LYMPHOMA
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Getting the Facts

Helpline: (800) 500-9976
helpline@lymphoma.org

Cutaneous T-Cell Lymphoma

Overview

Lymphoma is the most common blood cancer. The two main forms of lymphoma are Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Lymphoma occurs when cells of the immune system called lymphocytes, a type of white blood cell, grow and multiply uncontrollably. Cancerous lymphocytes can travel to many parts of the body, including the lymph nodes, spleen, bone marrow, blood, or other organs, and form a mass called a tumor. The body has two main types of lymphocytes that can develop into lymphomas: B lymphocytes (B cells) and T lymphocytes (T cells).

T-cell lymphomas account for about seven percent of all NHLs in the United States. There are many different forms of T-cell lymphomas, some of which are extremely rare. Most T-cell lymphomas can be classified into two broad categories: *aggressive* (fast-growing) or *indolent* (slow-growing).

Cutaneous T-cell lymphoma (CTCL) is a general term for T-cell lymphomas that involve the skin. There are many subtypes of CTCLs and the most common ones are named mycosis fungoides (MF) and Sézary syndrome (SS). The next most frequent subtype is a spectrum of T-cell neoplasms called the CD30-positive lymphoproliferative disorders. Some of the rare CTCL subtypes can be very aggressive. The skin symptoms and appearance, and kind of treatment used, varies depending on the subtypes of CTCL.

MF and SS can involve the blood, lymph nodes, and other internal organs. Symptoms can include dry skin, itching (which can be severe), a red rash, and enlarged lymph nodes. The disease affects men more often than women and usually occurs in people in their 50s and 60s.

Types of CTCL

Mycosis Fungoides (MF) is the most common type of CTCL, accounting for approximately one-half of all CTCLs. The majority of patients with MF experience only skin symptoms. Early stage MF might not progress to later stages at all in some patients, while it might progress rapidly in others, with the cancer spreading to the lymph nodes, blood, and/or internal organs.

MF looks different in each patient, with skin symptoms that can appear as patches, plaques, tumors, or *erythroderma* (reddening of the skin). Patches are usually flat, possibly scaly, and look like a rash; plaques are thicker, raised, usually itchy lesions that are often mistaken for eczema, psoriasis, or dermatitis; and tumors are raised bumps or nodules, which may or may not *ulcerate* (develop into an ulcer). It is possible to have more than one type of lesion. Patients with erythrodermic MF have diffuse scaly red skin eruptions that can be very itchy.

A medical history, physical examination, and skin biopsy are essential for diagnosis. A physician will examine lymph nodes, order various blood tests, and may conduct other screening tests, such as blood flow cytometry or whole-body imaging study such as a computed tomography (CT) or positron emission tomography (PET) scan.

MF is difficult to diagnose in its early stages because the symptoms and skin biopsy findings are similar to those of other skin conditions. This disease is usually indolent and develops slowly.

Sézary Syndrome is characterized as generalized erythroderma and the presence of a significant number of lymphoma cells in the blood. Extensive thin, red, itchy rashes typically appear on the skin. In certain patients, patches and tumors appear. Patients often experience severe itching and frequently have skin infections with *Staphylococcus aureus*. Patients may also experience changes in their nails, hair, or eyelids, or have enlarged lymph nodes.

Many of the same procedures used to diagnose and stage other types of CTCLs are used in Sézary syndrome. In addition, blood for Sézary flow cytometry and whole-body imaging tests may be needed to determine and follow the severity of the disease in the blood and determine if the cancer has spread to the lymph nodes or other organs (although that rarely occurs). These tests may include a CT scan, a PET scan, and/or magnetic resonance imaging (MRI). A bone marrow biopsy may also be performed but is usually not necessary.

Treatment Options

Once the diagnosis is made, patients undergo a staging work-up to assess the extent of their lymphoma, which determines the final clinical stage and prognosis. Because it is a rare disease, management of CTCL should be done at centers with expert experience treating it or in partnership with such centers. Patients' clinical stage is the primary factor for selecting the optimal treatment. Many other factors are also considered to identify the most appropriate treatment for each patient, including the extent of skin involvement, the type of skin lesion, and whether the cancer involves the blood, lymph nodes, or other internal organs. The treatment is highly tailored for each patient, and may be adjusted frequently depending on the treatment response and tolerability.

For MF, treatment is either directed at the skin or the entire body (systemic). Many patients with early-stage CTCL live normal lives while they treat their disease, and some are able to remain in remission for long periods of time. However, the disease is not considered curative and follows a chronic course, with treatments adjusted to treat it when it is active. Patients with advanced-stage MF often require systemic therapies at some point in their treatment course, and those with high-risk disease may receive allogeneic blood stem cell transplantation.

Since Sézary syndrome is *systemic*, disease in which both blood and skin involvement is noted, it is usually not treated with skin-directed therapies alone. Treatments may be prescribed alone or in combination to achieve the best long-term benefit.

Skin-Directed Therapies are generally used for earlier stage disease and are typically useful for patches and limited plaques. These therapies include topical corticosteroids, topical chemotherapy (for example, mechlorethamine), topical retinoids, or imiquimod; local or total skin radiation therapy, and ultraviolet light. Among these, bexarotene gel (Targretin) and mechlorethamine gel (Valchor) have been approved by the U.S. Food and Drug Administration (FDA) as a topical treatment for Stages 1A and 1B mycosis fungoides in patients

who have received previous skin treatment. However, the most frequently used skin-directed treatment is topical corticosteroids at different strengths for different parts of the body and severity of the skin disease.

Systemic treatment may be used in more advanced-stage disease and in those with earlier-stage disease in whom skin-directed therapies did not help, were not tolerated, or are not available.

Systemic treatments include milder systemic agents such as bexarotene (retinoid), low-dose methotrexate, interferons, extracorporeal photopheresis (ECP), histone deacetylase inhibitors (romidepsin and vorinostat), brentuximab vedotin (antibody-drug conjugate), and single-agent chemotherapies. Combination chemotherapy regimens are reserved for those with *refractory* (does not respond to treatment) or advanced disease or who have severe/extensive extracutaneous involvement. Some of the systemic therapies can be combined to improve the response. Patients also often use skin-directed treatments in conjunction with systemic therapies. Systemic therapies in MF/SS include:

- Acitretin (Soriatane)
- Bexarotene capsules (Targretin)
- Brentuximab vedotin (Adcetris)
- Extracorporeal photopheresis
- Gemcitabine (Gemzar)
- Interferons (alpha or gamma)
- Liposomal doxorubicin
- Methotrexate tablets
- Pralatrexate (Folotyn)
- Romidepsin (Istodax)
- Vorinostat (Zolinza)

Treatments Under Investigation

Many treatments at various stages of drug development are currently being tested in clinical trials and for various stages of CTCL, including E7777, MRG-106, carfilzomib (Kyprolis), lenalidomide (Revlimid), anti-CD47 monoclonal antibody, anti-KIR3DL2 monoclonal antibody, and others. The antibody treatment, mogamulizumab received breakthrough therapy designation in 2017 from the FDA for the treatment of MF and SS.

It is critical to remember that today's scientific research is continuously evolving. Treatment options may change as new treatments are discovered and current treatments are improved. Therefore, it is important that patients check with their physician or with the Lymphoma Research Foundation (LRF) for any treatment updates that may have recently emerged.

Clinical Trials

Clinical trials are crucial in identifying effective drugs and determining optimal doses for patients with lymphoma. Patients interested in participating in a clinical trial should view the *Understanding Clinical Trials* fact sheet on LRF's website at www.lymphoma.org/publications, talk to their physician, or contact the LRF Helpline for an individualized clinical trial search by calling (800) 500-9976 or emailing helpline@lymphoma.org.

Follow-up

Patients with lymphoma should have regular visits with a physician who is familiar with their medical history and the treatments they have received. Medical tests (such as blood tests, CT scans, and PET scans) may be required at various times during *remission* (disappearance of signs and symptoms) to evaluate the need for additional treatment.

Some treatments can cause long-term side effects or late side effects, which can vary based on the duration and frequency of treatments, age, gender, and the overall health of each patient at the time of treatment. A physician will check for these side effects during follow-up care. Visits may become less frequent the longer the disease remains in remission.

Patients and their caregivers are encouraged to keep copies of all medical records and test results as well as information on the types, amounts, and duration of all treatments received. This documentation will be important for keeping track of any side effects resulting from treatment or potential disease recurrences. LRF's award-winning *Focus On Lymphoma* mobile app (www.FocusOnLymphoma.org) can help patients manage this documentation.

Resources

LRF offers a wide range of resources that address treatment options, the latest research advances, and ways to cope with all aspects of lymphoma including our award-winning mobile app. LRF also provides many educational activities, from in-person meetings to teleconferences and webcasts for people with lymphoma, as well as patient guides and e-Updates that provide the latest disease-specific news and treatment options. To learn more about any of these resources, visit our website at www.lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.

The Cutaneous Lymphoma Foundation is dedicated to supporting every person affected by cutaneous lymphoma by promoting awareness and education, advancing patient care and fostering research for the best possible outcomes. To accomplish this, the Foundation provides an array of resources for patients, caregivers and physicians, including guide books, an online learning center with current videos and articles, as well as numerous live events for in-depth learning and social networking. For more information about this independent nonprofit patient advocacy organization please visit: www.clfoundation.org.

Contact the Lymphoma Research Foundation
Helpline: (800) 500-9976
helpline@lymphoma.org
Website: www.lymphoma.org
Email: LRF@lymphoma.org

Medical reviewer:
Youn H. Kim, MD
Stanford University

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