

# Understanding Peripheral T-Cell Lymphoma

Peripheral T-cell lymphoma (PTCL) refers to a group of different T-cell lymphomas (TCLs) that, together, account for about five percent of all patients diagnosed with non-Hodgkin Lymphoma (NHL) in the United States, according to the Surveillance, Epidemiology, and End Results (SEER) program.

PTCLs develop in lymphoid tissues outside of the bone marrow such as the lymph nodes, spleen, gastrointestinal tract, and skin. Most are *aggressive* (fast-growing) lymphomas, with the exception of some *indolent* (slow-growing) forms of cutaneous T-cell lymphoma (CTCL). Aggressive PTCL subtypes include, but are not limited to, PTCL-not otherwise specified (NOS), angioimmunoblastic T-cell lymphoma (AITL), anaplastic large cell lymphoma (ALCL), enteropathy-type T-cell lymphoma, and extranodal NK/T-cell lymphoma. The incidence of PTCL subtypes varies geographically. The NK/T-cell lymphomas and adult T-cell leukemia/lymphoma (ATLL) are more common in Asia and seem to be related to infections with human T-lymphotropic virus type 1 (HTLV-1) and Epstein-Barr virus, respectively. For more information on PTCL, please visit the Lymphoma Research Foundation's (LRF's) website at [www.lymphoma.org/ptcl](http://www.lymphoma.org/ptcl).

## SUBTYPES OF PERIPHERAL T-CELL LYMPHOMA

PTCLs are classified into various subtypes, each of which is typically considered to be a separate disease based on its distinct clinical features. Each particular subtype of PTCL is rare. The four most common subtypes of aggressive PTCL—PTCL-NOS, ALCL, AITL, and CTCL—account for approximately 88 percent of all cases in the United States.

### PERIPHERAL T-CELL LYMPHOMA, NOT OTHERWISE SPECIFIED (PTCL-NOS)

Peripheral T-Cell Lymphoma, Not Otherwise Specified (PTCL-NOS) is the most common subtype of PTCL, accounting for 30 to 40 percent of PTCLs, and refers to a group of diseases that do not fit into any of the other PTCL subtypes. PTCL-NOS usually occurs in adults in their 50s and 60s. Although most patients with PTCL-NOS are diagnosed with their disease confined to the lymph nodes, sites outside the lymph nodes such as the liver, bone marrow, gastrointestinal tract, and skin are frequently involved. This group of PTCLs is generally aggressive and requires urgent treatment. PTCL-NOS is potentially curable but tends to *relapse* (disease returns after treatment).

### ANAPLASTIC LARGE CELL LYMPHOMA (ALCL)

Anaplastic Large Cell Lymphoma (ALCL) is rare, accounting for about one percent of all NHLs and about 10 percent of all TCLs. Initial symptoms of ALCL can include fever, backache, painless swelling of lymph nodes, loss of appetite, and tiredness. ALCL occurs either *systemically* (throughout the body) or primarily *cutaneous* (affects the skin predominantly or only). All patients with ALCL express a protein called CD30 on the surface of tumor cells. Systemic ALCL can respond well to an antibody attached to a chemotherapy drug targeting the CD30 protein. Brentuximab vedotin and chemotherapy is potentially curable. *Cutaneous* (skin) ALCL is a less aggressive disease that may be preceded by a rare pre-cancerous condition called lymphomatoid papulosis.

Patients with systemic ALCL are divided into two groups, depending on whether or not the surface of their cells expresses an abnormal form of a protein called ALK. The outcome for ALCL varies depending on whether a patient is *ALK positive* (expresses the protein) or *ALK negative* (does not express the protein). ALK-positive disease responds more frequently to standard chemotherapy, putting most patients in long-term remission. Although a majority of patients with ALK-negative ALCL initially respond to treatment, they more frequently relapse within five years and are sometimes treated more aggressively, often with stem cell transplantation. For more information on ALCL, please visit LRF's website at [www.lymphoma.org/alcl](http://www.lymphoma.org/alcl).

## ANGIOIMMUNOBLASTIC T-CELL LYMPHOMA (AITL)

Angioimmunoblastic T-Cell Lymphoma (AITL) is a rare, aggressive PTCL that affects about 10 to 15 percent of all patients with PTCL in the United States. Most patients are middle-aged to elderly and are diagnosed with advanced-stage disease. Symptoms are common and include high fever, night sweats, skin rash, and some types of autoimmune disorders such as autoimmune hemolytic anemia (AIHA) and immune thrombocytopenia (ITP). As a result of these autoimmune disorders, the body's immune system does not recognize, and consequently destroys, its own cells or tissues, such as red blood cells (in the case of AIHA) or platelets (in the case of ITP).

Initially, AITL may be treated with steroids to relieve symptoms such as joint inflammation/pain and skin rash. Most patients are treated with combination chemotherapy and, sometimes, stem cell transplantation. For more information, view the *Angioimmunoblastic T-Cell Lymphoma* fact sheet and *Understanding the Stem Cell Transplantation Process* publication on LRF's website at [www.lymphoma.org/publications](http://www.lymphoma.org/publications).

## CUTANEOUS T-CELL LYMPHOMAS (CTCLS)

Cutaneous T-Cell Lymphomas (CTCLs) are a group of T-cell lymphomas that originate in the skin. These lymphomas are generally less aggressive, and have a different prognosis and treatment approaches than other types of TCLs.

The most common subtype of CTCL is **mycosis fungoides**, which is generally an indolent cancer that starts in the skin and can appear as patches, plaques, or tumors. Patches usually are flat, possibly scaly, and look like a rash; plaques are thicker, raised, often itchy lesions that can be mistaken for eczema, psoriasis, or dermatitis; and tumors are raised bumps or nodules, 1 cm or greater in diameter or height, that may or may not *ulcerate* (develop into an ulcer or open sore). It is possible to have more than one type of skin lesion. The rash can sometimes become thicker or more extensive to involve significant areas of the body. Treatments for CTCL are based on staging. They can be skin-directed – such as radiation therapy – as well as systemic (medication-based) and, often, several types of therapy may be used at once. Combination chemotherapy like CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone)-based regimens used for PTCLs are rarely used and only in specific circumstances.

## SÉZARY SYNDROME

Sézary Syndrome is a rare form of CTCL that affects both the skin and the peripheral blood. Most cases occur in adults over the age of 60 years. The most common symptom is a red, very itchy rash that covers large portions of the body. Abnormal T cells, called Sézary cells, are present in the blood. For more information on CTCLs, view the *Cutaneous T-Cell Lymphoma* fact sheet on LRF's website at [www.lymphoma.org/publications](http://www.lymphoma.org/publications).



## RARE TYPES

### ADULT T-CELL LEUKEMIA/LYMPHOMA (ATLL)

Adult T-Cell Leukemia/Lymphoma (ATLL) is a rare and often aggressive T-cell lymphoma that can be found in the blood (leukemia), lymph nodes (lymphoma), skin, or multiple areas of the body. ATLL only occurs in those who are infected by HTLV-1; however, less than five percent of individuals with HTLV-1 infection will ever develop ATLL.

The HTLV-1 virus is most common in parts of Japan, the Caribbean, and some areas of South and Central America and Africa. The HTLV-1 virus may be transmitted through sexual contact or exposure to contaminated blood, but it is most often passed from mother to child through the placenta, childbirth by Cesarean section, and breastfeeding. For more information, view the *Adult T-Cell Leukemia/Lymphoma* fact sheet on LRF's website at [www.lymphoma.org/publications](http://www.lymphoma.org/publications).

### ENTEROPATHY-TYPE T-CELL LYMPHOMA

Enteropathy-Type T-Cell Lymphoma is an extremely rare and aggressive subtype that appears in the intestines and was previously recognized in two forms: one that is preceded by celiac disease (Type 1) and one that is not preceded by celiac disease, previously Type 2 but now known as monomorphic epitheliotropic intestinal T-cell lymphoma. Chronic diarrhea and gluten sensitivity frequently precedes the former type. Other symptoms include abdominal pain and weight loss. Very specialized treatments are usually necessary to treat this unique subtype and may include surgery, combination chemotherapy such as CHOP, and stem cell transplantation in select patients.

### NASAL NK/T-CELL LYMPHOMA

Nasal NK/T-Cell Lymphoma develops from NK cells, which are closely related to and often have features that overlap with T cells. Although this aggressive lymphoma is very rare in the United States, it is more common in Asia and parts of Latin America. This subtype is associated with the Epstein-Barr virus. It typically originates in the lining of the nose or upper airway at the back of the throat but may appear in the gastrointestinal tract, skin, and other organs (in which case it is referred to as *nasal type*). Treatment of nasal NK/T-cell lymphoma usually consists of radiation treatments combined with chemotherapy. Chemotherapies for this rare disease include VIPD (etoposide, ifosfamide, cisplatin, and dexamethasone), peg-asparaginase (Oncaspar) or L-asparaginase alone or combined with methotrexate and dexamethasone (AspaMetDex), DeVIC (dexamethasone, etoposide, ifosfamide, and carboplatin), or SMILE (dexamethasone, methotrexate, ifosfamide, peg-asparaginase, and etoposide).

### HEPATOSPLENIC GAMMA-DELTA T-CELL LYMPHOMA

Hepatosplenic Gamma-Delta T-Cell Lymphoma is an extremely rare and aggressive disease that involves the liver and/or spleen. It can also involve blood and bone marrow. It most often occurs in young adults and is more common in males. This subtype of PTCL can be associated with immunosuppressive treatments. Patients, especially children, treated with

azathioprine and infliximab (Remicade) for Crohn disease may be more susceptible to this type of PTCL.

As with other rare cancers, patients with enteropathy-type, nasal NK/T-cell, or hepatosplenic gamma-delta T-cell lymphomas should discuss whether clinical trials offer potential treatment options with their healthcare team.

## TREATMENT OPTIONS

For most subtypes of PTCL, the initial treatment is typically a combination chemotherapy regimen, such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone), or other multidrug regimens. Recently, the addition of Brentuximab vedotin to initial chemotherapy was shown to significantly improve outcomes for patients with systemic ALCL and other types of PTCL that have the CD30 marker on their surface. Because many patients with PTCL will relapse, some physicians recommend high-dose chemotherapy followed by an autologous stem cell transplant (patient's own cells are infused after high-dose chemotherapy) for certain patients. For more information on stem cell transplants, view the *Understanding the Stem Cell Transplantation Process* publication on LRF's website at [www.lymphoma.org/publications](http://www.lymphoma.org/publications).

Patients with relapsed disease may be treated with combination chemotherapy such as ICE (ifosfamide, carboplatin, and etoposide) or other combination regimens, followed by stem cell transplantation. Increasingly, newer U.S. Food and Drug Administration (FDA)-approved therapies such as belinostat (Beleodaq), pralatrexate (Folotyn), romidepsin (Istodax), and brentuximab vedotin (Adcetris) are used to treat patients whose lymphoma has come back or never responded to initial therapy. Patients should discuss what treatments are most appropriate for them with their physician.

## TREATMENTS UNDER INVESTIGATION

Many new drugs are being studied in clinical trials for the treatment of PTCL, including:

- Alisertib
- ALRN-6942
- Bendamustine (Treanda)
- Carfilzomib (Kyprolis)
- Devimistat
- Durvalumab (Imfinzi)
- EDO-S101
- GDP (gemcitabine, dexamethasone, and cisplatin)
- Lenalidomide (Revlimid)
- Panobinostat (Farydak)
- Pembrolizumab (Keytruda)
- PI3K inhibitors such as duvelisib (Copiktra)
- Ruxolitinib (Jakafi)
- Valemetostat

Other immunotherapy and cellular therapies are also under investigation. 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 in identifying effective drugs and determining optimal doses for patients with lymphoma. Because PTCL is a rare disease and 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 most novel treatments are often available only through clinical trials. 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](http://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](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* (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](http://www.FocusOnLymphoma.org)) can help patients manage this documentation.



## PATIENT AND CAREGIVER SUPPORT SERVICES

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. One-to-one peer support programs, such as LRF's *Lymphoma Support Network*, connect patients and caregivers with volunteers who have experience with 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.

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.



## PATIENT EDUCATION

LRF offers a wide range of opportunities to learn about lymphoma.

*Ask the Doctor About Lymphoma* is a national series of two-hour, topic-specific, community-based programs that combine a presentation by a medical doctor with an extensive question-and-answer session.

*Lymphoma Workshops* are regional, full-day educational programs that provide the latest information about lymphoma, current treatment options, and patient support issues.

*The North American Educational Forum on Lymphoma* is held annually and provides critical information on treatment options, patient support issues, and the latest in lymphoma research.

*Webinars* are available on specific types of lymphoma, treatment options, and support topics.

Contact LRF:

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## PATIENT PUBLICATIONS

LRF offers a series of print and digital patient education publications. LRF offers comprehensive guides on non-Hodgkin lymphoma (NHL), Hodgkin lymphoma (HL), chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), and the transplantation process in lymphoma, along with a variety of disease- and topic-specific fact sheets. Contact the LRF Helpline at (800) 500-9976 or visit our website at [www.lymphoma.org/publications](http://www.lymphoma.org/publications).



## MOBILE APP

Focus On Lymphoma is the first mobile application (app) that provides patients and caregivers comprehensive content based on their lymphoma subtype and tools to help manage their disease such as: the ability to keep track of medications and blood work, track symptoms, and a way to 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 [www.FocusOnLymphoma.org](http://www.FocusOnLymphoma.org).

To learn more about any of these resources, visit our websites at [www.lymphoma.org/ptcl](http://www.lymphoma.org/ptcl), [www.lymphoma.org/alcl](http://www.lymphoma.org/alcl), or [www.lymphoma.org](http://www.lymphoma.org), or contact the LRF Helpline at (800) 500-9976 or [helpline@lymphoma.org](mailto:helpline@lymphoma.org).

## 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 and PTCL, including our award-winning mobile app. LRF also provides many educational activities, from in-person meetings to webinars for people with PTCL, as well as patient guides and e-Updates that provide the latest disease-specific news and treatment options.

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