommendations are known as the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®).

The NCCN Guidelines for Patients plainly explain these expert recommendations, so you can talk with your care team about the best care for you.

**These NCCN Guidelines for Patients are based on the NCCN Guidelines® for Melanoma: Cutaneous, Version 1.2026 — February 17, 2026.**

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# 1
# About melanoma


5 What is melanoma?

6 What are the signs of melanoma?

6 How is melanoma treated?

7 How can I get the best care?

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

## What is melanoma?

Melanoma is one of the most serious types of skin cancer because it spreads beyond the skin more often than other skin cancers. But if discovered early, it's curable with the right treatment. More than 3 in 4 are found early—before they have spread—and when they're easier to treat.

Melanoma occurs when something goes wrong in your melanocytes. Melanocytes are skin cells that make melanin, a pigment that gives your skin its color. When skin cells are damaged, new cells may grow out of control and can form a mass of cancerous cells. For more information on where melanoma starts and how to prevent it, see the next chapter: *Melanoma risk, prevention, and detection*.

Diagnosing and treating melanoma early can lead to better results. It's also encouraging that more effective treatments have become available in the past decade for melanoma that has spread (metastasized).

**Melanoma skin cancer**

**Melanoma usually has an irregular shape and different colors. It can show up as a change to an existing mole but also can appear as a new spot on the skin. See *Chapter 2* to learn about the ABCDE rule.**



Important note: While melanoma often occurs in people over 50 years of age, it can occur in anyone at any age—even children.

## What are the signs of melanoma?

Melanoma spots (also called lesions or tumors) can be found anywhere on your body. Most often, they are found in areas of high-intensity sun exposure, such as the trunk, legs, arms, and head. They may appear (develop) on normal skin or as a new mole or one that has changed.

Sometimes, melanoma can be found in areas that get little or no sun exposure and are called acral melanomas. These areas can include the soles of your feet, palms of your hands, and underneath your fingernails or toenails. 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, inside of the nose, on the tongue, in the intestines, and in the genital areas (mucosal melanoma); as well as 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 examines your skin, attention should be paid to the following:

- A mole that has changed in any way: size, shape, or color
- A new spot on the skin that persists, becomes raised, or bleeds easily
- Ugly duckling sign: a spot that looks different from other spots on your skin

To learn more about spotting melanoma on your own and about the ABCDE rule for moles, see *Chapter 2: Melanoma risk, prevention, and detection*.

## How is melanoma treated?

Treatment for melanoma depends on the extent of the cancer, known as its stage. Staging of melanoma happens twice: after biopsy and after surgery. The reason for 2 staging periods is because surgery often gives more specific information than the original biopsy. This means the melanoma could be changed to a higher stage (upstaged) and treated differently at that point.

There are 5 stages of melanoma that range from stage 0 (in situ) to stage 4 (metastatic melanoma). For more detailed information on staging, read *Chapter 4: Staging for melanoma*.

The lower the number, the earlier the stage and the easier the melanoma is to treat with fewer treatments needed. The good news is that most melanomas are found in earlier stages. And even if melanoma is diagnosed at a later stage, many potentially effective treatments are available.

Surgery is typically the primary treatment for earlier stages. To learn more, read *Chapter 6: Treatment for stages 0 to 2: Early stage*.

For melanoma that has spread regionally (locally), you might receive surgery along with other treatments, like immunotherapy, intralesional talimogene laherparepvec (T-VEC) injections, targeted therapy, or radiation therapy. For more information, read *Chapter 7: Treatment for stage 3: Regional spread*.

Sometimes melanoma can return, which is called recurrence. Recurrent melanoma is treated based on its pathological stage (assigned after surgery) and whether it has spread to another part of the body. You might receive treatment before surgery as well as after it. For more information on recurrence, read *Chapter 8: Treatment for recurrence*.

For stage 4 melanoma (metastatic or distant spread), you might have a combination of systemic treatment, surgery, radiation, intralesional T-VEC injections, or supportive care. Read *Chapter 9: Treatment for stage 4: Metastatic melanoma* for more specific information.

## How can I get the best care?

Advocate for yourself. You have an important role to play in your care. Many people feel more satisfied when they actively take part in planning their cancer care.

The NCCN Guidelines for Patients will help you play a larger role in your care. Discuss the recommendations in this guide with your care team. Ask questions about your options and share your goals and concerns.

Don’t know what to ask? You’re not alone. That’s why we include suggested questions to ask at the end of chapters.

Keep reading to find the best care for you.

## How this guide can help you

Making decisions about cancer care is stressful. There's a lot to learn, and you don't know what the future holds.

Use this guide to get the information and support you need.

Patients, doctors, and other health care professionals trust the NCCN Guidelines for Patients. This guide uses clear, everyday language to explain current cancer care recommendations made by respected experts in the field. Their recommendations are based on the latest research and practices at leading cancer centers.

Your health is unique to you, so your cancer care should be, too. As you read this guide, you'll learn which treatments are likely to provide the best results for you. And you'll be better prepared to talk with your care team.

**"It is important to understand what you are going through. If your doctor says something you do not understand, don't just nod like you do. Let them know 'I don't fully understand what __ means' or 'I don't fully understand what you just said. Can you please explain it in simpler terms?'"**

# 2

# Melanoma risk, prevention, and detection


10 Where does melanoma start?

11 What are the risk factors?

12 Genetic risk

13 Preventing melanoma

14 Early detection: ABCDE rule

15 Key points

15 Questions to ask

The last chapter gave a brief overview of melanoma and how this guide can help you. This chapter gives more details about the cancer, like where it starts and how to prevent and detect it.

To further understand melanoma, it's important to know where it forms and what its risk factors are. With that information, you can aim for prevention and detection.

## Where does melanoma start?

Your skin is your body's largest organ. It covers about 20 square feet—about the size of an oversized beach towel. 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:

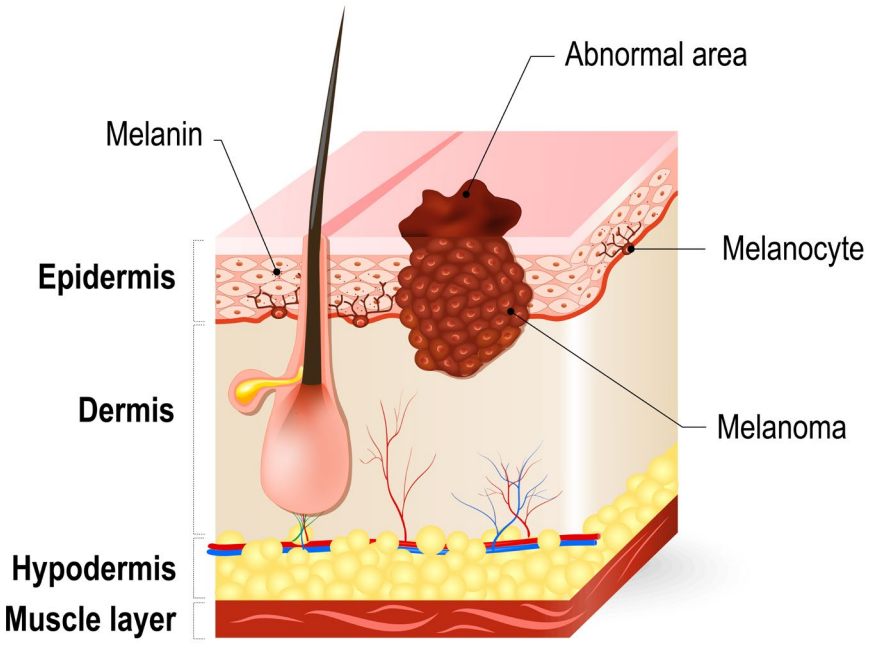
- **Epidermis** – The outermost layer of skin provides a waterproof barrier and creates skin color.
- **Dermis** – This second layer holds connective tissue, blood and lymphatic vessels, hair follicles, and sweat glands.
- **Hypodermis** – This deep skin tissue is made of subcutaneous fat, connective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

### Melanin

Located at the base of the epidermis are cells called melanocytes. These cells decide the color of your eyes and hair. Melanin is produced in these cells. This is the pigment (chemical) in skin that gives it color. In addition, melanin protects skin from harmful ultraviolet (UV) rays from the sun. When melanocytes grow uncontrollably, they start forming cancer known as melanoma. Melanocytes are found

**Where melanoma forms**

**Melanocytes are the cells located in the lower epidermis that, when damaged, can become melanoma.**



in other areas of the body, but the focus of this guide is cancer of sun-exposed and non–sun-exposed skin melanocytes, called melanoma.

### Causes

It's unclear how cell damage 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's important to know that UV radiation does not cause all melanomas. Some melanomas can occur in areas of your body that are not exposed to sunlight.

## What are the risk factors?

While the exact cause of melanoma is unknown, there are many risk factors that make it more likely that you will develop it. A risk factor increases the chance of developing cancer—it doesn't mean that you will get it. Some risk factors are associated with activities like spending time in the sun or tanning devices. Other risk factors are genetic, meaning they are passed down through genes (from parent to child). For more information on genetic risk factors, see the next section.

Here are some of the most common risk factors that make it more likely for a person to develop melanoma.

- **Lighter skin, hair, and eyes** – If you have less melanin (pigment) in your skin, it means less protection from UV radiation. People with light hair and blue/green eyes tend to have less melanin in their skin.
- **A tendency to sunburn** – If you sunburn easily or have a history of chronic sunburns, especially if you develop redness and blistering
- **Many moles** – If you have a high number of moles (more than 50) on your body or they're large and unusually shaped
- **UV light exposure** – If you spend extended time exposed to UV light (radiation that comes from the sun or tanning devices)
- **Earlier skin cancers** – If you've had conditions such as actinic keratosis, or other skin cancers, such as basal cell or squamous cell skin cancers
- **Childhood cancers** – If you had cancer as a child, this could increase your risk of melanoma as you get older
- **Weakened or suppressed immune systems** – If you have a weakened immune system from organ transplants or autoimmune diseases, or you take medicine that suppresses immune function
- **Rare inherited conditions** – If you have a skin condition such as xeroderma pigmentosum, or certain hereditary breast and ovarian syndromes

## Genetic risk

As mentioned, melanoma is a type of cancer that can run in families. About 1 in 10 people with melanoma have a family member who has or has had 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 of melanoma. For more information on family history, see *Chapter 3: Testing for melanoma*.

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

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 or eye (uveal) melanoma, especially among multiple blood relatives
- Pancreatic, kidney, gastrointestinal, and/or breast cancer

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

- *CDKN2A* mutation, which is the most common gene mutation for melanoma. It's also called p16INK4A or MTS1. This mutation is often found in families where several members developed melanoma at a young age.
- *CDK4* gene mutation, which significantly increases the risk of hereditary melanoma, but is considered rare.
- The melanocortin-1 receptor (*MC1R*) gene, which helps decide your skin's color. *MC1R* can determine if you or your family members have red hair and/or light skin, which increases your risk of melanoma.
- *BAP1* gene mutations, which can cause uveal and, less often, cutaneous melanoma.

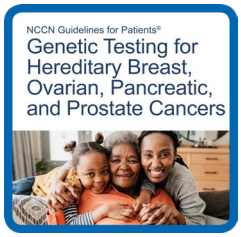
### Genetic testing

Your clinical and family history might call for multigene panel testing. This can help your care team know if you have a higher genetic risk of melanoma and other cancers. This information can also help guide recommendations for early detection and monitoring in both you and your family members.

You might be referred to genetic counseling and testing if you or someone in your family has a history of 2 or more instances of invasive cutaneous (skin) melanoma. You might also be referred if you or someone in your family has a history of 2 or more non-skin cancers, like pancreatic, kidney, gastrointestinal and/or breast cancer, especially in a first-degree relative.

Testing for other genes that can harbor melanoma-predisposing mutations may also be needed.

For more information about genetic testing, see *NCCN Guidelines for Patients: Genetic Testing for Hereditary Breast, Ovarian, Pancreatic, and Prostate Cancers*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.




## Preventing melanoma

Once you understand the risk factors, it's important to know that you can take steps to decrease the likelihood of new melanoma cells from forming. Taking preventive action is especially important if you're at higher risk, have sun sensitivity, or have a lighter complexion. Here are some of the leading ways to do that.

- **Reduce UV (ultraviolet) radiation exposure** – This means reducing your exposure to the sun and avoiding indoor tanning beds and other devices.
- **Prevent sun damage** – Limit your sun exposure between the 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. You should apply sunscreen 15 minutes before going outside to be most effective. Reapply at least once every 2 hours.
- **Check your skin regularly** – This includes both self-examinations and skin exams by a health care provider (see ABCDE rule next).

### 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.**



## Early detection: ABCDE rule

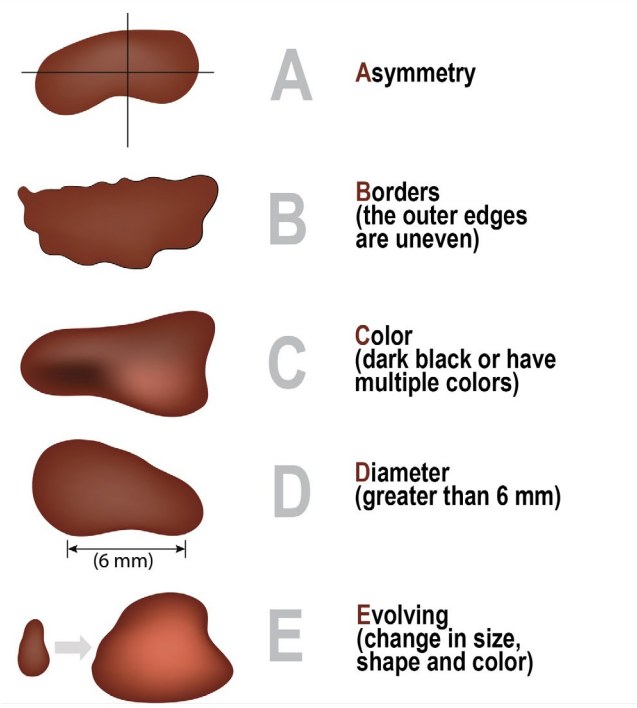
If you're diagnosed with melanoma or if you're trying to prevent another one from occurring, you'll likely need to see your doctor on a regular schedule for skin checks (see *Chapter 10: Follow-up care*). Between your regular visits, following the ABCDE rule is a good way to help detect the signs of melanoma. Check moles or spots (lesions) on your own in front of a mirror (a handheld mirror can help, too) or with a partner and keep this rule in mind:

- **Asymmetry** – This means the mole or spot is not uniform, and one half doesn't match the other half.
- **Border** – The edges of a spot seem irregular and lack definition.
- **Color** – The color of the spot is not the same throughout (may be brown or black or sometimes with patches of pink, red, white, or blue).
- **Diameter** – The spot is larger than 6 mm across (about the size of a pencil eraser).
- **Evolving** – The spot or mole changes size, shape, or color over time.

Understanding melanoma like how it forms and what it looks like can help with preventing new melanoma lesions and those that come back, called recurrences. For more information on melanoma recurrence, see *Chapter 8: Treatment for recurrence*.

**Early detection of melanoma: ABCDE rule**

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



## Key points

- Melanoma forms in the skin's top layer, the epidermis.
- Exposure to ultraviolet (UV) radiation is linked to melanoma.
- People with light hair and light eyes tend to have less melanin in their skin and are more at risk of melanoma.
- A risk factor means you are more likely to develop melanoma—it doesn't mean you will.
- Reducing your exposure to UV light (time in the sun and tanning beds) is one way to prevent melanoma.
- You can help detect melanoma on your own by following the ABCDE rule.
- You might be referred to genetic counseling if genetic tests show 2 or more instances of cancer diagnoses in your family.

## Questions to ask

- Does having risk factors for melanoma influence my chances of getting melanoma again?
- What number SPF is best for me?
- Can you recommend trusted brands of sunscreen?
- If I find a new spot or one that looks different than it did, what should I do?
- Do you have any recommendations for melanoma support groups?

## What's next

Now that you know the basics of melanoma, you might want to know about how it's officially detected. That happens through testing. Read the next chapter for the various tests that can help find and diagnose melanoma.

# 3
# Testing for melanoma


17 Medical history

18 Physical exam

20 Biopsy

21 Biopsy results

24 Imaging tests

26 Biomarker tests

27 Blood tests

28 Understanding test results

29 Key points

29 Questions to ask

You'll need testing to correctly identify the type and stage of melanoma as well as to see if it has spread and how far. With that information, you and your provider will talk about treatment next steps. This chapter presents an overview of the tests you might receive and what to expect — keep in mind you may not receive all of these tests.

Basic health tests help your doctor detect diseases, including melanoma (see **Guide 1**). Tests also help your care team judge 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 4: Staging for melanoma*.

**Guide 1**
**Common tests for melanoma**

| |
|---|
| Medical and family history |
| Physical exam |
| Complete skin exam |
| Biopsy |
| Imaging tests |
| Biomarker tests |
| Blood tests (for monitoring) |

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

## Medical history

A medical history is a record of all health issues and treatments you've had in your life. This information can help your doctor with treatment planning.

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've had any severe sunburns or other severe scarring in the past.

Your medical history also includes if you've had other types of skin cancer, such as basal cell skin cancer or squamous cell skin cancer. These are often less serious types of skin cancer.

More information on these skin cancers can be found in *NCCN Guidelines for Patients: Basal Cell Skin Cancer* and *NCCN Guidelines for Patients: Squamous Cell Skin Cancer*, 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 (including skin cancer), and diabetes, and at what age they were diagnosed. For more information on genetic risks, see *Chapter 10: Follow-up care*.

## 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

### Skin exams

It's important to have an experienced health care provider, such as a dermatologist, give you a thorough skin exam. Not only does your skin protect your body, but it also tells doctors a lot about your health. Providers take your pulse and blood pressure through your skin. They notice if the skin feels warm, hot, or cool to the touch.

**Skin exam**

**A health care provider may use a dermatoscope (a special magnifying lens and light source held near the skin) to see spots on the skin more clearly and in more detail.**



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
- Trunk, arms, and legs
- Hands and fingers
- Feet, toes, and toenails

Your doctor or other health care provider will look for spots that are unusual and need to be examined more closely or watched.

## Lesions

Your provider will examine your skin for lesions (spots). A skin lesion is defined as a change in skin color or texture. Skin lesions can appear anywhere on your body. They can be benign (not cancer) or cancer. Your doctor or other health care provider may use the ugly duckling or the ABCDE rule (discussed in *Chapter 2*) and/or a specialized device called a dermatoscope to thoroughly review any marks or lesions on your skin.

**When a melanoma lesion is diagnosed, it's considered a cancerous tumor, so it will be referred to that way throughout this guide.**

## Skin color

Your skin color is mainly based on the amount of melanin in your skin. You know your skin better than anyone. Show your provider any changes or differences where it looks abnormal or different to you.

### Pay attention to moles

**More than 50 moles on your body and the presence of large or unusual moles increase the risk of melanoma.**



## Biopsy

If you have a skin lesion that looks odd to you or your doctor, part or all of it will be removed. This is called a skin biopsy. A biopsy is needed to diagnose melanoma. It will be sent to a pathologist who will examine it under a microscope.

### 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'll 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 want to ask how the biopsy incision will be closed. Usually, the doctor will close it with stitches. Having a biopsy and incision usually means you'll have a scar. Feel free to ask your doctor about the incision and the potential for scarring before you have the biopsy.

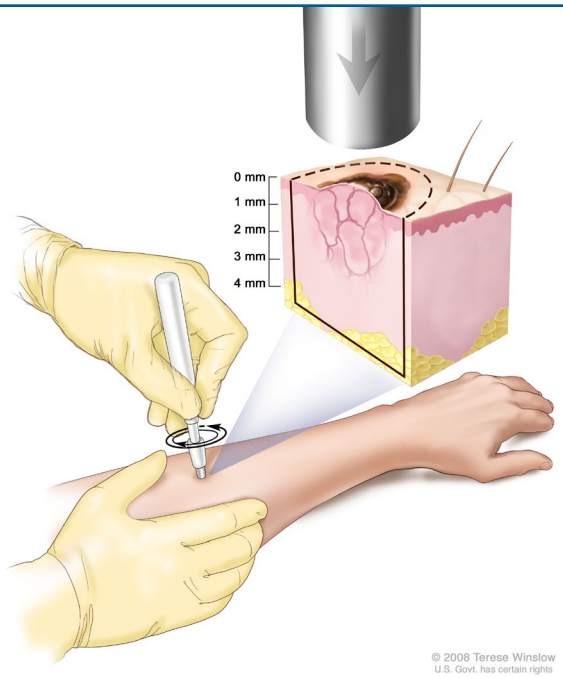
A skin biopsy can be done in several ways. The type of biopsy your provider does will depend on the lesion's size and location, as well as other factors. For the biopsy, either the entire lesion or a part of it will be removed and tested under a microscope to confirm melanoma.

A biopsy can be partial (incisional), in which only part of the lesion is removed, or complete (excisional), in which all of the lesion is removed.

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

**Skin punch biopsy**

**A small piece of skin and connective tissue are removed using a handheld tool.**



### Elliptical biopsy

An elliptical excisional biopsy removes an area of skin and underlying connective tissue, usually in the shape of a football. A rim of normal-looking tissue that surrounds the lesion will also be removed. The normal-looking tissue is called the margin. This method requires stitches to close the wound.

### Punch biopsy

For a punch biopsy, a small piece of skin and underlying connective tissue are removed with a handheld tool. The skin is then closed with a few stitches. 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 (lab) results.

### Shave biopsy

A shave biopsy can be done either on the skin surface (superficial) or deeper. Superficial shave biopsies can be used when a lesion is likely not cancerous. This type of biopsy is generally not recommended when melanoma is suspected, but may be useful for certain types of flat melanoma (mainly, lentigo maligna).

But deep shave biopsies (also called scoop or saucerization biopsies) are used for most melanoma lesions to completely remove the suspicious lesion. This type of biopsy uses a tool similar to a razor to remove the top layer of skin (epidermis) and part of the underlying layer (dermis). The sample is sent to a lab to be examined.

### Lymph node biopsy

A lymph node might be biopsied if your provider suspects it has cancer cells. Lymph nodes are small, bean-shaped filters of the immune system. Under normal circumstances, lymph nodes are usually too small to be seen or felt. But if a lymph node feels swollen, hard to the touch, or doesn't move when pushed (is fixed or immobile), it may be cancerous.

A lymph node biopsy can be done using a needle, which is preferred. It can also be done as a minor surgery to remove a lymph node, if it can't be biopsied with a needle.

## Biopsy results

Your biopsy sample should be reviewed by a pathologist or, preferably, by a dermatopathologist. These doctors specialize in diagnosing skin disorders, including melanoma and other skin tumors. This review is called a histopathology review. The pathologist will note the overall appearance and size, shape, and type of your cells, as well as other features. The melanoma will be given a stage based on this information and other factors. See the next chapter for more details on staging.

The pathologist or dermatopathologist will examine the following details.

### Breslow thickness

The Breslow thickness or depth is used to measure in millimeters (mm) how far the melanoma has gone into deeper layers of the skin (dermis). The deeper it goes, the more advanced the melanoma is. This is an important predictor and is used as part of melanoma staging to decide treatment.

## Ulceration status

Ulceration refers to a breakdown of skin on top of the melanoma, like an open sore. An ulcerated melanoma is considered more serious because it has a greater risk of spreading. Ulceration is considered during melanoma staging.

## Dermal mitotic rate

The dermal mitotic rate (DMR) or mitotic rate is a measure of how fast cancer cells grow and divide in the dermis. It is measured by looking at the surgically removed lesion under a microscope. The number of cells that show mitoses (cells dividing) are counted.

The more the cells divide (higher mitotic count), the more likely they are to invade the blood or lymph vessels and spread (metastasize) to other areas of the body.

## Margin status (deep and peripheral)

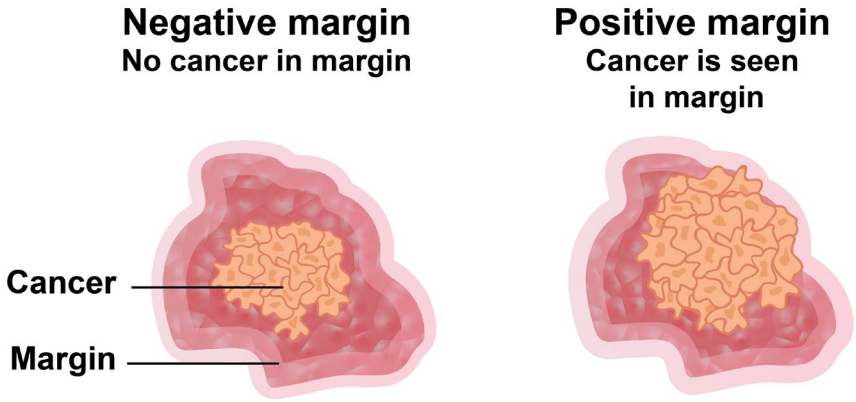
The edge, or border, of the tissue removed in cancer surgery is called the margin. Margin status of a biopsy or excision specimen refers to whether the lesion is present at the deep margin (the base of the sample) or the peripheral margin (side edges of the sample).

The margin is described as negative or clear 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 (first) biopsy, even if the margins are clear on the initial biopsy.

### Surgical margin

**The tumor will be removed along with some normal-looking tissue around its rim. The normal-looking tissue is called the surgical margin. The surgical margin will be tested for cancer. Postoperative therapy is based on if there is cancer in the margins.**



Expect your doctor to remove the melanoma tumor 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 provider 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.

One way it can spread is through microsatellitosis (having microsatellite tumors). This refers to tiny tumor deposits that have spread to lymph vessels in the skin near the first melanoma tumor. Microsatellitosis can only be seen with a microscope.

Microsatellites are different from satellite tumors, which are bigger and can be seen or felt. Satellite tumors are usually found within 2 centimeters (cm) from the melanoma site or scar and show as a nodule or bump. 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 usually found on the head, neck, and shoulders. It occurs in 1 out of 25 people who have melanoma.

DM is divided into 2 categories: pure and mixed. Pure desmoplastic melanoma may be associated with a higher risk of local recurrence on the skin but has a lower risk of lymph node involvement than mixed desmoplastic melanoma. Mixed desmoplastic melanoma has a higher risk of spreading to nearby lymph nodes.

## 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 or perineural invasion

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

For a list of what factors will be considered when pathologists analyze biopsies, see **Guide 2**. Your pathologist or dermatopathologist (pathologist specializing in diagnosing skin diseases) might also use specific immunohistochemical stains or molecular tests to detect markers on melanoma cells.

## Imaging 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 needs imaging, especially for the early stages of melanoma.

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

Most scans are done with IV contrast unless it's unsafe for you. This means it could cause a bad reaction if you have certain allergies or conditions or take certain medications. It's important to tell your doctors if you've ever had an allergic reaction to contrast.

After imaging, a radiologist, an expert in interpreting test images, will write a report and send it to your provider. Your test results will be discussed with you. The following are types of imaging tests.

**Guide 2**
**Factors examined in the biopsy**

| |
|---|
| Breslow thickness (how deep the melanoma tumor has grown into the skin) |
| Ulceration status (if there are breaks in 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 is fibrous tissue in a tumor) |
| Lymphovascular or angiolymphatic invasion (if cancer is in lymph nodes or fluid) |
| Neurotropism (invasion in, around, and through peripheral nerves) |

## CT scan

A computed tomography (CT or CAT) scan is done with a computerized x-ray machine. It takes many pictures (x-rays) from different angles of the same body part. Pictures are merged to form a 3D image.

## MRI scan

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

## PET scan

A positron emission tomography (PET) scan uses a radioactive drug called a tracer. A tracer is injected into a vein (through an IV). The needle is usually inserted in the inside of your elbow. You may need to wait for the tracer to be absorbed by your body, which takes about 1 hour.

Once inside of the body, the tracer will travel and collect in organs and tissues. 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.

Cancer cells show up as bright spots on PET scans, but not all bright spots are cancer. It's normal for the brain, heart, kidneys, and bladder to be bright on a PET scan since they need a lot of food for energy. When a PET scan is combined with CT, it's called a PET/CT scan. They are almost always used together.

## Ultrasound

Ultrasound uses sound waves to make pictures of areas inside of the body. Your provider might order a nodal basin (area of lymph nodes) ultrasound before removing lymph nodes. This is to get a clearer picture of the area before lymph node removal. Ultrasound imaging might also be

### 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.**



recommended if the doctor's physical exam of the nodal basin is unclear.

## 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 can lead to the development of a tumor.

Testing biomarkers involves studying a piece of tumor tissue in a lab 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* 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 changes that can be targeted to help guide your treatment. The results of biomarker testing can also be used to figure out whether you meet the criteria for certain clinical trials. An important development: Circulating tumor DNA blood tests (called ctDNA or liquid biopsy) that measure genetic changes are being investigated for use in monitoring melanoma.

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

### *BRAF* mutations

*BRAF* is a gene involved in controlling normal cell growth. But when a *BRAF* gene has mutated (changed), it can cause melanoma to grow more aggressively. A *BRAF* mutation is found in at least half of people who have melanoma of the skin.

It's helpful if the *BRAF* gene mutation is found before treatment for advanced cancer. 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 (the most common type of *BRAF* mutation), targeted therapy or immunotherapy may be a treatment possibility, 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 *BRAF* V600K and other mutations, like *NRAS* and *KIT*.

**Don't dwell on what you CAN'T do. Rather focus on what you CAN do."**

## 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 aren't used to diagnose melanoma or monitor early melanomas. However, they may be done before or during treatment, especially for more advanced melanomas.

The following are tests that your provider may request.

**Lactate dehydrogenase** – Lactate dehydrogenase (LDH) is a protein found in most cells. Dying cells release LDH into blood. A high level of LDH 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).

**Extra blood tests** – Other blood tests aren't regularly done before starting treatment. But they may be done to plan surgical treatment. If you have advanced melanoma, these tests might be done to check how well 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 can check liver and kidney health, blood glucose, protein levels, fluid and electrolytes, and metabolism.

## Understanding test results

The results of your physical exam, skin biopsy, and possible imaging scans will guide your treatment plan. It's important you understand what these tests mean. Don't hesitate to ask your care team questions.

Keep these other tips in mind:

- Bring someone with you to your appointments, if possible.
- Write down questions before your appointments and take notes during clinic visits.
- Get copies of blood tests, imaging results, and reports about the specific type of melanoma you have.
- Sign up for the patient portal. Once on the portal, in most cases you can get test results as soon as they're ready.
- Organize your papers. Create files for insurance forms, medical records, and test results. You can do the same with digital copies on a computer.

### 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 **cancer was found**. When you hear of a **negative** result, it means **cancer was not found**.

## Key points

- Basic health tests help your care team assess the extent (cancer stage) of the melanoma.
- A medical history is a record of all health issues and treatments you've had in your life, including other cancers.
- A head-to-toe skin exam should include a review of the scalp, face, mouth, eyes and eyelids, ears, trunk and extremities, hands, fingers, feet, toes, and toenails. This includes examining your skin for lesions (spots).
- A melanoma diagnosis is mostly based on the results of a skin biopsy. If you have an unusual lesion, it will be removed and sent to a lab to be examined.
- Imaging tests take pictures of the inside of your body, which are examined to look for cancer. Not everyone with melanoma needs imaging tests.
- Biomarker or molecular tests look for certain genes, proteins, or other molecules in a sample of tissue, blood, or other bodily fluid. These tests are sometimes used to help diagnose melanoma, and to stage and treat it.
- Blood tests are not often done to diagnose melanoma but may be done before or during treatment for advanced melanomas.

## Questions to ask

- Why did I get this specific test?
- Do the tests have any risks?
- Do I need other tests to confirm my diagnosis?
- How much scarring will there be from the biopsy?
- Should I use over-the-counter anti-scarring products to help minimize scarring?

## What's next

This chapter gave an overview of the different types of tests, from skin exams and genetic tests to imaging, which are used to diagnose melanoma. Now that you know the kinds of tests you might have, read the next chapter on the variety of treatments available. To find out more specifically how the melanoma might be treated, read about it in the stage-specific chapters.

# 4

# Staging for melanoma


31 TNM staging

32 Clinical vs. pathological

33 A summary of stages

34 Key points

34 Questions to ask

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

You may have heard of a cancer stage, but what exactly does it mean? It's essentially a number that's assigned based on the extent (severity) of the cancer to help guide the treatment. Read on for more details.

## 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 or spread) describe different areas of cancer growth. The TNM stages will be combined to assign the cancer stage group.

- **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). Tumor depth is measured in millimeters (mm). There are 5 tumor designations (Tis, T1, T2, T3 and T4). See the Figure on the next page.
- **Lymph node status (N)** describes 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. It also includes satellite, in-transit, and/or microsatellite tumors. For more information on these tumors, see *Chapter 7: Treatment for stage 3: Regional spread*.
- **Metastasis (M)** signifies whether the cancer has spread to parts of the body far from the primary tumor, like internal organs and distant lymph nodes. Areas of spread tends to be lungs, liver, bones, brain, and gastrointestinal (GI) tract. There are only 2 designations for metastasis: either the cancer has spread to distant areas (M1), or it has not (M0). For more information on metastatic melanoma, see *Chapter 9: Treatment for stage 4: Metastatic melanoma*.

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

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

Based on the cancer test results described in *Chapter 3*, 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) discussed futher on page 33.

The higher the stage, the thicker the tumor or the more the cancer has spread.

## Clinical vs. pathological

With melanoma, you'll be staged twice. The first time is called clinical staging. The second time is called pathological staging.

- **Clinical staging** happens after the biopsy. This is when you find out you have a diagnosis of melanoma and what stage it is.
- **Pathological staging** 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. The cancer may have changed from the clinical stage, or additional information from the surgery might alter the stage. This is especially true when a sentinel lymph node biopsy (SLNB) finds melanoma microscopically in nearby lymph nodes.

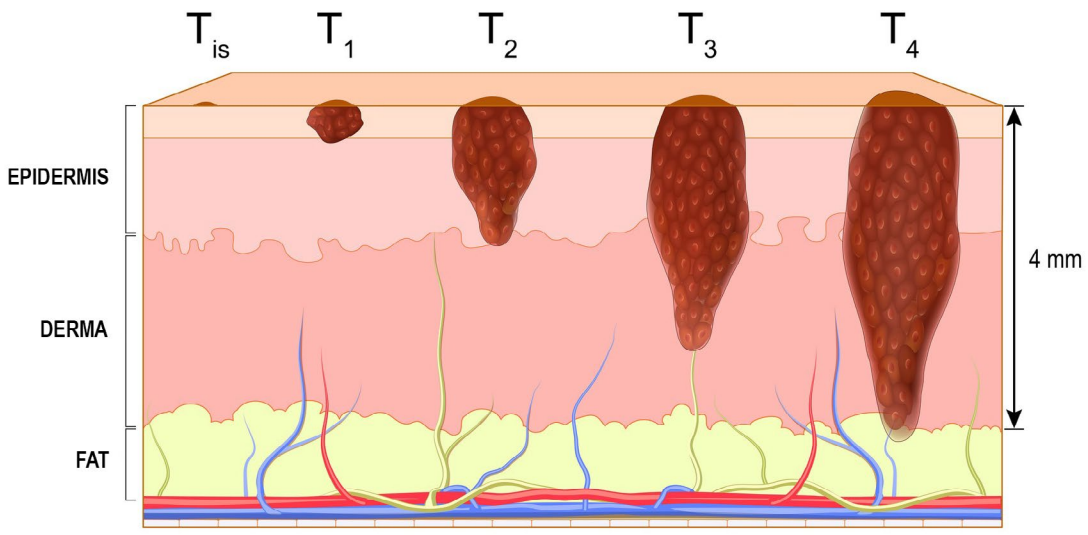
### Breslow thickness: What is it?

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.

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 clarify your diagnosis and to guide further treatment.

### Melanoma staging

**The TNM classification of malignant tumors reflecting tumor thickness**



## A summary of stages

Because it might be challenging to follow the clinical and pathological stages on their own, they're summarized below and described in more detail in the stage-specific chapters.

In general, **stage 0, stage 1, and stage 2** melanoma are early cancers of the skin that are not known to have spread elsewhere. Surgery is the most common treatment. For more detailed information on early-stage melanoma, see *Chapter 6: Treatment for stages 0 to 2: Early stage*.

**Stage 3** melanoma has spread but is considered regional (or local). Once the tumor is considered stage 3, it involves the lymph nodes and lymphatic vessels. After surgery, it's broken down into 4 pathological stages (3A, 3B, 3C, and 3D). For more detailed information on stage 3 melanoma, see *Chapter 7: Treatment for stage 3: Regional spread*.

**Stage 4** melanoma is cancer that has spread (metastasized) to distant areas of the body, such as the lungs, liver, brain, bones, or GI tract. For more detailed information on stage 4 melanoma, see *Chapter 9: Treatment for stage 4: Metastatic melanoma*.

If you have any questions, be sure to ask your provider to explain the melanoma in a way that you can best understand it.

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



## 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'll 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 is considered early-stage cancer.
- Stage 3 melanoma has spread only to nearby tissues, so it's called regional.
- Stage 4 melanoma refers to cancer that has spread (metastasized) to distant areas of the body.

## Questions to ask

- What stage is the melanoma at biopsy?
- When will I have surgery?
- Will I need recovery time from surgery?
- Are the lymph nodes involved?
- Other than surgery, what else might I expect?

## What's next

Now you've learned why and how melanoma is staged. The next step is treatment, which is the focus of the following chapter. Keep in mind that it's an overview, and no one will receive every treatment. When you know the melanoma's stage, you can read all about the treatment for it in the stage-specific treatment chapters that follow.

# 5
# Treatment overview


36 Who is on your care team?

37 Surgery

42 Systemic therapy

47 Radiation therapy

48 Clinical trials

50 Key points

50 Questions to ask

This chapter describes the kinds of treatments you may receive for melanoma. It's important to know that not everyone will receive the same treatment. Treatment for melanoma is based on its stage and location. For more information on your stage, read the stage-specific chapters.

After you've been diagnosed with melanoma, 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.

## Who is on your care team?

Depending on your diagnosis, your care team might include the following specialists.

### Doctors who treat cancer

**Dermatologists** diagnose and treat skin conditions, including skin cancer. They also do skin exams and help you learn how to do them on your own. Some dermatologists also perform surgery.

**Surgical oncologists** are trained to diagnose, surgically treat, and remove cancerous tumors.

**Medical oncologists** 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 (intravenously, or IV).

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

**Pathologists** study tissue and cells from a biopsy under a microscope to figure out the diagnosis and tumor stage. Dermatopathologists are experts in skin diseases.

**Plastic surgeons** 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** treat diseases (both cancerous and noncancerous) of the head and neck.

**Guide 3**
**Common treatments for melanoma**

| |
|---|
| Surgery |
| Systemic therapy |
| Radiation therapy |
| Clinical trials |

### Other health professionals

**Oncology nurses** 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 trained to prepare and give out medicine and teach about proper use and side effects. Some pharmacists specifically work with people with cancer.

**Geneticists** 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** help guide you on what foods are best for your diagnosis and treatment.

**Palliative care nurses** help provide an extra layer of support with cancer-related symptoms.

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

**Social workers** help people solve and cope with problems in their everyday lives while they are undergoing treatment.

Some members of your care team will be with you throughout your treatment and beyond, while others will 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 isn't
- Your goals for treatment

Keep a list of names and contact information for each member of your team. Add it to your cell phone, too, if you have one. Hang the list in an obvious place where anyone can access it in an emergency.

This will make it easier for you and anyone else involved in your care to know who to contact with questions or concerns.

Common treatments for melanoma are listed in **Guide 3** and discussed next.

## Surgery

Surgery is an operation or procedure to remove cancer from the body. The type of surgery depends on the size, number of tumors, and their location. Surgery is the primary treatment for most melanomas.

A person diagnosed with melanoma should expect to have surgery after the skin biopsy.

The goal of surgery for a primary melanoma tumor is to remove all the cancer. For melanomas that have a low risk of spreading, surgery may be the only treatment needed. Different types of surgery are used to treat melanoma. They are mentioned ahead.

## Wide excision

A wide excision surgery is the most common type of surgery. It removes the melanoma tumor as well as normal tissue surrounding it (the surgical margin). The surgical margin is measured in centimeters (cm). The size of the margin to be removed depends on the thickness of the primary tumor (see **Guide 4**). Still, margins can be even smaller in places like the face, ears, palms of the hands, and soles of the feet because of their delicate nature and narrower surface area. In some cases, Mohs micrographic surgery (also called Mohs surgery) or staged excision with permanent sections may be used, especially in early-stage melanoma. For more information, see *Chapter 6: Treatment for stages 0 to 2: Early stage*.

A wide excision may be done in a doctor's office, surgical center, or hospital (operating room).

You may receive local anesthesia before the surgery. Local anesthesia is 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 ahead) or more extensive surgery, general anesthesia may be used. You will be fully asleep during the surgery.

A wide excision is done even if the melanoma tumor was removed by biopsy. A wide excision also removes nearby microsatellites and lymph vessels in the skin because they could contain tumor cells.

A wide excision is often cut as an ellipse (football shape), which allows the wound to heal as a flat line. The surgical margin is cut based on the thickness of the melanoma tumor.

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

| If your tumor thickness is: | The recommended surgical margin is: |
|---|---|
| In situ (cancer hasn't spread) | 0.5 to 1 cm |
| Less than 1 mm | 1 cm |
| 1 to 2 mm | 1 to 2 cm |
| Greater than 2 to 4 mm | 2 cm |
| Greater than 4 mm | 2 cm |

## 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're concerned about scarring after the surgery.

Following the surgery, a skin graft might be recommended for larger incisions. A skin graft is when a surgeon takes skin from another part of your body and uses it to cover the wound.

Skin grafts are surgeries that can be performed in the clinic or hospital. Most larger skin grafts involve sedation (giving medicine to help you relax) 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 cover the wound so you can avoid a skin graft. A skin flap is a type of wound closure that takes skin from an area close to a wound and layers it to fill the removal of a skin lesion. Talk to your doctor about your options and how you can expect to heal after wide excision surgery.

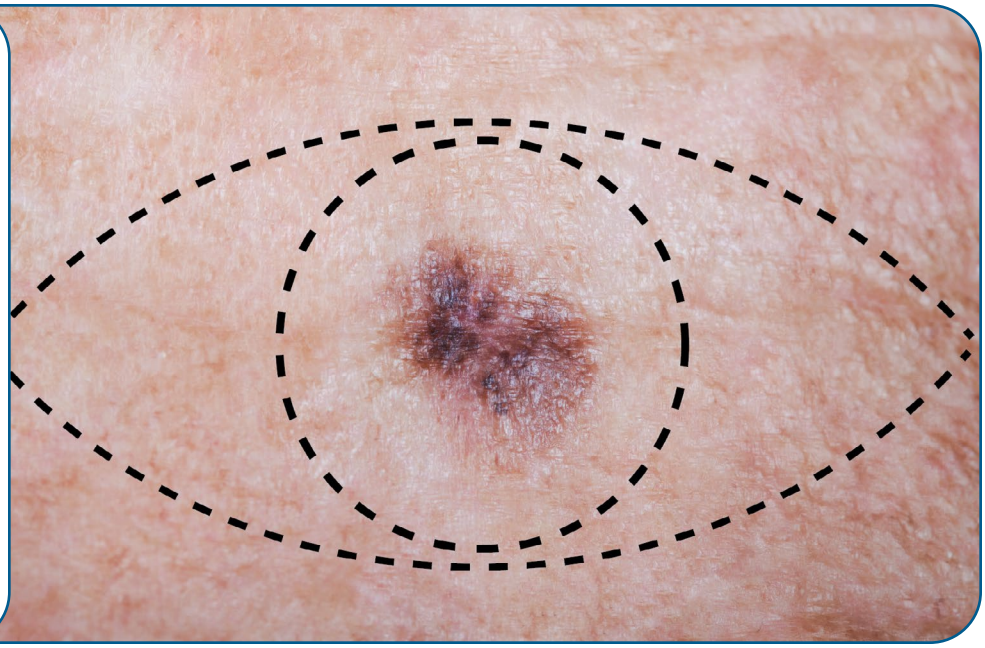
## Sentinel lymph node biopsy

A sentinel lymph node is the first lymph node where cancer cells are most likely to spread from a primary tumor on the skin. Sometimes there is more than one sentinel lymph node found, or multiple lymph node basins involved, like both armpit areas. The lymph node basin is the area of lymph nodes where lymph from the tumor drains.

A sentinel lymph node biopsy (SLNB) is a surgery that removes one or more lymph nodes to examine for any cancer cells. These nodes will be checked by a pathologist in a lab. (Most people with melanoma have an SLNB at the same time as wide excision surgery.)

### Wide excision

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



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

To find 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 use a special probe to find the radioactive nodes and remove them through a small cut in your skin. This procedure is typically 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 pocket of clear fluid in the lymph node basin. A seroma usually goes away on its own but sometimes it needs 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

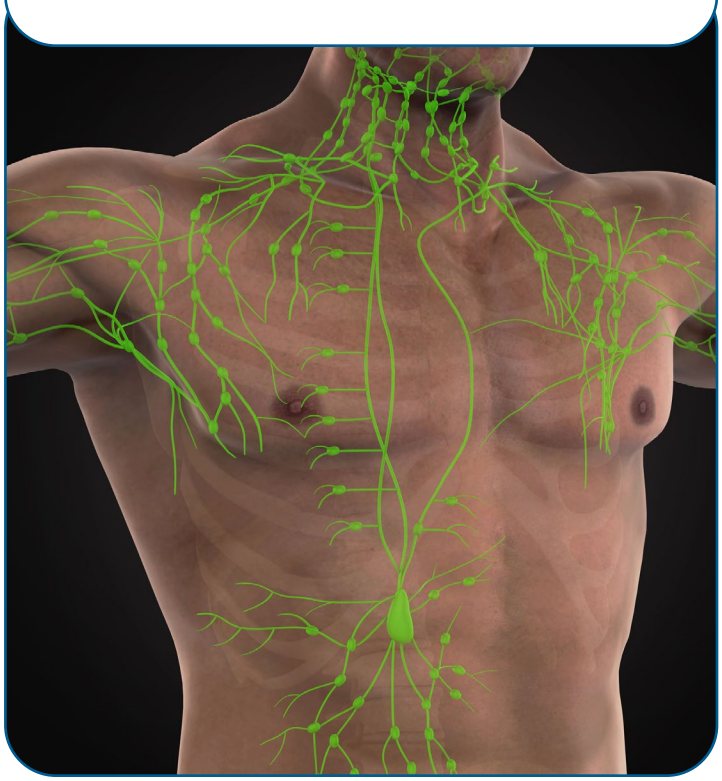
A lymph node dissection is a surgical procedure where lymph nodes are removed and checked for cancer. The procedure may be done if the cancer has spread to the lymph node basin. But it is not often done if there is cancer only in sentinel lymph node(s). A lymph node dissection removes nodes to prevent cancer from coming back or spreading. This surgery is done under general anesthesia.

**Complete (also known as completion) lymph node dissection (CLND)** is a dissection done after tiny amounts of cancer are found in the SLNB. Although it can be an option for some people, nodal basin ultrasound or other imaging tests are more commonly used to check the lymph nodes.

Lymph node dissection is generally recommended for advanced melanomas when enlarged lymph nodes are found on clinical exam or through imaging. Or it's done for nodes that have grown over time and have shown to contain melanoma.

### Lymph nodes

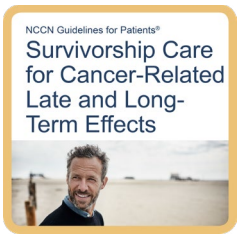
**There are hundreds of small, bean-shaped structures throughout the human body called lymph nodes. Lymph nodes catch and filter out foreign particles and harmful cells, including cancer cells.**



**Therapeutic lymph node dissection (TLND)** is when all of the lymph nodes in a nodal basin (area) are removed to help control the melanoma and prevent recurrence. TLND is often combined with systemic drug therapy (cancer drugs that travel throughout the body) given before and/or after surgery as a boost to help further control the melanoma.

Common side effects of TLND 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, most commonly in the arms or legs. It's 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.




## 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. In later stages, surgery is often combined with cancer drugs.

- **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.

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

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

## Systemic therapy

Systemic therapies are cancer drugs that travel throughout the body and are often used to treat more advanced melanoma. Depending on the stage, systemic therapies could be used as neoadjuvant treatments (before the primary treatment, which is often surgery) or adjuvant treatments (after the primary surgery treatment).

The most common types of systemic therapies that treat melanoma include targeted therapies and immunotherapies, and, less often, chemotherapies. Each type of treatment is explained below.

When it comes to systemic therapies, all treatments listed in this guide are recommended and appropriate. When helpful, NCCN experts also assign a level of preference to their recommendations for systemic therapies:

- **Preferred therapies** have the most evidence they may work better and be safer than other therapies.
- **Other recommended therapies** can provide effective results but may have less evidence, more side effects, or may not work quite as well as preferred therapies.
- **Therapies used in certain cases** work best for individuals with specific cancer features or health circumstances.

### Targeted therapy

Targeted therapy drugs are a type of systemic therapy designed to target and attack specific 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.

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

#### Cancer growth inhibitors

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

Cancer growth inhibitors 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 the following.

- **BRAF inhibitors:** When a *BRAF* gene mutates, it gives faulty instructions to proteins that can help cancer cells grow. BRAF inhibitors are drugs that directly attack these proteins. They can shrink or slow the growth of tumors in melanoma that has spread or can't be removed completely. Types of BRAF inhibitors include vemurafenib (Zelboraf), dabrafenib (Tafinlar), and encorafenib (Braftovi).
- **MEK inhibitors:** MEK is a protein that's activated when the *BRAF* gene mutates and causes melanoma cancer cells to grow. Drugs known as MEK inhibitors target and attack the MEK protein. They are often used in combination with

BRAF inhibitors. The MEK inhibitors include trametinib (Mekinist), cobimetinib (Cotellic), and binimetinib (Mektovi).

- **KIT inhibitors**: Mutations in the *KIT* gene can cause some rarer melanomas to develop, like those on the palms, on the soles, or under the nail beds. Types of KIT inhibitors include imatinib (Gleevec), dasatinib (Sprycel), and nilotinib (Tasigna).

In most cases, BRAF inhibitors are combined with MEK inhibitors to treat melanomas that have mutations in the *BRAF* genes. These combinations include:

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

As for side effects, BRAF and MEK inhibitors can cause non-melanoma skin cell cancers; photosensitivity (being sensitive to sunlight); 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 skin reaction (rash, itching, swelling) after any of the systemic therapies listed above, it's recommended that you see a dermatologist regularly for treatment.

### Immunotherapy

The immune system is the body's defense against infection and disease. Immunotherapy is a systemic treatment that uses the immune system to kill cancer cells.

Your immune system can tell the difference between normal cells and those it sees as foreign, like germs and cancer cells. And for the most part, it will do its job to fight the foreign cells but not the normal cells.

T cells are a key part of the immune system. T cells that kill infected cells and cancer cells are called cytotoxic or killer T cells.

But sometimes the proteins on tumor cells bind with T-cell proteins, which prevents the T cells from killing the tumor cells. These tumor cell proteins are called immune checkpoint proteins. PD-L1 is a tumor cell checkpoint protein that can bind with PD-1 checkpoint protein on T cells.

### Immune checkpoint inhibitors

Immune checkpoint inhibitors are a type of immunotherapy. They work by blocking the proteins from binding, which then frees the T cells to kill the tumor cells.

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

Examples of immune checkpoint inhibitors that treat melanoma include:

- Pembrolizumab (Keytruda)
- Pembrolizumab and berahyaluronidase alfa-pmph (Keytruda Qlex)
- Nivolumab (Opdivo)
- Nivolumab and hyaluronidase-nvhy (Opdivo Qvantig)
- Ipilimumab (Yervoy)
- Atezolizumab (Tecentriq)
- Atezolizumab and hyaluronidase-tqjs (Tecentriq Hybreza)
- Nivolumab and relatlimab-rmbw (Opdualag)

Immunotherapy can be given alone or combined with other types of treatment. In some cases, an immunotherapy combined with another immunotherapy, or an immunotherapy combined with a targeted therapy, is recommended for treatment. Two examples of combinations are:

- Nivolumab* and ipilimumab
- Nivolumab and relatlimab-rmbw

*Nivolumab and hyaluronidase injectable cannot be combined with ipilimumab.



## 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, they 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 through **systemic** or **local** treatment.

**Systemic** treatment is usually given through drugs that release antigens into 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 topical therapy (medicine in a lotion or cream applied directly to the skin) or therapies injected directly into melanoma in the skin or lymph nodes.

New forms of immune checkpoint inhibitors that can be injected under the skin (subcutaneously, and sometimes called sub-Q) are available. They can be given at different weekly intervals depending on the medicine and take much less time to give than an infusion. Three subcutaneous injections are currently available:

- Nivolumab and hyaluronidase-nvhy (known as Opdivo Qvantig)
- Pembrolizumab and berahyaluronidase alfa-pmph (known as Keytruda Qlex)
- Tezolizumab and hyaluronidase-tqjs (known as Tecentriq Hybreza).

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 can sometimes be lifelong.

For more information, see *NCCN Guidelines for Patients: Immunotherapy Side Effects*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.




## IL-2

Interleukin 2 (IL-2, Proleukin) is an immunotherapy that can be slowly injected into a vein (infusion) or directly into the tumor. IL-2 is a group of proteins made by white blood cells and other cells that handle increasing immune response. The therapy works by supercharging the immune system to target and kill cancer cells.

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.

IL-2 is now mainly used as part of TIL (tumor-infiltrating lymphocytes) therapy (see below).

## T-VEC

Talimogene laherparepvec (T-VEC) (Imlygic) is a modified form of the herpesvirus made in a lab. T-VEC is a type of viral immunotherapy that uses the genetically formed virus to stimulate the body's immune system. It's injected directly into the 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. Most people—about 9 out of 10—who receive T-VEC develop flu-like symptoms, which usually get better after a few days.

## TIL

Tumor-infiltrating lymphocyte (TIL) therapy (Lifileucel, Amtagvi) is an immune cell treatment approved as a second-line therapy for people whose melanoma hasn't responded to other immunotherapies. It uses the person's own cancer-fighting T cells, called tumor-infiltrating lymphocytes. These cells are collected from a person's own tumor. In a lab, the TILs are isolated from the tumor sample, grown into the billions, and infused (through an IV) back into the person.

TIL is used for melanoma that has a *BRAF* mutation and has progressed on prior immunotherapy and targeted therapy. It's a specialized type of cellular therapy given only in approved centers with experience in the technique.

Side effects are common and come from the chemotherapy (see next section) given along with the TIL. They include anemia, high fever, and drops in platelets and certain white blood cells. When used with IL-2, see side effects of IL-2 discussed on page 45. Side effects usually resolve within a couple of weeks.

## Chemotherapy

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

Because chemotherapy doesn't treat melanoma as well as immunotherapy and targeted therapy do, your care team will likely use those therapies first.

But if your cancer does not respond to immunotherapy or targeted therapy or if you have severe side effects, chemotherapy may be a possibility.

**Infusions are when cancer drugs are given through an IV (intravenously).**

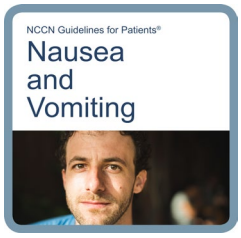


Chemotherapy drugs used to treat melanoma include:

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

Chemotherapy treatment may last several months. Side effects include tiredness, 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 in *NCCN Guidelines for Patients: Nausea and Vomiting*, available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.




## Radiation therapy

Radiation therapy is a painless treatment that focuses high-energy rays on tumor cells. The rays are delivered to the tumor area to damage the DNA inside of the tumor cells. This either kills the tumor cells or stops new tumor cells from being made. You won't see, hear, or feel the radiation. It passes through your skin and other tissues to reach the tumor.

Radiation therapy 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. Radiation therapy can also be used as a palliative treatment to help ease the pain or discomfort caused by cancer.

### External beam radiation therapy

External beam radiation therapy (EBRT) is the most commonly used method of radiation therapy. Radiation beams from a large machine are directed at the tumor. The beams overlap at the site of the tumor or cancer cells to target a 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 the exact location of the tumor both before and during treatments.

### Radiation therapy for distant cancer

Other radiation techniques used to treat distant metastatic melanoma are discussed next.

Stereotactic radiosurgery (SRS) treats small tumors with very precise, high-dose x-ray beams and is usually finished in 1 session. It's preferred for brain metastases.

- Stereotactic radiotherapy (SRT) is a form of SRS and is finished in 1 to 5 sessions.
- SRT is used to treat tumors in the body, not in the brain. It's sometimes called stereotactic body radiation therapy (SBRT) or stereotactic ablative body radiotherapy (SABR).

Side effects of radiation therapy may include:

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

## Clinical trials

Another treatment option at any stage of cancer is participating in a clinical trial. A clinical trial is a type of medical research study. After being developed and tested in a lab, 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. 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 and are done in phases.

- **Phase 1** trials study the safety and side effects of an investigational drug or treatment approach.
- **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 safety and benefit of an FDA-approved treatment.

## Who can enroll?

It depends on the clinical trial's rules, called eligibility criteria. The rules may be about age, cancer type and stage, treatment history, or general health. They 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 research team. This group of experts 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 people you trust. Keep in mind that you can leave and seek treatment outside of the clinical trial at any time.

## Will I get a placebo?

Placebos (inactive versions of real medicines) are almost never used alone in cancer clinical trials. It's 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. But you may need to pay for other services, like transportation or childcare, due to extra appointments. During the trial, you will continue to receive standard cancer care. This care is often covered by 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 its 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 the nodes most likely to have cancer if the cancer has spread. They will be checked for cancer cells by a pathologist.
- A lymph node dissection (removal) 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 on its own or combined with other types of treatment.

## Questions to ask

- How will I be involved in making decisions for my treatment?
- Should I bring someone with me to my appointments?
- Can you explain the treatment and side effects as simply as possible?
- What other health professionals will be a part of my care team?
- What if I decide to do nothing? What are the risks?

## What's next

This chapter explained the types of treatments for melanoma. What treatment you receive will depend on the stage of melanoma. Chapters 6, 7, and 9 are specific to the different stages of melanoma. At the end of the book, *Chapter 10: Follow-up care* describes how you'll be followed by your care team after treatment.

# 6

# Treatment for stages 0 to 2: Early stage


52 Stage 0 in situ

53 Stage 1

55 Stage 2

58 Key points

58 Questions to ask

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

The early stages of melanoma, especially stages 0 and 1, are when the cancer is highly treatable and curable. After your biopsy confirms melanoma and its stage, your doctor will do a physical exam and medical history. You'll only need imaging tests if you have any unusual symptoms or if it might help with planning for surgery or systemic therapy.

Keep reading to find out more about how the melanoma's stage reflects what treatment you may receive. See **Guide 5**.

## Stage 0 in situ

Stage 0 in situ refers to melanoma found only in the top layer of skin (epidermis). The melanoma at this stage is very unlikely to spread to other parts of the body. It's cured when completely removed.

### Treatment

The preferred 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). Some patients with stage 0 in situ may be offered nonsurgical treatment with the immunotherapy cream imiquimod (5%) or radiation therapy. Still, depending on your health and ability to have surgery, you might not have any treatment but instead will be closely observed by your doctor.

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

But surgery is the most common treatment for stage 0 in situ. There are some areas where it's harder to do surgery, such as on the face, ears, palms of the hands, and soles of the feet. In these cases, your doctor might consider alternative surgical techniques, like Mohs micrographic surgery (also called Mohs surgery) or staged excision with permanent sections.

Both types of surgery can provide a closer look at the edge of the removed tissue (called the histologic margin). With Mohs surgery, the surgeon removes thin layers of skin—one at a time—and checks each layer for cancer until reaching a layer where no more cancer cells are found. This whole procedure and lab results are done while you wait in the health care center.

**Guide 5**
**Possible treatments for early-stage melanoma**

| |
|---|
| Wide excision surgery |
| Wide excision surgery with SLNB |
| Immunotherapy |
| Radiation therapy |
| Clinical trials |

Staged excision with permanent sections is similar to Mohs surgery because the surgeon removes one layer at a time, but it's more precise. The sections are sent to a lab for more tests where it typically takes days to get results.

Other treatment options for certain types of melanoma in situ (specifically the lentigo maligna type) include imiquimod (5% cream). This topical treatment may be used if surgery isn't an option or if the entire tumor can't be removed. While not commonly used, radiation therapy is another possibility for in situ lentigo maligna-type melanoma.

### Follow-up for stage 0

Recommended steps after treatment for stage 0 melanoma include a medical history and skin exams at least once a year to check for 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's described as invasive. Stage 1 is defined as a lesion (tumor) that's 2 mm or thinner (Breslow depth or thickness). Stage 1 melanoma may or may not be ulcerated (broken skin), though most are not. Stage 1 melanoma has 2 subgroups: 1A and 1B.

### Stage 1A

This stage is defined as a tumor less than 0.8 mm thick that doesn't have a break on the skin (ulceration) when examined under a microscope. It's still considered localized to the skin but is invasive. This means it has gone through the top layer of skin (epidermis) into the next layer of skin (dermis).

**Early-stage melanoma is highly treatable. Be sure to ask questions if you need more information.**



### Treatment for stage 1A

The most common treatment for stage 1A is wide excision surgery. This removes the tumor as well as a margin of healthy tissue, which can help prevent the melanoma from coming back (called recurrence). Sentinel lymph node biopsy (SLNB) is usually not recommended at this stage. After surgery, you'll be observed through follow-up care (see "Follow-up for stage 1").

## Stage 1B

In stage 1B melanoma, the primary tumor has moved into the lower layer of skin but is still curable. Stage 1B includes tumors that are:

- Less than 0.8 mm thick with ulceration
- Between 0.8 and 1 mm thick with or without ulceration
- Between 1 and 2 mm thick without ulceration

### Treatment for stage 1B

Your doctor will discuss with you whether SLNB is needed at the time of a wide excision surgery. This procedure is considered for stage 1B melanoma and higher when no enlarged or abnormal nodes are felt during the physical exam. Your doctor may also consider nodal basin ultrasound imaging before SLNB if results of the physical exam were unclear. The nodal basin is the area of nearby lymph nodes. Even if the nodal basin ultrasound doesn't show cancer in the lymph nodes, you may still need an SLNB. Other imaging might also be ordered if you have signs or symptoms of cancer. See *Chapter 5: Treatment overview* for more information on SLNB.

The decision will be based on any health conditions you have, your age and general health, and your personal preferences. If the melanoma meets the criteria for SLNB, the procedure will figure out if cancer cells are in one or more nearby lymph nodes (see **Guide 6**).

If it's decided that you don't need an SLNB, then you'll have wide excision surgery and move to observation in follow-up care afterward (see "Follow-up for stage 1").

But if you need an SLNB, it will likely be done at the time of surgery. If the SLNB shows no cancer in the sentinel nodes (negative for cancer), then you'll move to follow-up care (see "Follow-up for stage 1").

## Cancer in SLNB

If cancer is found in the sentinel nodes (positive for cancer), then it could mean that cancer is also in other lymph nodes and your cancer stage will change (be upstaged) to stage 3. For more information on stage 3 melanoma treatment, see *Chapter 7: Treatment for stage 3: Regional spread*.

### Follow-up for stage 1

Recommended steps after treatment for stage 1A or stage 1B 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 at least once every year afterward. Imaging tests are done only to check for specific signs and symptoms.

## 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 3 subgroups: 2A, 2B, and 2C.

### Stage 2A

Stage 2A melanoma includes 2 types of tumors:

- Between 1 and 2 mm thick with ulceration
- Between 2 and 4 mm thick without ulceration

#### Treatment for stage 2A

Primary treatment for stage 2A starts with wide excision surgery.

**Guide 6**
**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 providers tell the stage of the melanoma and can help you and your care team make treatment decisions.**

| | | |
|---|---|---|
| **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 | Your doctor **will not likely** recommend an SLNB. |
| **If 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 | Your doctor **might** recommend an SLNB. |
| **If your cancer is stage 1B or higher and** | • The melanoma is more than 1 mm deep<br>• You had an in-transit metastasis or local recurrence of a melanoma but no sign of regional or distant metastases | Your doctor **will likely** recommend an SLNB. |

Before wide excision surgery, your provider may discuss with you having an SLNB at the same time as the surgery. They may consider nodal basin ultrasound imaging before the sentinel lymph node biopsy (SLNB), if results of the physical exam were unclear. Even if the nodal basin ultrasound doesn't show cancer in the nodes, you may still need an SLNB. Other imaging might also be ordered if signs or symptoms of cancer.

If your doctor doesn't think you need an SLNB, then you'll have standard wide excision surgery to remove the tumor. After surgery, you'll be observed in follow-up care (see "Follow-up for stage 2A").

Similarly, if you have the SLNB and cancer is not found in the sentinel nodes (negative for cancer), you'll be observed in follow-up care, usually by your dermatologist. Generally, no further treatment is needed.

However, a positive SLNB result shows that cancer is present in the sentinel lymph nodes and that other lymph nodes may be affected.

### Cancer in SLNB

If you have the SLNB and cancer is in sentinel nodes (positive for cancer), the cancer stage will be changed (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 7: Treatment for stage 3: Regional spread*.

### Follow-up for stage 2A

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

## Stage 2B or stage 2C

Stage 2B melanoma is defined as a lesion (tumor) thicker than 2 mm but not thicker than 4 mm with ulceration, or 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 for stage 2B or stage 2C

Primary treatment for stage 2B or 2C is the same and involves wide excision surgery and possibly SLNB. Your doctor will discuss SLNB with you and whether or not you need one. Imaging with PET/CT or CT of the chest, abdomen, and pelvis may be done beforehand if it's needed to plan surgery. You might also need imaging if you have any unusual signs or symptoms that need further workup. Imaging can also help guide shared decision-making between you and your medical oncologist about adjuvant systemic therapy after surgery.

An SLNB is typically recommended for complete (pathological) staging. It's also recommended before systemic therapy is started (pembrolizumab or nivolumab). This is because SLNB helps get the most accurate information on the melanoma to help guide treatment.

If your doctor doesn't think you need an SLNB, then you'll have standard wide excision surgery to remove the tumor with the option of receiving adjuvant (after surgery) therapy (see 3 options below). Similarly, if you have surgery with an SLNB and it shows no cancer in the sentinel nodes, then you also have these 3 options after surgery:

- Observation by your care team in follow-up care (see "Follow-up for stage 2B or 2C" for description)
- Systemic therapy with pembrolizumab or nivolumab
- Radiation therapy at the tumor site (for melanoma at high risk of recurrence)

Systemic immunotherapies can help reduce the chance of cancer returning. However, you could have long-term immunotherapy-related side effects.

Your doctor should discuss the pros and cons of pembrolizumab or nivolumab with you. Factors to consider, in addition to the cancer stage, include your age, how active you are, your personal and family history of autoimmune disease, and how toxic systemic therapies might be for you.

### Cancer in SLNB

If you have stage 2B or 2C melanoma and cancer is found in the sentinel nodes (sentinel node positive) during wide excision surgery with SLNB, your melanoma will be upstaged to stage 3. For more information on stage 3 treatment options, see *Chapter 7: Treatment for stage 3: Regional spread*.

### Follow-up for stage 2B or 2C

Recommended steps after treatment for stage 2B and 2C melanomas include a physical exam and medical history, with a focus on the skin and lymph nodes. Follow-up visits should occur every 3 to 6 months for 2 years, then every 3 to 12 months for 3 years, and then yearly after that.

Imaging tests are done to evaluate any concerning signs and symptoms and usually after receiving adjuvant treatment. 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 recurrence (return) or metastasis (spread) of melanoma.

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

## Key points

- Stage 0 through stage 2A melanomas are considered early-stage cancer. They are highly treatable and curable.
- The standard treatment for stage 0 in situ and stage 1A melanoma 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'll be upstaged to stage 3.
- Adjuvant therapy (after primary treatment) may be used for stage 2B and stage 2C melanoma. It can help reduce the chance of cancer returning.
- If you're considered for adjuvant therapy, pretreatment imaging will be needed to help guide treatment.
- Depending on your signs and symptoms after treatment, you may undergo regular monitoring of your skin and lymph nodes for up to 3 years.

## Questions to ask

- What are the chances of the melanoma coming back after my treatment?
- Will insurance cover my treatment?
- Should I be using a patient portal to get my test results or should I wait to hear from you?
- How long until I receive test results after an SLNB?

## What's next

This chapter explained treatments for early-stage melanoma. At these stages, melanoma is often curable. After successful treatment, regular follow-up care is needed. Be sure to check out *Chapter 10* to learn more about follow-up care.



**Let us know what you think!**

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

# 7

# Treatment for stage 3: Regional spread


60 Features of regional spread

61 Staging subgroups

62 Cancer in the sentinel nodes

63 Cancer in the lymph nodes

65 Microsatellites

66 Satellite or in-transit tumors

70 Follow-up for stage 3

71 Key points

71 Questions to ask

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 melanoma means the cancer has spread from the main skin tumor to nearby areas. This is called regional melanoma because the cancer has spread locally but not to distant parts of the body.

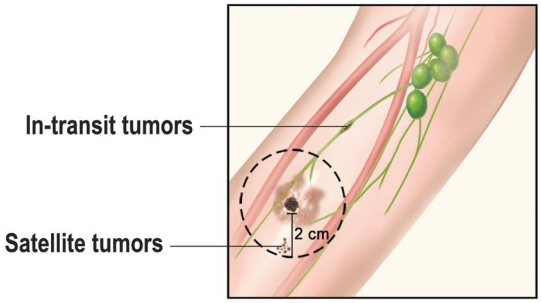
## Features of regional spread

Stage 3 melanoma has 1 or more of these 4 features:

- **Nearby lymph nodes with cancer** may be found. (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 further than 2 cm from the main tumor but haven't reached the lymph nodes.

### Satellite and in-transit tumors

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




Microsatellite tumors (only seen with a microscope)

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For more information on staging, see *Chapter 4: Staging for melanoma*.

## Staging 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.

Treatment of stage 3 depends on its features, which help determine the subgroup. This chapter is organized based on the treatment of the main features and then mentions the subgroup within the features.

### Stage 3A

Stage 3A melanoma includes tumors that may be:

- 1 mm thick or less with or without ulceration (broken skin)
- 2 mm thick or less without ulceration

This stage also means that between 1 to 3 lymph nodes have cancer detected microscopically after a sentinel lymph node biopsy (SLNB).

### Stage 3B

Stage 3B indicates tumors that have:

- Thickness less than 1 mm or up to 4 mm with or without ulceration
- 1 to 3 lymph nodes found to have cancer by physical exam or imaging tests
- Microsatellite, satellite, or in-transit tumors on or under the skin

### Stage 3C

A stage 3C tumor is identified as:

- Less than 2 mm thick to no more than 4 mm thick, with or without ulceration
- Involving anywhere from 1 to 4 lymph nodes found by physical exam or imaging tests, and/or any number of lymph nodes clumped (matted) together
- Having microsatellite, satellite, or in-transit tumors on or under the skin

### Stage 3D

Stage 3D means the tumor is:

- More than 4 mm thick with ulceration
- Found with cancer in 4 or more lymph nodes or any number of lymph nodes clumped (matted) together
- Associated with 2 or more lymph nodes and/or any number of lymph nodes clumped together. There are also microsatellite, satellite, and/or in-transit tumors 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 (lab) 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. Cancer is found in the lymph nodes in 2 ways:

- The pathologist confirms cancer in abnormal nodes that were first detected by a doctor's physical exam, or through imaging and a biopsybefore treatment.
- The pathologist finds cancer in the SLNB.

## Cancer in the sentinel nodes

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

### Tests

For stage 3A melanoma, your care team may consider imaging to help with 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 figure out whether targeted therapy is a possibility.

When cancer is found in sentinel lymph nodes, other nearby nodes may have cancer, too. Cancer care options include a series of imaging tests to check nearby lymph nodes called the nodal basin.

### Treatment

Active nodal basin ultrasound or other types of imaging (CT, PET/CT, or MRI) without further lymph node removal (called complete lymph node dissection, or CLND) are considered the preferred next step. Active nodal basin ultrasound is the usual imaging to monitor the lymph node location with cancer in the sentinel node, but is done more frequently. See **Guide 7**.

CLND should only be used for certain people and circumstances because of its risk of severe side effects like lymphedema (swelling due to buildup of lymph fluid in the fatty tissue just under your skin near the surgery site). CLND also involves extensive surgery, longer recovery time, and hospitalization. If signs of cancer appear, you can have adjuvant (after surgery) treatment at that time.

For most stage 3A tumors, no further treatment is needed. Instead, observation is preferred. Observation means periodic doctor visits or follow-up care that includes skin and lymph node exams; attention to any concerning signs and symptoms; and/or imaging scans, when needed (see "Follow-up for stage 3").

But the next step for cancer in the sentinel nodes, especially for stage 3B, 3C, or 3D, could be adjuvant (after surgery) treatment that's either systemic therapy or observation

**Guide 7**
**Possible treatments for cancer in sentinel lymph nodes**

| |
|---|
| Active nodal basin ultrasound without CLND |
| CLND (for certain people) |
| Systemic therapy |
| Observation |

in follow-up care. But before choosing one of the systemic therapies, your care team should consider both your risk of cancer recurrence (returning) and how toxic systemic therapies might be for you.

For example, if the cancer is considered low risk, the toxicity of adjuvant therapy may outweigh any potential benefit. Because of that, adjuvant therapy may not be recommended.

But if your doctor recommends adjuvant therapy, the preferred options are:

- Nivolumab
- Pembrolizumab
- Dabrafenib/trametinib for people with *BRAF* V600 mutation

As mentioned previously, another possibility is undergoing observation in follow-up care.

After all treatment, you'll move to follow-up care (see "Follow-up for stage 3").

## Cancer in the lymph nodes

Your care team may have detected abnormal (enlarged or hard) lymph nodes before you started treatment, possibly during your physical exam or through imaging. Then a biopsy, either core (a thicker needle, which is preferred) or fine-needle aspiration, confirmed cancer in these nodes, which are referred to as clinically positive lymph nodes. Melanoma at this stage could be 3B, 3C, or 3D.

### Tests

Further recommended tests to guide treatment 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 of the melanoma (meaning it's resectable). See **Guide 8** for treatment options.

### Treatment

Before surgery, you may receive drug treatment (called neoadjuvant systemic therapy), which could help shrink the tumor as well as make drug treatment after surgery more effective. Neoadjuvant therapy may consist of immunotherapy, targeted therapy, or both. This is typically done before a wide excision surgery with therapeutic lymph node dissection (TLND). This surgery consists of wide excision of the tumor while removing nearby lymph nodes. The number of lymph nodes removed depends on the involved lymph node basin (area). TLND is recommended if you had neoadjuvant therapy first, or it can be done without neoadjuvant therapy if neoadjuvant therapy isn't an option for you.

Important to know: Sometimes other targeted therapy combinations may be considered if the side effects are too much for you (known as toxicity).

Another option is to have surgery without neoadjuvant therapy first. This would consist of wide excision surgery of the tumor and TLND.

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, the preferred adjuvant systemic therapy options include:

- Nivolumab
- Pembrolizumab
- Dabrafenib/trametinib (for people with *BRAF* V600 mutation)

You may also receive adjuvant radiation therapy, although its use has mostly been replaced by the cancer drugs listed above. Adjuvant radiation therapy is not usually recommended since it only treats the region where the lymph nodes were removed and not other areas. But it's sometimes used locally at the skin or lymph node sites for melanoma at high risk of recurrence.

One other option is observation. The decision to use observation is based on your care team's assessment of the risk of the melanoma's recurrence and the risk of treatment side effects (toxicity). Observation in follow-up care involves periodic doctor visits that include skin and lymph node exams; attention to any concerning signs and symptoms; and/or imaging scans, when needed.

**Guide 8**
**Treatment of melanoma with clinically positive nodes**

| | |
|---|---|
| **If cancer can be treated with surgery (resectable)** | Treatment may have 3 phases:<br>• Neoadjuvant therapy with immunotherapy, targeted therapy, or both<br>• Wide excision surgery and (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 |

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

### Unresectable melanoma

If surgery is not an option for you or the tumor is considered unresectable (not removable with surgery), the preferred treatment is systemic therapy mentioned on page 64.

In addition, you may get relief from one or more of these treatments:

- Palliative radiation therapy
- Talimogene laherparepvec (T-VEC), virus is injected into the skin tumor and triggers your body to find and attack nearby cancer cells
- Best supportive care, also known as palliative 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.




## 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 of a clinical stage 3A melanoma, it can be upstaged to pathological stage 3B melanoma. For all stages, microsatellites are found in either:

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

Possible treatments for microsatellites are listed in **Guide 9**.

### Tests

The tests for melanoma with microscopic satellites include:

- Imaging tests for staging
- Imaging tests to assess signs or symptoms of cancer

**Guide 9**
**Possible treatments for cancer with microsatellites**

| |
|---|
| Wide excision surgery |
| Wide excision surgery with SLNB |
| Observation |
| Systemic therapy |

- *BRAF* mutation testing if you might have adjuvant therapy (described on page 66) or if you might 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 not have 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, treatment options include participation in a clinical trial or systemic therapy with:

- Nivolumab
- Pembrolizumab
- Dabrafenib and trametinib (for people with *BRAF* V600 mutation)

Observation in follow-up care is also a possibility. Observation involves having regular doctor visits that include skin and lymph node exams; attention to any concerning signs and symptoms; and/or imaging scans, when needed (see "Follow-up for stage 3").

### Cancer in SLNB

If you had wide excision surgery with an SLNB and the SLNB was positive for cancer, you'll receive the following tests:

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

For the treatment of SLNB-positive microsatellite melanoma, read the treatment section in "Cancer in the sentinel nodes" because it's the same treatment as microsatellites.

## 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 by biopsy to be cancer. Treatments are listed in **Guide 10**.

**Guide 10**
**Possible treatments for cancer with satellite or in-transit tumors**

| |
|---|
| Neoadjuvant systemic therapy |
| Surgery (complete excision) to clear margins |
| T-VEC/intralesional therapy |
| Systemic therapy |
| Radiation therapy |
| Observation |

## 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's called resectable. Cancer that cannot be treated with surgery is called unresectable. Sometimes satellite or in-transit tumors can be considered either resectable or unresectable/borderline resectable. Unresectable/borderline resectable means the tumor is on the border (outside limit) of what surgery might be able to accomplish. Resectable means the tumor could be surgically removed if treatment shrinks the tumor first.

## Treatment: Resectable cancer

There are 4 options for initial treatment of resectable cancer:

- Neoadjuvant (before surgery) systemic therapy (see **Guide 11**)
- Surgery (complete excision) to clear margins
- T-VEC injectable intralesional therapy
- Systemic therapy as the initial treatment (see **Guide 16**, *Chapter 9*, for first-line options)

**Guide 11**
**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 |

*Only IV nivolumab can be used with ipilimumab, not the injectable form.

### Surgery with neoadjuvant therapy

If you received neoadjuvant (before surgery) systemic therapy to shrink the tumor and/or to help drug therapy after surgery to be more effective, the next step is surgery. The cancer will be removed with complete excision to clear margins. Clear margins mean there is no evidence (signs) of disease (cancer) on the edges of the surgical excision or elsewhere.

Following surgery, the preferred options for adjuvant systemic therapy include nivolumab; pembrolizumab; or dabrafenib and trametinib, if you have *BRAF* V600 mutation.

One other possibility is observation. This involves regular clinical exams and imaging scans for any new cancer signs or symptoms (see "Follow-up for stage 3").

### Surgery without neoadjuvant therapy

If you received a complete excision to clear margins as initial treatment without neoadjuvant systemic therapy and there are no signs of remaining cancer cells, you might receive the adjuvant (after surgery) systemic treatment options or observation.

If cancer cells remain after complete excision, read the "Treatment: Unresectable/borderline resectable cancer" section ahead for treatment options.

### Systemic therapy and T-VEC

If you had systemic therapy or T-VEC/intralesional therapy as your initial treatment, you may receive any combination of clinical exams (skin exam or physical exam), a lab test (like another biopsy), or imaging to determine the cancer's response to the treatment.

If cancer that is considered unresectable is still present and has progressed after those therapies, then you'll be treated following the "Treatment: Unresectable/borderline resectable cancer" discussed below.

But if the remaining cancer is resectable, you'll likely have the same treatment (1 of the 4 options) for resectable cancer, noted above, or possibly another treatment, like radiation.

### No evidence of cancer after T-VEC

If there is no evidence of cancer after T-VEC/intralesional therapy and further exams, then your provider will likely consider one of these adjuvant therapy options:

- Nivolumab
- Pembrolizumab
- Dabrafenib/trametinib if you have *BRAF* V600 mutation
- Observation in follow-up care

If there's no evidence of cancer after you've had systemic therapy as an initial treatment and further exams, you'll move to observation as part of follow-up care.

## Treatment: Unresectable/borderline resectable cancer

Instead of up-front surgery because it's considered unresectable/borderline resectable, initial treatment options include systemic therapy, which is preferred (see **Guide 16**, *Chapter 9*, for first-line therapy options).

Or you could have the following local therapy options.

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

Regional chemotherapy is another option for local satellite/in-transit melanoma confined to an arm or a leg. The treatment is called isolated limb infusion/isolated limb perfusion (ILI/ILP) with melphalan and treats just the limb that has the melanoma. This procedure should only be done at centers experienced in providing ILI/ILP.

After treatment, your doctor may perform another skin exam or biopsy, and you may undergo imaging. The next treatment is based on those test results.

- If some cancer remains and appears to be unresectable, you may have the same treatment as in the intial treatment section.
- If there is some resectable melanoma remaining, you'll have the same treatment as resectable cancer.
- If there are no signs of cancer after local or regional therapy, you may start adjuvant systemic therapy (nivolumab; pembrolizumab; or dabrafenib/trametinib, if you have *BRAF* V600 mutation) or start observation as part of follow-up care.
- If no cancer remains after systemic therapy, you'll move to observation as part of follow-up care.

**If you need support while dealing with a melanoma diagnosis, find a nearby in-person or online cancer support group.**



## Follow-up for stage 3

For all stage 3 melanomas, follow-up care involves ongoing testing for new signs and symptoms of cancer, also known as observation. It's further described in *Chapter 10: 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 then every year as needed.
- Imaging tests as needed based on cancer signs and symptoms. Imaging might be done 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.

### Supportive Care

Supportive care is an important part of cancer care. The goal is to improve your quality of life during and after cancer treatment. Supportive care is for everyone with cancer and their families, not just for those at the end of life. It's also known as palliative care.

Supportive care includes a wide range of services. Supportive care prevents or manages the symptoms of cancer and the side effects of cancer treatment, like pain and cancer-related fatigue. It also addresses the mental, social, emotional, and spiritual concerns faced by people with cancer.

Supportive care provides help with additional needs, such as:

- Making treatment decisions
- Coordinating your care
- Paying for care
- Planning for advance care and end of life

## Key points

- Stage 3 melanoma has spread to nearby lymph nodes, lymph vessels, or other areas of the skin.
- 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 found in enlarged lymph nodes can often be treated with surgery.
- Neoadjuvant therapy is often recommended to shrink a tumor prior to surgery and then can be followed by adjuvant therapy.
- Melanoma may spread and form more skin tumors, called satellite or in-transit tumors.

## Questions to ask

- How far has the cancer spread?
- Will I need *BRAF* mutation testing?
- What are the side effects from systemic therapies?
- How can you tell that melanoma could be in my lymph nodes?
- Will I need imaging tests?

## What's next

In this chapter, you learned about stage 3 melanoma, which is considered regional—it has spread locally and not far in the body. The next step is regular follow-up care to prevent and find another skin cancer. Read *Chapter 2* to learn how you can spot and prevent skin cancers, as well as information about genetic risks. If the melanoma returns, it's called recurrence. For more information on recurrence, read the next chapter (*Chapter 8: Treatment for recurrence*).

# 8
# Treatment for recurrence


73 True scar recurrence

74 Local satellite and in-transit recurrence

76 Nodal recurrence

78 Key points

79 Questions to ask

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

When melanoma recurs, it often doesn't 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 9: Treatment for stage 4: Metastatic melanoma* for options.

## True scar recurrence

True scar recurrence, also known as persistent cancer, 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.

**Guide 12**
**Possible treatments for true scar recurrence**

| |
|---|
| Re-excision of tumor site |
| Lymphatic mapping or SLNB |
| Radiation therapy |
| Immunotherapy |
| Observation |

This tumor looks like the original melanoma. It's 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'll receive are based on the stage and features of the recurrent melanoma. Tests could include lymphatic mapping (the use of dyes and radioactive substances to find cancer in lymph nodes) or sentinel lymph node biopsy (SLNB). Ask your care team about any other testing you may have.

### Treatment

Treatment options for true scar recurrence are listed in **Guide 12**. They 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:

- 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's 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 2 types of recurrence are tested and treated the same way.

**Guide 13**
**Possible treatments for local satellite and in-transit recurrence**

| |
|---|
| Neoadjuvant systemic therapy |
| Surgery (complete excision) to clear margins |
| T-VEC/intralesional therapy |
| Systemic therapy |
| Adjuvant systemic therapy |
| Regional therapy |
| Palliation (limited excision or local ablation) |
| Observation |

## Tests

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

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

## Treatment

Treatment of recurrent satellite or in-transit tumors (**Guide 13**) is almost the same as the treatment for these tumors when they're found at diagnosis. (For treatment at diagnosis, see *Chapter 7: Treatment for stage 3: Regional spread*.) Treatment of recurrence depends on if the cancer can be removed with surgery (resectable cancer) or not (unresectable/ borderline resectable).

### Resectable

When the recurrent cancer is classified as resectable, your first treatment options may be:

- Neoadjuvant systemic therapy (see **Guide 11**, *Chapter 7*)
- Surgery with complete excision to clear margins and removal of all cancer
- Talimogene laherparepvec (T-VEC)/ intralesional therapy
- Systemic therapy (see **Guide 16**, *Chapter 9*)

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

After you've had either neoadjuvant systemic therapy before surgery or surgery alone to clear margins and there is no evidence of cancer, you could undergo observation in follow up care (see *Chapter 10: Follow-up care*) or have one of the preferred systemic therapy options:

- Nivolumab
- Pembrolizumab
- Dabrafenib/trametinib if you have *BRAF* V600 mutation
- If you had anti-PD-1 therapy, you might have ipilimumab

If the surgery cannot completely remove the cancer, you'll follow the treatment in the "Unresectable/borderline resectable" section.

But if you received T-VEC or systemic therapy (known as local or regional therapy) as the initial treatment, your provider may recommend another biopsy and more imaging to see if the cancer is responding to treatment.

At that point, if there is residual/progressive unresectable cancer, you'll receive the same treatment as discussed in the "Unresectable/borderline resectable" section.

But if there is residual cancer that is resectable, then you might receive 1 of the following 4 treatment options:

- Neoadjuvant systemic therapy (see **Guide 11**, *Chapter 7*)
- Surgery with complete excision to clear margins and removal of all cancer
- T-VEC/intralesional therapy
- Systemic therapy (see **Guide 16**, *Chapter 9*)

Still, if you've had T-VEC/intralesional therapy and the testing afterward shows no evidence of cancer, then you could undergo observation (see *Chapter 10: Follow-up care*) or have one of the preferred adjuvant systemic therapy options:

- Nivolumab
- Pembrolizumab
- Dabrafenib/trametinib if you have *BRAF* V600 mutation
- Ipilimumab (if you had anti-PD-1 therapy)

If no cancer remains after systemic therapy, you can begin observation in follow-up care.

### Unresectable/bordeline resectable

When the melanoma can't be treated with surgery, it's unresectable/borderline resectable cancer, and there are many other options.

The preferred initial treatment is systemic therapy, as described in *Chapter 9*, which discusses metastatic cancer (see **Guide 16**).

Other treatment includes local therapy options, such as:

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

Regional therapy, such as isolated limb infusion/perfusion (ILI/ILP) with melphalan-based regimens, is another possibility for unresectable/borderline resectable recurrent melanoma. This is a procedure where a high dose of drugs is injected directly into a tumor in an arm or a leg, and the cancer is only in that limb. This therapy should only be done in centers with experience in ILI/ILP.

After initial treatment, your provider will examine you and may need more information in the form of another biopsy and more imaging to see if your cancer is responding to treatment.

The next treatment is based on those results.

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

If no cancer remains after systemic therapy, you will move to observation in follow-up care. See *Chapter 10: Follow-up care*.

## Nodal recurrence

Nodal recurrence means the cancer has returned 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 first located.

**Guide 14**
**Possible treatments for nodal recurrence**

| |
|---|
| Neoadjuvant systemic therapy |
| Surgery (excision of recurrence) with TLND |
| Surgery (excision recurrence) without TLND |
| Adjuvant systemic therapy |
| Locoregional therapy |
| Observation |

## Tests

Testing for nodal recurrence can include:

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

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

If tests find the melanoma has spread further than nearby lymph nodes, see *Chapter 9: Treatment for stage 4: Metastatic melanoma* to learn what treatment options are available.

If you have recurrent melanoma limited to the lymph nodes, treatment depends on whether it's resectable or unresectable.

## Resectable cancer

If the cancer is considered resectable, you might first have neoadjuvant systemic therapy, which is preferred (see **Guide 11**, *Chapter 6*), before surgery to help shrink the tumor and to reduce the risk of recurrence.

After neoadjuvant therapy, you'll have surgery to remove the enlarged lymph nodes. Other lymph nodes that may have cancer might be removed, too. This is called a therapeutic lymph node dissection (TLND).

Or you might not have neoadjuvant therapy and instead just have surgery and TLND to remove the cancer recurrence in the lymph nodes if you didn't have a lymph node removal before.

**Palliative options mean they aim to ease the suffering from cancer symptoms.**

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

- One of the following preferred treatments: Nivolumab; pembrolizumab; dabrafenib/trametinib or other BRAF or MEK inhibitors if you have *BRAF* V600 mutation
- Ipilimumab if you already had anti-PD-1 therapy, used in some cases

You might also have one or both of the following:

- Regional radiation therapy to nodal basin if you have a higher risk of another recurrence
- Observation as part of follow-up care

For more information on follow-up care, see *Chapter 10: Follow-up care*.

### Unresectable cancer

Whether or not you had a lymph node removal before, if the cancer is unresectable then the preferred treatment is the same: systemic therapy (see **Guide 16**, *Chapter 9*). Other options include palliative radiation therapy, intralesional T-VEC, and/or 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.




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

**“Any time is the right time to bring up clinical trials.”**

## 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 have 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 a possibility. 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.
- If the recurrent melanoma is considered resectable, you might first have neoadjuvant systemic therapy before the surgery to help shrink the tumor and to reduce risk of recurrence.

## Questions to ask

- Is the cancer considered metastatic?
- Do my lymph nodes need to be removed?
- Am I eligible for a clinical trial?
- What is my risk of another recurrence?
- Am I a candidate for neoadjuvant systemic therapy?

## What's next

In this chapter, you learned about the different types of recurrence, which is when melanoma returns. If the recurrent melanoma is considered metastatic (has spread to distant areas), read the next chapter, *Treatment for stage 4: Metastatic melanoma*. If it's not metastatic, then you'll receive follow-up care. Read *Chapter 10: Follow-up care* for more information on regular doctor visits and imaging.

# 9

# Treatment for stage 4: Metastatic melanoma


81 Tests for metastatic melanoma

82 Limited spread

84 Widely spread and/or brain metastases

85 Ask for help

86 Key points

86 Questions to ask

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, the brain, bones, liver, lungs, or gastrointestinal (GI) tract.

It's important to know that stage 4 melanoma is treatable (**Guide 15**). Find a care team that's experienced in treating the type and stage of cancer and explore clinical trial options. Always ask questions. This increases your chances of getting the best possible outcome.

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 16** 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.

## Tests for metastatic melanoma

Tests to evaluate the extent of stage 4 melanoma may involve one or more of the following:

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

After you get the test results, your care team will meet to discuss options with you. Melanoma experts recommend that the team include a surgical oncologist, radiation

**Guide 15**
**Possible treatments for metastatic melanoma**

| |
|---|
| Surgery (resection) |
| Stereotactic ablative radiation therapy |
| T-VEC injection therapy |
| Systemic therapy |
| Palliative resection |
| Radiation therapy |
| Supportive care |
| Observation |

oncologist, and medical oncologist. A neurosurgeon should also be included if the melanoma has spread to your brain. There are 2 types of metastatic melanoma: limited spread and widely spread (which may include brain metastases).

## Limited spread

When cancer has spread to only a few distant sites, it's called limited spread or limited metastatic cancer. It's also referred to as oligometastatic cancer. Your care team will meet with you to discuss primary treatment, which could include options like:

- Systemic therapy (preferred for people who have not had systemic therapy before—see **Guide 16**)
- Surgery (resection)
- Stereotactic ablative radiation therapy (also called stereotactic body radiation therapy, or SBRT), which uses special equipment to position the person and precisely deliver radiation to a tumor
- Talimogene laherparepvec (T-VEC) injections into accessible tumors

### After systemic therapy as primary treatment

If you received systemic therapy for limited metastases, you'll have imaging tests to assess whether the therapy worked. With that information, you'll have the following options:

- If the cancer has spread, see treatment options in the "Widely spread and/or brain metastases" section.
- If the cancer stayed the same, you may have surgery. If there are no signs of cancer after surgery, you may receive systemic therapy (see **Guide 16**). Or you'll have observation in follow-up care described on page 84 and in more detail in *Chapter 10*.
- If there is still cancer after surgery (called residual disease), then you'll have the same treatment for widely spread metastases (see the "Widely spread and/or brain metastases" section).

### After surgery, radiation, or injections

After treatment for limited spread melanoma, your care team will assess if there are still signs of cancer. If there are none, you may be treated with adjuvant therapy or start observation in follow-up care described in *Chapter 10*. Preferred adjuvant therapy options are:

- Nivolumab
- Pembrolizumab
- Nivolumab/ipilimumab (only IV nivolumab, not injectable, can be combined with ipilimumab)

Other recommended therapy if you have *BRAF* V600 mutation is as follows:

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

In some cases, ipilimumab might be used as adjuvant therapy if you already had anti-PD-1 therapy.

## Guide 16
## 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 | ○ | ● |
| Lifileucel (tumor-infiltrating lymphocyte therapy, or TIL) | | ● |
| Pembrolizumab/low-dose ipilimumab | ○ | ● |
| Ipilimumab | | ○ |
| High-dose IL-2 | | ○ |
| Imatinib, dasatinib, nilotinib, or ripretinib for *KIT* mutations | | ○ |
| Crizotinib or entrectinib for *ROS1* fusions | | ○ |
| Larotrectinib or entrectinib for *NTRK* fusions | | ○ |
| Trametinib for *BRAF* fusions | | ○ |
| Binimetinib for *NRAS* mutation | | ○ |
| Pembrolizumab/lenvatinib | | ○ |
| Ipilimumab/intralesional T-VEC | | ○ |
| Dabrafenib/trametinib plus pembrolizumab or vemurafenib/cobimetinib plus atezolizumab for *BRAF* V600 mutation | | ○ |
| Chemotherapy | | ○ |

● preferred option ○ not a preferred option

*Only IV nivolumab can be used with ipilimumab, not the injectable form.

**Injectable forms of this therapy are available to treat melanoma.

If cancer remains (called residual cancer) after any treatment, see the next section on widely spread or brain metastases for treatment options. Otherwise, if there is no cancer remaining, you will move to observation in follow-up care.

### Follow-up for limited spread

Recommended follow-up tests for stage 4 melanoma with limited spread 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 then 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 5 years, routine imaging is not recommended.

## Widely spread and/or brain metastases

Widely spread (disseminated) refers to melanoma that has spread to many distant sites and/or to the brain as brain metastases. It's unresectable, which means it cannot be completely removed with surgery.

### Treatment

The first step in treating widely spread 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 with you to discuss treatment options.

Preferred treatment for widely spread and/or brain metastases includes systemic therapy listed in **Guide 16**. For skin lesions that have spread to other skin sites, T-VEC injections are a treatment option.

Otherwise, surgery is an option if large brain metastases are causing symptoms or if there is a single metastasis—this is called a palliative resection (surgery) because it's intended to relieve symptoms vs. removing the cancer (discussed further below).

Or you may receive radiation therapy after surgery. The preferred radiation method is stereotactic ablative radiation therapy (SBRT). This is therapy that uses a high dose of radiation directly into the tumor. If SBRT is not an option, whole brain radiation therapy may be considered.

Sometimes, brain metastases are treated with the goal of relieving symptoms and not removing the cancer. This is called palliative care. Palliative options for brain metastases include:

- Corticosteroids to relieve swelling
- Anticonvulsant therapy to control seizures
- Bevacizumab to help with quality of life

To summarize, treatment options for widely spread and/or brain metastases include:

- Systemic therapy (preferred)
- Palliative surgery
- Radiation therapy
- T-VEC injections to treat metastatic skin lesions
- Best supportive/palliative 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.




## Ask for help

Cancer and its treatment can be very overwhelming. Getting help when you're feeling worried or hopeless is an important part of cancer care. And if you have a caregiver, this could apply to them, too. If you're both feeling anxious or overwhelmed, ask your care team for help.

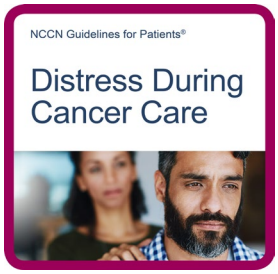
Part of asking for help could also mean talking to other people who have the same type of cancer as you. Often the best advice comes from others who've been there. And dozens of online and in-person support groups are available where you can share your feelings and worries or anything on your mind.

Most cancer centers have patient-to-patient peer support groups. Don't hesitate to ask your care team (like a social worker or a behavioral health expert) to recommend support groups, or do an online search of groups that meet near you or others that might meet virtually.

If you're looking for spiritual help and guidance, ask your care team about any resources for that, too.

### It's normal to feel worried

Depression, anxiety, fear, and distress are very common feelings in people with cancer. These feelings can make it harder to deal with cancer and cancer treatment. They can hold you back even when you want to move forward. Getting help when you're feeling worried is an important part of cancer care. If you're feeling anxious or overwhelmed, ask your treatment team for help.




Read more about cancer and distress in *NCCN Guidelines for Patients: Distress During Cancer Care,* available at NCCN.org/patientguidelines and on the NCCN Patient Guides for Cancer app.

## Key points

- Stage 4 melanoma, also referred to as metastatic cancer, is cancer that has spread from where it started to other parts of the body.
- Metastatic melanoma is treatable and has many options.
- Cancer that has spread to only a few distant sites is referred to as limited spread cancer or limited metastases.
- Limited spread cancer can be considered resectable, which means it can be treated with surgery.
- Widely spread metastatic cancer refers to cancer that has spread to many distant sites.
- Brain metastases are often treated with both systemic therapy and local treatment.
- The preferred treatment for widely spread metastases is systemic therapy.

## Questions to ask

- What is your experience treating metastatic melanoma?
- How many of your patients have had complications? What were the complications?
- Who will manage my day-to-day care?
- Is a clinical trial an option for me?
- I would like a second opinion. Is there someone you can recommend?

## What's next

In this chapter, you learned about stage 4 metastatic melanoma. Cancer that spreads can be treated in a variety of ways. It's important to ask your care team questions throughout your treatment as well as to ask for support if you need it. The next chapter discusses follow-up care and includes information on the type of exams you might receive on a regular basis. If you need additional resources, be sure to check out *Chapter 11: Other resources,* which includes many helpful links.



**From a patient's perspective, having a combination of a supportive team of medical professionals and the experiences from other patients gives one a sense of confidence and control that is invaluable when it comes to making decisions about their treatment options."**

# 10
# Follow-up care


88 Melanoma tests

89 Be your own detector

89 Key points

89 Questions to ask

After treatment for melanoma, your care team will want to check you for any new skin cancers—often called follow-up, observation, surveillance, or monitoring. This chapter briefly explains ongoing care for everyone who's had melanoma.

You've gone through your melanoma treatment, so the next step is attending regular visits with your doctor to look for any new lesions and to make sure the melanoma hasn't spread.

## Melanoma tests

You may receive more than one type of test for melanoma in follow-up care.

### Skin and lymph node exams

Your provider may examine 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 lymph nodes at home. It's important to regularly look for any new, changing, or unusual spots on both sun-exposed and non–sun-exposed skin.

What you can do:

- Examine your skin regularly—If you spot anything that seems out of the ordinary or doesn't look normal, have it checked as soon as possible. See *Chapter 2* for detection information.
- Visit your health care provider annually and ask for a full-body skin exam by a skin care provider, like a dermatologist, at least once a year. You may want to consider a skin exam more often if you're at higher risk of skin cancer.

### Skin devices

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

- A dermatoscope—a handheld device to provide a closer look at suspicious lesions

**It's good practice to look at your skin for anything unusual at least once a month.**



- Total-body photography—to help with ongoing monitoring of moles on the skin

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

### Imaging tests

If you had a lymph node exam that showed cancer in the past, your doctor might consider more imaging scans (for example, an ultrasound or CT scan). This could be followed by more thorough imaging or a biopsy if your doctor feels it's needed.

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

## Be your own detector

You can look for and find any suspicious spots on your own, too. Your doctor will likely encourage you to do so as part of your follow-up care about once a month. Be sure to read *Chapter 2: Melanoma risk, detection, and prevention* for ways to do that.

## Key points

- Your doctor or other health care provider should examine your skin and lymph nodes at least once a year.
- How often you receive follow-up testing depends on how likely it is that the cancer will return.
- Your doctor or other health care provider should also explain how you can do self-exams of your skin and lymph nodes.
- Your care team might use devices to help detect new melanomas early.
- If you had a past lymph node exam that showed cancer, your doctor might consider more imaging.
- Your risk of future melanomas is part of the decision of how frequently you should have follow-up testing.

## Questions to ask

- If I find an unusual spot, what should I do?
- Should I always let you know about new spots? Is there a way to tell it's suspicious?
- Will I need imaging tests?
- What else can I do to prevent another melanoma?

**"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."**

# 11
# Other resources


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Want to learn more? Here's how you can get additional help.

## What else to know

This guide helps you know your options so you can make informed decisions and improve your cancer care. But it's not the only resource that you have.

Ask for as much information and help as you need. Many people are interested in learning more about:

- The details of melanoma treatment and its side effects
- Being a part of a care team
- Getting financial help
- Finding a cancer care professional who's an expert in melanoma
- Coping with other health problems

## What else to do

Your health care center can help you with next steps. It often has on-site resources to help meet your needs and find answers to your questions. Health care centers can also inform you of resources in your community.

In addition to help from your providers, the resources listed in the next section provide support for many people like yourself.

## Where to get help

Look through the list below and visit the related websites to learn more about these organizations.

**AIM at Melanoma**
aimatmelanoma.org

**AIM at Skin Cancer**
aimatskincancer.org

**Cancer*Care***
cancercare.org

**Cancer Hope Network**
cancerhopenetwork.org

**Clear Cell Sarcoma**
clearcellsarcoma.org

**GRACE**
cancergrace.org

**Imerman Angels**
imermanangels.org

**Melanoma Research Alliance**
curemelanoma.org

**Melanoma Research Foundation**
melanoma.org

**My Faulty Gene**
myfaultygene.org

**PAN Foundation**
panfoundation.org

**Save Your Skin Foundation**
saveyourskin.ca

**The Skin Cancer Foundation**
skincancer.org

**Triage Cancer**
triagecancer.org

## Questions to ask

- Who can I talk to about help with housing, food, and other basic needs?
- What assistance is available for transportation, childcare, and home care?
- How much will I have to pay for treatment?
- What help is available to pay for medicines and other treatment?
- What other services are available to me and my caregivers?



**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**



# Words to know

**ABCDE rule**
A memory device to recognize the characteristics of moles or skin lesions that might be cancer.

**adjuvant treatment**
Treatment (usually medicine or radiation) 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**
A characteristic of possible skin cancer in which one half or side of a mole does not match the other half or side.

**best supportive care**
Health care for the symptoms of cancer and the side effects of cancer treatment. Also called palliative care.

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

***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.

**complete lymph node dissection (CLND)**
A type of surgery that removes the remaining lymph nodes after a positive sentinel lymph node biopsy. Also called completion lymph node dissection.

**computed tomography (CT) scan**
An imaging scan that uses x-rays from many angles to make detailed pictures of the inside of the body.

**contrast**
A substance put into the body to make clearer pictures during imaging.

**dermal mitotic rate (DMR)**
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 beneath the top layer (epidermis).

**distant metastasis**
Spread of cancer cells 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**
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 drug-induced, sleep-like state for pain relief.

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

**hypodermis**
Deep skin tissue made of subcutaneous fat, connective tissue, and blood and lymphatic vessels.

**imaging**
Any radiology test that makes pictures (images) of the inside 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**
The spread of skin cancer through a lymph vessel.

**lentigo maligna**
A slow-growing, early-stage melanoma often found in older adults and appears as brown patches on the face or neck.

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

**lymph node**
A small, disease-fighting structure located throughout the body.

**lymph node basin**
A group of lymph nodes that receive and filter 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**
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) 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 illnesses.

**radiation therapy**
Treatment that uses high-energy rays to kill cancer cells.

**recurrence**
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)**
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 filters out UV rays and protects skin against sunburn.

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

**targeted therapy**
Drug treatment that identifies and attacks a specific feature of cancer cells with less harm to normal cells.

**tumor**
An abnormal mass of tissue from cells growing or dividing too much that can be benign (not cancer) or cancer. In melanoma, a lesion or a spot is also called a tumor.

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

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

**unresectable**
Cancer that can't be surgically removed.

# NCCN Contributors

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# NCCN Cancer Centers

For contact information, visit NCCN.org/cancercenters.

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*Philadelphia, Pennsylvania*

Case Comprehensive Cancer Center/
University Hospitals Seidman Cancer Center and
Cleveland Clinic Taussig Cancer Institute
*Cleveland, Ohio*

City of Hope National Medical Center
*Duarte, California*

Dana-Farber/Brigham and Women's Cancer Center |
Mass General Cancer Center
*Boston, Massachusetts*

Duke Cancer Institute
*Durham, North Carolina*

Fox Chase Cancer Center
*Philadelphia, Pennsylvania*

Fred & Pamela Buffett Cancer Center
*Omaha, Nebraska*

Fred Hutchinson Cancer Center
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Johns Hopkins Kimmel Cancer Center
*Baltimore, Maryland*

Mayo Clinic Comprehensive Cancer Center
*Phoenix/Scottsdale, Arizona*
*Jacksonville, Florida*
*Rochester, Minnesota*

Memorial Sloan Kettering Cancer Center
*New York, New York*

Moffitt Cancer Center
*Tampa, Florida*

O'Neal Comprehensive Cancer Center at UAB
*Birmingham, Alabama*

Robert H. Lurie Comprehensive Cancer Center
of Northwestern University
*Chicago, Illinois*

Roswell Park Comprehensive Cancer Center
*Buffalo, New York*

Siteman Cancer Center at Barnes-Jewish Hospital
and Washington University School of Medicine
*St. Louis, Missouri*

St. Jude Children's Research Hospital/
The University of Tennessee Health Science Center
*Memphis, Tennessee*

Stanford Cancer Institute
*Stanford, California*

The Ohio State University Comprehensive Cancer Center -
James Cancer Hospital and Solove Research Institute
*Columbus, Ohio*

The UChicago Medicine Comprehensive Cancer Center
*Chicago, Illinois*

The University of Texas MD Anderson Cancer Center
*Houston, Texas*

UC Davis Comprehensive Cancer Center
*Sacramento, California*

UC San Diego Moores Cancer Center
*La Jolla, California*

UCLA Jonsson Comprehensive Cancer Center
*Los Angeles, California*

UCSF Helen Diller Family Comprehensive Cancer Center
*San Francisco, California*

University of Colorado Cancer Center
*Aurora, Colorado*

University of Michigan Rogel Cancer Center
*Ann Arbor, Michigan*

University of Wisconsin Carbone Cancer Center
*Madison, Wisconsin*

UT Southwestern Simmons
Comprehensive Cancer Center
*Dallas, Texas*

Vanderbilt-Ingram Cancer Center
*Nashville, Tennessee*

Yale Cancer Center/Smilow Cancer Hospital
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**tumor** 19, 22–24, 26

**wide excision** 38–39, 50, 52, 54–58



# NCCN Guidelines for Patients®

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# Melanoma

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