

# Understanding Lymphoma

## T-Cell Lymphoma

T-cell lymphomas can develop in lymphoid tissues such as the lymph nodes and spleen, or outside of lymphoid tissues (i.e., gastrointestinal tract, liver, nasal cavity, skin, and others).

A similar lymphocyte called a natural killer (NK) cell shares many features with T cells. When NK cells become cancerous, the cancer is called NK or NK/T-cell lymphoma and is generally grouped with other T-cell lymphomas. T-cell lymphomas account for less than 15 percent of all non-Hodgkin Lymphomas (NHLs) in the United States. Each particular subtype of T-cell lymphoma tends to be uncommon. They can be *aggressive* (fast-growing) or *indolent* (slow-growing).

Lymphomas are often named from a description of the normal cell that leads to cancer. Lymphomas that arise from mature T cells include peripheral T-cell lymphoma (PTCL) and cutaneous T-cell lymphomas (CTCL), which distinguishes them from the lymphomas that arise from immature T cells like lymphoblastic lymphoma. Of the new cases of mature T-cell lymphomas in the United States each year, approximately 60 percent are PTCL and 40 percent are CTCL. Some subtypes of T-cell lymphoma are listed below.



### COMMON SUBTYPES OF PERIPHERAL T-CELL LYMPHOMA

**Peripheral T-Cell Lymphoma, Not Otherwise Specified (PTCL-NOS)** refers to a group of diseases that do not fit into any of the other PTCL subtypes. PTCL-NOS accounts for about 25-35 percent of T cell lymphomas and is the most common PTCL subtype. Although most patients with PTCL-NOS are diagnosed when the disease is confined to the lymph nodes, extranodal sites such as the liver, bone marrow, gastrointestinal tract, and skin, may also be involved. This subtype of PTCL is generally aggressive and patients will frequently have symptoms such as fevers, serious night sweats, and unexplained weight loss. For more information, view the *Peripheral T-Cell Lymphoma* fact sheet on the Lymphoma Research Foundation's (LRF's) website (visit [lymphoma.org/publications](http://lymphoma.org/publications)).

**Anaplastic Large Cell Lymphoma (ALCL)** describes several types of T-cell lymphomas and accounts for approximately 10-20 percent of all T-cell lymphomas. Initial symptoms of ALCL can include fever, backache, painless swelling of lymph nodes, loss of appetite, itching, skin rash, and tiredness. All patients with ALCL express a protein called CD30 on the surface of tumor cells. ALCL can be either *systemic* (occurring throughout the body), *cutaneous* (limited to the skin), and can rarely be seen around breast implants.

Systemic ALCL is typically in an advanced stage at diagnosis and can progress rapidly. Patients with systemic ALCL are divided into two groups, depending on whether or not the surface of their cells express an abnormal form of a protein called anaplastic lymphoma kinase (ALK). Systemic ALCL, especially *ALK-positive*

(expresses the protein) disease, can respond well to treatment and is potentially curable. Patients with *ALK-negative* (does not express the protein) disease, may require more aggressive treatments, and relapse (disease returns after treatment) occurs more frequently than in ALK-positive disease.

Primary cutaneous ALCL appears only on the skin, and has a good prognosis (is less aggressive). A rare type of ALCL called breast implant-associated (BIA)-ALCL has been observed in some patients who have a history of breast implants, particularly those with implants with textured (non-smooth) surfaces. Most patients with BIA-ALCL may be treated with surgery alone. For more information on ALCL, please visit LRF's *Focus On Anaplastic Large Cell Lymphoma* website at [www.FocusOnALCL.org](http://www.FocusOnALCL.org) or view the Anaplastic Large Cell Lymphoma fact sheet (visit [lymphoma.org/publications](http://lymphoma.org/publications)).

**Angioimmunoblastic T-Cell Lymphoma (AITL)** is a rare, aggressive type accounting for about 10-20 percent of all patients with PTCL in the United States. Most patients are middle-aged to elderly and are diagnosed with advanced-stage disease. Initial symptoms often include fever, night sweats, skin rash, itching, and some autoimmune disorders such as autoimmune hemolytic anemia (AIHA; where the immune system attacks the body's own red blood cells) and immune thrombocytopenia (ITP; where the immune system attacks the body's own platelets). For more information, view the *Angioimmunoblastic T-Cell Lymphoma* fact sheet on LRF's website (visit [lymphoma.org/publications](http://lymphoma.org/publications)).



## UNCOMMON SUBTYPES OF PERIPHERAL T-CELL LYMPHOMA

**Adult T-Cell Leukemia/Lymphoma (ATLL)** is a rare and often aggressive form of T-cell lymphoma that can be found in the blood (leukemia), lymph nodes (lymphoma), skin, or multiple areas of the body. ATLL has been linked to infection with human T-lymphotropic virus type 1 (HTLV-1). This virus is commonly found in people from the Caribbean, parts of Japan, and some areas of South and Central America and Africa. The HTLV-1 virus is believed to be transmitted through sexual contact or exposure to contaminated blood, but it is most often passed from mother to child through the placenta, childbirth, and breastfeeding. Less than 5 percent of those who carry the virus will develop lymphoma. This lymphoma requires urgent treatment in most patients and stem cell transplantation is frequently needed for cure. For more information, view the *Adult T-Cell Leukemia/Lymphoma* fact sheet on LRF's website (visit [lymphoma.org/lymphoma](http://lymphoma.org/lymphoma)).

**Enteropathy-Associated T-Cell Lymphoma and Monomorphic Epitheliotropic Intestinal T-cell Lymphoma** are extremely rare and aggressive subtypes of T-cell lymphoma that appear in the intestines. Enteropathy-Associated T-Cell Lymphoma is frequently preceded by chronic diarrhea and gluten sensitivity and is associated with celiac disease. Monomorphic epitheliotropic intestinal T-cell lymphoma is not generally associated with celiac disease. Other symptoms include abdominal pain and weight loss. Both require aggressive treatment that frequently is followed by stem cell transplantation in select patients.

**Hepatosplenic Gamma-Delta T-Cell Lymphoma** is an extremely rare and aggressive disease that starts in and involves the liver and/or spleen. It can spread into the blood and bone marrow. It most often occurs in teenagers and young adults and is more common in males. This lymphoma is associated with immunosuppressive treatments. Patients, especially children, who have been treated with immunosuppressants such as azathioprine and infliximab (Remicade) for Crohn's disease, may be more susceptible to this type of lymphoma.

**Extranodal NK/T-Cell Lymphomas** develop from NK cells, which are closely related to and often have features that overlap with T cells. This aggressive lymphoma is relatively rare in the United States, but common in Asia and parts of Latin America. It typically originates in the lining of the nose or upper airway at the back of the throat (in which case it is referred to as nasal type) but may appear in the gastrointestinal tract, skin, and other organs. The NK/T-cell lymphomas seem to be related to infections with Epstein-Barr virus.

**Treatment-Related T-Cell Lymphomas** sometimes referred to as post-transplant lymphoproliferative disorder (PTLD), appear in patients who are intentionally immunosuppressed after solid organ or bone marrow transplantation. While this subtype is more commonly a proliferation of B cells, it can occasionally arise from T cells. The immune system suppression that is required to prevent rejection of the transplanted organ puts patients at risk for this type of lymphoma.

**Lymphoblastic Lymphoma** can arise from either immature B cells or T cells, but more commonly comes from T cells, comprising more than 80 percent of all lymphoblastic lymphomas. This type of lymphoma is most often diagnosed in adolescents and young adults and is a bit more common in

males. It can progress rapidly, if not properly treated. Tumors frequently arise in the middle of the chest, or mediastinum, and immature white blood cells (called lymphoblasts) appear in the lymph nodes, bone marrow or spleen. Central nervous system involvement is more common than in other T-cell lymphomas. It behaves similarly to acute lymphoblastic leukemia (lymphoblasts are found in the bone marrow and blood) and is often treated with intensive chemotherapy. This lymphoma, like other subtypes, can result in impaired immunity and opportunistic infections, and interfere with the body's ability to make blood cells. With intensive chemotherapy, the complete *remission* (disappearance of signs and symptoms of the disease) rate can be very high and many patients can be cured.



## COMMON SUBTYPES OF CUTANEOUS T-CELL LYMPHOMA

**Cutaneous T-Cell Lymphoma (CTCL)** accounts for about 40 percent of all T-cell lymphomas and usually affects adults. The term cutaneous T-cell lymphoma describes a group of typically indolent lymphomas that appear on, and are most often confined to, the skin. Some patients may develop lymphoma in their blood, lymph nodes and more rarely, other organs.

**Mycosis fungoides** is the most common type of CTCL, and usually appears as skin patches, plaques, or tumors. 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, which may or may not *ulcerate* (develop into an ulcer). More than one type of lesion may be present at any time.

**Sézary syndrome** is a less common form of CTCL that affects both the skin and with a higher proportion of lymphoma cells in the blood. Most cases occur in adults over the age of 60 years. The most common symptoms are swollen lymph nodes and a red, very itchy rash that covers large portions of the body. Abnormal T cells, called Sézary cells, can be seen under a microscope and are present in both the skin and blood.

There are other more rare forms of CTCL as well. For more information, view the *Cutaneous T-Cell Lymphoma* fact sheet on LRF's website (visit [lymphoma.org/publications](http://lymphoma.org/publications)).



## TREATMENT OPTIONS

Because there are so many different subtypes of T-cell lymphoma, treatment varies widely. Standard lymphoma therapies may include chemotherapy, targeted therapy, immunotherapy (like antibody-drug conjugates) immunomodulatory agents, radiation, stem cell transplantation, and surgery. Patients diagnosed with rare forms of lymphoma should consult their medical team to find new promising therapies or to enroll into clinical trials.

Initial treatment for the more common types of PTCL typically includes combination chemotherapy regimen, such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), CHOEP (CHOP plus etoposide), BV-CHP (brentuximab vedotin, cyclophosphamide, doxorubicin, prednisone) or EPOCH (etoposide, vincristine, doxorubicin, cyclophosphamide, and prednisone), or other multidrug regimens. Treatments vary

depending on the subtype of lymphoma that you have.

Three histone deacetylase inhibitors—a type of targeted therapy— have been approved by the U.S. Food and Drug Administration (FDA) in the past decade: belinostat (Beleodaq) for PTCL and romidepsin (Istodax) and vorinostat (Zolinza) for CTCL. Romidepsin (Istodax) was previously FDA approved for PTCL and remains available to these patients, as it is National Comprehensive Cancer Network (NCCN) compendium listed. Romidepsin (Istodax) remains FDA approved for CTCL.

In some cases, stem cell transplantation (allogeneic or autologous) is recommended for either relapsed disease or to increase the chance of cure from some forms of PTCL. For more information on transplants, view the *Understanding the Stem Cell Transplantation Process* publication on LRF’s website (visit [lymphoma.org/publications](http://lymphoma.org/publications)).

Therapy for CTCL often includes treatments directed at the skin to improve quality of life. Effective skin directed treatments include topical corticosteroids, topical retinoids, topical chemotherapy, ultraviolet light therapy, or *electron beam radiation therapy* (a type of radiation that does not penetrate to internal organs).

In addition, for some patients with CTCL that involves the bloodstream, a procedure called extracorporeal photopheresis (ECP) is approved. For this procedure, blood is removed from the patient and treated with ultraviolet light, and with drugs that become active when exposed to ultraviolet light. Once the blood has been treated, it is then returned back into the patient’s body.

Patients with relapsed disease are usually treated with combination chemotherapy or with other approved agents. In some patients with PTCL, stem cell transplantation is contemplated as a next step in therapy. However, some regimens or transplant might not be suited for everyone because of their high toxicity levels. Less toxic single-agent therapies are also available and might induce a long-lasting remission in such patients. Belinostat (Beleodaq) or pralatrexate (Folotyn) may be recommended for PTCL and mogamulizumab (Poteligeo) may be a treatment option for CTCL. The antibody-drug conjugate brentuximab vedotin (Adcetris) is approved for both PTCL and CTCL. Patients with an ALK negative ALCL may be also treated with crizotinib (Xalkori). These drugs are approved by the FDA for patients who have relapsed or those who have not responded to their first line of chemotherapy.

## TREATMENTS UNDER INVESTIGATION

Treatment options for the different types of T-cell lymphomas are expanding as new treatments are discovered and current treatments are improved. Treatments currently being investigated singly or in combination include:

- Anti-CD30 chimeric antigen receptor (CAR) T cells
- Azacitidine (CC-486)
- Bendamustine (Treanda)
- Bortezomib (Velcade)
- Devimistat (CPI 613)
- Durvalumab (Imfinzi)
- Duvelisib (Copiktra)
- Lacutamab (IPH4102)
- Lenalidomide (Revlimid)

- MEDI-570
- Nivolumab (Opdivo)
- Pembrolizumab (Keytruda)
- Tenisolip (RP6530)
- Ruxolitinib (Jakafi)
- Venetoclax (Venclexta)

In addition, a number of promising clinical trials are exploring combinations of these new agents which in some cases may be more active than the single agent alone. 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 LRF for any treatment updates that may have recently emerged.

## CLINICAL TRIALS

Clinical trials are crucial for identifying effective drugs and determining optimal doses for patients with lymphoma. In many of the rare subtypes of T-cell lymphoma, no standard of care is established.

Clinical trial enrollment is critical for establishing more effective, less toxic treatments. The rarity of the disease also means that the latest treatments are also often only available through clinical trials. Patients interested in participating in a clinical trial should view the *Understanding Clinical Trials* fact sheet on LRF’s website (visit [lymphoma.org/publications](http://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](mailto: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, computed tomography [CT] scans, and positron emission tomography [PET] scans) may be required at various times during remission 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](http://www.FocusOnLymphoma.org)) can help patients manage this documentation.



## LRF'S HELPLINE AND LYMPHOMA SUPPORT NETWORK

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. The LRF Helpline staff members are available to answer your general questions about a lymphoma diagnosis and treatment information, as well as provide individual support and referrals to you and your loved ones. Callers may request the services of a language interpreter. A part of the Helpline is LRF's one-to-one peer support programs, Lymphoma Support Network. This program connects patients and caregivers with volunteers who have experience with T cell lymphoma, similar treatments, or challenges, for mutual emotional support and encouragement. Patients and loved ones may find this useful whether the patient is newly diagnosed, in treatment, or in remission.



## MOBILE APP

*Focus On Lymphoma* is the first mobile application (app) that provides patients and caregivers comprehensive content based on their lymphoma subtype, including T cell lymphoma, and tools to help manage their lymphoma such as, keep track of medications and blood work, track symptoms, and document treatment side effects. The *Focus On Lymphoma* mobile app is available for download for iOS and Android devices in the Apple App Store and Google Play. For additional information on the mobile app, visit [FocusOnLymphoma.org](http://FocusOnLymphoma.org). To learn more about any of these resources, visit our website at [lymphoma.org](http://lymphoma.org), or contact the LRF Helpline at (800) 500-9976 or [helpline@lymphoma.org](mailto:helpline@lymphoma.org).



## LYMPHOMA CARE PLAN

Keeping your information in one location can help you feel more organized and in control. This also makes it easier to find information pertaining to your care and saves valuable time. LRF offers a Lymphoma Care Plan as a resource for patients and their caregivers. LRF's Lymphoma Care Plan document organizes information on your health care team, treatment regimen, and follow-up care. You can also keep track of health screenings and any symptoms you experience to discuss with your health care provider during future appointments. The Lymphoma Care Plan document can be accessed by visiting [lymphoma.org/publications](http://lymphoma.org/publications).

### Resources

LRF offers a wide range of free resources that address treatment options, the latest research advances, and ways to cope with all aspects of lymphoma and T cell lymphoma. LRF also provides many educational activities, including our in-person meetings, and webinars for people with lymphoma. For more information about any of these resources, visit our websites at [lymphoma.org/Tcelllymphoma](http://lymphoma.org/Tcelllymphoma) or [lymphoma.org](http://lymphoma.org), or contact the LRF Helpline at (800) 500-9976 or [helpline@lymphoma.org](mailto:helpline@lymphoma.org).

Para información en Español, por favor visite [lymphoma.org/es](http://lymphoma.org/es). (For Information in Spanish please visit [lymphoma.org/es](http://lymphoma.org/es).)

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