Understanding
T-cell Lymphomas



Resource Center
Lymphoma Research Foundation

Overview

T-cell lymphomas can develop in lymphoid tissues such as the lymph nodes (small bean-shaped structures that help the body fight disease, Figure 1) and spleen, or outside of lymphoid tissues such as the gastrointestinal tract (digestive system which includes esophagus, stomach, and intestines), liver, nasal cavity, skin, bone marrow (the spongy tissue inside the bone) and others.

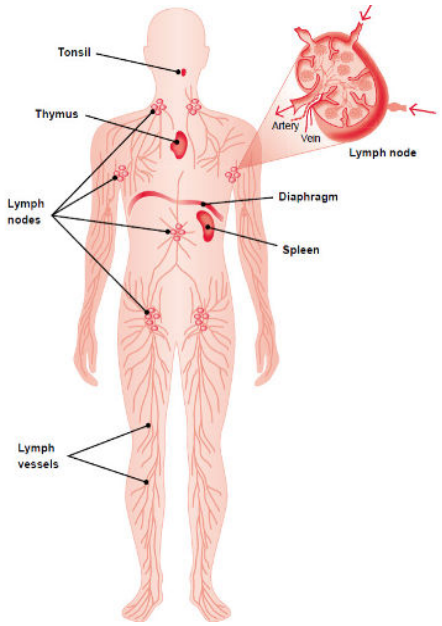


Figure 1. The lymphatic system (tissues and organs that produce, store and carry white blood cells) and the lymph nodes.



T-cell lymphomas develop from white blood cells called T-lymphocytes (also called T-cells) or natural killer (NK) cells (a type of T-cell), and account for less than 15% of all non-Hodgkin Lymphomas (NHLs) in the United States. T-cells direct the immune response by binding and signaling the cancer cells, while NK cells directly and rapidly kill cancer cells.

Most T-cell lymphomas appear from mature T-cells (T-cells that are fully developed). T-cell lymphomas can be aggressive (fast-growing) or indolent (slow-growing) and are mainly found in the skin (cutaneous T-cell lymphomas, CTCL) or throughout the body (peripheral T-cell lymphomas, PTCL):

- PTCL account for about 10% of all cases of NHL.
- CTCL account for about 4% of all NHL.

In rare cases (about 1% of all lymphomas), T-cell lymphoma develops from immature (early stages of development) T-cells in the thymus and is called T-lymphoblastic lymphoma. When cancer develops from NK cells (which share many characteristics with T-cells), it is called NK or NK/T-cell lymphoma and is generally grouped with other T-cell lymphomas. Some subtypes of T-cell lymphoma are listed in Figure 2 and described below.

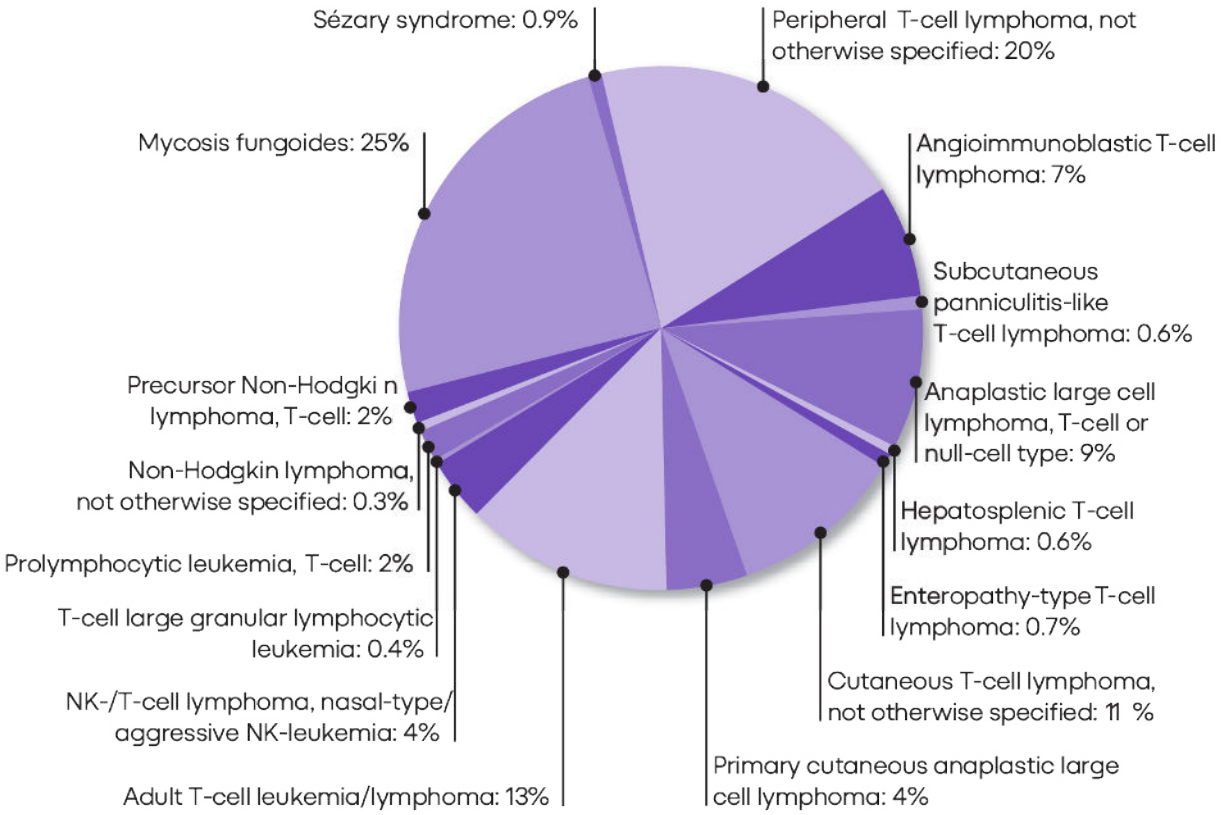


Figure 2. Relative frequencies (probability of T-cell lymphoma happening relative to all lymphomas) of T-cell lymphomas in the United States. Percentages are based on the National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER, an official source for cancer statistics) data, 2008-2017. Some very rare types are not shown in the graph. NK, natural killer.

Symptoms, Staging, and Diagnostic Procedure



Symptoms

Some patients with T-cell lymphoma do not have any obvious signs or symptoms of the disease. Their doctors might detect lymphoma during routine blood tests and/or a physical examination. For others, lymphoma is discovered when symptoms occur and patients go to the doctor because they are worried, uncomfortable, or not feeling well.

T-cell lymphomas may cause different signs and symptoms depending on the type of lymphoma and where it is located in the body. Keep in mind that many of these signs and symptoms are not specific to T-cell lymphoma and can be caused by other conditions. The signs and symptoms commonly found in patients with T-cell lymphoma are:

- Lumps under the skin on the sides of the neck, above the collarbone, or in the underarms, elbows, or groin. Lumps are usually not painful
- Swollen, tender abdomen ("belly" or "stomach")
- Abdominal pain, nausea, vomiting, decreased appetite, or feeling full more easily
- Coughing, trouble breathing, or chest pain or pressure
- Headache, trouble thinking, weakness in extremities (legs or arms), personality changes, double or blurred vision, facial numbness, trouble speaking, or seizures (sudden, uncontrolled burst of electrical activity in the brain)
- Rash or itchy red or purple lumps or nodules under the skin
- "B symptoms" including fever for no known reason, unexplained drastic weight loss, or drenching night sweats that soak clothing and sheets
- Severe or frequent infections
- Autoimmune disorders (group of diseases where the immune system attacks the body's own healthy tissues), such as autoimmune hemolytic anemia (the body immune system attacks its own red blood cells) and immune thrombocytopenia (the body immune system attacks its own platelets)

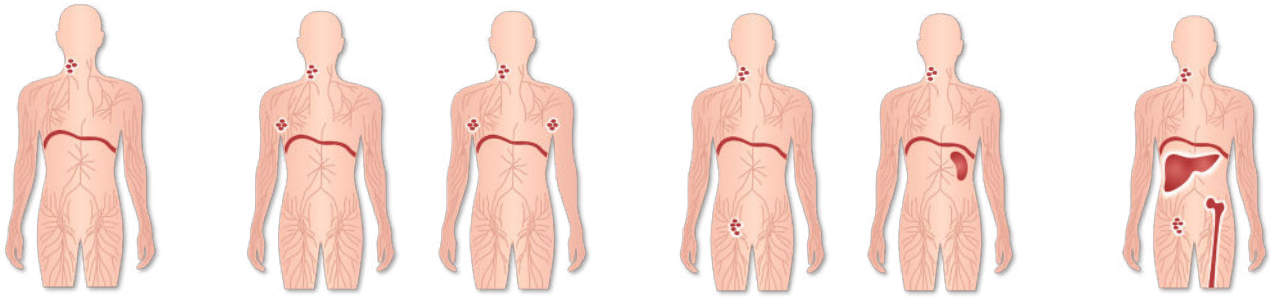
Diagnostic Procedure

To make a definite diagnosis of T-cell lymphoma, doctors need to collect a sample of the affected lymph node. This procedure is called a biopsy (a procedure in which a piece of the abnormal tissue is removed from the body and examined under a microscope). Biopsies where an entire lymph node or tumor is removed (called excisional biopsies) are preferred to ensure there is enough sample to determine the type of lymphoma. However, in some cases, core needle biopsies (a large needle is inserted into a lymph node suspected to be cancerous and a small tissue sample is withdrawn) can be sufficient for diagnosis. The biopsy is typically studied by a pathologist (doctor who specializes in the diagnosis of diseases by studying the cells from a patient's body fluids and tissue samples) and preferably a hematopathologist (pathologist who has undergone additional training in the diagnosis of blood cancers, including lymphoma) who is experienced in diagnosing lymphoma. There are multiple subtypes of T-cell lymphoma, some very uncommon, and additional tests may be needed to make an accurate diagnosis. Determining the exact T-cell lymphoma subtype helps to identify the appropriate treatment options for the patient.

Staging

After a diagnosis of T-cell lymphoma, it is important to determine if and how far the lymphoma has spread. This process is called staging, and it uses the results of the different tests (such as biopsies and scans) to determine the severity of the disease and the appropriate treatment. The Lugano staging system is used for T-cell lymphomas and is depicted in Figure 3 below. This system categorizes lymphoma from Stage I (least severe) to IV (most severe), based on whether the disease is restricted to a single group of lymph nodes, has spread to other lymph nodes, or has reached the bone marrow and/or other organs (like the liver or lungs).





Stage I:
Involvement of a single lymph node or group of adjacent nodes

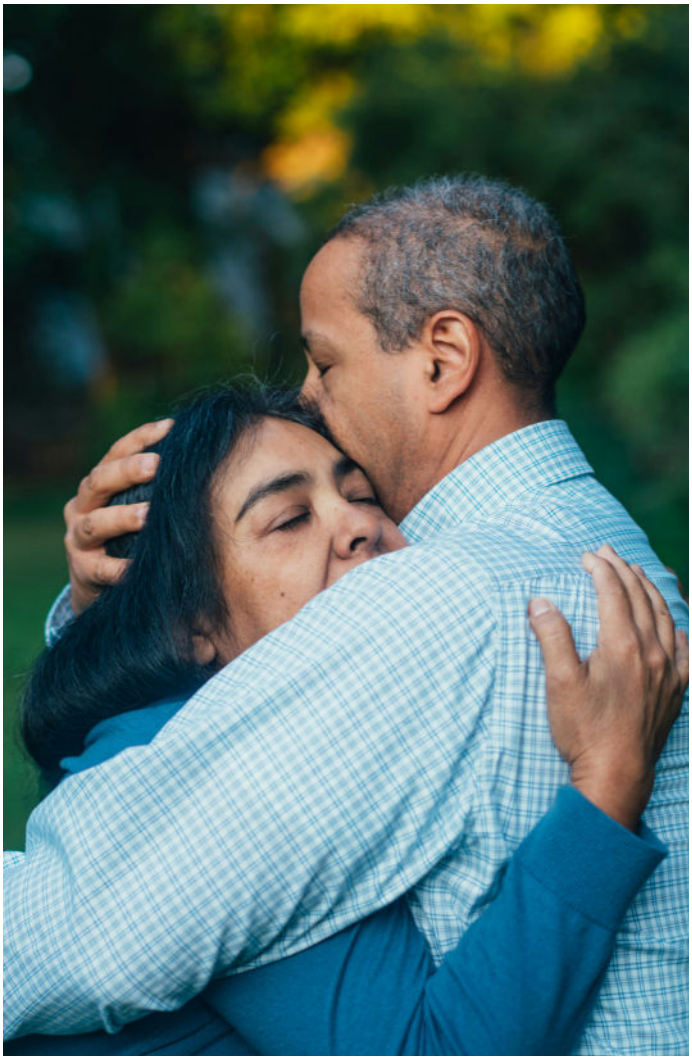
Stage II:
Involvement of two or more groups of lymph nodes on the same side of the ***diaphragm*** (muscle that separates the chest from the abdomen)

Stage III:
- Involvement of lymph nodes on both sides of the diaphragm, or
- Involvement of lymph nodes above the diaphragm plus spleen involvement

Stage IV:
Widespread disease in lymph nodes, bone marrow, and organ involvement, such as liver or lungs

Figure 3. Staging of lymphoma according to the Lugano system.

To stage a lymphoma, the patient might need imaging tests such as a positron emission tomography (PET) scan or abdominal and chest computed tomography [CT] scans. A CT scan allows the physician to see inside the chest and abdomen, locating the tumor. A PET scan is a form of imaging that uses a special dye to locate the lymphoma cells in the body. Other staging tests may include a bone marrow biopsy, spinal tap (lumbar puncture, a procedure where a small needle is inserted into the back and spinal fluid is withdrawn), endoscopy/colonoscopy (medical procedures where an instrument is introduced into the body to give a view of the stomach or colon, respectively), and magnetic resonance imaging (MRI, a type of scan that uses a strong magnet and radio waves to produce detailed images of the inside of the body). Physicians may also request blood tests and an echocardiogram (a type of scan that uses sound waves to produce images of the heart and nearby blood vessels) to help evaluate overall health and risks with chemotherapy.



Subtypes

Common PTCLs

Peripheral T-cell lymphoma, not otherwise specified (PTCL-NOS), the most common subtype of PTCL (around 30% of PTCLs in the United States), and refers to a group of lymphomas that do not fit into any of the other PTCL subtypes. PTCL-NOS usually occurs in adults in their 60s. Although most patients with PTCL-NOS are diagnosed when the disease is only located in the lymph nodes, extranodal sites (sites in the body 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. Patients are most often treated with chemotherapy and may be considered for an autologous stem cell transplant (SCT, patient's own cells are infused after high-dose chemotherapy) following initial chemotherapy. While PTCL-NOS is potentially curable, in some patients the disease tends to relapse (disease returns after treatment).

Anaplastic large cell lymphoma (ALCL) accounts for around 15% of all T-cell lymphomas. There are several different subtypes of ALCLs. All patients with ALCL have a protein called CD30 on the surface of cancer cells, which helps detect and diagnose ALCL. CD30 is characteristic of some forms of NHLs, while the majority of Hodgkin's lymphoma cells are positive for CD30.

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 (disease has grown in size and/or spread throughout the body) at diagnosis and can progress (grow and/or spread) rapidly. Patients with systemic ALCL are divided into two groups, depending on whether or not the surface of their cells have an abnormal form of a protein called anaplastic lymphoma kinase (ALK):

- ALK-positive (ALK protein is present in cancer cells) disease can respond well to chemotherapy treatment and is potentially curable.

- ALK-negative (ALK protein is not present in cancer cells) disease may require stronger treatments than ALK-positive disease. It can be cured with chemotherapy, but relapse occurs more frequently than in ALK positive disease.

Primary cutaneous ALCL appears only on the skin and is often less aggressive (it grows slower). A rare type of ALCL called breast implant-associated (BIA)-ALCL has been observed in some patients who have or had breast implants, especially implants with textured (non-smooth) surfaces. Most patients with BIA-ALCL may be treated with surgery alone. While chemotherapy or radiation therapy is considered for some patients with these diseases, there are patients who may not require additional therapy.

Angioimmunoblastic T-cell lymphoma (AITL) is a rare and often fast-growing form of PTCL. It accounts for about 15-30% of PTCLs and is more common in older people (median age at diagnosis is 65 years), though it can affect young adults as well. Most patients with AITL are diagnosed with advanced-stage disease (Stage III or Stage IV disease). Patients are most often treated with chemotherapy and may be considered for an autologous SCT following initial chemotherapy. While AITL is potentially curable, in some patients the disease tends to relapse.

Nodal T-follicular helper phenotype lymphomas (nTFHL) including:

- nTFHL angioimmunoblastic-type (nTFHL-AI)
- nTFHL follicular-type (nTFHL-F)
- nTFHL not otherwise specified (nTFHL-NOS)

These are a rare and aggressive family of T-cell lymphomas, accounting for about 25-40% of all patients with PTCL in the United States. The most common type is the nTFHL-AI which was previously called angioimmunoblastic T-cell lymphoma (AITL). These lymphomas are more common in older adults (median age at diagnosis of around 65 years) and are usually diagnosed in an advanced stage. Patients are most often treated with chemotherapy and may be considered for an autologous SCT following initial chemotherapy. While nTFHL is potentially curable, in some patients the disease tends to relapse.



Uncommon PTCLs

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 other areas of the body. ATLL has been linked to infection with human T-lymphotropic virus type 1 (HTLV-1). However, not all individuals that are positive for HTLV-1 will develop ATLL.

This virus is commonly found in people from the Caribbean, parts of Japan, and some areas of South and Central America, Africa, Middle East, and more rarely in Australia and Asia. The HTLV-1 virus is believed to be passed through sexual contact or contact with blood, but it is most often passed from mother to child through the placenta, at

childbirth, or during breastfeeding. Only 5% of those who carry the virus will develop lymphoma. Treatment commonly includes chemotherapy and antivirals to treat the underlying HTLV-1 infection. In some patients, allogeneic SCT (patients receive stem cells from a familiar or unrelated donor) may be appropriate following remission (disappearance of signs and symptoms). The acute and lymphoma subtypes are aggressive forms of ATLL, whereas chronic and smoldering are indolent.

- Acute: Symptoms develop rapidly and may include fatigue (extreme tiredness), skin rash, and enlarged lymph nodes in the neck, underarm, or groin. The characteristics of acute ATLL are a high level of white blood cells (cells that help the body fight infections and cancer) often with hypercalcemia (elevated calcium levels in the blood), which can cause confusion, irregular heartbeat and severe constipation (a condition in which stool becomes hard, dry, and difficult to pass, and bowel movements don't happen very often). Acute ATLL may spread to extranodal sites.

- Lymphoma: This aggressive type of ATLL is found primarily in the lymph nodes, causes swollen or enlarged lymph nodes and may cause an increase in the level of white blood cells, skin rash, and hypercalcemia.

- Chronic: This slow-growing type of ATLL can result in elevated lymphocytes in the blood, enlarged lymph nodes, skin rash, or fatigue. It can also be found in other areas of the body such as the spleen and liver.

Smoldering: This slow-growing type of ATLL is associated with very mild symptoms, such as a few skin lesions and/or rash.

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. Patients with enteropathy-Associated T-Cell Lymphoma frequently have chronic diarrhea, gluten sensitivity (feeling sick after eating gluten), and celiac disease (autoimmune disease where the ingestion of gluten leads to damage of the small intestine). 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 SCT in selected patients.

Hepatosplenic gamma-delta T-cell lymphoma is an extremely rare and aggressive disease that affects the liver and/or spleen. It can spread into the blood and bone marrow. It most often occurs in adolescents and young adults and is more common in males. This lymphoma is associated with immunosuppressive treatments (drugs that lower the activity of the immune system). Patients, especially children, who have been treated with immunosuppressants such as azathioprine and infliximab (Remicade) for Crohn's disease (a type of inflammatory bowel disease), may be more susceptible to this type of lymphoma. Allogeneic SCT are also considered after initial treatment for selected patients.

Extranodal NK/T-cell lymphomas (ENKTL) develop from NK cells. This aggressive lymphoma is relatively rare in the United States, but common in Asia and parts of Latin America. It typically develops in the interior of the nose or upper airway (nose, nasal cavity, mouth, throat, and larynx) at the back of the throat (in which case it is referred to as nasal type) but may appear in the gastrointestinal tract, skin, bone marrow, 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 received immunosuppressants after an organ or bone marrow transplant (to prevent rejection of the transplanted organ). These treatments put patients at risk for this type of lymphoma. While PTLD more commonly leads to B-cell lymphomas, it can sometimes lead to a T-cell lymphoma.

Lymphoblastic lymphoma can appear from either immature B-cells or T-cells (B- or T-cells that are not fully developed), but more commonly comes from T-cells, making up to 90% 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.

This lymphoma can progress rapidly, if not properly treated, and frequently appears in the middle of the chest, or mediastinum (area between the lungs including heart, throat, thymus, and lymph nodes). In this type of lymphoma, immature white blood cells (called lymphoblasts) can appear in the lymph nodes, bone marrow or spleen.

Lymphoblastic lymphomas, like other subtypes of lymphoma, can result in opportunistic infections (infections that happen more often or are more serious in patients with a weaker immune system), and affect the body's ability to make blood cells.

This subtype of T-cell lymphoma spreads to the central nervous system (brain and spinal cord) more often than 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 (high-dose or over several months) chemotherapy which is associated with a very high rate of complete remission and cure.



Common CTCL

Cutaneous T-cell lymphoma (CTCL) describes a group of typically indolent lymphomas that appear on, and most often only affect the skin. Some patients may develop lymphoma in their blood, lymph nodes and, more rarely, other organs.

Mycosis fungoides (MF) is the most common subtype of CTCL (around 60% of all cases). It usually appears as skin patches (flat and often scaly rashes), plaques (thick, raised and often itchy lesions, similar to those found in eczema, psoriasis or dermatitis), or tumors (raised bumps or nodules with a diameter or height ≥ 1cm, which may turn into an open sore). More than one type of lesion may be present at any time.

Sézary syndrome (SS) is a less common and more aggressive form of CTCL that affects both the skin and the blood. Most individuals with SS are adults between the ages of 55 and 60 years. The most common symptoms are swollen lymph nodes and a red, very itchy rash that covers large portions of the body. Cancer T-cells, called Sézary cells, can be seen under a microscope and are present in both the skin and blood. There are other rarer forms of CTCL as well.

For more information, view the Cutaneous Lymphomas guide on the Foundation's website (visit lymphoma.org/publications).



Treatment Options

First Line Therapies

Peripheral T-cell Lymphoma (PTCL)

Because there are so many different subtypes of T-cell lymphoma, treatment types vary widely, but initial treatment for the more common types of PTCL typically includes combination chemotherapy regimens usually for curative intent. Standard lymphoma therapies include:

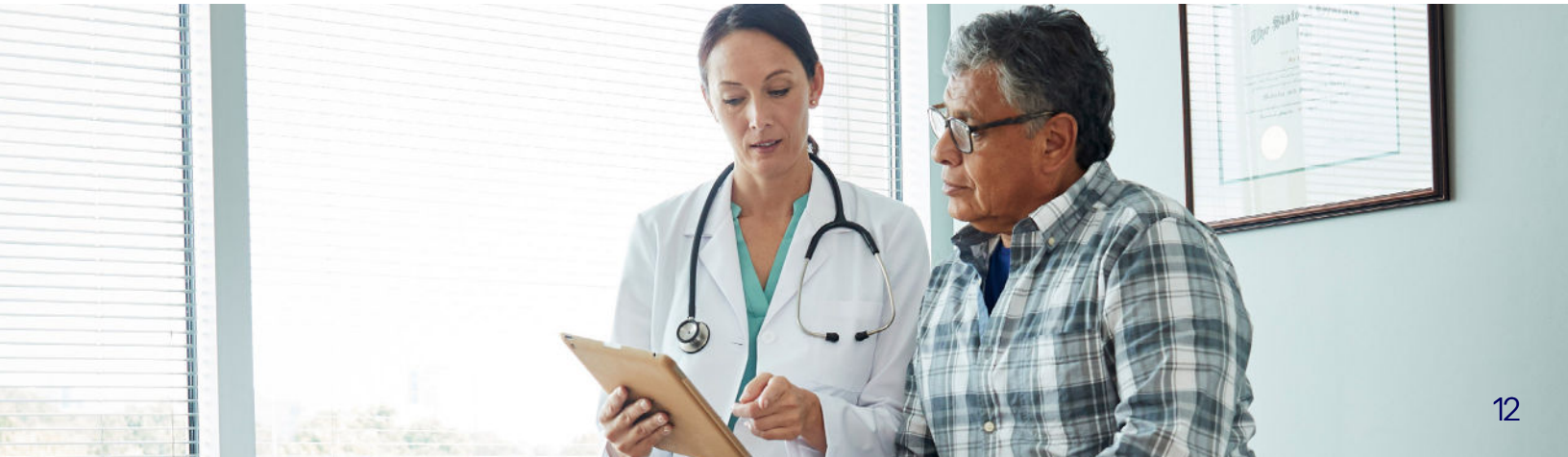
- Chemotherapy (drugs that stop the growth of or kill cancer cells):
  - CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone).
  - CHOEP (CHOP plus etoposide).
  - Dose-adjusted EPOCH (etoposide, vincristine, doxorubicin, cyclophosphamide, and prednisone).

- Chemoimmunotherapy: a combination of chemotherapy (drugs that stop the growth of or kill cancer cells) with immunotherapy (drugs that use the body's immune system to fight cancer):
  - An ADC is a monoclonal antibody (a protein made in the laboratory that binds to cancer cells and helps the immune system destroy them) attached to a chemotherapy drug. The monoclonal antibody in the ADC recognizes and binds to a protein on the cancer cell surface. Once the ADC is inside the cell, the chemotherapy drug separates from the ADC and kills the cancer cell by targeting cell multiplication.
  - BV-CHP is a combination of the ADC brentuximab vedotin (Adcetris) and the chemotherapy regimen cyclophosphamide, doxorubicin, and prednisone (CHP). This combination is used for the treatment of lymphomas that are positive for CD30 (molecule present on the surface of certain lymphomas) and has been approved for ALCL and CTCL.

- Immunotherapy such as:
  - Immunomodulatory agents, drugs that work on the immune system directly by regulating (activating or slowing down) the activity of specific proteins.

- Radiation which uses high-energy radiation to kill cancer cells.

- SCT (the patient is treated with high-dose chemotherapy or radiation to remove their blood-forming cells or stem cells and then



receives healthy stem cells to restore the immune system and the bone marrow's ability to make new blood cells). For more information about SCT, please view the Understanding Cellular Therapy Guide, also on the Foundation's website (lymphoma.org/publications).
  - Allogeneic SCT (patients receive stem cells from a familiar or unrelated donor)
  - Autologous SCT (patient receives own stem cells)

- Antiviral therapy (treatment of infections caused by a virus). Zidovudine (Retrovir, AZT) in combination with interferon-alpha, to treat the underlying HTLV-1 infection (in patients with slow-growing ATLL).

Patients diagnosed with rare forms of lymphoma should consult their medical team to find new promising therapies or to enroll in clinical trials.

For some patients who have one of the slower-growing subtypes of ATLL with mild or no symptoms, physicians may recommend not treating the disease right away. This is called active surveillance (also known as "watchful waiting" or "observation"). In this case, patients are monitored through regular physical exams (to check for any swollen lymph nodes) or periodic imaging tests (like CT scans). If patients begin to have symptoms or signs of disease progression, treatment is initiated. For more information about active surveillance, please see the Active Surveillance publication on the Foundation's website (lymphoma.org/publications).

Patients diagnosed with rare forms of lymphoma should consult their medical team to find new promising therapies or to enroll in clinical trials.

Cutaneous T-cell lymphoma (CTCL) Therapy for CTCL often includes treatments directed at the skin (also called topical therapies which are applied directly to the skin) to improve quality of life, such as:

- Corticosteroids
- Retinoids
- Chemotherapy
- Phototherapy (use of ultraviolet light to kill cancer cells on the skin)
- Electron beam radiation therapy (a type of radiation therapy that only affects the skin and does not reach the internal organs).

When skin directed therapies do not provide sufficient disease control or when the disease affects other areas of the body, systemic therapy is considered. For some patients with CTCL that has spread to the bloodstream, a procedure called extracorporeal photopheresis (ECP) is approved. During 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.



Relapsed or Refractory

Peripheral T-cell Lymphoma (PTCL)

Some patients with T-cell lymphomas respond to initial treatment and go into remission. In other cases, the disease may relapse or become refractory (does not respond to treatment). For these patients, different therapies may result in improved treatment outcomes.

Patients with relapsed or refractory T-cell lymphomas are usually treated with:

- Chemotherapy such as pralatrexate (Folotyn), which works as a dihydrofolate reductase inhibitor and blocks the cells' ability to divide and multiply.

- Targeted therapies (drugs that target molecules that cancer cells use to grow and spread). This includes inhibitors of proteins involved in cell signaling and growth.
  - Histone deacetylase (HDAC) inhibitors such as belinostat (Beleodaq) or vorinostat (Zolinza)
  - ALK inhibitors such as crizotinib (Xalkori)

- Immunotherapy, including:
  - Monoclonal antibody such as the anti-CCR4 mogamulizumab (Poteligeo)
  - ADC such as brentuximab vedotin (Adcetris).
  - Immunomodulatory drugs such as lenalidomide (Revlimid).

In some patients with PTCL, SCT is considered the next step in therapy after combined chemotherapy. However, for some patients, chemotherapy regimens or SCT might not be recommended because of their side effects. Single-agent therapies with less side effects are also available and might cause a long-lasting remission in such patients.



Table 1 shows the drugs approved by the FDA for patients who have relapsed or became refractory to first-line chemotherapy.

Cutaneous T-cell lymphoma (CTCL)

Patients with high-risk disease (advanced disease that has failed to adequately respond to multiple forms of systemic therapy) may receive an allogeneic SCT. To know more about SCT, please view the Understanding Cellular Therapy guide at the Foundation's website (lymphoma.org/publications).

Some other drugs used in other types of lymphoma that may occasionally be considered for the treatment of patients with AITL include targeted therapies like romidepsin (Istodax), duvelisib (Copiktra), and ruxolitinib (Jakafi), and chemotherapies like gemcitabine (Gemzar), bendamustine (Treanda), and azacitidine (Vidaza). Immunosuppressive agents like cyclosporin can also be used in patients who have autoimmune disorders. Alemtuzumab (Campath) is a monoclonal antibody also occasionally considered, although it is no longer commercially available and is provided only through the Campath Distribution Program.

Table 1. FDA-approved treatments for relapsed/refractory T-cell lymphomas.

Agent (Drug)	Indication
Belinostat (Beleodaq)	Indicated for PTCL.
Pralatrexate (Folotyn)	Indicated for PTCL.
Mogamulizumab (Poteligeo)	Indicated for CTCL.
Brentuximab vedotin (Adcetris)	Indicated for PTCL
Crizotinib (Xalkori)	Indicated for relapsed or refractory ALK-positive ALCL.
Vorinostat (Zolinza)	Indicated for CTCL
Denileukin diftitox (Lymphir)	Indicated for CTCL

ALCL, anaplastic large cell lymphoma; ALK, anaplastic lymphoma kinase; CTCL, cutaneous T-cell lymphomas; PTCL, peripheral T-cell lymphoma.

Treatments Under Investigation

Treatment options for the different types of newly diagnosed and relapsed/refractory T-cell lymphomas are expanding as new treatments are discovered, and current treatments are improved. Treatments currently being investigated alone or in combination are described in the table below.

Table 2. Selected agents under investigation for T-cell lymphomas in Phase 2-3 clinical trials

Agent (Drugs)	Class (Type of treatment)	Type of lymphoma
Azacitidine (CC-486)	Chemotherapy	R/R PTCL, untreated PTCL-NOS, untreated nTFHL
Bendamustine (Treanda)	Chemotherapy	R/R nTFHL
Cemiplimab (Libtayo)	Immunotherapy; immune checkpoint inhibitor, anti-PD-1	R/R ENKTL
DR-01	Immunotherapy; monoclonal antibody, anti-CD94	R/R CTCL, R/R PTCL-NOS
Durvalumab (Imfinzi)	Immunotherapy; immune checkpoint inhibitor, anti-PD-1	R/R MF, untreated SS, R/R CTCL, R/R PTCL-NOS
Duvelisib (Copiktra)	Targeted therapy; PI3K inhibitor	R/R PTCL, untreated PTCL
Golidocitinib (AZD4205)	Targeted therapy; JAK1 inhibitor	R/R ENKTL, untreated PTCL
Lacutamab (IPH4102)	Immunotherapy; monoclonal antibody, anti-KIR3DL2	R/R PTCL, R/R MF, R/R SS
MB-105	CAR T-cell therapy; anti-CD5	R/R PTCL

Agent (Drugs)	Class (Type of treatment)	Type of Lymphoma
Nivolumab (Opdivo)	Immunotherapy; immune checkpoint inhibitor, anti-PD-1	R/R ALCL
Pembrolizumab (Keytruda)	Immunotherapy; immune checkpoint inhibitor, anti-PD-1	R/R ALCL, R/R AITL, R/R nTFHL
PTX-100 (GGTI-2418)	Targeted therapy; GGTase I inhibitor	R/R CTCL
Ruxolitinib (Jakafi)	Targeted therapy; JAK1/2 inhibitor	Untreated ATLL
Soquelitinib (CPI-818)	Targeted therapy; ITK inhibitor	R/R PTCL-NOS, R/R ATCL, R/R nTFHL
Valemetostat (DS-3201b)	Targeted therapy; EZH1/2 dual inhibitor	R/R ATLL
Venetoclax (Venclexta)	Targeted therapy; BCL-2 inhibitor	R/R PTCL

AITL, angioimmunoblastic T-cell lymphoma; ALCL, anaplastic large cell lymphoma; ATLL, adult T-cell leukemia/lymphoma; BCL-2, B-cell lymphoma 2; CTCL, cutaneous T-cell lymphoma; ENKTL, extranodal natural killer T-cell lymphomas; EZH1/2, enhancer of zeste homologue 1 and 2; ITK: interleukin-2-inducible T-cell kinase; JAK1/2, Janus kinase 1/2; PD-1, programmed cell death protein 1; PI3K, phosphoinositide 3-kinase; PTCL-NOS, peripheral T-cell lymphoma-not otherwise specified; MF, mycosis fungoides; nTFHL, nodal T-follicular helper phenotype lymphomas; KIR3DL2, killer cell immunoglobulin like receptor three Ig domains and long cytoplasmic tail 2; R/R, relapsed and/or refractory; SS, Sézary syndrome.

In addition, a number of promising clinical trials are studying combinations (two or more drugs given at the same time) of these new treatments which in some cases may be more effective than the single agent (one drug) alone. It is critical to remember that scientific research is always evolving. Treatment options may change as new treatments are discovered, and current treatments are improved. Therefore, it is important that patients check with their physician or with the Foundation for any treatment updates that may have recently appeared. It is also very important that all patients with T-cell lymphoma consult a specialist to clear up any questions.

Clinical Trials

Clinical trials are important in finding effective drugs and best treatment doses for patients with T-cell lymphoma. In many of the rare subtypes of T-cell lymphoma, no standard of care is defined. Clinical trial enrollment is critical for establishing more effective, less toxic treatments.

The rarity of the disease also means that the latest treatments are often only available through clinical trials. Patients interested in participating in a clinical trial should view the Understanding Clinical Trials fact sheet on the Foundation's website (visit lymphoma.org/publications) talk to their physician, or contact the Foundation's Treatment Navigation Service to receive personalized educational materials, a comprehensive overview of standard and emerging treatments, and a customized clinical trials search list tailored to your diagnosis by calling **(800) 500-9976** or emailing **connect@lymphoma.org.**





How to Be a Self-Advocate

Being a self-advocate and an active participant in healthcare decisions can be a positive experience. It may help patients regain a sense of control that they may have lost following the lymphoma diagnosis by making sure patients receive the best care. Patients and care partners should remember they are partners in their treatment plan.

- Do not be afraid to ask your doctors or nurses questions about your care. An educated patient asking questions is not 'being a challenge to your physician' (or 'being a difficult patient').
- Learn more about lymphoma by asking your doctor for information and visiting reliable websites, such as the Foundation's at www.lymphoma.org.
- Take advantage of counseling, support groups, nutritional counseling, fitness classes, expressive arts, and other services offered at your doctor's office, cancer center, or hospital.
- Consider joining the Foundation's Lymphoma Support Network, a nationwide peer support program that matches patients and care partners with people who have had similar experiences. For information about the program, call **(800) 500-9976** or email connect@lymphoma.org.
- Finally, it is important that patients not be afraid to talk with the healthcare team about nonmedical issues such as transportation, finances, insurance, working through treatment or taking time off, and childcare. There are nurses, social workers, and physician's assistants that are able to provide the support and resources to help.



Follow-Up

Living with Treatment Side Effects

After your treatments have ended you may still experience side effects. Some side effects develop during treatment and last for months or longer (called "long-term side effects") and others appear long after the treatment has ended (called "late side effects"). These effects may vary for each survivor and depend on the type of lymphoma you had, the treatment you received, and your age and overall health. While blood cancer survivors don't always have serious long-term or late effects of treatment, it is important to know that some side effects may take time to go away and may even be permanent. Talk to your healthcare team about what these possible effects might be and ask for ways to prevent and/or relieve them.

Long-term and late treatment effect may include "chemo brain" or "brain fog" (decreased memory, concentration and inability to multitask), psychological effects (anxiety, depression and post-traumatic stress disorder) or a variety of physical effects, which are highly dependent on the treatment:

- Fertility issues
- Infections
- Thyroid problems
- Heart disease
- Lung damage
- Decreased bone density and osteoporosis (a condition that weakens bones, making them fragile and more likely to break)
- Eye and vision problems
- Nerve damage
- Dental and mouth problems
- Other cancers

Long Term Follow-Up Care Plan

All lymphoma survivors should have a long term follow up plan (also called a "survivorship care plan") after treatment ends. This plan is arranged by your healthcare team and includes a summary of the treatments you received, recommendations for follow-up care based on your medical history, and schedules for medical exams to check if the lymphoma has come back (recurrence). This allows your healthcare team to monitor your overall health and look out for long-term effects or other problems that may occur at any point after treatment. Your doctor will let you know how often you need to return for checkup appointments and which physical exams and blood tests are necessary. These checkups usually include a review of your medical history, physical exam and bloodwork, as well as specific exams or screenings recommended by your doctor (see Health Screenings to Consider on next page).

A follow-up care plan may also provide information to help you meet any emotional, social, legal, and/or financial needs. Your health care team can help you decide which doctor to see for your follow-up care plan (the same doctor who treated your lymphoma, a health care provider specialized in caring or cancer survivors, or your primary care provider [PCP]). Some clinics specialized in follow-up cancer plans offer comprehensive support to cancer survivors (called "survivorship clinics"). You can visit oncolink.org/clinics/search to check for survivorship clinics in your area.

Health Screenings To Consider

As a survivor, there are specific health screenings and exams that you may do at an earlier age than the general population. These will be adapted to the type of lymphoma you had and the treatment you received. For instance, due to the increased risk of secondary breast cancer from radiation therapy, women who received radiation therapy to the chest area during childhood, adolescence, or young adulthood should have clinical breast examinations yearly until age 25, then every six months thereafter. In addition, these women should receive yearly mammograms and breast magnetic resonance imaging (MRI) beginning at age 25 or eight years after completion of the radiation therapy, whichever comes last.

Other health screenings the physician may suggest include:

- Bone density scans
- Cardiovascular monitoring
- Chest or whole body imaging
- Screening for other cancers (e.g. colorectal or skin)
- Dental screenings
- Eye exams
- Lipid blood tests
- Thyroid function tests

Because everyone is different, survivors should talk with their physicians about which screenings are most appropriate and when they should be started.

Survivorship

As a cancer survivor, it is important that you practice self-care regularly to reset your physical and emotional well-being. Adopting routines of self-care will help you recharge your batteries and stay healthy. Talk with your healthcare team about developing a wellness plan to help you stay physically and emotionally healthy and improve your mood. Consider the following suggestions:

- Watch your health. Stay up-to-date with your own medical appointments and take any medications as prescribed.
- Exercise. Stay active with short periods of daily exercise (30 minutes of power walking, jogging or biking). If not possible, take the stairs instead of the elevator or park farther away than usual.
- Eat well. Include fruits and vegetables in your meals and maintain a balanced diet.
- Cut down on risk factors. Quit smoking and reduce alcohol intake.
- Sleep. Try to get 7 hours of sleep per night, or take naps when needed.
- Rest. Meditation, deep breathing and stretching can help you relax and reduce stress.
- Write it down. Keeping a journal with thoughts and feelings may help to let go of worries and fears.

Care Partners

There are many ways you can help a loved one with lymphoma, as follows:

- Be present. The most important thing that a care partner can do is to "just show up."
- Be prepared. Talk with the healthcare team so that you know what to expect throughout the treatment, how to manage symptoms and when to ask for help.
- Listen. Each person asks for help in different ways, verbally (through words) and nonverbally, and some may require more comfort while others are more action oriented.
- Avoid "cheerleading". Do not disregard your love one's negative feelings (sadness, anger or worry).
- Organize the help. A rush of sudden help upon diagnosis can make the situation harder to manage and create unproductive tension.
- Set up remote access with computer and/or phone access. This is helpful for regular communication with your loved one.
- Offer rides. This is important for people with decreased mobility or limited resources.
- Take notes. If you go into the appointments, write down notes with the doctor's plan, medications, potential side effects and other relevant information.

Patients and their care partner are encouraged to keep copies of all medical records. This includes test results as well as information on the types, amounts, and duration of all treatments received. Medical records are important for keeping track of any side effects resulting from treatment or potential disease recurrences. The Foundation can help patients manage this documentation.

View the Care Partners fact sheet on the Foundation's website at lymphoma.org/publication for more info.

Questions to Ask Your Healthcare Team

- What is my exact diagnosis? What subtype of lymphoma do I have? May I have a copy of the report from the pathologist?
- What is the stage of my disease? In what area of the body is it specifically located?
- What are my treatment choices? Which do you recommend for me and why? Would choosing one treatment prevent me from getting a different kind of treatment later on? How are the different treatments administered?
- Do I need more than one type of treatment?
- What is the goal of treatment? What are the expected benefits of each type of treatment?
- How will we know if the treatment is working? What tests will I need to determine if treatment is working, and how often will I need to be tested?
- How long will the treatment last?
- What are the chances the treatment will be successful?
- What is a clinical trial? Are clinical trials available that are studying new treatments for my type of lymphoma? Would a clinical trial be appropriate for me? How would I benefit? Are there any drawbacks of participating in a clinical trial?
- Will I be able to work during treatment? Will I be able to drive or take public transportation during my treatment?
- Should I take care of other medical or dental issues before I start treatment?
- How much will the treatment cost? Will my insurance cover some or all of it? What will my out-of-pocket costs be?



The Foundation's Programs and Services

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. The Foundation's Lymphoma Care Plans organize information on your health care team, treatment regimen, and follow-up care. The Foundation also provides a Lymphoma Care Plan for Aggressive Lymphomas, Chronic Lymphocytic Leukemia (CLL), and one dealing with Survivorship. 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.**

Patient Education Programs

The Foundation also offers a variety of educational activities, including live meetings and webinars for individuals looking to learn directly from lymphoma experts. These programs provide the lymphoma community with important information about the diagnosis and treatment of lymphoma, as well as information about clinical trials, research advances and how to manage/cope with the disease. These programs are designed to meet the needs of a lymphoma patient from the point of diagnosis through long-term survivorship. To view our schedule of upcoming programs, please visit lymphoma.org/programs.

Lymphoma Resource Center

The Foundation's Lymphoma Resource Center staff are available to answer your general questions about lymphoma 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. The Foundation also offers a one-to-one peer support program called the Lymphoma Support Network and clinical trials information through our Treatment Navigation Service. For more information about any of these resources, visit our website at lymphoma.org, or contact The Foundation's Lymphoma Resource Center at **(800) 500-9976** or **connect@lymphoma.org.**

Para información en español, por favor visite **lymphoma.org/es** (For Information in Spanish please visit **lymphoma.org/es**).

Lymphoma Support Network

The Foundation's one-to-one peer support program – Lymphoma Support Network – connects patients and care partners with volunteers who have experience with lymphomas, similar treatments, or challenges, for mutual emotional support and encouragement. You may find this useful whether you or a loved one is newly diagnosed, in treatment, or in remission.
For more information about this program, please contact the Foundation's Lymphoma Resource Center at **(800) 500-9976** or visit lymphoma.org/resources/supportservices/lsn.

Treatment Navigation Service

A lymphoma diagnosis can bring a lot of questions about your subtype, your treatment options, and what comes next. The Lymphoma Resource Center's Treatment Navigation Service is here to help you find answers. Through a one-on-one consultation with the Resource Center team, you'll receive personalized educational materials, a comprehensive overview of standard and emerging treatments, and a customized clinical trials search list tailored to your diagnosis. You'll walk into your next appointment feeling prepared and empowered to ask the right questions and take the next step in your journey. This free service is available to every member of our community, patients, survivors, and care partners alike. Reach out to the Lymphoma Resource Center to take your next step with confidence.

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For individuals outside of the U.S. seeking information, the Foundation recommends the Lymphoma Coalition. The Lymphoma Coalition is a global network of worldwide nonprofit/NGO lymphoma patient organizations with information appropriate for non-U.S.-based audiences. Additional information can be found by visiting their website at https://lymphomacoalition.org/.

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