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## Treating Melanoma Skin Cancer

If you've been diagnosed with melanoma, your treatment team will discuss your treatment options with you. It's important to weigh the benefits of each treatment option against the possible risks and side effects.

**How is melanoma skin cancer treated?**



the art cancer treatment. In some cases they may be the only way to get access to newer treatments. They are also the best way for doctors to learn better methods to treat cancer.

If you would like to learn more about clinical trials that might be right for you, start by asking your doctor if your clinic or hospital conducts clinical trials.

- [Clinical Trials](#)

## Considering complementary and alternative methods

You may hear about alternative or complementary methods to relieve symptoms or treat your cancer that your doctors haven't mentioned. These methods can include vitamins, herbs, and special diets, or other methods such as acupuncture or massage, to name a few.

**Complementary** methods are treatments that are used **along with** your regular medical care. **Alternative** treatments are used **instead of** standard medical treatment. Although some of these methods might be helpful in relieving symptoms or helping you feel better, many have not been proven to work. Some might even be harmful.

Be sure to talk to your cancer care team about any method you are thinking about using. They can help you learn what is known (or not known) about the method, which can help you make an informed decision.

- [Complementary and Integrative Medicine](#)

## Help getting through cancer treatment

People with cancer need support and information, no matter what stage of illness they may be in. Knowing all of your options and finding the resources you need will help you make informed decisions about your care.

Whether you are thinking about treatment, getting treatment, or not being treated at all,



- [Wide excision](#)
- [Lymph node dissection](#)
- [Surgery for metastatic melanoma](#)
- [More information about Surgery](#)

## Wide excision

When melanoma is diagnosed by [skin biopsy](#)<sup>1</sup>, more surgery will probably be needed to help make sure the cancer has been removed (excised) completely. This fairly minor operation will cure most thin melanomas.

Local anesthesia is injected into the area to numb it before the excision. The site of the tumor is then cut out, along with a small amount of normal skin around the edges (called the **margins**). The wound is usually stitched back together afterward. This will leave a scar.

The removed sample is then viewed with a microscope to make sure that no cancer cells were left behind at the edges of the skin that was removed.

Wide excision differs from an [excisional biopsy](#)<sup>2</sup>. The margins are wider because the diagnosis is already known. The recommended margins vary depending on the thickness of the tumor. Thicker tumors need larger margins (both at the edges and in the depth of the excision).

The margins can also vary based on where the melanoma is on the body and other factors. For example, if the melanoma is on the face, the margins may be smaller to avoid large scars or other problems. Smaller margins might increase the risk of the cancer coming back, so be sure to discuss the options with your doctor.

## Mohs surgery

Mohs surgery (also known as Mohs micrographic surgery, or MMS) might be an option for some very early-stage melanomas that are in areas where a wide excision would be hard to do (such as the face or ears). This type of surgery is used for melanomas that are in areas where a wide excision



limb swelling, which may or may not go away. If it's severe enough, it can cause skin problems and an increased risk of infections in the limb. Elastic stockings or compression sleeves can help some people with this condition. For more information, see [Lymphedema](#)<sup>7</sup>.

Lymphedema, along with the pain from the surgery itself, is a main reason why lymph node dissection is not done unless the doctor feels it is really necessary. Sentinel lymph node biopsy, however, is unlikely to have this effect. It's important to discuss the risks of side effects with your doctor before having either of these procedures.

## **Surgery for metastatic melanoma**

If melanoma has spread (metastasized) from the skin to other organs such as the lungs or brain, the cancer is very unlikely to be curable by surgery. Even when only 1 or 2 areas of spread are [found by imaging tests](#)<sup>8</sup> such as CT, MRI, or PET scans, there are likely to be others that are too small to be found by these scans.

Surgery is sometimes done in these circumstances, but the goal is usually to try to control the cancer rather than to cure it. If 1 or even a few metastases are present and can be removed completely, this surgery may help some people live longer. Removing metastases in some places, such as the brain, might also help prevent or relieve symptoms and improve a person's quality of life.

If you have metastatic melanoma and your doctor suggests surgery as a treatment option, be sure you understand what the goal of the surgery would be, as well as its possible benefits and risks.

## **More information about Surgery**

For more general information about surgery as a treatment for cancer, see [Cancer Surgery](#)<sup>9</sup>.

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#)<sup>10</sup>.

## **Hyperlinks**

1. [www.cancer.org/cancer/types/melanoma-skin-cancer/detection-diagnosis-](http://www.cancer.org/cancer/types/melanoma-skin-cancer/detection-diagnosis-)

- [staging/how-diagnosed.html](#)
2. [www.cancer.org/cancer/types/melanoma-skin-cancer/detection-diagnosis-staging/how-diagnosed.html](http://www.cancer.org/cancer/types/melanoma-skin-cancer/detection-diagnosis-staging/how-diagnosed.html)
  3. [www.cancer.org/cancer/types/skin-cancer/skin-biopsy-treatment-procedures/mohs-surgery.html](http://www.cancer.org/cancer/types/skin-cancer/skin-biopsy-treatment-procedures/mohs-surgery.html)
  4. [www.cancer.org/cancer/diagnosis-staging/lymph-nodes-and-cancer.html](http://www.cancer.org/cancer/diagnosis-staging/lymph-nodes-and-cancer.html)
  5. [www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/imaging-radiology-tests-for-cancer.html](http://www.cancer.org/cancer/diagnosis-staging/tests/imaging-tests/imaging-radiology-tests-for-cancer.html)
  6. [www.cancer.org/cancer/types/melanoma-skin-cancer/detection-diagnosis-staging/how-diagnosed.html](http://www.cancer.org/cancer/types/melanoma-skin-cancer/detection-diagnosis-staging/how-diagnosed.html)  
[www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html](http://www.cancer.org/cancer/managing-cancer/side-effects/swelling/lymphedema.html)
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# Immunotherapy for Melanoma Skin Cancer

Immunotherapy is the use of medicines to help a person's own immune system recognize and destroy cancer cells more effectively. Several types of immunotherapy can be used to treat melanoma.

[Immune checkpoint inhibitors](#)

response against melanoma cells.

They can be used to treat melanomas:

- That can't be removed by surgery
- That have spread to other parts of the body
- After surgery (as **adjuvant** treatment) for certain [stage II, III, or IV<sup>1</sup>](#) melanomas that have been removed completely, to try to lower the risk of the cancer coming back

treatments (although it may be given for longer when used as an adjuvant treatment).

### **LAG-3 inhibitor**

**Relatlimab** targets LAG-3, another checkpoint protein on certain immune cells that normally helps keep the immune system in check.

This drug is given along with the PD-1 inhibitor nivolumab (in a combination known as **Opdualag**). It can be used to treat melanomas that can't be removed by surgery or that have spread to other parts of the body.

This drug is given as an intravenous (IV) infusion, typically once every 4 weeks.

### **Possible side effects of immune checkpoint inhibitors**

Some of the more common side effects of these drugs can include fatigue, cough, nausea, skin rash, poor appetite, constipation, joint pain, and diarrhea.

Other, more serious side effects occur less often.

**Infusion reactions:** Some people might have an infusion reaction while getting these

melanomas when used alone. It is not used as much as in the past, because the immune checkpoint inhibitors are more likely to help people and tend to have fewer side effects. But IL-2 might be an option if these drugs are no longer working.

When treating advanced melanoma, IL-2 is given as intravenous (IV) infusions, at least at first. Some patients or caregivers may be able to learn how to give injections under the skin at home.

Side effects of IL-2 can include flu-like symptoms, such as fever, chills, aches, severe tiredness, drowsiness, and low blood cell counts. In high doses, IL-2 can cause fluid to build up in the body so that the person swells up and can feel quite sick. Because of this and other possible serious side effects, high-dose IL-2 is given only in the hospital, in centers that have experience with this type of treatment.

**For some earlier-stage melanomas:** Melanomas that have reached the nearby lymph nodes are more likely to come back in another part of the body, even if all of the cancer is thought to have been removed. IL-2 can sometimes be injected into the tumors (known as **intralesional therapy**) to help lower this risk. Side effects tend to be milder when IL-2 is injected directly into the tumor.

When deciding whether to use IL-2, it's important to consider the potential benefits and side effects of this treatment. Because of the risk of serious side effects, high-dose IL-2 is not usually a good option for people who have other serious health problems.

## Tumor-infiltrating lymphocyte (TIL) therapy

TILs are immune system cells called T cells that have entered (infiltrated) a tumor to attack the cancer cells. Treatments that use these cells can help shrink some melanomas. This type of treatment is also known as **tumor-derived autologous T cell immunotherapy**.

**Lifileucel (Amtagvi)** is a type of TIL therapy that can be used to treat people with advanced melanomas, after other treatments have been tried.

For this treatment, a melanoma tumor is removed with surgery and is sent to a lab, where the TILs are separated out and then multiplied over a few weeks. They are then sent back to be given to the person as an infusion into a vein (IV). Once in the body, the TILs seek out and attack the melanoma cells.

People getting this treatment are first given chemotherapy for about a week to help the body accept the TILs. After getting the TILs, the person is also given IL-2 (see above),

which helps these immune cells attack the cancer.

This treatment can cause serious or even life-threatening side effects, so it needs to be given in a hospital. Serious side effects can include:

- Very low blood cell counts, which can increase the risk of serious bleeding and infections
- Internal bleeding
- Serious infections
- Heart problems
- Lung problems
- Kidney problems
- [Infusion reactions](#)<sup>2</sup>

Other side effects are also possible, including fever, chills, feeling very tired, skin rash, low blood pressure, and diarrhea.

## Oncolytic virus therapy

Viruses are a type of germ that can infect and kill cells. Some viruses can be altered in the lab so that they infect and kill mainly cancer cells. These are known as **oncolytic viruses**. Along with killing the cells directly, the viruses can also alert the immune system to attack the cancer cells.

**Talimogene laherparepvec (Imlygic)**, also known as **T-VEC**, is an oncolytic virus that can be used to treat melanomas in the skin or lymph nodes that can't be removed with surgery. The virus is injected directly into the tumors, typically every 2 weeks. This treatment can sometimes shrink these tumors, and it might also shrink tumors in other parts of the body.

Side effects can include flu-like symptoms and pain at the injection site.

## Bacille Calmette-Guerin (BCG) vaccine

BCG is a vaccine that contains a germ related to the one that causes tuberculosis. BCG doesn't cause serious disease in humans, but it does activate the immune system. The BCG vaccine can be used to help treat stage III melanomas by injecting it directly into tumors, although it isn't used very often anymore.

## Imiquimod cream

Imiquimod (Zyclara) is a topical drug that is put on the skin as a cream. It stimulates a local immune response against skin cancer cells.

For very early (stage 0) melanomas in sensitive areas on the face, some doctors may use imiquimod if surgery isn't able to remove all of the tumor.

Imiquimod might also be an option to treat some melanomas that have spread along the skin, especially if surgery can't be done for some reason.

The cream is usually applied 2 to 5 times a week for around 3 months. Some people have serious skin reactions to this drug, and some might develop flu-like symptoms during treatment.

## Newer treatments

Some other types of immunotherapy have shown promise in treating melanoma in early studies. Other studies are now looking at combining different types of immunotherapy to see if it might help them work better. To learn more, see [What's New in Melanoma Skin Cancer Research?](#)<sup>3</sup>

## More information about immunotherapy

To learn more about how drugs that work on the immune system are used to treat cancer, see [Cancer Immunotherapy](#)<sup>4</sup>.

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#)<sup>5</sup>.

## Hyperlinks

1. [www.cancer.org/cancer/types/melanoma-skin-cancer/detection-diagnosis-staging/melanoma-skin-cancer-stages.html](http://www.cancer.org/cancer/types/melanoma-skin-cancer/detection-diagnosis-staging/melanoma-skin-cancer-stages.html)
2. [www.cancer.org/cancer/managing-cancer/side-effects/infusion-immune-reactions.html](http://www.cancer.org/cancer/managing-cancer/side-effects/infusion-immune-reactions.html)
3. [www.cancer.org/cancer/types/melanoma-skin-cancer/about/new-research.html](http://www.cancer.org/cancer/types/melanoma-skin-cancer/about/new-research.html)

4. [www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/immunotherapy.html)
5. [www.cancer.org/cancer/managing-cancer/side-effects.html](http://www.cancer.org/cancer/managing-cancer/side-effects.html)

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# Targeted Therapy Drugs for Melanoma Skin Cancer

Targeted drugs target parts of melanoma cells that make them different from normal cells. Targeted drugs work differently from standard chemotherapy drugs, which basically attack any quickly dividing cells.

- [Drugs that target cells with BRAF gene changes](#)
- [Drugs that target cells with C-KIT gene changes](#)
- [Drugs that target cells with other gene changes](#)
- [More information about targeted therapy](#)

Targeted drugs can be very helpful in treating advanced melanomas when the cancer cells have certain gene changes.

If you have melanoma that has spread beyond where it started, a [biopsy](#)<sup>1</sup> sample of it will likely be tested to see if the cancer cells have one of these gene changes. This is known as [biomarker testing](#)<sup>2</sup>.

## Drugs that target cells with *BRAF* gene changes

About half of all melanomas have changes (mutations) in the *BRAF* gene. Melanoma cells with these changes make an altered *BRAF* protein that helps them grow.



These drugs are taken as pills or capsules, typically once or twice a day.

Common **side effects** can include skin thickening, rash, itching, sensitivity to the sun, headache, fever, joint pain, fatigue, hair loss, and nausea. Less common but serious side effects can include heart rhythm problems, liver problems, kidney failure, severe allergic reactions, severe skin or eye problems, bleeding, and increased blood sugar levels.

Some people treated with these drugs develop new [squamous cell skin cancers](#)<sup>4</sup>. These cancers are usually less serious than melanoma and can be treated by removing them. Still, your doctor will want to check your skin often during treatment and for several months afterward. You should also let your doctor know right away if you notice any new growths or abnormal areas on your skin.

### **MEK inhibitors**

The *MEK* gene works together with the *BRAF* gene, so drugs that block MEK proteins can also help treat melanomas with *BRAF* gene changes. MEK inhibitors include **trametinib (Mekinist)**, **cobimetinib (Cotellic)**, and **binimetinib (Mektovi)**.

These drugs can be used to treat melanoma that has spread or can't be removed completely.

Trametinib can also be used along with dabrafenib after surgery in people with stage III melanoma, where it can help lower the risk of the cancer coming back.

Again, the most common approach is to combine a MEK inhibitor with a BRAF inhibitor. This seems to shrink tumors for longer than when using either type of drug alone. Some side effects (such as the development of other skin cancers) are actually *less* common with the combination.

MEK inhibitors are pills taken once or twice a day.

Common **side effects** can include rash, nausea, diarrhea, swelling, and sensitivity to sunlight. Rare but serious side effects can include heart, lung, or liver damage; bleeding or blood clots; vision problems; muscle damage; and skin infections.

### **Drugs that target cells with *C-KIT* gene changes**

A small portion of melanomas have changes in the *C-KIT* gene that help them grow. These changes are more common in melanomas that start in certain parts of the body:



5. [www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/targeted-therapy.html)
6. [www.cancer.org/cancer/managing-cancer/side-effects.html](http://www.cancer.org/cancer/managing-cancer/side-effects.html)

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# Chemotherapy for Melanoma Skin Cancer



infusion into a vein (IV). Some chemo drugs, such as temozolomide, can be taken by mouth as capsules.

**Isolated limb perfusion (ILP) and isolated limb infusion (ILI):** These are ways of giving chemo that are sometimes used to treat melanoma that is confined to an arm or leg but that can't be removed with surgery. The idea with this approach is to keep the chemo in the limb and not allow it to reach other parts of the body, where it could cause more side effects.

This is done during a surgical procedure. The blood flow of the arm or leg is cut off from the rest of the body, and a high dose of chemotherapy is circulated through the limb for a short time. This lets doctors give high doses to the area of the tumor without exposing other parts of the body to these doses.

To do this, a tube is placed into the artery that feeds blood into the limb, and a second tube is placed into the vein that drains blood from it.

- For **ILP**, the artery and vein are first surgically separated from the circulation to the rest of the body, and are then hooked up to tubes going to a special machine in the operating room.
- For **ILI**, long tubes (catheters) are inserted through the skin and into the artery and vein. This method is less complex and takes less time, and it might not require general anesthesia (where you are in a deep sleep).

In either approach, a tourniquet is tied around the limb to help make sure the chemo doesn't enter the rest of the body. Chemotherapy (usually with a drug called melphalan) is then infused into the blood in the limb through the artery. (This is done by the machine in ILP, and by using a syringe in ILI.) During the treatment session, the blood exits the limb through the tube in the vein, the chemo is added, and then the blood is returned back to the limb through the tube in the artery. (During ILP, the drug can also be heated by the machine to help the chemo work better.)

By the end of the treatment the drug is washed out of the limb, and the tubes are removed (and for ILP the blood vessels are stitched back together) so that the circulation is returned to normal.

## **Possible side effects of chemotherapy**

Chemo drugs can cause side effects. These depend on the type and dose of drugs given and how long they are used. The side effects of chemo can include:



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# Radiation Therapy for Melanoma Skin Cancer

- [How is radiation therapy given?](#)
- [Possible side effects of radiation therapy](#)
- [More information about radiation therapy](#)

## When might radiation therapy be used?

Radiation therapy is not needed for most people with melanoma on the skin, although it might be useful in certain situations:

- Radiation might be an option to treat some early-stage melanomas, if [surgery](#) can't be done for some reason.
- Radiation might be used after surgery (as an **adjuvant** treatment) in some situations if there's a high risk that the melanoma might come back. For example, it's often used after surgery for an uncommon type of melanoma known as **desmoplastic melanoma**, which has a higher risk of recurring after surgery alone.
- Sometimes, adjuvant radiation is given after surgery in the area where lymph nodes were removed, especially if many of the nodes contained cancer cells. This is to try to lower the chance that the cancer will come back.
- Radiation might be used to treat melanoma that has come back after surgery, either in the skin or lymph nodes, or to help treat distant spread of the disease.
- Radiation therapy can be used to relieve symptoms caused by the spread of melanoma to other parts of the body, especially to the brain or bones. Treatment with the goal of relieving symptoms is called [palliative therapy](#)<sup>1</sup>. Palliative radiation therapy is not expected to cure the cancer, but it might help shrink it or slow its growth for a time to help control some of the symptoms.

## How is radiation therapy given?

The type of radiation most often used to treat melanoma, known as **external beam radiation therapy**, focuses radiation from a source outside of the body on the cancer.

Before treatments start, your radiation team will take careful measurements to find the correct angles for aiming the radiation beams and the proper dose of radiation. This planning session is called **simulation**.

The treatment schedule can vary based on the goal of treatment and where the melanoma is.



The treatment itself is much like getting an x-ray, but the radiation is stronger. The procedure itself is painless. Each treatment lasts only a few minutes, although the setup

Radiation therapy to the brain can sometimes cause memory loss, headaches, trouble thinking, or reduced sexual desire. Usually, these symptoms are minor compared with those caused by a tumor in the brain, but they might still affect a person's quality of life.

## More information about radiation therapy

To learn more about how radiation is used to treat cancer, see [Radiation Therapy](#)<sup>2</sup>.

To learn about some of the side effects listed here and how to manage them, see [Managing Cancer-related Side Effects](#)<sup>3</sup>.

## Hyperlinks

1. [www.cancer.org/cancer/managing-cancer/palliative-care.html](http://www.cancer.org/cancer/managing-cancer/palliative-care.html)
2. [www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html](http://www.cancer.org/cancer/managing-cancer/treatment-types/radiation.html)
3. [www.cancer.org/cancer/managing-cancer/side-effects.html](http://www.cancer.org/cancer/managing-cancer/side-effects.html)

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# Treatment of Melanoma Skin Cancer, by Stage

The type of treatment(s) your doctor recommends will depend mainly on the [stage](#)<sup>1</sup> and location of the melanoma. But other factors can be important as well, such as the risk of the cancer returning after treatment, if the cancer cells have certain gene changes, and your overall health.

- [Treating stage 0 melanoma](#)
- [Treating stage I melanoma](#)
- [Treating stage II melanoma](#)
- [Treating stage III melanoma](#)
- [Treating stage IV melanoma](#)
- [Treating recurrent melanoma](#)

## Treating stage 0 melanoma

Stage 0 melanoma (melanoma in situ) has not grown deeper than the top layer. It has not grown

beyond the area where they started.

These cancers are typically treated by wide excision ([surgery](#) to remove the tumor as well as a margin of normal skin around it). The width of the margin depends on the thickness and location of the melanoma. Most often, no other treatment is needed.

Some doctors may recommend a [sentinel lymph node biopsy](#) (SLNB) to look for cancer in nearby lymph nodes, especially if the melanoma is stage IB or has other traits that make it more likely to have spread. You and your doctor should discuss this option.

**If the SLNB does not find cancer cells in the lymph nodes**, then no further treatment is needed, although close [follow-up](#)<sup>2</sup> is still important.

**If cancer cells are found on the SLNB** (which changes the cancer stage to stage III – see below), a lymph node dissection (removal of all lymph nodes near the cancer) might be recommended. Another option might be to watch the lymph nodes closely by getting an imaging test such as [ultrasound](#)<sup>3</sup> of the nodes every few months.

If the SLNB found cancer, adjuvant (additional) treatment with [immune checkpoint inhibitors](#) or [targeted therapy drugs](#) (if the melanoma has a *BRAF* gene mutation) might be recommended to try to lower the chance the melanoma will come back. Other drugs or perhaps vaccines might also be options as part of a [clinical trial](#)<sup>4</sup>.

## Treating stage II melanoma

Stage II melanomas have grown deeper into the skin than stage I melanomas, but they still haven't grown beyond the area in the skin where they started.

Wide excision ([surgery](#) to remove the melanoma and a margin of normal skin around it) is the standard treatment for these cancers. The width of the margin depends on the thickness and location of the melanoma.

Because the melanoma may have spread to nearby lymph nodes, many doctors recommend a [sentinel lymph node biopsy](#) (SLNB) as well. This is an option that you and your doctor should discuss.

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or *C-KIT* gene change), [immunotherapy](#), or chemotherapy.

Some stage III melanomas might be hard to cure with current treatments, so taking part in a [clinical trial](#)<sup>8</sup> of newer treatments might be a good option.

## Treating stage IV melanoma

Stage IV melanomas have already spread (metastasized) to other parts of the body, such as distant lymph nodes, areas of skin, or other organs.

Skin tumors or enlarged lymph nodes causing symptoms can often be removed by [surgery](#) or treated with [radiation therapy](#).

**If there are only a few metastases**, surgery to remove them might sometimes be an option, depending on where they are and how likely they are to cause symptoms. Metastases that can't be removed may be treated with radiation or with injections of the [T-VEC vaccine \(Imlygic\)](#) directly into the tumors. In either case, this is often followed by adjuvant treatment with medicines such as [immunotherapy](#) or [targeted therapy](#) drugs.

The **treatment of widespread melanomas** has changed in recent years as newer forms of immunotherapy and targeted drugs have been shown to be more effective than chemotherapy.

[Immunotherapy](#) drugs called **checkpoint inhibitors** are often the first treatment. These drugs can shrink tumors for long periods of time in some people. Options might include:

- Pembrolizumab (Keytruda) or nivolumab (Opdivo) alone
- Nivolumab combined with relatlimab (Opdualag)
- Nivolumab or pembrolizumab, plus ipilimumab (Yervoy)

Combinations of checkpoint inhibitors seem to be more effective, although they're also more likely to result in serious side effects, especially if they contain ipilimumab.

People who get any of these drugs need to be watched closely for serious side effects.

In about half of all melanomas, the cancer cells have ***BRAF* gene changes**. These melanomas often respond to treatment with [targeted therapy](#) drugs – typically a combination of a *BRAF* inhibitor and a *MEK* inhibitor. However, the immune checkpoint inhibitors mentioned above are often tried first, as this seems to be more likely to help for longer periods of time. Another option might be a combination of targeted drugs plus the immune checkpoint inhibitor atezolizumab (Tecentriq).

While immunotherapy is often used before targeted therapy, there might be situations where it makes sense to use targeted therapy first. For example, the targeted drugs are more likely to shrink tumors quickly, so they might be preferred in cases where this is important. In either case, if one type of treatment isn't working, the other can be tried.

A small portion of melanomas have changes in the *C-KIT* gene. These melanomas might be helped by targeted drugs such as imatinib (Gleevec) and nilotinib (Tasigna), although these drugs often stop working eventually.

Rarely, melanomas might have changes in other genes such as *NRAS*, *ROS1*, *ALK*, or the *NTRK* genes, which can be treated with targeted drugs.

**Immunotherapy** using other medicines might be an option if immune checkpoint inhibitors or other treatments aren't working. Options might include:

- Interleukin-2 (IL-2) (also known as aldesleukin)
- Lifileucel (Amtagvi), a type of tumor-infiltrating lymphocyte (TIL) therapy

These treatments can cause serious side effects in some people, so they are usually given in the hospital.

**Chemotherapy** (chemo) can help some people with stage IV melanoma, but other treatments are usually tried first. Dacarbazine (DTIC) and temozolomide (Temodar) are the chemo drugs used most often, either by themselves or combined with other drugs. Even when chemo shrinks these cancers, the cancer usually starts growing again over time.

It's important to carefully consider the possible benefits and side effects of any recommended treatment before starting it.

Because stage IV melanoma is often hard to cure with current treatments, people may want to think about taking part in a [clinical trial](#)<sup>9</sup>. Many studies are now looking at new targeted drugs, immunotherapies, and combinations of different types of treatments. (See [What's New in Melanoma Skin Cancer Research?](#)<sup>10</sup>)

## Treating recurrent melanoma

Treatment of melanoma that comes back after initial treatment depends on where in the body the melanoma is.

## Local recurrence

Melanoma might come back in the skin near the site of the original tumor, sometimes even in the scar from the surgery. In general, these local (skin) recurrences are treated with [surgery](#) similar to what would be recommended for a primary melanoma. This might include a [sentinel lymph node biopsy](#)<sup>11</sup> (SLNB). Depending on the results of the SLNB, other treatments might be recommended as well.

## In-transit recurrence

If melanoma recurs in nearby lymph vessels in or just under the skin (known as **in-transit recurrence**), it should be removed with surgery, if possible. Other options might include injections of the [T-VEC vaccine \(Imlygic\)](#), [interleukin-2 \(IL-2\)](#), or [Bacille Calmette-Guerin \(BCG\) vaccine](#) directly into the melanoma; [radiation therapy](#); or applying [imiquimod cream](#). For melanomas on an arm or leg, another option might be isolated limb perfusion or isolated limb infusion (infusing just the limb with [chemotherapy](#)). Other treatments might include [targeted therapy](#) (for melanomas with a *BRAF* or *C-KIT* gene change), [immunotherapy](#), or chemotherapy.

## Recurrence in nearby lymph nodes

If the nearby lymph nodes weren't removed during the initial treatment, the melanoma might come back in these lymph nodes. Lymph node recurrence is typically treated by [lymph node dissection](#) if it can be done, sometimes followed by adjuvant (additional) treatments such as [radiation therapy](#) and/or [immunotherapy](#) or [targeted therapy](#) (for cancers with *BRAF* gene changes). If surgery is not an option, radiation therapy or systemic treatment (immunotherapy, targeted therapy, or chemo) can be used.

## Recurrence in other parts of the body

Melanoma might also come back in distant parts of the body. Almost any organ can be affected. Most often, the melanoma comes back in the lungs, bones, liver, or brain. Treatment for these recurrences is generally the same as for stage IV melanoma (see above). Melanomas that recur on an arm or leg may be treated with isolated limb perfusion/infusion [chemotherapy](#).

Melanoma that comes back in the brain can be hard to treat. Single tumors can sometimes be removed by [surgery](#). [Radiation therapy](#) to the brain (stereotactic radiosurgery or whole-brain radiation therapy) may help as well. Systemic treatments ([immunotherapy](#), [targeted therapy](#), or chemo) might also be options.



As with other stages of melanoma, people with recurrent melanoma may want to think about taking part in a [clinical trial](#)<sup>12</sup> of newer treatments.

## Hyperlinks

1. [www.cancer.org/cancer/types/melanoma-skin-cancer/detection-diagnosis-staging/melanoma-skin-cancer-stages.html](http://www.cancer.org/cancer/types/melanoma-skin-cancer/detection-diagnosis-staging/melanoma-skin-cancer-stages.html)
  2. [www.cancer.org/cancer/types/melanoma-skin-cancer/after-treatment/follow-up.html](http://www.cancer.org/cancer/types/melanoma-skin-cancer/after-treatment/follow-up.html)
  3. [www.cancer.org/cancer/types/melanoma-skin-cancer/detection-diagnosis-staging/how-diagnosed.html](http://www.cancer.org/cancer/types/melanoma-skin-cancer/detection-diagnosis-staging/how-diagnosed.html)
  4. [www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html](http://www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-trials.html)
  5. [www.cancer.org/cancer/types/melanoma-skin-cancer/after-treatment/follow-up.html](http://www.cancer.org/cancer/types/melanoma-skin-cancer/after-treatment/follow-up.html)
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[https://www.nccn.org/professionals/physician\\_gls/pdf/cutaneous\\_melanoma.pdf](https://www.nccn.org/professionals/physician_gls/pdf/cutaneous_melanoma.pdf) on September 26, 2023.

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