LYMPHOMA RESEARCH • FOUNDATION

Understanding Adult T-Cell Leukemia/Lymphoma

Adult T-cell leukemia/lymphoma (ATLL) is a rare and often *aggressive* (fast-growing) T-cell lymphoma that can be found in the *blood* (leukemia), *lymph nodes* (lymphoma), skin, or multiple areas of the body.

ATLL has been linked to infection with the human T-cell lymphotropic virus type 1 (HTLV-1); however, less than five percent of individuals with HTLV-1 will develop ATLL. Currently, physicians have no way of predicting which infected patients will 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 is rarely transmitted through sexual contact or exposure to contaminated blood; it is most often passed from mother to child through breastfeeding.

SUBTYPES OF ATLL

There are four subtypes of ATLL: acute, lymphoma, chronic, and smoldering. Acute and lymphoma subtypes are fast-growing forms of ATLL, whereas chronic and smoldering are less aggressive.

Acute: In individuals with acute ATLL, symptoms develop rapidly and may include *fatigue* (extreme tiredness), skin rash, and enlarged lymph nodes in the neck, underarm, or groin. The hallmarks of acute ATLL are a high white blood cell count often accompanied by *hypercalcemia* (elevated calcium levels in the blood), which can cause confusion, irregular heart rhythms and severe constipation. Acute ATLL may spread to extranodal tissues.

Lymphoma: This aggressive type of ATLL is found primarily in the lymph nodes, causes swollen or enlarged lymph nodes (lymphadenopathy) and may cause high white blood cell counts 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.

Depending on the subtype, diagnosing ATLL will require removing a small sample of tumor tissue or abnormal skin tissue, called a biopsy, and looking at the cells under a microscope. A blood test will also be necessary to measure the white blood cell count and calcium levels, and to test for exposure to the HTLV-1 virus. Other tests, such as a bone marrow biopsy, a computed tomography (CT) scan of the chest, abdomen, liver, and spleen, and/or a positron emission tomography (PET) scan may be used to determine where the cancer is located.

TREATMENT OPTIONS

Observation without treatment, called *active surveillance*, also known as *watchful waiting* (observation with no treatment [drug therapy, radiation therapy, or stem cell transplantation] given) may be appropriate for some patients who have one of the slower-growing subtypes of ATLL with mild or no symptoms, although follow-up monitoring is required. For ATLL affecting the skin, skin-directed therapies (for example, topical steroids or local radiation) may be prescribed.

Because ATLL is such a rare disease, there have not been enough patients enrolled in clinical trials to establish treatment standards in the United States and Europe, especially for the acute and lymphoma subtypes. As a result, common *frontline* (initial) therapies used to treat ATLL are the same as those used to treat other types of T-cell lymphomas. These include:

- CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone)
- CHOEP (cyclophosphamide, doxorubicin, vincristine, etoposide, and prednisone)
- Dose-adjusted EPOCH (etoposide, vincristine, doxorubicin, cyclophosphamide, and prednisone)
- Hyper-CVAD (cyclophosphamide, vincristine, doxorubicin, and dexamethasone) alternating with high-dose methotrexate and cytarabine (Cytosar)
- BV-CHP [Brentuximab vedotin (Adcetris) + CHP (cyclophosphamide, doxorubicin, and prednisone)] for CD30-positive cases

VCAP-AMP-VECP (vincristine, cyclophosphamide, doxorubicin, prednisone, ranimustine, vindesine, etoposide, and carboplatin) is a regimen piloted in Japan. Other treatments may include zidovudine (Retrovir), also known as AZT, in combination with interferon-alpha to treat the underlying HTLV-1 virus infection. This may be effective in patients with the slower-growing forms of ATLL. In some patients, stem cell transplantation may be appropriate following *remission* (disappearance of signs and symptoms). Similar to the frontline setting, standard treatment for *relapsed* (disease returns after treatment) ATLL has not been established.

Many regimens used to treat other T-cell lymphomas following relapse are also being used to treat ATLL, including the following:

- DHAP (dexamethasone, cytarabine, and cisplatin)
- ESHAP (etoposide, methylprednisolone, cytarabine, and cisplatin)
- GDP (gemcitabine, dexamethasone, and cisplatin)
- ICE (ifosfamide, carboplatin, and etoposide)
- Pralatrexate (Folotyn), belinostat (Beleodaq) and romidepsin (Istodax)

TREATMENTS UNDER INVESTIGATION

Several new drugs are being studied in clinical trials for ATLL, as single-agent therapy or as part of a combination therapy regimen, including the following:

- Bendamustine (Treanda)
- Bortezomib (Velcade)
- Mogamulizumab (Poteligeo)
- Nelarabine (Arranon)
- Ruxolitinib (Jakafi)
- Lenalidomide (Revlimid)
- Tolinapant (ASTX660)
- Valemetostat

High-dose chemotherapy followed by *allogeneic stem cell transplantation* (patients receive stem cells from a donor) is also being evaluated as a potential treatment for patients with ATLL.

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 the Lymphoma Research Foundation (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 ATLL 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 latest 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 (click **here**) 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

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/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.

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 our *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 ATLL, 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 ATLL, 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. For additional information on the mobile app, visit FocusOnLymphoma.org. 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.

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, including our award-winning mobile app. LRF also provides many educational activities, from in-person meetings to webinars for people living with lymphoma or ATLL, as well as e-Updates that provide the latest disease-specific news and treatment options. For more information about any of these resources, visit our websites at lymphoma.org/ATLL or lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.

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Contact LRF:

Helpline: (800) 500-9976

Email: helpline@lymphoma.org

www.lymphoma.org

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