Cutaneous T-Cell Lymphoma (CTCL): Staging and Treatment

What is staging for cancer?

Staging is the process of learning how much cancer is in your body and where it is. Tests like a skin biopsy, CT, MRI, and PET scan may be done to help stage your cancer. Your providers need to know about your cancer and your health so that they can plan the best treatment for you.

Staging looks at the size of the tumor and where it is on the skin, and if it has spread to other organs. There are a few different kinds of cutaneous T-cell lymphoma, making staging more complex. There are two main staging systems, as described by the International Society for Cutaneous Lymphomas (ISCL) and the European Organization for Research and Treatment of Cancer (EORTC):

- **TNMB system** for staging both mycosis fungoides and Sezary syndrome (the two most common types of CTCL).
  - T- describes how much of your skin is affected by the tumor.
  - N- describes if the cancer has spread to the lymph nodes.
  - M- describes if your cancer has spread to other organs (called metastases).
  - B- describes if there are lymphoma cells in your blood.

- **TNM system** for staging all other types of CTCL*. This system is newer and it is not clear how helpful it is for treatment options.
  - T- describes how much of your skin is affected by the tumor.
  - N- describes if the cancer has spread to the lymph nodes.
  - M- describes if your cancer has spread to other organs (called metastases).

*For these types of CTCL, if the lymphoma has spread to anywhere other than the skin (N and M), it will be staged as non-Hodgkin lymphoma and not a skin lymphoma.

How is cutaneous T-cell lymphoma staged?

Staging for cutaneous T-cell lymphoma is based on:

- How much of your skin is affected by the lymphoma.
- Any evidence of spread to other organs (metastasis).
- If your lymph nodes have cancer cells in them.

The staging system is very complex. Below is a summary. Talk to your provider about the stage of your cancer.

**TNMB System (for mycosis fungoides and Sezary syndrome)**

**Stage IA (T1, N0, M0, B0, or B1)**

- There are skin lesions but no tumors. Skin lesions cover less than 10% of the skin surface, the lymph nodes are not larger than normal, lymphoma cells have not spread to other organs, and there is not a high number of Sezary cells in the blood.

**Stage IB (T2, N0, M0, B0, or B1)**

- There are skin lesions but no tumors. Skin lesions cover at least 10% of the skin surface, the lymph nodes are not larger than normal, lymphoma cells have not spread to other organs, and there is not a high number of Sezary cells in the blood.
Stage IIA (T1 or T2, N1 or N2, M0, B0 or B1)

- There are skin lesions but no tumors. Skin lesions cover up to 80% of the skin surface. Lymph nodes are larger than normal, but the patterns of cells do not look too abnormal under the microscope. Lymphoma cells have not spread to other organs, and there is not a high number of Sezary cells in the blood.

Stage IIB (T3, N0 to N2, M0, B0 or B1)

- At least one of the skin lesions is a tumor that is 1 cm wide or bigger. The lymph nodes are either normal or are larger than normal, but the patterns of cells do not look too abnormal under the microscope. Lymphoma cells have not spread to other organs, and there is not a high number of Sezary cells in the blood.

Stage IIIA (T4, N0 to N2, M0, B0)

- Skin lesions cover at least 80% of the skin. The lymph nodes are either normal or are larger than normal, but the patterns of cells do not look too abnormal under the microscope. Lymphoma cells have not spread to other organs or tissues, and 5% or less of the lymphocytes in the blood are Sezary cells.

Stage IIIB (T4, N0 to N2, M0, B1)

- Skin lesions cover at least 80% of the skin. The lymph nodes are either normal or are larger than normal, but the patterns of cells do not look too abnormal under the microscope. Lymphoma cells have not spread to other organs, and there is a low number of Sezary cells in the blood.

Stage IVA1 (Any T, N0 to N2, M0, B2)

- Skin lesions can cover any amount of the skin. The lymph nodes are either normal or are larger than normal, but the patterns of cells do not look too abnormal under the microscope. Lymphoma cells have not spread to other organs, and there is a high number of Sezary cells in the blood.

Stage IVA2 (Any T, N3, M0, any B)

- Skin lesions can cover any amount of the skin surface. Some lymph nodes are larger than normal, and the patterns of cells look very abnormal under the microscope. Lymphoma cells have not spread to other organs. Sezary cells may or may not be in the blood.

Stage IVB (Any T, any N, M1, any B)

- Skin lesions can cover any amount of the skin surface. The lymph nodes may be normal or larger than normal, and Sezary cells may or may not be in the blood. Lymphoma cells have spread to other organs, like the liver or spleen.

TNM system for staging all other types of CTCL

This system does not assign an overall stage at the end. Instead, your provider will tell you the score from each lettered category: T, N, and M.

T1: There is only a single skin lesion.

- T1a: The skin lesion is less than 5 cm (about 2 inches) across.
- T1b: The skin lesion is at least 5 cm across.

T2: There are 2 or more lesions on the skin. These may be in a single body region or in 2 body regions that are next to each other.

- T2a: All of the skin lesions could be placed within a circle that is 15 cm (about 6 inches) across.
- T2b: The circle needed to surround all of the skin lesions is larger than 15 cm across but smaller than 30 cm (about 1 foot) across.
- T2c: The circle needed to surround all of the skin lesions is larger than 30 cm across.
T3: There are skin lesions in body regions that aren’t next to each other, or in at least 3 different body regions.

- **T3a:** There are skin lesions involving 2 body regions that aren’t next to each other.
- **T3b:** There are skin lesions involving 3 or more body regions.

N0: No lymph nodes are enlarged or contain lymphoma cells.

N1: There are lymphoma cells in the lymph nodes that drain an area where skin contained lymphoma.

N2: One of the following is true:

- At least 2 sets of lymph nodes from different areas contain lymphoma cells.
- There are lymphoma cells in lymph nodes that do not drain areas where the skin contained lymphoma.

N3: Lymph nodes deep inside the chest or abdomen contain lymphoma cells.

M0: No signs of lymphoma outside of the skin or lymph nodes.

M1: Lymphoma has spread to other organs or tissues.

**How is CTCL treated?**

Treatment for CTCL depends on many factors, like the type of CTCL, your cancer stage, age, overall health, and testing results. CTCL is a chronic disease for most patients, meaning you can live with this cancer for many years. There are more than 30 treatments for CTCL. Unlike a lot of other cancers, progression on one treatment does not mean that the same treatment won’t work better in the future. Your treatment may include some or all of the following:

- Topical therapies (medications put on the skin).
- Phototherapy (UV light).
- Systemic therapies (photopheresis, bexarotene, and various other medication therapies).
- Chemotherapy.
- Targeted therapy.
- Allogenic stem cell transplant.

**Topical therapies**

Topical therapies are put on the skin a few times a day as an ointment, cream, or gel to the affected areas. Corticosteroids can be used to treat small areas with few side effects but are not often applied to the whole body. They can cause thinning of the skin after long-term use.

- **Nitrogen Mustard (Mechlorethamine gel),** a chemotherapy agent, can be added to an ointment for large areas of the skin. It works by slowing or stopping the growth of cancer cells. Nitrogen Mustard can cause itching, redness, or rash and should be applied using gloves and only to the skin that is affected.
- **Topical retinoids** such as **bexarotene** and tazarotene affect how tumor cells are made and come in topical (gel) and oral (by mouth) formulations. Retinoids work by causing tumor cell death and boosting the immune reaction. Almost all patients taking **oral bexarotene** will develop hypothyroidism (underactive thyroid) and higher cholesterol levels, both of which can be treated with other medications. These problems get better on their own after the medication is stopped. Other side effects are headache, nausea, fatigue, and sun sensitivity. Diabetics may have hypoglycemia (low sugar) and should track their blood sugar carefully.

**Phototherapy (UV Light)**

Phototherapy, or UV light, uses a source of light to treat some skin diseases.

- **PUVA (psoralen plus UVA light) and UVB** are types of phototherapy.
  - **PUVA:** Psoralen, a photosensitizer, is given about 90 minutes before PUVA therapy to make the T cells more sensitive to the effects of the light. The skin is then exposed to UVA rays from a "lightbox" in the provider’s office.
The psoralen stays in the system for 24 hours, so you will need to protect your skin and eyes from sunlight during those 24 hours. There is an increased risk of cataracts and nausea from the psoralen and red, dry, or itchy skin from the UVA rays.

- **UVB therapy** does not penetrate the skin as deeply as UVA and can be used (without a photosensitizer) for thin skin lesions. Side effects include redness or burning of the skin.

As with any UVA/B exposure, there is a risk for melanoma and basal and squamous cell cancers due to this therapy.

- Electron beam **radiation therapy** is a type of x-ray therapy that delivers radiation to the outer layers of the skin, keeping deeper tissues safe from damage. This therapy helps with clearing the skin lesions and in some cases, can be given to the whole body. Side effects of therapy are skin burn, itching, and fatigue. Long-term effects can include skin cancers, changes in color or hair distribution, and a loss of sweat/oil secretion from the area treated.

### Systemic Therapies

Systemic therapies are those that treat the entire body by circulating through the bloodstream. These include photopheresis, bexarotene, and other medication therapies, which can be given alone or in combination with other systemic or topical therapies.

**Photopheresis** is used to treat patients with erythrodermic stage or blood involvement of the disease. It is basically a form of PUVA for the blood. You will have two IV catheters placed, one used to remove blood, the other to return the treated blood to your system. The blood is passed through a machine that separates the white blood cells from the rest of the blood, mixes them with a liquid form of psoralen (photosensitizer), exposes them to UVA light, and returns them to the body. The process damages the cancerous T cells, but other types of white blood cells resist this damage and help create an immune response in the body. The procedure takes 3-4 hours and is done on two consecutive days about once a month. It has minor side effects, including fever, increased skin redness, and dizziness.

**Interferons** are substances the body produces normally to rev up the immune system. By giving synthetic (manmade) forms of interferon-alpha (called interferon alfa 2b and alfa 2a), the body’s immune system is stimulated to attack the cancer cells. It is given by injection several times a week, often along with other therapies and may work well with photopheresis. Side effects are related to the stimulation of the immune system and include fever, chills, muscle aches, and fatigue—often called "flu-like" symptoms. Other side effects include depression, sleep disturbances, anxiety, hair loss, and nausea. If patients have stopped responding to interferon alfa, a synthetic form of interferon-gamma may be used.

**Chemotherapy** may be used in advanced cases of CTCL. Your provider will create a regimen for you including which drugs you will receive, the dose of each drug, and how often you will receive them. The first-line therapies often are brentuximab, gemcitabine, liposomal doxorubicin, or pralatrexate. Some other less common chemotherapies are chlorambucil, pentostatin, etoposide, cyclophosphamide, and temozolomide.

**Targeted therapies** attack a specific target found on the cancer cells, causing fewer side effects compared to traditional chemotherapy. Targeted therapies include Alemtuzumab and vorinostat.

**Allogeneic stem cell transplants** may be used in a small number of patients. Allogenic stem cell transplants are thought to be the only cure for advanced stages of CTCL.

### Clinical Trials

You may be offered a clinical trial as part of your treatment plan. To find out more about current clinical trials, visit the OncoLink Clinical Trials Matching Service.

### Making Treatment Decisions

Your care team will make sure you are included in choosing your treatment plan. This can be overwhelming as you may be given a few options to choose from. It feels like an emergency, but you can often take a few weeks to meet with different providers and think about your options and what is best for you. This is a personal decision. Friends and family can help you talk through the options and the pros and cons of each, but they cannot make the decision for you. You need to be comfortable
with your decision – this will help you move on to the next steps. If you ever have any questions or concerns, be sure to call your team.

You can learn more about lymphoma at OncoLink.org.

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