

Understanding Anaplastic Large Cell Lymphoma

Anaplastic large cell lymphoma (ALCL) is a rare type of non-Hodgkin lymphoma (NHL), and one of the subtypes of T-cell lymphoma.

ALCL comprises about one percent of all NHLs and approximately 10-20 percent of all T-cell lymphomas. Initial symptoms of ALCL can include fever, backache, painless swelling of lymph nodes, loss of appetite, night sweats, weight loss, itching, skin rash and tiredness.

One characteristic that distinguishes ALCL is that the cancer cells have a marker on their surface called CD30. The disease can be either cutaneous (limited to the skin), systemic (occurring throughout the body), or around breast implants.

Patients with systemic ALCL are divided into two groups, depending on whether their cells produce an abnormal form of a protein called anaplastic lymphoma kinase (ALK). Although both systemic lymphomas are treated as *aggressive* (fast-growing) lymphomas, the disease course may be different in patients who have ALK-positive ALCL compared with those with ALK-negative ALCL. The ALK-positive form of ALCL generally responds better to standard chemotherapy treatments, putting most patients into long-term *remission* (disappearance of signs and symptoms). In contrast, while most patients with ALK-negative ALCL initially respond to treatment as well, the disease is more likely to *relapse* (disease returns after treatment) compared to those with ALK positive ALCL. Sometimes ALK-negative patients (and some ALK-positive patients with certain risk factors) are treated more aggressively and stem cell transplant can be considered after remission. While ALK-positive ALCL usually affects children and young adults, ALK-negative ALCL is more common in patients over the age of 55 years.

Primary cutaneous ALCL (disease appears first in the skin) is almost always ALK negative and has a less aggressive disease course than the *systemic* types. The characteristic features of primary cutaneous ALCL include the appearance of solitary or multiple raised, red skin lesions that are usually greater in size than a quarter that do not go away, may ulcerate, and may itch. These ALCL lesions are tumors, which can appear on any part of the skin, often grow very slowly, and may be present for a long time before being diagnosed. Only about 10 percent of the time does primary cutaneous ALCL extend beyond the skin to lymph nodes or organs. If this occurs, it is usually treated like systemic ALCL.

A rare type of ALCL called breast implant-associated (BIA)-ALCL has been observed in some patients who get breast implants, particularly those with *textured* (non-smooth) surfaces. The U.S. Food and Drug Administration (FDA) recommends that patients with such implants, and their doctors, consider the possibility of BIA-ALCL if they experience any late-onset symptoms such as pain, lumps, or swelling in the breast.

A diagnosis of ALCL requires taking a *biopsy* (sample of the tumor tissue) and looking at the cells under a microscope. Additional tests may be conducted to give physicians more information about the disease and how far it has spread in the body. 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.



TREATMENT OPTIONS

Many patients with newly diagnosed systemic ALCL respond well to common *frontline* (initial) chemotherapy. The combination of brentuximab vedotin (Adcetris) and cyclophosphamide, doxorubicin, and prednisone (BV-CHP) were found to have superior survival when compared to the prior standard of CHOP chemotherapy (cyclophosphamide, doxorubicin, vincristine, prednisone). Therefore, for patients with systemic ALCL, ALK positive or ALK negative, BV-CHP is the preferred first line treatment option and was approved by the FDA in 2018. In some circumstances, higher doses of chemotherapy followed by stem cell transplantation may be prescribed after having a remission to BV-CHP.

Brentuximab vedotin (Adcetris) is also approved by the FDA for the treatment of patients with *relapsed* (disease returns after treatment) or *refractory* (does not respond to treatment) systemic ALCL after the failure of at least one prior multiagent chemotherapy regimen. Other treatment options for relapsed/refractory disease include romidepsin (Istodax), which is FDA approved for relapsed systemic T-cell lymphomas, including systemic ALCL. Belinostat (Beleodaq) is another histone deacetylase inhibitor that is approved for relapsed peripheral T-cell lymphomas, including systemic ALCL, but not for cutaneous T-cell lymphomas. Pralatrexate (Folotyn) is also approved for the treatment of relapsed/refractory peripheral T-cell lymphomas. Finally, kinase inhibitor crizotinib (Xalkori) is approved for pediatric patients 1 year of age and older and young adults with relapsed or refractory, systemic ALK-positive ALCL.

Treatment of primary cutaneous ALCL depends on the extent of skin lesions. Overall it is treated similarly to a chronic skin disease. If the disease is confined to a single lesion or area, radiation therapy or surgical excision will result in remission in approximately 95 percent of patients and some patients may have recurrent lesions in the future. If there are multiple lesions or recurrent lesions in the skin, radiation can eradicate individual skin lesions but will not reduce the likelihood of new lesions developing. Those with primary cutaneous ALCL appearing in multiple sites on the body are considered for systemic treatment, which travels through the blood and affects many parts of the body. There are very few studies of primary cutaneous ALCL; however, brentuximab vedotin (Adcetris) has been used successfully in such patients in clinical trials and is now FDA approved for this purpose. Although primary cutaneous ALCL tends to relapse in about 40 percent of cases, the long-term prognosis remains excellent if relapses are confined to the skin.

Patients with BIA-ALCL generally undergo surgery to remove the lymphoma, the implant(s), and some surrounding tissue. Most patients have lymphoma limited to the fluid around the breast implant and its capsule, and the majority of patients are cured with a complete excision of the implant and capsule. If the lymphoma cannot be removed by surgery, or if it has spread outside the breast, radiation therapy, chemotherapy, and/or brentuximab vedotin (Adcetris) may be given.



TREATMENTS UNDER INVESTIGATION

There are several drugs showing promising results in clinical trials, including:

- Duvelisib (NCT03372057)
- Valemtostat (NCT04703192)
- Umbralisib
- Combination of brentuximab vedotin (Adcetris) and chemotherapy
- Entrectinib (Rozlytrek)
- Lenalidomide (Revlimid)
- Brigatinib (Alunbrig)
- Lorlatinib (Lorbrena)
- Immune checkpoint inhibitors like nivolumab (Opdivo) and tislelizumab

It is critical to remember that today's scientific research is continuously evolving. New treatments for ALCL are being researched all the time. Patients should check with their physician or with the Lymphoma Research Foundation (LRF) for any updates that may have recently emerged.



CLINICAL TRIALS

Clinical trials are crucial in identifying effective drugs and determining optimal doses for patients with lymphoma. 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, CT scans, and PET scans) may be required at various times during remission to evaluate the need for additional treatment.

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 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 ALCL, 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 ALCL, 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 free resources that address treatment options, the latest research advances, and ways to cope with all aspects of lymphoma and ALCL. LRF also provides many educational activities, including our in-person meetings, podcasts, and webinars for people with lymphoma. For more information about any of these resources, visit our websites at lymphoma.org/ALCL or lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.

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