

# **Treating Lymphoma of the Skin**

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

#### How is skin lymphoma treated?

Several types of treatment can be used for skin lymphoma. Some are directed only at the skin. Other treatments (systemic treatments) can affect the whole body.

- Skin-Directed Treatments for Skin Lymphomas
- Whole-Body (Systemic) Treatments for Skin Lymphomas

#### **Common treatment approaches**

Which treatments are used will depend on the type of lymphoma and its stage, as well as other factors such as your overall health and preferences. Treatment options are tailored to each person's situation.

Treatment for Specific Types of Skin Lymphoma

#### Who treats skin lymphomas?

Based on your treatment options, you might have different types of doctors on your

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.

treatments. Whether or not you continue treatment, there are still things you can do to help maintain or improve your quality of life.

Some people, especially if the cancer is advanced, might not want to be treated at all. There are many reasons you might decide not to get cancer treatment, but it's important to talk to your doctors as you make that decision. Remember that even if you choose not to treat the cancer, you can still get supportive care to help with pain or other symptoms.

If Cancer Treatments Stop Working

The treatment information given here is not official policy of the American Cancer Society and is not intended as medical advice to replace the expertise and judgment of your cancer care team. It is intended to help you and your family make informed decisions, together with your doctor. Your doctor may have reasons for suggesting a treatment plan different from these general treatment options. Don't hesitate to ask your cancer care team any questions you may have about your treatment options.

# Skin-Directed Treatments for Skin Lymphomas

For many skin lymphomas (especially early-stage lymphomas), the first treatment is directed at the skin lesions themselves, while trying to avoid harmful side effects on the rest of the body. There are many ways to treat skin lesions. Sometimes more than one type of treatment is used, either at the same time or one after another.

- Surgery
- Radiation therapy
- Phototherapy (UV light therapy)
- Topical medicines

# Surgery

Surgery is not usually the only treatment for skin lymphoma, but it can be helpful in some situations. Surgery may be used to <u>biopsy</u><sup>1</sup> a skin lesion, lymph node, or other

tissue to diagnose and classify a lymphoma. It might also be used to treat some types of skin lymphomas when there is only one or a few skin lesions that can be removed completely. Even then, other types of treatment may be used as well.

# **Radiation therapy**

Radiation therapy uses high-energy rays to kill cancer cells. The treatment is much like getting an x-ray, but the radiation is stronger. The procedure itself is painless. Treatment might be given in just one dose or on several days, depending on how much of the skin is being treated.

The type of radiation used most often for skin lymphomas is called **electron beam radiation**. The beam of electrons only penetrates as far as the skin, so there are few side effects to other organs and tissues. The main side effect of electron beam therapy is a skin reaction similar to a sunburn. For mycosis fungoides and Sezary syndrome covering a large part of the skin, electron beam therapy is sometimes given to the entire body. This is called **total skin electron beam therapy (TSEBT)**. Along with skin changes, this can sometimes cause loss of all hair on the body, dry skin, a reduced ability to sweat for several months, and even the loss of fingernails and toenails.

Some thicker lymphomas that are not widespread (especially single lesions) are treated with high energy radiation (like x-rays or gamma rays) instead of electrons. This kind of radiation can penetrate deeper into the body. Because it can damage internal organs, the treatment is planned carefully so that most of the radiation goes only to the skin.

To learn more, see <u>Radiation Therapy</u><sup>2</sup>.

# Phototherapy (UV light therapy)

Ultraviolet (UV) light is the higher-energy part of sunlight that causes sunburn and can lead to skin cancer. Phototherapy uses UV light to kill cancer cells in the skin. This is a

Some chemo drugs can be used to treat earlier forms of skin lymphoma by putting them directly on the skin (usually in a cream, ointment, or gel). The drugs most often used to treat skin lymphoma include mechlorethamine (nitrogen mustard) and carmustine (BCNU). Possible side effects include redness, swelling, or irritation where the drug is applied, as well as an 6u4 Tm 0 0 0 rg /GS229 gs (/F2 12 Tf 0 0 liskm)Tjo8 Tr typeem

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# Whole-Body (Systemic) Treatments for Skin Lymphomas

Systemic treatments can affect the whole body. They are most useful for more advanced or quickly growing skin lymphomas. In some cases, a systemic treatment is combined with a skin-directed treatment or with another systemic treatment.

- Photopheresis (photoimmune therapy)
- Systemic chemotherapy
- Targeted and biologic therapies
- Systemic retinoids
- High-dose chemotherapy with stem cell transplant (SCT)

# Photopheresis (photoimmune therapy)

This treatment is also called **extracorporeal photopheresis (ECP)**. It is sometimes used for T-cell skin lymphomas, especially <u>Sezary syndrome</u><sup>1</sup>. It is thought to work by killing some lymphoma cells directly, as well as by boosting the body's immune response against lymphoma cells.

The procedure is similar to donating blood, but instead of going into a collecting bag, the blood goes into a special machine that separates out the lymphocytes (including lymphoma cells). They are then treated with a psoralen (a light-sensitizing drug) and ultraviolet A (UVA) light before they are mixed back in with the rest of the blood and infused back into the person. Each procedure usually takes a few hours. Treatments are

typically given for 2 days in a row, and then repeated every few weeks or so.

Side effects are usually minor. The most significant side effect is sensitivity to sunlight for about a day after each treatment, which might result in sunburn or other problems. It's very important to protect yourself from sunlight as much as possible during this time.

# Systemic chemotherapy

Chemotherapy (chemo) uses strong drugs to treat cancer. When the drugs are injected into a vein or a muscle or taken by mouth, they enter the bloodstream and reach all areas of the body.

Systemic chemo is not often used for early skin lymphomas, but it may be used if the disease in the skin is more advanced and no longer getting better with other treatments. It can also be helpful if the lymphoma has spread to the lymph nodes, blood, or to other parts of the body.

Many chemo drugs can be useful in treating people with skin lymphoma, including:

- Gemcitabine
- Liposomal doxorubicin (Doxil)
- Methotrexate
- Chlorambucil
- Cyclophosphamide
- Fludarabine
- Cladribine
- Pentostatin
- Etoposide
- Temozolomide
- Pralatrexate

Often a single drug is tried first, but sometimes combinations of drugs are used, like those used for non-Hodgkin lymphoma not involving the skin.

Chemo treatments are given on different schedules, but usually they are repeated several times in cycles given 3 or 4 weeks apart. Most chemo treatments are given on an outpatient basis (in the doctor's office, clinic, or hospital outpatient department), but some require a hospital stay.

People often get chemo for 2 or 3 cycles and then have tests<sup>2</sup> (such as PET or CT

scans) to see if it is working. If the first chemo regimen doesn't seem to be working, different drugs may be tried.

For more information about chemo for non-Hodgkin lymphoma, see <u>Non-Hodgkin</u> <u>Lymphoma</u><sup>3</sup>.

#### Possible side effects of chemotherapy

Chemo drugs can cause side effects. These depend on the drugs used, their dose, and the length of treatment. Some common <u>side effects</u><sup>4</sup> include:

- Hair loss
- Mouth sores
- Loss of appetite
- Nausea and vomiting
- Diarrhea
- Increased chance of infection (from a shortage of white blood cells)
- Bleeding or bruising after minor cuts or injuries (from a shortage of platelets)
- Fatigue or shortness of breath (from a shortage of red blood cells)

These side effects usually go away after treatment is finished. If serious side effects occur, the chemo may have to be delayed or the doses reduced. There are often ways to lessen side effects. For example, drugs can be given to 180.58 Tm 0 0t1to 180.5revIf s g Ee ofte2 3

Side effects from this drug are usually mild, but some people might have serious side effects, such as an <u>infusion reaction</u><sup>10</sup> while getting the drug or a serious autoimmune reaction (in which the immune system attacks other organs in the body).

**Denileukin diftitox (Lymphir)**: This drug combines part of an interleukin-2 (IL-2) molecule with diphtheria toxin. The drug attaches to the IL-2 receptor on certain lymphocytes and lymphoma cells, where the diphtheria toxin can kill these cells.

Denileukin diftitox may be an option to treat people whose skin lymphoma has gotten worse (or come back) after another treatment. The drug is given as an infusion into a vein (IV) daily for 5 days in a row of a 21-day cycle.

Common side effects can include tiredness, nausea, fevers, chills, changes in liver tests, and swelling in the hands and feet. A rare but serious side effect is capillary leak syndrome (CLS), which can cause low blood pressure and possible organ damage.

# **Systemic retinoids**

Retinoids are drugs related to vitamin A. Retinoids such as acitretin, isotretinoin (Accutane), and bexarotene (Targretin) can be used to treat some skin lymphomas, especially mycosis fungoides and Sezary syndrome. Bexarotene can be used as a topical treatment when only a few small skin lesions are present, but retinoids are often taken in pill form for skin lymphomas that are more widespread.

Side effects of systemic retinoids can include headache, nausea, fever, increased blood levels of triglycerides (fats), thyroid problems, and eye problems. Some retinoids can cause more serious side effects, like fluid buildup in the body. These drugs should never be given to a woman who is pregnant or who might become pregnant, as they can cause serious birth defects.

# High-dose chemotherapy with stem cell transplant (SCT)

A stem cell transplant (SCT) is sometimes an option to treat lymphoma when standard treatments are no longer working.

The doses of chemotherapy (chemo) drugs normally are limited by the side effects these drugs can cause. Higher doses can't be used, even if they might kill more cancer cells, because they would severely damage the bone marrow, where new blood cells are made.

A stem cell transplant (also known as a bone marrow transplant) lets doctors give

higher doses of chemo (sometimes along with radiation therapy). This is because after getting high-dose chemo treatment, the patient receives a transplant of blood-forming stem cells to restore the bone marrow. The blood-forming stem cells used for a transplant can come either from the blood or from the bone marrow.

The main types of transplants, based on the source of the stem cells are:

**Allogeneic SCT:** For this type of transplant, the blood-forming stem cells come from another person (instead of using the patient's own stem cells). The ideal donor is a relative (often a brother or sister) whose tissue type (HLA type) matches the individual's. This lowers the chance of having serious problems with the transplant. This is often the preferred type of transplant if it can be done, but it is often hard to find a matched donor. Another drawback is that side effects of this treatment might be too severe for many older patients.

**Autologous SCT:** In this type of transplant, a patient's own stem cells are removed from their bone marrow or blood. They are collected over several days in the weeks before treatment. The cells are frozen and stored while the person gets treatment (high-dose chemo and/or radiation) and are then are reinfused (put back) into the patient's blood. Autologous transplants are not used much for skin lymphomas.

A stem cell transplant is a complex treatment that can cause life-threatening side effects. It should be done at a cancer center where the staff has experience with the procedure and with managing the recovery phase.

To learn more about stem cell transplants, including how they are done and their potential side effects, see <u>Stem Cell or Bone Marrow Transplant</u><sup>11</sup>.

# **Hyperlinks**

- 1. www.cancer.org/cancer/types/skin-lymphoma/about/types-of-skin-lymphoma.html
- 2. <u>www.cancer.org/cancer/types/skin-lymphoma/detection-diagnosis-staging/how-diagnosed.html</u>
- 3. www.cancer.org/cancer/types/non-hodgkin-lymphoma.html
- 4. www.cancer.org/cancer/managing-cancer/side-effects.html
- 5. <u>www.cancer.org/cancer/managing-cancer/side-effects/pain/peripheral-neuropathy.html</u>

- 7. <u>www.cancer.org/cancer/managing-cancer/treatment-types/biosimilar-</u> drugs/list.html
- 8. www.cancer.org/cancer/managing-cancer/side-effects/infections.html
- 9. <u>www.cancer.org/cancer/managing-cancer/treatment-</u> types/immunotherapy/immune-checkpoint-inhibitors.html
- 10. <u>www.cancer.org/cancer/managing-cancer/side-effects/infusion-immune-reactions.html</u>
- 11. <u>www.cancer.org/cancer/managing-cancer/treatment-types/stem-cell-</u> <u>transplant.html</u>

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- Local radiation treatments, if there is only one or a few lesions
- Total skin electron beam therapy (TSEBT) if MF covers most of the skin

Sometimes more than one type of skin-directed treatment is used.

**Systemic (whole-body) treatments:** Mycosis fungoides might stay just in the skin for many years. But eventually it might spread, which might require systemic treatment. Several types of treatment can be used, such as:

- Retinoids (taken by mouth)
- Targeted drugs like vorinostat (Zolinza) or romidepsin (Istodax)
- Photopheresis
- Interferons
- Brentuximab vedotin (Adcetris)
- Mogamulizumab (Poteligeo)
- Pembrolizumab (Keytruda)
- Low-dose methotrexate (a chemo drug)

Chemotherapy (usually with a single drug) or other medicines might also be options, but they are often reserved for lymphomas that are no longer responding to the treatments above. If single chemo drugs are not effective, combinations of drugs (similar to those used for other types of <u>non-Hodgkin lymphoma</u><sup>3</sup>) might be recommended.

More than one type of treatment might be used at the same time. This could include combinations of skin-directed and systemic treatments (such as TSEBT plus photopheresis) or combined systemic treatments (such as an oral retinoid plus interferon).

Many people can be helped by these treatments, sometimes for many years, but they rarely cure the lymphoma. If other treatments are no longer working, a <u>stem cell</u> <u>transplant</u><sup>4</sup> may be an option. Newer treatments are also being studied, so it might be worth considering entering a <u>clinical trial</u><sup>5</sup>.

#### Sezary syndrome

The systemic treatments used for advanced MF (see above) are also used to treat Sezary syndrome. This disease usually has spread beyond the skin at the time it is diagnosed, so treatments directed only at the skin are less useful than in MF (although some might still be part of treatment).

Photopheresis may be helpful in treating the disease, as may retinoids, such as bexarotene. The targeted drugs vorinostat (Zolinza) and romidepsin (Istodax) might also be used, as might interferon, brentuximab vedotin (Adcetris), or mogamulizumab (Poteligeo). Chemotherapy or other drugs such as alemtuzumab or pembrolizumab (Keytruda) might also be useful, but these are usually reserved for lymphomas that are no longer responding to other treatments. A stem cell transplant might be another option if other treatments are no longer working.

As with advanced MF, these treatments are often helpful for a time, but they rarely result in a cure. Newer treatments are now being studied, so it might be worth considering entering a <u>clinical trial</u><sup>6</sup> of one of these.

## Primary cutaneous anaplastic large cell lymphoma (C-ALCL)

This lymphoma usually stays confined to the skin. It can come back after treatment, but it seldom spreads inside the body and is rarely fatal. If it's not causing symptoms, it can often be watched closely without needing to be treated right away. The skin lesions may even go away on their own, without any treatment.

If treatment is needed, options depend on how extensive the lymphoma is:

- For single skin lesions (or small groups of lesions), surgery and/or radiation therapy are the most common options.
- If there are skin lesions in several places, the targeted drug brentuximab vedotin (Adcetris) or chemotherapy (often methotrexate, taken as a pill) is often the first treatment. Other chemotherapy, targeted therapy, or retinoid drugs might also be options, as well as radiation therapy (and possibly other skin-directed treatments).

If the lymphoma comes back in the same place after treatment, the same treatment often can be used again. If one treatment is no longer helpful, another can be tried.

If the lymphoma spreads to the lymph nodes or (rarely) internal organs, brentuximab vedotin (Adcetris), chemotherapy, or a combination of the two might be options. Sometimes radiation therapy might be given as well.

## Lymphomatoid papulosis

This disease often comes and goes on its own and usually has such a good outlook that treatment isn't needed right away, especially if the lesions aren't causing any symptoms. If treatment is needed, options depend on how extensive it is:

- If there are only a few skin lesions, topical corticosteroids or phototherapy is the most common treatment.
- If the lesions are more extensive, skin-directed treatments (such as phototherapy or topical chemotherapy or corticosteroids) or systemic treatments (such as oral retinoids or low-dose methotrexate) are options.

More intensive systemic therapies are rarely needed.

#### Subcutaneous panniculitis-like T-cell lymphoma

People with this rare type of lymphoma can live a long time and generally have an excellent outlook. This disease can often be controlled for long periods with just corticosteroids. Chemotherapy, radiation, or newer treatments might also be options, if needed.

#### Primary cutaneous peripheral T-cell lymphoma, rare subtypes

**Primary cutaneous gamma/delta T-cell lymphoma** tends to grow and spread very quickly. It is treated with systemic chemotherapy using a combination of drugs, but even with treatment it can often be hard to control.

**Primary cutaneous CD8+ aggressive epidermotropic cytotoxic T-cell lymphoma** usually grows quickly and is treated with systemic chemotherapy using a combination of drugs. Even with treatment, it can often be hard to control.

**Primary cutaneous acral CD8+ T-cell lymphoma** tends to grow slowly, and can usually be treated effectively with surgery or radiation therapy. It can sometimes come back, but it can often be treated again in the same way.

**Primary cutaneous CD4+ small/medium T-cell lymphoproliferative disorder** sometimes goes away on its own. If treatment is needed, it is usually surgery or radiation therapy, or by injecting a corticosteroid into the tumor. People with this lymphoma generally have a very good outlook, especially if they have only one tumor.

be less likely to work or more likely to cause side effects.

When a cancer comes back after treatment it is called <u>recurrent<sup>10</sup></u> or relapsed. In general, if a skin lymphoma comes back it tends to be in the skin. If this is the case, skin-directed therapies that haven't been used yet may be effective.

Some skin lymphomas eventually spread inside the body as well. Often, the lymph nodes are the first site of relapse. After that, the lymphoma might spread to organs such as the liver or spleen, or bone marrow. Different types of <u>systemic treatments</u> may be helpful in this situation. Chemotherapy might be used, especially if a person hasn't had chemo before. Depending on the type of lymphoma and treatments a person has had before, other options might include drugs such as vorinostat (Zolinza), romidepsin (Istodax), brentuximab vedotin (Adcetris), mogamulizumab (Poteligeo), or pembrolizumab (Keytruda). A stem cell transplant may be another option at some point.

Advanced skin lymphomas can be very hard to cure. Different systemic treatments may be effective for some time, but in general, the more treatments a person has had, the less likely it is that the next treatment will be helpful.

A good option for some people might be to consider entering a <u>clinical trial</u><sup>11</sup> that's testing a newer type of treatment. Many newer treatments are now being studied. For more info, see <u>What's New in Skin Lymphoma Research?</u><sup>12</sup>

# **Hyperlinks**

1. /cancer/skin-lymphoma/about/types-of-skin-lymphoma.html

- 8. <u>www.cancer.org/cancer/types/non-hodgkin-lymphoma/treating/b-cell-lymphoma.html</u>
- 9. www.cancer.org/cancer/types/non-hodgkin-lymphoma/treating/b-celllymphoma.html
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- 11. <u>www.cancer.org/cancer/managing-cancer/making-treatment-decisions/clinical-</u> <u>trials.html</u>
- 12. www.cancer.org/cancer/types/skin-lymphoma/about/new-research.html

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