LYMPHOMA
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Getting the Facts

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Anaplastic Large Cell Lymphoma

Overview

Lymphoma is the most common blood cancer. The two main forms of lymphoma are Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL). Lymphoma occurs when cells of the immune system called lymphocytes, a type of white blood cell, grow and multiply uncontrollably. Cancerous lymphocytes can travel to many parts of the body, including the lymph nodes, spleen, bone marrow, blood, or other organs, and form a mass called a tumor. The body has two main types of lymphocytes that can develop into lymphomas: B lymphocytes (B cells) and T lymphocytes (T cells).

Anaplastic large cell lymphoma (ALCL) is a rare type of NHL, and one of the subtypes of T-cell lymphoma. ALCL comprises about one percent of all NHLs and approximately 16 percent of all T-cell lymphomas. Initial symptoms of ALCL can include fever, backache, painless swelling of lymph nodes, loss of appetite, and tiredness.

ALCL can initially appear either in the skin, in the lymph nodes, or in organs throughout the body. ALCL that appears in the skin is most often called primary cutaneous ALCL, and it typically has a less aggressive disease course than the *systemic* (throughout the body) types. The characteristic features of primary cutaneous ALCL include the appearance of solitary or multiple raised, red skin lesions that do not go away, have a tendency to ulcerate, and may itch. These ALCL lesions are tumors, and they can appear on any part of the body, 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.

Patients with systemic ALCL are divided into two groups, depending on whether or not their cells have an abnormal form of a protein on their surface 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 responds well to standard chemotherapy treatments, putting most patients into long-term remission. In contrast, while most people with ALK-negative ALCL initially respond to treatment as well, the disease is more likely to *relapse* (disease returns after treatment) within five years in these people than in those with ALK-positive ALCL. Sometimes ALK-negative patients (and some ALK-positive patients with certain risk factors) are treated more aggressively, often with a stem cell transplant 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 is always ALK-negative.

A diagnosis of ALCL requires taking a *biopsy* (small sample of tumor tissue or abnormal skin 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

Treatment of primary cutaneous ALCL depends on the extent of skin lesions. If the disease is confined to a single lesion or area, radiation therapy or surgical excision will result in complete remission in approximately 95 percent of patients. If there are multiple lesions or relapsed disease in the skin, radiation can eradicate the skin lesions but will not reduce the likelihood of new lesions developing. Those with primary cutaneous ALCL appearing in multiple sites on the body usually need systemic treatment, which travels through the blood and affects many parts of the body. There are very few studies of primary cutaneous ALCL; however, vorinostat (Zolinza) and romidepsin (Istodax), which are histone *deacetylase inhibitors* (drugs that inhibit the growth of tumor cells), and bexarotene (Targretin), a *retinoid* (drug derived from vitamin A that targets skin cell growth), are approved for cutaneous T-cell lymphoma and can be used to treat the cutaneous form of ALCL. Although primary cutaneous ALCL tends to relapse in about 40 percent of cases, the long-term prognosis remains excellent as long as relapses are confined to the skin.

Many patients with newly diagnosed systemic ALCL respond well to common first-line chemotherapy regimens such as CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), although long-term disease outcome varies depending on the subtype and other factors. Patients with ALK-positive disease usually respond very well to CHOP or CHOEP (CHOP plus etoposide). In contrast, patients with ALK-negative disease have slightly lower survival rates with similar treatments. In some circumstances, higher doses of chemotherapy followed by stem cell transplantation may be prescribed.

Brentuximab vedotin (Adcetris) is approved by the U.S. Food and Drug Administration (FDA) for the treatment of patients with relapsed or *refractory* (disease does not respond to treatment) systemic ALCL after the failure of at least one prior multiagent chemotherapy regimen. Accelerated approval was granted for the

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systemic ALCL indication based on overall response rate. Recent studies show similarly good activity in cutaneous T-cell lymphomas, and ongoing clinical trials are combining brentuximab vedotin with chemotherapy for people newly diagnosed with systemic ALCL.

Other treatment options for relapsed/refractory disease include romidepsin, which is FDA-approved for relapsed systemic T-cell lymphomas, including systemic ALCL. Belinostat is a newer histone deacetylase inhibitor that is approved for relapsed peripheral T-cell lymphomas, including systemic ALCL, but not for cutaneous T-cell lymphomas. Finally, pralatrexate (Folotyn) is also approved for the treatment of relapsed/refractory peripheral T-cell lymphomas.

Treatments Under Investigation

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

- Bortezomib (Velcade)
- Combination of brentuximab vedotin and chemotherapy
- Crizotinib (Xalkori)
- Lenalidomide (Revlimid)

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 for identifying effective drugs and determining optimal doses for patients with lymphoma. Patients interested in participating in a clinical trial should 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 in remission 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, MRI, and PET scans) may be required at various times to evaluate the need for additional treatment.

Some treatments can cause long-term effects or late effects, which can vary based on duration and frequency of treatments, age, gender, and overall health. A physician will check for these effects during follow-up care.

Patients 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 help in keeping track of any effects resulting from treatment or potential disease recurrences.

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 teleconferences and webcasts, as well as E-Updates that provide the latest disease-specific news and treatment options. LRF's T-Cell Lymphoma Transportation Assistance Fund grant program provides financial assistance to T-cell lymphoma patients who are uninsured or have adequate medical insurance but struggle to pay for transportation costs (e.g., mileage, parking, tolls, gas, train tickets, etc.) to get to and from treatment. For more information about any of these resources, visit our websites at www.FocusOnALCL.org or www.lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.