LYMPHOMA RESEARCH • FOUNDATION

# Understanding Lymphoma: Angioimmunoblastic T-Cell Lymphoma

**Angioimmunoblastic T-cell lymphoma (AITL) is a rare and often fast-growing form of peripheral T-cell lymphoma (PTCL).** It accounts for about 20%-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. Symptoms of AITL include:

- Fatigue
- High fever
- Night sweats
- Skin rash
- Autoimmune disorders (group of diseases where the immune system attacks the body's own healthy tissues), such as autoimmune hemolytic anemia (AIHA, the body's immune system attacks its own red blood cells) and immune thrombocytopenia (ITP, the body's immune system attacks its own platelets)

Diagnosing AITL requires taking a biopsy (sample of the tumor tissue) and looking at the cells under a microscope. The cells are also analyzed by flow cytometry (a technique that uses a laser to detect and count the different types of blood cells according to their size and number of small particles). Testing for specific genetic mutations (permanent changes) in the DNA (deoxyribonucleic acid, the molecule that carries the genetic information inside the cells) is also required. Other tests may be done to determine the extent, or stage (how much the disease has grown and the different locations in the body it affects) of the disease. These can include blood tests, a computed tomography (CT) scan (a procedure that uses X-rays to take detailed pictures of areas inside the body), a positron emission tomography (PET) scan (a procedure that uses a special dye to locate the cancer in the body), and a bone marrow (the spongy tissue inside the bones) biopsy. Rarely, a lumbar puncture (a needle is inserted into the lower back to collect a sample of the fluid that surrounds the brain and spinal cord) and a magnetic resonance imaging (MRI) scan (a procedure that takes detailed pictures of areas inside the body using a powerful magnet and radio waves) may also be recommended. Some patients with AITL can have active Epstein-Barr virus (EBV, the virus that causes mononucleosis) infection.

Most patients with AITL are diagnosed with advanced-stage disease (Stage III or Stage IV disease). This means that the disease has grown and/or affects many areas of the body (Figure 1) and requires treatment. Less-extensive disease, Stage I (localized disease that has not spread beyond one lymph node or other location) or Stage II (disease that has spread only to nearby lymph nodes), is rare in AITL. In Stage III, affected lymph nodes are found both above and below the diaphragm (the muscle that separates the chest from the abdomen). In Stage IV, one or more organs beyond the lymph nodes are affected, such as the bone, bone marrow, skin, or liver.

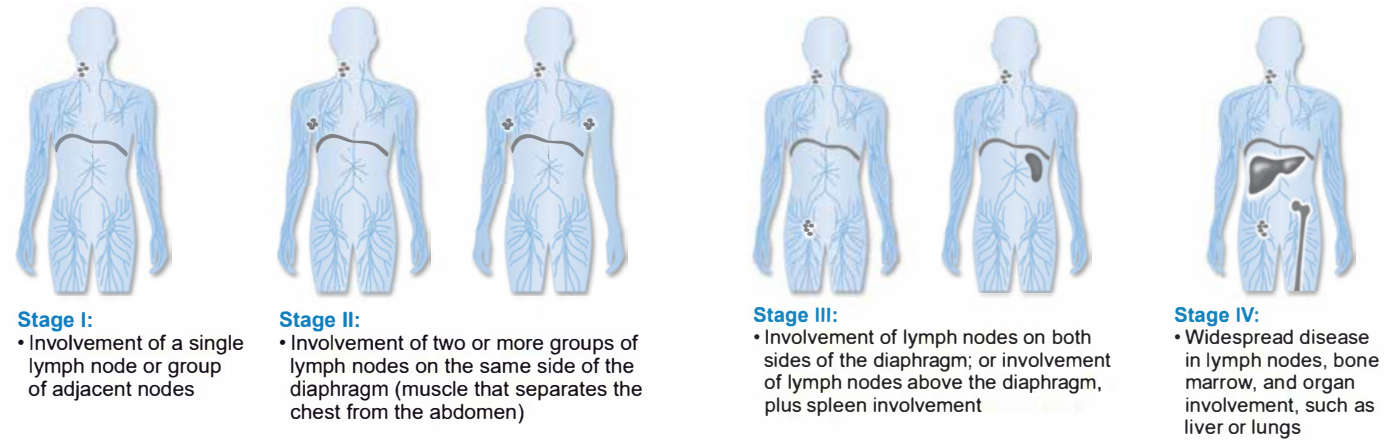


**Figure 1.** Staging of NHL according to the Lugano system. This system categorizes NHL from Stage I (limited disease) to IV (advanced disease) based on whether the cancer is restricted to a single group of lymph nodes, has spread to other lymph nodes, or has reached the bone marrow (the spongy tissue inside the bones) and/or other organs (like the liver or lungs).

## PROGNOSIS

A new prognostic tool (predicts how well the patient will do) called the AITL Score was recently developed to predict the outcome in patients with AITL. The AITL Score categorizes patients by level of risk (low-, intermediate-, and high-risk). The risk categories are determined by age, Eastern Cooperative Oncology Group (ECOG) performance status (a scale of 0 to 5 that describes the patient's ability to take care of themselves and perform daily activities like walking or working), and levels of C-reactive protein (CRP, a protein made in the liver in response to inflammation or tissue damage) and β2 microglobulin (a protein that is increased in some types of cancer, like lymphoma).

Patients aged 60 years or older with an ECOG performance status greater than 2 and elevated CRP and β2 microglobulin have an increased risk of severe disease when compared to other patients. However, keep in mind that no two patients are alike and that statistics can only predict how a large group of patients will do (not what will happen to an individual patient). The doctor most familiar with the patient's situation is in the best position to interpret the increased risk, understand how it applies to a patient's particular situation, and respond to any questions the patient might have.

## TREATMENT OPTIONS

Patients with AITL are usually treated with combinations of chemotherapy drugs. Recommended frontline (initial) therapy for the treatment of AITL is either a clinical trial (a research study that evaluates the best dose, safety, and efficacy of a new treatment in human patients) or a course of chemotherapy using a combination of drugs, such as:

- CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone)
- CHOEP (doxorubicin, vincristine, cyclophosphamide, etoposide, prednisone)
- BV-CHP (Brentuximab vedotin [Adcetris] in combination with cyclophosphamide, doxorubicin, and prednisone) is the standard of care (the proper treatment that is widely used by health care professionals and accepted by medical experts) for cancers that have the CD30 marker (a protein involved in cell growth and survival found in increased amounts on some white blood cells), like in some cases of AITL

The goal of such therapy is often to achieve durable remission (no signs and symptoms of cancer for a long time). In cases where the treatment goal is mostly to relieve symptoms, steroids may be used. Sometimes higher doses of chemotherapy followed by stem cell transplantation (SCT, patient receives new blood-forming [stem] cells after a high-dose chemotherapy with or without radiation) may be added at the end of treatment with the multidrug chemotherapy. The aim is to increase the chance of the patient reaching durable remission. In some cases, patients may be treated with radiation therapy.

Disease relapse (returns after treatment) is common with this cancer. If the cancer returns or is refractory (does not respond to treatment), there are several other treatment options available:

- Brentuximab vedotin (Adcetris), an antibody-drug conjugate (ADC) that targets CD30
- Pralatrexate (Folotyn), a chemotherapy drug that works as a dihydrofolate reductase (DHFR) inhibitor and blocks the cells' ability to divide and multiply
- Belinostat (Beleodaq), a histone deacetylase (HDAC) inhibitor that blocks tumor cells from growing and dividing, causing cell death

Treatments following relapse may include high-dose chemotherapy followed by an autologous SCT (patients receive their own stem cells) or an allogeneic SCT (patients receive stem cells from a donor). For additional information about stem cell transplantation, view the *Understanding Cellular Therapy* publication on the Lymphoma Research Foundation's (LRF's) website (**lymphoma.org/publications**).

## OTHER TREATMENT POSSIBILITIES

Lenalidomide (Revlimid) is an immunomodulatory drug (a drug that works by increasing or reducing the immune response) that has been tested alone or in combination with current chemotherapy regimens and shows promise for the treatment of AITL. Some other drugs used in other types of lymphoma that may occasionally be considered for the treatment of patients with AITL include targeted therapies (drugs that target specific molecules that cancer cells use to grow and/or spread), like romidepsin (Istodax) and bortezomib (Velcade), and chemotherapies, like gemcitabine (Gemzar), bendamustine (Treanda), azacitidine (Vidaza), or others. Alemtuzumab (Campath) is a monoclonal antibody (a protein made in the laboratory that binds to cancer cells and helps the immune system destroy them) also occasionally considered, although it is no longer commercially available and is provided only through the Campath Distribution Program.

## TREATMENTS UNDER INVESTIGATION

Many treatments (also referred to as investigational drugs) are currently being tested in clinical trials in patients who are previously untreated and relapsed/refractory AITL. Results from these clinical trials may improve or change the current standard of care (the proper treatment that is widely used by healthcare professionals and accepted by medical experts). The table below lists some of these investigational drugs that can be accessed through a clinical trial.

**Table 1. Selected Agents Under Investigation for AITL in Phase 2 or 3 Clinical Trials.**

| Agent (Drug) | Class (Type of treatment) |
|---|---|
| **AUTO4** | Immunotherapy; CAR T-cell therapy, anti-TRBC1 |
| **Daratumumab (Darzalex)** | Immunotherapy; monoclonal antibody, anti-CD38 |
| **Duvelisib (Copiktra)** | Targeted therapy; PI3K inhibitor |
| **Pembrolizumab (Keytruda)** | Immunotherapy; immune checkpoint inhibitor, anti-PD-1 |
| **Sintilimab (Tyvyt)** | Immunotherapy; immune checkpoint inhibitor, anti-PD-1 |
| **Venetoclax (Venclexta)** | Targeted therapy; BCL-2 inhibitor |

AITL, angioimmunoblastic T-cell lymphoma; BCL-2, B-cell lymphoma protein; CAR, chimeric antigen receptor; PD-1, programmed cell death protein 1; PI3K, phosphoinositide 3-kinase; TRBC1, T-cell receptor beta constant 1.

It is important to remember that today's 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 Lymphoma Research Foundation for any treatment updates that may have recently appeared. It is also very important that patients consult with a specialist to clear up any questions.

## CLINICAL TRIALS

Clinical trials are crucial in identifying effective drugs and the best treatment doses for patients with AITL. Because AITL is a rare disease, clinical trial enrollment is critical for establishing more effective, less toxic treatments. The rarity of the disease also means that the new treatments are often available only through clinical trials. Patients interested in participating in a clinical trial should view the *Understanding Clinical Trials* fact sheet (**lymphoma.org/publications**) and the *Clinical Trials Search Request Form* (**lymphoma.org**), talk to their physician, or contact the LRF Helpline for an individualized clinical trial search by calling **(800) 500-9976** or emailing **helpline@lymphoma.org**

## FOLLOW-UP

Disease relapse and infections are common with this cancer. It is important to seek medical attention for fever or other symptoms related to improper functioning of the immune system.

Patients with AITL should have regular visits with their physician. During these visits, medical tests (such as blood tests, CT scans, or, at times, PET scans) may be required to evaluate the need for additional treatment.

Some treatments can cause long-term side effects (occur **during** treatment and continue for months or years) or late side effects (appear only months, years, or decades **after** treatment has ended). These side effects can vary based on the following factors:

- Duration of treatment (how long the treatment was given)
- Frequency of treatment (how often the treatment was administered)
- Type of treatment given
- Age and gender of the patient
- Patient overall health 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. These include 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. LRF's award-winning *Focus on Lymphoma* mobile app (**lymphoma.org/mobileapp**) or the *Lymphoma Care Plan* (**lymphoma.org/publications**) can help patients manage this documentation.

## LYMPHOMA CARE PLAN AND PATIENT EDUCATION PROGRAMS

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'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**. LRF also offers a variety of educational activities, including live meetings and webinars, for individuals looking to learn directly from lymphoma experts. To view our schedule of upcoming programs, please visit **lymphoma.org/programs**.

### LRF Helpline

The LRF Helpline 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. LRF also offers a one-to-one peer support program called the Lymphoma Support Network and clinical trials information through our Clinical Trials Information Service. For more information about any of these resources, visit our website at **lymphoma.org**, or contact the LRF Helpline at **(800) 500-9976** or **helpline@lymphoma.org**.

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

## LRF FOCUS ON LYMPHOMA MOBILE APP

Focus on Lymphoma is the first app to provide patients and their caregivers with tailored content based on lymphoma subtype and actionable tools to better manage diagnosis and treatment. It provides convenient and comprehensive lymphoma management in one secure and easy-to-navigate app, no matter where you are on the care continuum. Get the right information, first, with resources from the entire Lymphoma Research Foundation content library, use unique tracking and reminder tools, and connect with a community of specialists and patients. To learn more about this resource, visit our website at **lymphoma.org/mobileapp**, or contact the LRF Helpline at **800-500-9976** or **helpline@lymphoma.org**.

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