

## Adult T-Cell Leukemia/Lymphoma (HTLV-1)

*Expert review by:*

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### What is Lymphoma?

Lymphoma is a cancer of the white blood cells, namely lymphocytes, that constitute the lymphatic system. The two main types of lymphoma are Hodgkin lymphoma and non-Hodgkin lymphoma. Lymphoma is the most common blood cancer and the third most common cancer of childhood. Lymphoma occurs when lymphocytes grow abnormally. The body has two types of lymphocytes: B lymphocytes, or B-cells, and T lymphocytes, or T-cells. B-cells play an important role in making antibodies to fight bacterial infections and T-cells play a role in fighting viruses and organ rejection in transplant patients. Although both cell types can develop into lymphomas, B-cell lymphomas are more common, comprising nearly 85 percent of all non-Hodgkin lymphomas. Like normal lymphocytes, those that become malignant can grow in any part of the body, including the lymph nodes, spleen, bone marrow, blood or other organs.

### What Is Non-Hodgkin Lymphoma?

Of the more than 30 types of lymphoma, over 25 are classified as non-Hodgkin lymphoma (NHL). Nearly all non-Hodgkin lymphoma cases occur in adults, with the average age of diagnosis in the 60s. While scientists do not know the exact causes of non-Hodgkin lymphoma, they do know that it is not caused by injury or by coming into contact with someone with the disease. Most people diagnosed with NHL have no known risk factors, although increasingly many scientists believe infections may play an important role in causing select types of non-Hodgkin lymphoma to develop.

### What Is T-Cell Lymphoma?

T-cell lymphoma is a rare disease in which T lymphocyte cells become cancerous. These lymphomas account for between 10 percent and 15 percent of all cases of non-Hodgkin lymphoma in the United States (approximately 5,000 to 6,000 cases) a year, although some forms of T-cell lymphoma are more common in Asia, Africa and the Caribbean. There are many different types of T-cell lymphoma, most of which are extremely rare, occurring in only a few patients per year throughout the world. Like the B-cell lymphomas, T-cell lymphomas are classified into two broad categories: aggressive (fast-growing) or indolent (slow-growing).

Most T-cell lymphomas are diagnosed by taking a small sample, called a biopsy, of the tumor and looking at the cells under a microscope. However, since the cells of many forms of lymphoma look similar, making an accurate diagnosis can be difficult and oftentimes other diagnostic tools such as genetic tests of the tumor, blood tests, CT (computerized axial tomography), MRI (magnetic resonance imaging) and PET (positron emission tomography) scans and a bone marrow biopsy may be done to determine the type and extent (or stage) of the disease. One of the most common forms of T-cell lymphoma is cutaneous, or skin lymphoma, because it starts in the lymphocytes in the skin. Cutaneous lymphoma actually describes many different disorders with various signs and symptoms, outcomes and treatment considerations.

### What Is Adult T-Cell Leukemia/Lymphoma?

Adult T-cell leukemia/lymphoma (ATLL) is a rare and aggressive T-cell lymphoma that is linked to infection by the human T-cell lymphotropic virus 1 (HTLV-1). Human T-cell lymphotropic virus 1 is a retrovirus—meaning that

these viruses do not contain genetic material made of DNA, but instead carry RNA. These viruses selectively infect only T-cells. Only about 2 percent to 5 percent of patients infected with the HTLV-1 virus will develop ATLL. Currently, physicians have no way of telling which infected patients will develop the lymphoma.

The HTLV-1 virus is in the same class of virus as the HIV/AIDS virus and is endemic to certain parts of the world such as Japan, the Caribbean, South and Central America, West Africa and the southeastern United States. The HTLV-1 virus is believed to be transmitted through sexual contact, exposure to contaminated blood from either a blood transfusion or used needles and can be passed from mother to child through breastfeeding.

### **How Adult T-Cell Leukemia/Lymphoma Is Diagnosed**

Cancerous T-cells in ATLL may present only in the blood (leukemia) or in the lymph nodes (lymphoma) or in both. There are four subtypes of adult T-cell leukemia/lymphoma:

- **Acute**—In this type of ATLL, symptoms develop rapidly and may include fatigue; skin rash; and enlarged lymph nodes in the neck, armpit and groin. One of the hallmarks of this cancer is an elevated level of calcium in the blood (hypercalcemia), which may result in irregular heart rhythms and severe constipation.
- **Lymphomatous**—This subtype of ATLL is found only in the lymph nodes.
- **Chronic**—Although this type is slow growing, it is characterized by enlarged lymph nodes that may be found anywhere in the body and in organs such as the spleen and liver. Common symptoms include skin rash and fatigue.
- **Smouldering**—This form of ATLL develops slowly and presents with very mild symptoms, such as a few skin lesions.

Depending on the subtype of ATLL, diagnosing the cancer may require taking a small sample of tumor tissue or abnormal skin tissue, called a biopsy, and looking at the cells under a microscope and a blood test to measure the white blood cell count and calcium levels. Other diagnostic tests may be used to confirm a diagnosis and determine the extent of the disease, including a CT (computerized axial

tomography) scan of the chest, abdomen, liver and spleen and a bone marrow biopsy.

### **How Adult T-Cell Leukemia/Lymphoma Is Treated**

Because ATLL is such a rare disease, there have not been enough patients enrolled in clinical trials to establish treatment standards. As a result, the common frontline therapy used to treat ATLL is the same therapy used to treat other types of T-cell lymphomas, and may include such regimens as CHOP (cyclophosphamide, doxorubicin, vincristine and prednisone) or EPOCH (etoposide, vincristine, doxorubicin, cyclophosphamide and prednisone). Other treatments may include using drugs such as the nucleoside analogue acyclovir (Zovirax) and combinations of interferon-alpha to treat the underlying HTLV-1 virus infection. In some patients, a bone marrow transplant may be recommended following remission.

Just like in the frontline setting, standard treatment in the relapsed setting of ATLL has not been established, although, again, many of the same drugs used to treat other T-cell lymphomas following relapse are being used to treat ATLL, including such chemotherapy regimens as GND (gemcitabine, vinorelbine (Navelbine) and doxorubicin); ICE (ifosfamide, carboplatin and etoposide); DHAP (dexamethasone, cytarabine and cisplatin); and CEPP (cyclophosphamide, etoposide, procarbazine and prednisone).

### **Treatments Under Investigation**

Because adult T-cell leukemia/lymphoma is such a rare disease, finding enough patients to enroll in clinical trials is difficult. However, several new drugs being studied in clinical trials for other T-cell lymphomas are emerging as potential treatments for ATLL, including:

- PDX (pralatrexate)
- Vorinostat (Zolinza)
- Lenalidomide (Revlimid)
- Bortezomib (Velcade)

The role of using allogeneic stem cell transplant (high-dose chemotherapy followed by donor cell transplantation) is also being evaluated as a promising treatment for ATLL patients who have relapsed.

## Are Complementary and Alternative Therapies Safe and Effective?

Complementary and alternative medicines are nonstandard therapies that may help patients cope with their cancer and its treatment, but that should not be used in place of standard treatment. No alternative therapy has ever been proven effective against lymphoma. However, complementary therapies such as meditation, yoga, acupuncture, exercise, diet and relaxation techniques have been shown to be effective in combating some treatment side effects. Before embarking on any complementary therapies, patients should discuss the matter with their healthcare team. Certain unproven treatments, including some herbal supplements, can interfere with standard lymphoma treatments or may cause serious side effects.

## How to Prepare for Follow-Up Appointments

It is important for patients both during and after treatment to be proactive in their healthcare, including keeping a master file of medical records, asking questions, reporting new symptoms, exercising and eating a balanced diet. Some patients find it helpful to keep a diary of their symptoms, which can help the physician promptly address concerns. In addition, patients who smoke should strongly consider stopping. Follow-up visits, usually scheduled every few months, typically include physical examinations, blood tests and occasionally CT scans. Since lymphoma symptoms may resemble those of less serious illnesses, like colds or viral infections, maintaining regular medical care is imperative. Besides looking for signs of a recurrence of cancer, follow-up care can help identify and resolve unusual side effects of treatment.

## Finding Support

A lymphoma diagnosis may provoke a range of feelings and raise many concerns. In addition, cancer treatment can cause physical and emotional discomfort. Connecting with other people who have lymphoma, or have been cured of it, can provide enormous relief. Support groups and online message boards are often useful. One-to-one peer support programs, such as the Lymphoma Research Foundation's Lymphoma Support Network, matches lymphoma survivors (or caregivers) with volunteers who have gone through similar experiences.

## Staying Informed

The Lymphoma Research Foundation offers a wide range of resources that address treatment issues, the latest research advances and how to cope with all aspects of lymphoma. For more information about any of these resources, visit [www.lymphoma.org](http://www.lymphoma.org); send an e-mail to [Helpline@lymphoma.org](mailto:Helpline@lymphoma.org) or call 800-500-9976.

## Participating in Clinical Trials

T-cell lymphomas comprise such a rare group of diseases it is often difficult to find enough patients to enroll in clinical trials. Clinical trials are crucial in identifying effective drugs and determining optimal doses for lymphoma patients. If you are interested in participating in a clinical trial, talk to your doctor about an appropriate trial for you. To learn more about clinical trials, visit [www.lymphoma.org](http://www.lymphoma.org).

## The Basics of Clinical Trials

Clinical trials are done to study new drugs and treatment strategies. Examples of what clinical trials might investigate include the following:

- A novel drug that is not approved by the FDA nor proven effective as treatment
- A new indication (use) for a drug already approved by the FDA as a treatment for a different disease
- Compare a new treatment with a standard treatment to determine which one is more effective or has fewer side effects
- See how lifestyle changes can help cancer patients
- Look for ways to prevent cancer from occurring

New drugs must pass through a rigorous approval process governed by the FDA before it becomes a standard therapy for use in hospitals and clinics. The trials used to assess these drugs are typically divided into three types, called phases, each of which is designed to determine certain information. Phase I tries to determine whether a potential treatment is well tolerated; phase II tests the drug's effectiveness in a small group of patients; and phase III tests the drug's effectiveness compared to standard therapies or other available treatments in a large, varied group of patients with a specific cancer. Patients may be eligible to take part in different stages depending on their condition, type and stage of lymphoma and the type of treatment, if any, previously given.

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The Lymphoma Research Foundation offers a comprehensive array of patient education and support programs, including:

- *Lymphoma Helpline and Clinical Trials Information Service*
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## Glossary of Terms

**Allogeneic transplant** A procedure in which a patient receives bone marrow or stem cells donated by another person.

**Aggressive lymphomas** Lymphomas that are fast growing. These types of lymphoma generally need to be treated immediately, but there is a good chance for a long-term cure. These lymphomas are also called intermediate-grade or high-grade lymphomas.

**Autologous transplant** A type of bone marrow or stem cell transplantation in which a patient receives his or her own cells.

**Chemotherapy** Treatment with "chemo" drugs to stop the growth of rapidly dividing cancer cells, including lymphoma cells.

**Chemotherapy regimen** Combinations of anti-cancer drugs given at a certain dose in a specific sequence according to a strict schedule.

**CT or CAT (computerized axial tomography) scan:** This imaging test provides a series of detailed pictures of the inside of the body using an x-ray machine linked to a computer.

**Lymph nodes** Small bean-shaped glands located in the small vessels of the lymphatic system. Thousands are located throughout the body and are most easily felt in the neck, armpits and groin.

**Lymphatic system** The vessels, tissues and organs that store and carry lymphocytes that fight infection and other diseases.

**Lymphocyte** A type of white blood cell.

**Partial remission** The term used when a cancer has shrunk in size by least in half, but has not totally disappeared. The cancer can still be detected and other treatments may be recommended.

**PET (positron emission tomography) scan** PET scans may be used instead of gallium scans to identify areas in the body that are affected by lymphoma. This test evaluates metabolic activity in different parts of the body using a radioisotope.

**Relapse** The return of cancer after treatment. Lymphoma may recur in the area where it first started, or it may relapse in another place.

**Remission** The absence of disease. Remission does not necessarily mean cure. A patient is considered in remission when the lymphoma has been treated and tumors have diminished by at least 50 percent (partial) or have totally disappeared (complete).

**Stage** The extent of cancer in the body, including whether the disease has spread from the original site to other body parts.

**Toxicities** The unwanted side effects of cancer therapies, such as a decrease in blood cells, nausea and vomiting, and hair loss.

**Virus** A particle of nuclei acid that has the potential to inject its genetic material (DNA or RNA) into normal cells. Once inside the normal cells, the virus's genetic material can take control of the normal cells, making them malignant.