LYMPHOMA RESEARCH • FOUNDATION

Understanding Lymphoma Angioimmunoblastic T-Cell Lymphoma

Angioimmunoblastic T-cell lymphoma (AITL) is a rare but very distinct and often fast-growing form of peripheral T-cell lymphoma (PTCL).

AITL accounts for about 20-30 percent of PTCLs. AITL is more common in older people but can sometimes affect young adults as well. Symptoms of AITL include fatigue, high fever, night sweats, skin rash, and autoimmune disorders such as autoimmune hemolytic anemia (AIHA) and immune thrombocytopenia (ITP). As a result of these autoimmune disorders, the body's immune system attacks its own red blood cells (in the case of AIHA) or platelets (in the case of ITP). Other autoimmune disorders can also be seen in AITL.

Diagnosing AITL requires taking a *biopsy* (sample of the tumor tissue) and looking at the cells under a microscope, after the appropriate stains have been performed. Flow cytometric analysis of the cells and testing for specific genetic mutations are also required. Other tests may be done to determine the extent, or stage, of the disease. These can include blood tests, a computed tomography (CT) scan, a positron emission tomography (PET) scan, a magnetic resonance imaging (MRI) scan, and a bone marrow biopsy. Rarely, a lumbar puncture might also be recommended. Some patients with AITL can have active Epstein-Barr virus infection in their lymph nodes and blood.

Most patients with AITL are diagnosed with advanced-stage disease, either Stage III or Stage IV. In Stage III, affected lymph nodes are found both above and below the diaphragm. In Stage IV, one or more organs beyond the lymph nodes are affected, such as the bone, bone marrow, skin, or liver. Less-extensive disease, Stage I or II, is rare in AITL. Patients with Stage I have localized disease that has not spread beyond one lymph node or other location; Stage II disease has spread only to nearby lymph nodes.

PROGNOSIS

The prognosis of AITL remains poor. A new prognostic tool called the AITL Score was recently developed to predict several measures of survival in patients with AITL. The AITL Score categorizes patients by level of risk. The risk categories are determined by age, Eastern Cooperative Oncology Group (ECOG) performance status, and levels of C-reactive protein (CRP) and >2 microglobulin. The 5-year overall and progression free survival rates are predicted to be highest for the low risk category, as shown in Table 1 below.

Table 1. AITL Score Prognostic Tool

Risk Category	5-Year Overall Survival	5-Year Progression Free Survival
Low	**63%**	**41%**
Intermediate	**54%**	**37%**
High	**21%**	**13%**

AITL, Angioimmunoblastic T-cell lymphoma

Age ⩾60 years, ECOG performance status >2, and elevated CRP and >2 microglobulin are associated with poorer outcomes. Progression of disease within two years was also determined to be a powerful prognostic factor.

TREATMENT OPTIONS

Patients with AITL are most commonly treated with combinations of chemotherapy drugs. Recommended *frontline* (initial) therapy for the treatment of AITL is either a clinical trial 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 for cancers expressing the CD30 marker. Some cases of AITL express CD30.

The goal of such therapy is often to get rid of the lymphoma permanently or at least for a long time. In cases where the goal is to treat the disease more mildly, mostly to relieve symptoms, steroids may be used. Sometimes radiation therapy or higher doses of chemotherapy, followed by stem cell transplantation, may be added at the end of treatment with the multidrug chemotherapy.

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 also may be used in patients with T-cell lymphomas with CD30 expression including AITL.
- Pralatrexate (Folotyn) was the first drug to be approved by the U.S. Food and Drug Administration (FDA) for the treatment of relapsed or refractory PTCL; patients with AITL were included in the clinical study that supported this approved use.
- Romidepsin (Istodax) and belinostat (Beleodaq) are histone deacetylase (HDAC) inhibitors that block tumor cells from growing and dividing, causing cell death.

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

OTHER TREATMENT POSSIBILITIES

Lenalidomide (Revlimid) 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 gemcitabine (Gemzar), bortezomib (Velcade), and bendamustine (Treanda), or other chemotherapies. Alemtuzumab (Campath) is also occasionally considered, although it is no longer commercially available and is provided only through the Campath Distribution Program.

TREATMENTS UNDER INVESTIGATION

New treatments for AITL are being researched all the time. There are several drugs currently in clinical trials that are showing promising results, including:

- AUTO4 (chimeric antigen receptor [CAR] T-cell therapy)
- Azacitidine (Vidaza)
- Chidamide
- Clofarabine
- Daratumumab (in combination with chemotherapy)
- Duvelisib (Copiktra)
- Pembrolizumab (Keytruda)
- Ruxolitinib
- Sintilimab
- Valemetostat
- Venetoclax

New drugs such as lenalidomide (Revlimid), romidepsin (Istodax), and others are also being studied in combination with chemotherapy such as CHOP (doxorubicin, vincristine, cyclophosphamide, prednisone) or CHOEP (doxorubicin, vincristine, cyclophosphamide, etoposide, prednisone) as frontline therapy. In relapsed patients, combinations of some of the new drugs listed above are also being studied. It is important to remember that today's scientific research is continuously evolving. Treatment options may change as new treatments are discovered and current treatments are improved. Because the science is always changing, it is important for patients to check in with their doctor or with LRF to find out about any new treatments that become available.

CLINICAL TRIALS

Clinical trials are crucial in identifying effective drugs and determining optimal doses for patients with lymphoma. 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 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 (visit **lymphoma.org/publications**), and the *Clinical Trials Search Request Form* at 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 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 and CT scans or at times 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 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 (**lymphoma.org/mobileapp**) or the *Lymphoma Care Plan* (**lymphoma.org/publications**) 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 AITL, 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 AITL, 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. To learn more about any of these resources, visit our website at **lymphoma.org**, or contact the LRF Helpline at **800-500-9976** or **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**.

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 AITL. 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**, 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**.)

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