LEUKEMIA & LYMPHOMA SOCIETY®

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Cutaneous T-Cell Lymphoma

Revised **2019**

Support for this publication provided by SeattleGenetics®

A six-word narrative about living with blood cancer from patients in our LLS Community

Stay strong and keep moving forward. Find the positive in every day. Be your own best patient advocate. Changed my life for the better. Accept, learn and focus on present. Learning to live a different life. Sudden and life changing—be positive. Waiting, worrying, anxiousness/ happy I'm alive! Embrace a new normal each day. 5 years, 41 infusions, constant fatigue. Patience, positive attitude, hope and faith. Test to test, I will survive! Treatment, fatigue, treatment, fatigue and survival. Love life, live better every day. I don't look back only forward. So far, so good, live life. Meditation, mindfulness, wellness, faith, nutrition and optimism. Finding the joy while living with uncertainty. Watch, wait, treat, regroup, rest, re-energize. Blessed to be doing so well! Eye opening needed learning and healing. Feel great: uncertain travel plans annoying. Renewed faith, meditation, diet, mindfulness, gratitude. Watchful waiting can be watchful worrying. Scary, expensive, grateful, blessings, hope, faith. Thank god for stem cell transplants! Do not know what to expect. Extraordinarily grateful, I love my life. Diagnosed; frightened; tested; treating; waiting; hoping. I'm more generous, impatient less often. Embrace your treatment day after day. Live today, accept tomorrow, forget yesterday. Strength you never realized you had. Challenging to our hearts and minds. Life is what we make it. Live life in a beautiful way.

Discover what thousands already have at **www.LLS.org/Community**

Join our online social network for people who are living with or supporting someone who has a blood cancer. Members will find

- Thousands of patients and caregivers sharing experiences and information, with support from knowledgeable staff
- Accurate and cutting-edge disease updates
- The opportunity to participate in surveys that will help improve care.

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Acknowledgement

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Drugs may have been approved since this book was printed. Check www.LLS.org/DrugUpdates or call (800) 955-4572.

Introduction

Lymphomas are cancers that originate in the lymphatic system, specifically from a type of white blood cell called a "lymphocyte." The lymphatic system is an important part of the immune system and consists of the bone marrow, lymph nodes, thymus, liver, skin and spleen. Lymphocytes are present in almost every organ. Therefore, lymphomas can begin to grow in any organ system, including the skin (which is considered the largest lymphoid organ in the human body). There are three different types of lymphocytes, each with a distinct function: B lymphocytes (B cells) that make antibodies to fight infections, T lymphocytes (T cells) that provide a response to specific threats posed by viruses and possibly cancers, and natural killer (NK) cells that are part of the innate immune response. It is important to determine the cell of origin, the B cell, T cell or NK cell, because that information determines the particular type of lymphoma and how to classify it.

Classification of lymphomas is forever evolving; however, they are broadly divided into two major categories: Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Depending on the cell of origin, NHL can be subdivided into over 80 subtypes with differing growth patterns and biology. Treatment approaches for these subtypes vary, so it is important to know the patient's NHL subtype. When NHL begins in the skin (not in another part of the lymphatic system such as the lymph nodes, organs or lymph tissue) it is called a "cutaneous (skin) lymphoma." A lymphoma that begins in the lymph nodes or another part of the body and then spreads to the skin is not considered a cutaneous lymphoma because it did not start in the skin. B-cell lymphomas have a higher incidence than T-cell lymphomas except in the skin.

While there are several types of CTCLs, this booklet provides descriptions of the two main types: mycosis fungoides (MF) and Sézary syndrome (SS). It also includes specific information on the diagnosis and treatment of these diseases, new treatments undergoing investigation in clinical trials and support resources.

For additional free information about NHL subtypes, please see the LLS booklet *Non-Hodgkin Lymphoma*.

About Cutaneous T-Cell Lymphoma (CTCL)

Cutaneous T-cell lymphomas (CTCLs) result from a malignant change that occurs in a single T cell located in the skin. These changes cause a normal, healthy T cell to start growing and dividing uncontrollably. These cells accumulate in the skin and show up as skin abnormalities called "skin lesions." The original cancerous T cell (and all clones of that cell) can easily be distinguished from healthy cells by various laboratory techniques including molecular methods. The skin lesions contain cancerous T cells, but the skin cells themselves are not cancerous. In certain CTCLs, these cancerous T cells may also circulate in the bloodstream (as they do in Sézary syndrome) or they may accumulate in the lymph nodes or other internal organs.

Cutaneous T-cell lymphomas are a rare group of non-Hodgkin lymphomas. While approximately 74,680 new cases of NHL are expected to be diagnosed in the United States in 2018, CTCLs account for approximately 4 percent of all NHL cases. Cutaneous T-cell lymphoma is twice as common in men as in women and it is most common in African Americans. The incidence of CTCL increases with age, with an average onset between 50 and 60 years. Rarely, it can affect children and young adults.

Cutaneous T-cell lymphomas have various signs and symptoms, treatment options and outcomes. The two most common types of CTCL are mycosis fungoides (MF) and Sézary syndrome (SS). Other less common CTCL subtypes include

- Cutaneous cluster of differentiation (CD) 30+ (CD30+) expressing anaplastic large-cell lymphoma
- Panniculitislike T-cell lymphoma
- Cutaneous CD8+ expressing aggressive epidermotropic T-cell lymphoma
- Gamma-delta (**γ-δ**)T-cell lymphoma.

A smaller number of skin lymphomas arise from malignant changes in B lymphocytes and are referred to as "cutaneous B-cell lymphomas." In most cases, patients with B-cell lymphomas respond well to treatment and have relatively good outcomes. See **Table 1**, on *page 4*.

Mycosis fungoides accounts for approximately 50 to 70 percent of CTCLs. The name comes from the mushroomlike skin tumors that may appear in the advanced stages of the disease although the disease is not related to a fungus. For most patients, MF progresses slowly. It may start with dry skin and a red rash, either with or without itching. In its earliest stage, it can be difficult to diagnose because of its resemblance to other skin conditions. There may be red patches or raised areas of the skin that often have scaling on the surface and cover either small or large portions of the skin. Large bumps or tumor

World Health Organization—European Organization for Research and Treatment of Cancer Classification for Cutaneous Lymphomas

Cutaneous T-cell and NK-cell lymphomas

- Mycosis fungoides
  - Mycosis fungoides variants and subtypes
  - Folliculotropic mycosis fungoides
  - Pagetoid reticulosis
  - Granulomatous slack skin
  - Hypopigmented/vitiligenous MF
- Sézary syndrome
- Adult T-cell leukemia/lymphoma
- Primary cutaneous CD30+ lymphoproliferative disorders
  - Primary cutaneous anaplastic large cell lymphoma
  - Lymphomatoid papulosis
- Subcutaneous panniculitis-like T-cell lymphoma
- Extranodal NK/T-cell lymphoma, nasal type
- Primary cutaneous peripheral T-cell lymphoma, rare subtypes
  - Primary cutaneous gamma-delta T-cell lymphoma
  - Primary cutaneous aggressive epidermotropic CD8+ T-cell lymphoma (provisional)
  - Primary cutaneous CD4+ small/medium-sized pleomorphic T-cell lymphoproliferative disorder (provisional)
  - Primary cutaneous acral CD8+ T-cell lymphoma (provisional)
- Primary cutaneous peripheral T-cell lymphoma, not otherwise specified

Cutaneous B cell lymphomas

- Primary cutaneous marginal zone B-cell lymphoma
- Primary cutaneous follicle center lymphoma
- Primary cutaneous diffuse large B-cell lymphoma, leg type

Abbreviations: MF, mycosis fungoides; SS: Sézary syndrome; CD: cluster of differentiation; NK: natural killer; acral: affecting extremities such as hands, feet, nose and ears.

Table 1. Classification from the World Health Organization and the European Organization for Research and Treatment of Cancer. Source: UpToDate (2018). Table 1 Frequency and prognosis of main types of primary cutaneous lymphomas according to the 2018 revision of the WHO-EORTC classification from the article Classification of primary cutaneous lymphomas. www.uptodate.com/contents/classification-of-primary-cutaneous-lymphomas

nodules with significant thickness may develop initially or later in disease progression. For most patients, MF remains confined to the skin and does not spread to the lymph nodes or internal organs. Sometimes lymph nodes can enlarge in the vicinity of skin lesions due to a response to infection or inflammation associated with the skin lesion. These are called “dermatopathic nodes” and do not indicate spread of the actual cancer.

Sézary syndrome is a leukemic form of CTCL and is more difficult to treat. It accounts for only 1 to 3 percent of CTCLs. The disease is characterized by

- Generalized redness of the skin called “erythroderma” along with severe itching (pruritus)
- Enlarged lymph nodes and the presence of circulating malignant T cells (the Sézary cells) found in the bloodstream that match the malignant clone present in the skin.

These patients, like leukemia patients, can present with a very high white blood cell count. Sézary syndrome tends to have more aggressive features than the typically slower-growing MF, and it can result in markedly reduced median survivals in affected patients. These SS patients need specific treatment approaches that are different from those used for other CTCL subtypes.

Due to the rarity and heterogeneity of the disease, there are no hard and fast guidelines for either diagnosis or therapy. The disease, particularly in the early stages, can mimic other skin conditions and can remain undiagnosed for years. It is recommended that patients either be treated or at least get a second opinion at a medical center specializing in the diagnosis and treatment of cutaneous lymphomas. **See the free LLS booklet *Choosing a Blood Cancer Specialist or Treatment Center* for more information.**

Signs and Symptoms

The signs and symptoms of cutaneous T-cell lymphomas (CTCLs) vary depending on the type. In mycosis fungoides (MF) the lesions tend to start in sun-protected areas of the body and may vary from either a single or a few lesions to extensive skin involvement, even at the patient’s first presentation. The lesions may come and go adding to the complexity of diagnosis. Types of skin lesions seen in patients with MF include

- Patches—flat, scaly, pink or red areas on the skin. Patches are flat but may be scaly. They can disappear and reappear or remain stable. They may be hypopigmented.
- Papules—small, solid, raised bumps on the skin by hair follicles. Papules may be red, pink, purple or brown.

- Plaques—abnormal, thickened patches of skin that are raised or hard. They can be smooth, scaly, crusted or ulcerated. They are typically red, purple or brown in color.
- Tumors—solid dome-shaped masses at least 1 cm in size. They are raised nodules that are thicker and deeper than plaques.
- Erythroderma—redness of the skin covering more than 80 percent of the skin surface. This condition may lack distinct skin lesions.

Mycosis fungoides often progresses slowly. It may manifest as a few areas of either patches or plaques that persist for many years. The disease may be difficult to diagnose as the appearance of the skin lesions tend to resemble other benign skin conditions. Other manifestations may involve more extensive lesions and a more rapid pace of progression to advanced stages. Patients with these lesions will show evidence of plaques and tumors early on in the course of the disease. The pace of the disease can shift during the course at any time. Thicker tumors that are extensive, ulcerate and subsequently become infected and painful are hallmarks of more advanced stages of CTCL. Lymphadenopathy (enlarged lymph nodes), especially if shown to be due to an accumulation of malignant cells, indicates a more advanced stage. Rarely, the tumor cells can metastasize (spread) to other organs.

Blood involvement can vary from minimal to extensive resulting in Sézary syndrome (SS). It is important to note that blood involvement with the malignant clone may be seen in the earliest stages of the disease and may require special testing to be identified. See *Diagnosis* on *page 7*.

Sézary syndrome is characterized by erythroderma, an extensive red, severely itch rash that covers more than 80 percent of the skin surface. There may also be patches, plaques or tumors on the skin. Other common signs and symptoms of SS may include

- Thickened skin on the palms of the hands and the soles of the feet
- Abnormalities of the fingernails and toenails
- Swelling of the skin
- Hair loss
- Enlarged lymph nodes
- A high white blood cell count.

Diagnosis

A diagnosis of mycosis fungoides (MF) can only be made by performing a series of tests on a biopsy of a suspicious skin lesion. A diagnosis of Sézary syndrome (SS) requires specific signs and symptoms and the presence of a specific amount of Sézary cells in the bloodstream. Early MF lesions cannot easily be distinguished from other benign (noncancerous) conditions, either on a clinical basis or on microscopic examination. Sometimes it takes the intuition of an astute dermatologist to suspect MF and to order the specific tests that are necessary to confirm an MF diagnosis. It is very important for the patient to consider getting a second opinion from a center with appropriate expertise in the diagnosis and treatment of cutaneous lymphomas. This includes a clinical evaluation by a dermatologist as well as review of the skin biopsy slides by a dermatopathologist. The following tests and procedures are used to confirm a diagnosis of MF and SS.

Medical History. A complete medical history should focus on information about a person's health including past illnesses, injuries, treatments and medications. Often, people with MF have had skin lesions for months or even years before being diagnosed with the disease.

Physical Examination. The physical examination should involve a complete skin examination of the entire body including the scalp, between the legs, and between the fingers and toes. The doctor will observe the type of skin lesions and determine the percentage of skin that is affected. Lymph node evaluation by palpation (feeling with the fingers and hands during an exam) of neck, armpits and groin as well as an assessment of an enlarged liver or spleen is essential. Other systems may need examination based on the patient's presenting symptoms.

Skin Biopsy. A skin biopsy is crucial for correct diagnosis. It is a simple procedure that can be performed in the office under mild local anesthesia. Depending on the number and type of lesions, multiple biopsies may be taken at the time of diagnosis. The sample is then sent to a laboratory for the following tests:

- Histology—the study of tissues and cells under the microscope. The pathologist studies the size and shape of the cells and how they are arranged in the layers of skin and around other structures such as hair follicles. There may be patterns of abnormal cells that are characteristic of MF but it is not always the case and further tests may be needed to confirm the diagnosis. Subtypes of MF such as folliculotropic MF, pagetoid reticulosis, or granulomatous slack skin can also be determined by the histologic examination. Transformed MF indicates genetic progression of the cancer. Transformed MF lesions have an aggressive clinical course.

- Immunophenotyping—a test that is used to classify cells based on the type of proteins (markers) on the surface of the cells. Malignant cells in cutaneous lymphomas, including MF and SS cells, have a characteristic surface protein pattern that allow them to be differentiated from healthy T cells and other types of leukemia and lymphoma. Typically, MF or SS have T cells that test positive for specific proteins, cluster of differentiation (CD) 2, CD3, CD4, CD5 and they lack certain T-cell markers, CD7 and CD26. However, there are some subtypes of MF that test positive for CD8 (especially the hypopigmented variant). In most MF cases, CD30 is found on at least a few cells but it can be more heavily expressed in the large transformed cells.
- Molecular testing—makes use of very sensitive DNA (deoxyribonucleic acid) tests that identify specific genetic mutations in the cancerous cells. Often patients with MF and SS have rearrangements in the clonal *TCR* (T-cell receptor) genes that are unique to that patient's cancer and are used to establish clonality. This test may be valuable to confirm a diagnosis when histology and immunophenotyping cannot clearly confirm a diagnosis.

- **Blood tests.** Laboratory studies should include
  - A complete blood count (CBC) with differential
  - A Sézary screen to identify the number of abnormally shaped Sézary cells in the blood—under the microscope a Sézary cell has a characteristic large flower-shaped nucleus so SS cells can be identified and counted. Healthy people may have a very small number of cells that look like Sézary cells in their blood. There are more sensitive tests that are used to find cancerous circulating T cells in the bloodstream such as flow cytometry (to look for the unique expression of proteins on the surface of the cells) and molecular testing. Subtle involvement of blood that does not meet criteria of SS can also alter the determination of the SS stage and the prognosis of the patient. It can be present in the earliest stages of disease.
  - An assessment of lactate dehydrogenase (LDH) levels—LDH is one of a group of enzymes found in the blood. An elevated LDH level may be a sign of tissue damage and is a nonspecific marker for aggressive lymphomas. It may be elevated in cases of transformed or advanced-stage MF.
  - Molecular testing of lymphocytes in the blood for rearrangements of the clonal *TCR* gene
  - Evaluations of liver and kidney function—important evaluations that help to identify optimal therapies for the patients who may need systemic treatments
  - Serum testing—it is recommended that serum is tested for the presence of human immunodeficiency virus (HIV), human T-lymphotropic virus 1 (HTLV-1) and infectious hepatitis B and C. Serum is collected from blood draws.

Lymph Node Biopsy. It is important to evaluate enlarged lymph nodes for the presence of disease. Optimal testing requires removal of the entire node for complete evaluation by the pathologist as the malignant cells need to be examined along with any changes present in the node. In cases where it is not clinically feasible to obtain a full excisional (removal of the whole node) biopsy, a core biopsy may be performed using a thick needle to obtain adequate tissue sampling. A fine needle aspiration is not very useful and should not be used to establish a diagnosis of any lymphoma. Once an adequate tissue sample has been obtained, it is reviewed by an expert hematopathologist using microscopic evaluations to look at the structure and distribution of the malignant T cells, analyze the immunophenotype and test for rearrangements of the clonal *TCR* gene.

Imaging Tests. Imaging tests are done to obtain detailed pictures of areas inside the body. They help to detect any cancer that has spread inside the body so that the doctor can determine the stage of the cancer (see more information on *Staging, below*) and plan appropriate treatment. Appropriate staging tests for lymphomas consist of computed tomography (CT) scans, fluorodeoxyglucose-positron emission tomography (FDG-PET) scans, or magnetic resonance imaging (MRI), and ultrasonography. Not all patients who have cutaneous lymphomas need imaging with scans and the determination is made by the treating doctor. Imaging tests are recommended for patients with significant skin lesions, enlarged lymph nodes, abnormal blood test results, large-cell transformation and MF folliculotropic subtype.

Treatment Planning

Optimal management of cutaneous lymphoma involves a collaborative, multidisciplinary approach between the dermatologist, dermatopathologist, hematologist-oncologist and a radiation oncologist at every stage of the disease. It is important for patients and members of their medical team to discuss all treatment options, including treatments being studied in clinical trials.

Staging. Once mycosis fungoides (MF) or Sézary syndrome (SS) is diagnosed, doctors will perform tests to see if the cancer has spread, and if so, how far. This process is called “staging.” Doctors may use the findings from physical examinations, laboratory tests and imaging tests to determine the extent of the cancer within the body. Staging helps the patient and doctor plan the best treatment.

The International Society for Cutaneous Lymphomas (ISCL) and the European Organization for Research and Treatment of Cancer (EORTC) have developed a standard staging system for MF and SS (see **Table 2** on *page 11*) based on the classification of the following four factors:

- T (tumor)—refers to the percentage of skin affected by the lymphoma and the type of lesions
- N (node)—describes the level of lymphoma in the lymph nodes
- M (viscera [internal organs])—refers to organ involvement
- B (blood)—refers to the number of lymphoma cells in the blood.

The physical examination, laboratory and imaging data are used to determine the T, N, M and B status (disease classification) of a patient and then T, N, M, B are grouped according to class and assigned a stage that ranges from one (I) through four (IV). See **Table 3**, on *page 12*. A higher stage indicates more extensive tumor. Each stage may further be divided into categories using letters "a" and "b." Within a stage, "A" refers to a lower stage while "B" refers to a higher stage.

Stage I

- Stage IA (T1, N0, M0, B0 or B1)—less than 10 percent of the skin surface is covered with patches, papules and/or plaques but no skin tumors. The lymph nodes are not enlarged, lymphoma cells have not spread to other organs. There can be minimal blood involvement.
- Stage IB (T2, N0, M0, B0 or B1)—10 percent or more of the skin surface is covered with patches, papules and/or plaques but no skin tumors. The lymph nodes are not enlarged, lymphoma cells have not spread to other organs and the number of Sézary cells in the blood is low.

Stage II

- Stage IIA (T1 or T2, N1 or N2, M0, B0 or B1)—up to 80 percent of the skin surface is covered with patches, papules and/or plaques but no skin tumors. Lymph nodes are enlarged but do not contain cancerous cells. Lymphoma cells have not spread to other organs, and the number of Sézary cells in the blood is not high.
- Stage IIB (T3, N0 to N2, M0, B0 or B1)—At least one of the skin lesions is a tumor. Lymph nodes may be enlarged but do not contain cancerous cells. Lymphoma cells have not spread to other organs, and the number of Sézary cells in the blood is not high.

Stage III

- Stage IIIA (T4, N0 to N2, M0, B0)—skin lesions cover at least 80 percent of the skin. The lymph nodes are either normal or are enlarged but do not contain cancerous cells. Lymphoma cells have not spread to other organs and the number of Sézary cells in the blood is not high.

- Stage IIIB (T4, N0 to N2, M0, B1)—skin lesions cover at least 80 percent of the skin. Lymph nodes may be enlarged but do not contain cancerous cells. More than 80 percent of the skin is reddened (erythrodermic) and may have patches, papules, plaques or tumors. Lymphoma cells have not spread to other organs, the number of Sézary cells in the blood is low.

TNMB Classification and Staging of Mycosis Fungoides/Sézary Syndrome

T (skin)

T1 Limited patches, papules, and/or plaques covering less than 10% of the skin surface

T2 Patches, papules, and/or plaques covering greater than or equal to 10% of the skin surface

T3 One or more tumors (greater than or equal to 1 cm in diameter)

T4 Confluence of erythema greater than or equal to 80% body surface area

N (lymph node)

N0 No abnormal lymph nodes; biopsy not required

N1 Abnormal lymph nodes; histologically uninvolved

N2 Abnormal lymph nodes; histologically involved (nodal architecture uneffaced)

N3 Abnormal lymph nodes; histologically involved (nodal architecture [partially] effaced)

NX Abnormal lymph nodes; no histologic confirmation

M (metastasis)

M0 No visceral organ involvement

M1 Visceral involvement (must have pathology confirmation and organ involved should be specified)

B (blood)

B0 Absence of significant blood involvement

B1 Low blood tumor burden

B2 High blood tumor burden

Abbreviations: MF, mycosis fungoides; SS, Sézary syndrome; TNMB, tumor, node, metastasis, blood; patch, dry and/or red skin; plaque, skin that becomes harder and thicker but is still flat; tumor, forms in patients with advanced disease.

Table 2. Classification and staging in MF and SS. Source: NCCN Guidelines Version 4. 2018. Mycosis Fungoides/ Sézary Syndrome and Willemze R, Hodak E, Zinzani PL, et al. Primary cutaneous lymphomas: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Annals of Oncology.* 2018;29(4): iv30-iv40.

Stage IV

- Stage IVA_1 (T1 to T4, N0 to N2, M0, B2)—skin lesions can cover any amount of skin. The lymph nodes are either normal or are enlarged but the cells do not look very abnormal under the microscope, and the lymphoma cells have not spread to other organs. The number of Sézary cells in the blood is high.
- Stage IVA_2 (T1 to T4, N3, M0, B0 to B2)—skin lesions can cover any amount of the skin. Some lymph nodes are enlarged, and the cells appear abnormal under the microscope. Lymphoma cells have not spread to other organs. There may be either high or low numbers of Sézary cells in the blood.
- Stage IVB (T1 to T4, any N, M1, any B)—skin lesions can cover any amount of the skin. The lymph nodes may be either normal or abnormal. The lymphoma cells have spread to other organs, and Sézary cells either may or may not be in the bloodstream.

The International Society for Cutaneous Lymphomas/European Organization of Research and Treatment of Cancer Staging and TNMB Classification

Stage	T	N	M	B
IA	1	0	0	0, 1
IB	2	0	0	0, 1
IIA	1, 2	1,2	0	0, 1
IIB	3	0-2	0	0, 1
IIIA	4	0-2	0	0
IIIB	4	0-2	0	1
IVA_1	1-4	0-2	0	2
IVA_2	1-4	3	0	0-2
IVB	1-4	0-3	1	0-2

Table 3. TNMB classification.

Abbreviation: TNMB: tumor, node, metastasis, blood

Source: NCCN Guidelines Version 4. 2018. Mycosis Fungoides/Sézary Syndrome and Willemze R, Hodak E, Zinzani PL, et al. Primary cutaneous lymphomas: ESMO clinical practice guidelines for diagnosis, treatment and follow-up. *Annals of Oncology.* 2018;29(4):iv30-iv40.

Prognosis. A prognosis is a prediction of the outcome of the patient's disease. It is an educated guess on how well a person will respond to treatment. It is a consideration when planning treatment.

The prognosis for an individual with MF or SS may depend on the following factors:

- The stage of the cancer
- The patient's age
- The extent of skin involvement and type of lesions (T classification)
- The presence of extracutaneous disease (whether the disease has spread from the skin to the lymph nodes or other organs in the body)
- The extent of peripheral blood involvement (amount of Sézary cells in the blood)
- The level of lactate dehydrogenase (LDH) in the bloodstream
- The presence of large-cell transformation (LCT) or folliculotropic MF.

Prognosis is determined by using statistics, collected over many years, about patients with the same type of cancer. These statistics are based on large groups of patients, so they cannot predict precisely what will happen to any individual patient. Every person is different. Treatments, and patients' responses to treatments, vary significantly.

Treatment

Drugs may have been approved since this book was printed. Check www.LLS.org/DrugUpdates or call (800) 955-4572.

Mycosis fungoides (MF) and Sézary syndrome (SS) are chronic conditions that are generally considered incurable; however, these diseases are treatable and are not life threatening in most cases. Typically, the goals of treatment are to relieve symptoms, induce remission and postpone disease progression. While patients with early-stage disease may respond well to skin-directed therapies alone, patients with more advanced disease may require a combination of skin-directed and systemic (affecting the entire body) therapies. These are considered "standard" treatments. Standard treatments are accepted by medical experts as being the proper treatments for a disease. Some treatments are being tested in clinical trials. A clinical trial is a research study that is intended to improve current treatments for patients. When clinical trials demonstrate that a new treatment is better than the standard treatment, the new treatment may become the standard treatment.

The selection of a specific therapy or therapies should be individualized, the risks versus the benefits carefully weighed and the patient's general health and his or her social situation taken into account. The patient should actively participate in the decision-making process for determining the optimal treatment that is suitable for him or her.

Specific treatments include watch and wait, skin-directed therapies and systemic therapies. For a list of all treatments, see **Table 4** on *page 20*.

Watch and Wait. Patients with MF stage IA disease have a low risk of disease progression. For some of these patients "watch and wait" may be a reasonable first option. This means that treatment is deferred or delayed until signs of the disease progression occur. Frequent and careful observation by a doctor is required so that effective treatment can be started if the disease starts advancing. **See the free LLS fact sheet *Watch and Wait* at www.LLS.org/booklets or call an Information Specialist at (800) 955-4572 for a copy.**

Skin-Directed Therapies

- Topical corticosteroids—corticosteroids are part of the treatment regimen for some lymphomas and can temporarily reduce the associated symptoms of lymphoma such as itching. These drugs are also good at reducing the swelling and inflammation associated with rapidly growing tumors. For cutaneous lymphomas they may be used in the treatment of individual lesions to help alleviate red, swollen and inflamed skin. Topical corticosteroids may be prescribed in a cream, lotion, foam, gel or ointment formulation. Long-term use of topical corticosteroids can have side effects such as thinning of the skin and stretch marks.
- Topical chemotherapy—some chemotherapy drugs can be applied directly to skin lesions. **Nitrogen mustard (mechlorethamine HCl, Valchlor gel®)** is approved by the Federal Drug Administration (FDA) for the topical treatment of stage IA and IB MF-type cutaneous T-cell lymphoma (CTCL) in patients who have received previous skin treatment. Mechlorethamine HCL gel is in a class of medications called "alkylating agents." It works by slowing or stopping the growth of cancer cells. Most common side effects include redness, swelling, itching, skin ulcers or blisters, skin infection and darkening of areas of the skin.
- Topical retinoids—retinoids are drugs related to vitamin A that can slow the growth of certain types of cancer cells. **Bexarotene gel (Targretin®)** and **tazarotene (Avage®, Tazorac®)** are topical retinoids that can be applied directly to skin lesions. Bexarotene is the only topical retinoid approved by the FDA for the treatment of cutaneous lesions in patients who have CTCL (stages IA and IB) and who have refractory or persistent disease after other therapies or in patients who have not been able to tolerate other therapies. Topical retinoids frequently cause skin irritation, but this side effect typically

disappears once the drugs are stopped. Retinoids can cause severe harm to unborn babies and should never be used by pregnant women.

- Topical **imiquimod (Aldara®)**—imiquimod cream is a type of immunotherapy that is applied to skin lesions. Several research groups have reported the effectiveness of imiquimod in early-stage MF. While the FDA has not approved imiquimod for the treatment of MF, it is already approved to treat basal cell carcinoma, actinic keratosis and genital warts. Some doctors use it off-label to treat skin lymphomas. Side effects may include redness, itching, flaking, scaling or thickening of the skin.
- Electron beam therapy—electron beam therapy is a form of radiation therapy that is used to treat skin lesions. Electrons do not penetrate deeply into the body, so they are less likely to harm the tissue and organs beneath the skin. Patients with one lesion or a few lesions can be treated with localized electron beam therapy. For patients with widespread lesions, total skin electron beam therapy can treat the entire skin surface. Typically treatment is given a few times each week over a period of 3 to 4 weeks.
  - Localized electron beam therapy—localized radiation therapy has been helpful for patients who have a few lesions. Prior to treatment, the patient undergoes a treatment planning procedure called a "simulation." The simulation ensures that the treatment site is mapped out correctly on the patient's body. During the simulation, the radiation therapist will take pictures of the patient's skin and use a felt marker to outline the area(s) of the skin that need to be treated.

    During an actual treatment, the patient will be positioned on the table in exactly the same way as in the simulation. Once the patient is in the correct position, the radiation therapist will leave the room and begin the treatment. Patients will neither see nor feel the radiation, although they may hear the machine as it turns on and off and moves around them. Patients who receive spot treatment usually have minor side effects that involve the skin, hair, and nails in the treated areas.
  - Total skin electron beam therapy is appropriate for patients with widespread thick plaques, either with or without skin tumors. During treatment, the patient stands on a platform that rotates so that the entire surface of the patient's skin can be treated from different angles. Usually receiving the radiation just takes a few minutes. Side effects typically involve the skin, hair, fingernails and toenails. The skin may become red, dry, and irritated over the entire body. The redness and irritation typically improve after the treatment is finished. A patient may lose body hair including the scalp, eyebrows and pubic hair. This loss is usually temporary and hair will begin to grow back in 3 to 6 months after treatment is completed. A patient's fingernails and toenails may also fall out, but new ones will eventually begin to grow.

- Phototherapy (light therapy)—phototherapy, also known as "light therapy," is a treatment that uses ultraviolet (UV) light which is also found in sunlight. Ultraviolet light consists of ultraviolet A (UVA) rays and ultraviolet B (UVB) rays. Ultraviolet A and UVB radiation therapy is given using a special lamp or laser that directs the radiation beam to the target area on the skin. Phototherapy can be given to a specific area of the body or to the entire body and it can be used with other topical therapies.

There are two main types of phototherapy, they are

- Ultraviolet B phototherapy—UVB phototherapy uses UVB light to treat patches and thin plaques. It can be either broadband or the more commonly used narrowband. The patient will stand undressed in a "cabinet" or "box" that is fitted with fluorescent light tubes for approximately 30 minutes. Some parts of the body, such as the eyes, will be covered. The dose of UVB is usually increased at each visit. Visits typically occur three to five times a week. Skin lesions often begin to fade in 20 to 40 visits. Once the lesions are gone, the number of visits are reduced and then eventually stopped. Side effects may include red, painful skin that resembles a sunburn.
- Psoralen plus ultraviolet A (PUVA)—this type of therapy uses UVA light and an oral medication called **"psoralen."** For patients who have skin plaques, PUVA is often recommended instead of UVB. Ultraviolet A is able to penetrate deeper into the skin than UVB so PUVA may be more effective for the treatment of thick lesions. Approximately 1 to 2 hours before a PUVA treatment, the patient will receive the medication psoralen. Typically, it is given in pill form. The patient waits for the psoralen to be absorbed. Patients then remove their clothing and wear goggles to protect the eyes and a visor if their faces are unaffected. They stand in a "cabinet" that has many UVA bulbs. Patients are usually exposed to the UVA for 30 minutes. This therapy is often given two to three times a week until the lesions are gone. This can often take 4 to 6 months.

  After treatment, a patient's skin may appear red and blistered. It may also feel dry and itchy. Psoralen makes the skin more sensitive to light so patients may burn more easily than usual in the sun. Patients should protect their skin from the sun for at least 24 hours after treatment.

Long-term phototherapy is associated with an increased risk of skin cancer (basal cell and squamous cell cancers and melanoma). Thus, patients who have a strong personal or family history of these skin cancers should discuss the risks and benefits of phototherapy with their doctor.

Systemic Therapies

- Oral retinoids—while some retinoids are applied directly to the skin, other retinoids are formulated as pills. Doctors use oral retinoids **bexarotene (Targretin®)**, **acitretin (Soriatane®)**, **isotretinoin (Accutane®)** and **tretinoin (Vesanoid®)** to treat MF and SS, but only bexarotene is approved by the FDA for treating MF. Common side effects include high numbers of fat particles in the bloodstream (hyperlipidemia) and low levels of thyroid hormones (hypothyroidism). Patients may also develop dry skin, muscle and joint pain, headaches and light sensitivity. Most side effects of retinoids diminish once treatment has been completed. Retinoids can cause severe harm to unborn babies and should never be used by pregnant women.
- Interferons **(interferon (IFN)-alfa, interferon (IFN)-gamma)**—interferons are a type of immunotherapy that uses the immune system to fight cancer. Interferon alfa and interferon gamma are proteins called "cytokines." Cytokines exist in the body as part of the immune system. They can also be made in the laboratory and used to help the body fight cancer, infections and other diseases. Cytokines can trigger the immune system to attack cancer cells. Interferon alfa and interferon gamma can be given as injections under the skin. Interferon alfa can also be given as an injection into the vein. These treatments are given several times a week. Common side effects include a low white blood cell count (neutropenia), flulike symptoms, fatigue, nausea, vomiting, depression, hair thinning and heart and liver damage.
- Histone deacetylase (HDAC) inhibitors—HDAC inhibitors are a class of anticancer agents that modify abnormal cancer genes and cause the cancer cells to stop dividing and die. The following drugs are approved by the FDA for the treatment of MF and SS:
  - **Vorinostat (Zolinza®)**—vorinostat is a pill that is taken once a day. Vorinostat is approved for the treatment of cutaneous manifestations in patients with CTCL who have progressive, persistent or recurrent disease on or following two systemic therapies. Common side effects include nausea, diarrhea, fatigue, dry mouth, hair loss, fever, headaches, and changes in taste.
  - **Romidepsin (Istodax®)**—this drug is FDA approved for the treatment of CTCL in patients who have received at least one prior systemic therapy. Romidepsin is a liquid that is slowly infused into a vein over a 4-hour period. The infusion is given once a week for the first 3 weeks of a 28-day cycle. The doctor will discuss how many additional cycles are needed. Common side effects include nausea, fatigue, changes in taste and low platelet counts.
- Extracorporeal photopheresis—extracorporeal photopheresis is a method of treating T cells outside of the body. In this procedure, blood is removed through a patient's vein. The photopheresis machine separates the white

blood cells from the rest of the blood. The red blood cells and plasma are returned to the patient's body. The white blood cells are then treated with a medication called **"methoxsalen"** and exposed to UV light which activates the methoxsalen. The treated white blood cells are subsequently returned to the body. This process injures the cancerous T cells and helps stimulate the immune system to fight the cancer. This procedure takes about 3 to 4 hours and is usually repeated multiple times to obtain the full effect. Extracorporeal photopheresis is most effective in patients with blood involvement, people who have SS, for example.

- Monoclonal antibodies—these are immunotherapy drugs that are designed to target specific proteins in cancer cells while minimizing harm to healthy cells. Some of these drugs work by themselves while others are coupled with chemotherapy drugs, toxins or radioactive substances to target malignant cells.

  The anti-CC chemokine receptor 4 (CCR4) monoclonal antibody **mogamulizumab-kpkc (Poteligeo®)** targets the CCR4 protein, which is frequently found on the surface of cancer cells in patients with CTCLs. Mogamulizumab, administered intravenously (IV), is approved by the FDA for the treatment of adult patients who have either relapsed or refractory mycosis fungoides or Sézary syndrome after they have had at least one prior systemic therapy.

- Targeted therapies—these agents target a specific molecule on the cancer cell killing the malignant cells and not the healthy ones. Cluster of differentiation 30 (CD30) is a protein that is sometimes expressed in MF, especially the aggressive transformed MF. This protein can be targeted with anticancer therapies. One such agent **brentuximab vedotin (Adcetris®)** attaches to cells that express CD30 antigens and penetrates the lymphoma cells. Once brentuximab vedotin is in the bloodstream it targets and kills the lymphoma cells. It is FDA approved for the treatment of CD30-expressing MF for patients who have received prior systemic therapy. Brentuximab vedotin is given every 3 weeks by IV. The most common side effects include a low white blood cell count (neutropenia), anemia, peripheral sensory neuropathy, nausea, fatigue, constipation, diarrhea and vomiting.

- Chemotherapy—conventional chemotherapy drugs kill cancer cells that divide rapidly. Some chemotherapy drugs can be applied directly to the skin, but most chemotherapy drugs for MF and SS are not applied to the skin. They are given systemically either as intravenous or oral agents. These treatments travel in the bloodstream to treat cancer throughout the body. Systemic chemotherapy is generally used in patients with advanced-stage MF or SS whose disease has relapsed multiple times and who have few therapeutic options. Responses to chemotherapy are rarely durable in patients with MF and SS. As a result, eventually, MF and SS both relapse in most patients treated with chemotherapy.

Side effects of chemotherapy depend on many factors, including the type of treatment and dosage, the age of the patient and coexisting medical conditions. Therapy may cause fever or chills, fatigue, nausea, loss of appetite, mouth sores, peripheral neuropathy (tingling, burning, numbness or pain in the hands or feet), changes in blood cell counts, infection, rash, vomiting, diarrhea, shortness of breath, swelling, temporary loss of hair and other side effects.

Most side effects are temporary and resolve when treatment is completed. However, other side effects persist over the long term and may appear years after the treatment has been completed. Late side effects may include developing another type of cancer, heart disease, low levels of thyroid hormones (hypothyroidism), nerve damage and loss of fertility.

Some systemic chemotherapies for patients with MF and SS include

- **Methotrexate, pralatrexate (Folotyn®)**—antifolate agents that interfere with the growth of tumor cells
- **Gemcitabine (Gemzar®), pentostatin (Nipent®)**—purine analogues that interfere with the tumor growth
- **Liposomal doxorubicin (Doxil®)**—a chemotherapy that binds to DNA (deoxyribonucleic acid)
- **Chlorambucil (Leukeran®), cyclophosphamide (Cytoxan®)**—alkylating agents, which interfere with the growth of cancer cells
- **Etoposide (VP-16, VePesid®, Etopophos®), temozolomide (Temodar®)**—antineoplastic agents that interfere with the growth of cancer cells.

Treatments for Cutaneous T-Cell Lymphoma

Skin-Directed Therapies	Systemic Therapies	Combination Therapies
For limited/localized skin involvement • Topical corticosteroids • Topical chemotherapy • Local radiation • Topical retinoids • Phototherapy • Topical imiquimod **For generalized skin involvement** • Topical corticosteroids • Topical chemotherapy • Phototherapy • Total skin electron beam therapy	• Oral retinoids • Interferons • Histone deacetylase (HDAC) inhibitors • Extracorporeal photopheresis • Targeted therapies • Brentuximab vedotin • Chemotherapy • Methotrexate • Pralatrexate • Gemcitabine • Pentostatin • Liposomal doxorubicin • Chlorambucil • Cyclophosphamide • Etoposide • Temozolomide	**Skin-directed + Systemic** • Phototherapy + retinoid • Phototherapy + interferon • Phototherapy + photopheresis • Total skin electron beam + photopheresis **Systemic + Systemic** • Retinoid + interferon • Photopheresis + retinoid • Photopheresis + interferon • Photopheresis + retinoid + interferon

Table 4. **A list of treatment options for cutaneous T-cell lymphoma. Source: NCCN Guidelines Version 4. 2018. Slide 34.**

Drugs may have been approved since this book was printed. Check www.LLS.org/DrugUpdates or call (800) 955-4572.

Treatment Under Investigation

A clinical trial is a research study in which a new treatment option is being evaluated for the treatment of a particular condition. There are many different types of clinical trials and each has specific objectives such as establishing a safe dose of an agent (phase I), evaluating the efficacy of a specific dose or type of therapy in a specific disease and establishing a response rate (phase II) and comparing the new agent against a known treatment for that particular stage of cancer (phase III). Clinical trials are conducted under the oversight of regulatory committees and the Federal Drug Administration (FDA) and patients are followed very closely by a team of physicians and their research staff. A patient has to fully understand and consent to the trial before treatment can be initiated and he or she has the right to withdraw from the trial at any time.

While there are many treatments available to patients with mycosis fungoides (MF) and Sézary syndrome (SS), there are few rigorously tested guidelines about standard treatments and none of the treatments are considered to be curative. Participation in a carefully conducted clinical trial may be the best available therapy. Patient participation in past clinical trials has resulted in the therapies we have today. As we are improving our understanding of the pathogenesis of MF and SS, it is likely that there will be more targeted treatments available through clinical trials. Patients should be encouraged to keep informed about any available trials in their areas.

LLS Information Specialists, at (800) 955-4572, can offer guidance on how patients can work with their doctors to determine if a specific clinical trial is an appropriate treatment option. They can provide information and conduct individualized clinical-trial searches for patients, family members and healthcare professionals. When appropriate, Information Specialists refer patients for personalized clinical-trial navigation by trained nurses, a service which is available through the Clinical Trial Support Center. Visit www.LLS.org/CTSC for more information.

Research Approaches. There are clinical trials for newly diagnosed patients and for patients who have relapsed or refractory disease. Researchers are studying novel therapies and drugs as well as looking at ways of combining drugs already known to be effective in new ways or using different doses.

Some classes of novel therapies and drugs under investigation include

- Immune checkpoint inhibitors—a type of immunotherapy which helps a person's own immune system attack cancer cells. Cancer cells can make proteins that allow them to "hide" from the patient's immune system. When these proteins are blocked, T cells are better able to detect and attack cancer cells. **Pembrolizumab (Keytruda®)** and **durvalumab (Imfinzi®)** are

immune checkpoint inhibitors that are approved to treat other types of cancer and are now being studied to treat cutaneous T-cell lymphomas (CTCLs).

- **Cobomarsen (MRG-106)**—designed to inhibit a molecule called miR-155 that is found at high levels in certain types of cancer, including mycosis fungoides (MF), and which may be important for the cancer cells to survive and grow. Cobomarsen is currently in clinical trials for patients with MF.
- Photodynamic therapy (PDT)—researchers are studying PDT for MF patients whose disease has not responded to other treatments. For this treatment, a light-activated drug such as **aminolevulinic acid hydrochloride** is applied to skin lesions. A type of laser is then focused on the lesions. The light from the laser activates the drug which then kills the lymphoma cells. The advantage of PDT is that it can kill cancer cells with very little harm to normal cells. But because the chemical must be activated by light, it can only kill cancer cells near the surface of the skin.
- Allogeneic stem cell transplantation—a promising therapeutic strategy for patients with advanced CTCLs. Allogeneic stem cell transplantation may induce remissions in patients with MF and SS. Researchers continue to improve stem cell transplantation methods, including new ways to harvest stem cells and reduce side effects. Multiple studies have shown successful results with reduced-intensity allogeneic stem cell transplantation in patients with MF and SS. Clinical trials are under way to determine whether milder or alternative regimens of allogeneic stem cell transplants for patients with CTCL may improve clinical benefit and reduce the harmful outcome of graft-versus-host disease, which can be a complication in allogeneic transplantation. **For more information about transplantation, see the free LLS booklet *Blood and Marrow Stem Cell Transplantation*.**

Side Effects of Treatment for Mycosis Fungoides (MF) and Sézary Syndrome (SS)

The side effects of treatment will depend on many factors including type of treatment, the drug dosage, the age of the patient and any coexisting medical conditions. Therapy may induce fatigue, nausea, fever, chills, dizziness, blood clots, infertility and other effects. Some treatment options, such as retinoids, can cause severe birth defects; it is strongly recommended that women of childbearing age use birth control when using these drugs.

Managing the side effects of treatment is important. Patients should discuss side effects with their doctors to get help. Most side effects can be managed without compromising the effectiveness of treatment. In fact, aggressive management of side effects often leads to better treatment outcomes. Most

side effects are temporary and resolve when treatment is completed. However, some side effects are long term and may appear years after the treatment has been completed. Late side effects may include developing another type of cancer, heart disease, low levels of thyroid hormones (hypothyroidism) and loss of fertility. **For specific drug and side effects information, see the free LLS booklet *Understanding Side Effects of Drug Therapy*.**

Supportive Care

In addition to cancer treatment, patients may also receive supportive care to prevent or control other health conditions. The abnormal scaling, flaking and cracking of the skin in mycosis fungoides (MF) and Sézary syndrome (SS) patients can lead to considerable discomfort. Severe itching (pruritus) and skin infections are also serious concerns for these patients.

To protect the skin, it is important for MF and SS patients to keep their skin well moisturized. Dry, cracked skin can intensify itching and can allow infectious agents to penetrate the skin. To protect the skin, patients should

- Take shorter showers or baths (10 to 15 minutes maximum) in warm, not hot, water.
- Use a mild cleanser that is scent-free and dye-free.
- Wash the skin gently and avoid rubbing the skin with a wash cloth or sponge.
- Pat off water gently and apply a thick ointment or moisturizer after showering or bathing.
- Apply moisturizers frequently, at least two to three times a day.
- Use fragrance-free laundry detergents and fabric softeners. The fragrances in these products can come in contact with the skin and cause irritation.
- Keep the skin comfortable by wearing loose-fitting clothes made of fabrics that “breathe” such as cotton.
- Avoid becoming over-heated. Sweating can worsen the itch.

Most patients with MF and SS suffer from severe itching that may be difficult to control. Patients should be evaluated for itching at each visit to the doctor. Supportive therapies that may help manage itching include

- Placing ice packs on itchy area
- Soaking in an oatmeal bath
- Using topical corticosteroids (either with or without occlusion). Occlusion involves covering the treated area with a dry, protective dressing (wrapping it in cloth).

- Taking oral medications such as
  - Antihistamines, such as **diphenhydramine (Benadryl®)** or **hydroxyzine (Atarax®)**, may relieve itching. The major side effects of these drugs are drowsiness so they are frequently prescribed for use at night. Nonsedating antihistamines such as **loratadine (Claritin®), cetirizine (Zyrtec®),** and **fexofenadine (Allegra®)** can be prescribed for daytime use but these drugs are generally less effective.
  - Antidepressants **doxepin (Zonalon®)** and **mirtazapine (Remeron®)** may help manage itching.
  - **Aprepitant (Emend®)** is a prescription medication used for preventing chemotherapy-induced nausea that has been shown to reduce itching.
  - **Gabapentin (Neurontin®)**, an anticonvulsant prescribed to individuals prone to seizures, has been effective in treating severe itching.

Because patients with MF and SS frequently have cracked and ulcerated skin, they are susceptible to infections. Infections are frequent among patients with MF and SS, particularly bacterial skin infections and viral herpes skin infections. Patients should consider taking the following preventive measures to minimize infections:

- Routinely, use skin moisturizers to protect the skin.
- Wash skin gently with an antibacterial soap and apply an antibiotic ointment to skin lesions.
- Take bleach baths or soaks (for limited areas only).
- Avoid central lines (particularly for erythrodermic patients).

It is important for patients to recognize the signs of skin infections. Signs of skin infection may include redness, swelling, increased pain or pus (weeping fluid). Patients with infections may need aggressive antibiotic treatment.

Treatment Outcomes

The prognosis for patients with mycosis fungoides (MF) and Sézary syndrome (SS) depends on a number of factors, including patient age, disease type and stage, rate of disease progression and response to therapy. Some patients may have stable or slowly progressive disease, while others may have a more rapidly progressive disease. Many MF patients will have disease limited to the skin. These patients may live normal lives for many years while being treated for their disease and some are able to remain in remission for long periods of time. For these patients, a normal life span can be expected. A minority of patients will experience a more progressive disease with the disease spreading to the lymph nodes and/or other organs. It is important to emphasize that outcomes for patients with advanced disease is improving as a result of new treatment options.

Feedback. Please visit www.LLS.org/PublicationFeedback to make suggestions about the content of this booklet.

Resources and Information

LLS offers free information and services for patients and families affected by blood cancers. This section of the booklet lists various resources available to you. Use this information to learn more, to ask questions, and to make the most of your healthcare team.

For Help and Information

Consult with an Information Specialist. Information Specialists are master's level oncology social workers, nurses and health educators. They offer up-to-date information about disease, treatment and support. Language services are available. For more information, please

- Call: (800) 955-4572 (Monday through Friday, 9 am to 9 pm ET)
- Email: infocenter@LLS.org
- Live chat: www.LLS.org/InformationSpecialists
- Visit: www.LLS.org/InformationSpecialists

Clinical Trials (Research Studies). New treatments for patients are under-way. Patients can learn about clinical trials and how to access them. For more information, please call (800) 955-4572 to speak with an LLS Information Specialist who can help conduct clinical-trial searches. When appropriate, personalized clinical-trial navigation by trained nurses is also available. Visit www.LLS.org/CTSC for more information.

Free Information Booklets. LLS offers free education and support publications that can either be read online or ordered. Please visit www.LLS.org/booklets for more information.

Telephone/Web Education Programs. LLS offers free telephone/Web and video education programs for patients, caregivers and healthcare professionals. Please visit www.LLS.org/programs for more information.

Financial Assistance. LLS offers financial assistance to individuals with blood cancer. Visit www.LLS.org/finances for more information.

***Co-Pay Assistance Program*.** LLS offers insurance premium and medication co-pay assistance for certain eligible patients. For more information, please

- Call: (877) 557-2672
- Visit: www.LLS.org/copay

One-on One Nutrition Consultations. Access free one-on-one nutrition consultations by a registered dietitian with experience in oncology nutrition. Dietitians assist callers with information about healthy eating strategies, side effect management, and survivorship nutrition. They also provide additional nutrition resources. Please visit www.LLS.org/nutrition for more information.

Podcast. Listen in as experts and patients guide listeners in understanding diagnosis, treatment, and resources available to blood cancer patients. *The Bloodline with LLS* is here to remind you that after a diagnosis comes hope. Visit www.LLS.org/TheBloodline for more information and to subscribe.

Suggested Reading. LLS provides a list of selected books recommended for patients, caregivers, children and teens. Visit www.LLS.org/SuggestedReading to find out more.

Community Resources and Networking

LLS Community. The one-stop virtual meeting place for talking with other patients and receiving the latest blood cancer resources and information. Share your experiences with other patients and caregivers and get personalized support from trained LLS staff. Visit www.LLS.org/community to join.

Weekly Online Chats. Moderated online chats can provide support and help cancer patients reach out and share information. Please visit www.LLS.org/chat for more information.

LLS Chapters. LLS offers community support and services in the United States and Canada including the *Patti Robinson Kaufmann First Connection Program* (a peer-to-peer support program), in-person support groups and other great resources. For more information about these programs or to contact your chapter, please

- Call: (800) 955-4572
- Visit: www.LLS.org/ChapterFind

Other Helpful Organizations. LLS offers an extensive list of resources for patients and families. There are resources that provide help with financial assistance, counseling, transportation, patient care and other needs. For more information, please visit www.LLS.org/ResourceDirectory to obtain our directory.

Advocacy. The LLS Office of Public Policy (OPP) enlists volunteers to advocate for policies and laws to speed new treatments and improve access to quality medical care. For more information, please

- Call: (800) 955-4572
- Visit: www.LLS.org/advocacy

Additional Help for Specific Populations

Información en Español (LLS information in Spanish). Please visit www.LLS.org/espanol for more information.

Language Services. Let your doctor know if you need a language interpreter or other helper, such as a sign language interpreter. Often, these services are free.

Information for Veterans. Veterans with lymphoma who were exposed to Agent Orange while serving in Vietnam may be able to get help from the United States Department of Veterans Affairs. For more information visit www.publichealth.va.gov/exposures/agentorange or call the Department of Veterans Affairs at (877) 222-8387.

World Trade Center Survivors. People involved in the aftermath of the 9/11 attacks and subsequently diagnosed with a blood cancer may be able to get help from the World Trade Center (WTC) Health Program. People eligible for help include

- Responders
- Workers and volunteers who helped with rescue, recovery and cleanup at the WTC-related sites in New York City (NYC)
- Survivors who were in the NYC disaster area and those who lived, worked or were in school in that area
- Responders to the Pentagon and the Shanksville, PA, crashes

For more information, please

- Call: WTC Health Program at (888) 982-4748
- Visit: www.cdc.gov/wtc/faq.html

People Suffering from Depression. Treating depression has benefits for cancer patients. Seek medical advice if your mood does not improve over time, for example, if you feel depressed every day for a two-week period.
For more information, please

- Call: The National Institute of Mental Health (NIMH) at (866) 615-6464
- Visit: NIMH at www.nimh.nih.gov and enter “depression” in the search box

Questions to Ask Your Doctor

It may be helpful to prepare some questions to ask the members of your treatment team at your next appointment. Here are some suggestions of questions to ask.

About the Disease and Testing

1. What tests do I need to have?
2. How do I prepare for these tests?
3. Will my medical insurance pay for the tests?
4. When will I have the results? Who will explain the results?
5. I am experiencing symptoms right now, what does that mean for my treatment?
6. What test is done to confirm my lymphoma subtype?

About Treatment Options and Side Effects

1. Do I need treatment for cutaneous T-cell lymphoma (CTCL)?
2. Is the "watch-and-wait" approach the right option for me?
3. What treatment options do I have?
4. Are there any available clinical trials for my diagnosis?
5. Does this hospital/center offer treatment for my disease?
6. How long will the treatment last?
7. What are the side effects of this treatment? How long will they last?
8. How will I know if the treatment is effective? What will happen if the treatment does not work?
9. Are there any long-term side effects of this treatment?

About Cost

1. Will my medical insurance pay for my treatment?
2. For clinical trial participants: Am I responsible for any costs associated with the clinical trial?
3. What additional costs should I be thinking about (ie., transportation, parking, food, etc)?

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LEUKEMIA & LYMPHOMA SOCIETY®

Get support. Reach out to our **INFORMATION SPECIALISTS**

The Leukemia & Lymphoma Society team consists of master's level oncology social workers, nurses and health educators who are available by phone Monday through Friday, 9 a.m. to 9 p.m. (ET).

- Get one-on-one personalized support and information about blood cancers
- Know the questions to ask your doctor
- Discuss financial resources
- Receive individual clinical-trial searches

Contact us at
800-955-4572 or
www.LLS.org/informationspecialists
(Language interpreters can be requested)

LEUKEMIA & LYMPHOMA SOCIETY®

For more information, please contact our Information Specialists **800.955.4572** (Language interpreters available upon request).

National Office 3 International Drive, Suite 200 Rye Brook, NY 10573

The mission of The Leukemia & Lymphoma Society (LLS) is to cure leukemia, lymphoma, Hodgkin's disease and myeloma, and improve the quality of life of patients and their families. Find out more at **www.LLS.org**.

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