

Burkitt 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).

NHL is broadly categorized as B-cell lymphomas or T-cell lymphomas. B-cell lymphomas develop from abnormal B cells and account for 85 percent of all NHLs. T-cell lymphomas develop from abnormal T cells and account for the remaining 15 percent of all NHLs. NHL may also be classified as *indolent* (slow-growing) or *aggressive* (fast-growing).

Burkitt lymphoma is a rare but highly aggressive B-cell NHL that is a form of mature B-cell lymphoma. This disease may affect the jaw, central nervous system, bowel, kidneys, ovaries, or other organs. There are three main types of Burkitt lymphoma: endemic, sporadic, and immunodeficiency-related. Endemic Burkitt lymphoma is the most common of the three forms, originating in Africa, where it is still the most common childhood cancer; endemic Burkitt lymphoma is rare outside of Africa. Sporadic Burkitt lymphoma occurs throughout the world. The immunodeficiency-related variety of Burkitt lymphoma is most common in people with human immunodeficiency virus/acquired immunodeficiency syndrome (HIV/AIDS). Immunodeficiency-related Burkitt lymphoma can also occur in patients who have inherited immune deficiencies or those who take immunosuppressive medications to prevent rejection after organ transplant. The Epstein-Barr virus (EBV) has been shown to be linked to the development of Burkitt lymphoma; the greatest association between EBV and Burkitt lymphoma is seen with the endemic form.

The sporadic form seen in the United States (U.S.) and Western Europe accounts for less than one percent of B-cell NHLs in adults; however, it accounts for 30 percent of all childhood lymphomas. In comparison, an endemic form found in equatorial Africa and New Guinea has an incidence rate about 50 times higher than that seen in the U.S. The most common site of endemic disease is the jaw; for sporadic and immunodeficiency-related Burkitt lymphoma, abdominal tumor is the most common site of disease occurrence. Burkitt lymphoma may spread to the central nervous system (CNS; i.e., brain and spinal cord). At diagnosis, a sample of cerebrospinal fluid may be taken to determine if the disease has spread to the CNS.

Translocation of the *MYC* gene is a hallmark of Burkitt lymphoma, making this an important finding for diagnosis of the disease; however, abnormalities in this gene are found in other aggressive

mature B-cell lymphomas as well. In fact, in adults, Burkitt lymphoma is often indistinguishable from diffuse large B-cell lymphoma (DLBCL)—another aggressive mature B-cell lymphoma that is a much more common form of NHL. Accurately diagnosing Burkitt lymphoma is critical because Burkitt lymphoma and DLBCL are treated differently.

Patients with Burkitt lymphoma may experience tumor lysis syndrome, a condition that occurs when tumor cells release their contents into the bloodstream. Symptoms of tumor lysis syndrome may include nausea and vomiting, shortness of breath, irregular heartbeat, clouding of the urine, lethargy, or joint discomfort. This condition can occur spontaneously or after patients have received chemotherapy, and it can be very serious. Tumor lysis syndrome can cause kidney damage, irregular heartbeat, seizures, loss of muscle control, and in some cases death. However, this condition can be managed with increased fluids and supportive medications like allopurinol (Aloprim, Lopurin, Zylprim) or rasburicase (Elitek).

Treatment Options

Because Burkitt lymphoma is extremely aggressive, diagnosis of this disease is frequently a medical emergency, requiring urgent hospitalization and rapid institution of therapy. However, Burkitt lymphoma is often very responsive to the currently recommended intensive combination chemotherapy regimens, and cure rates for this disease remain high. Treatment options are determined based on low- versus high-risk status. CNS involvement at diagnosis is recognized as the strongest risk factor for *relapse* (disease returns after treatment); therefore, recommended treatment regimens include treatment to protect the CNS, which may be given *intrathecally* (injected into the spinal fluid).

The combination of agents used for low- versus high-risk disease is similar, but high-risk patients are given additional treatment. All of the treatments used are very intensive, using high doses of toxic drugs given very frequently; however, most of the treatments are of short duration. The monoclonal antibody rituximab (Rituxan) may be added to any of these regimens. Specific treatment options for adults include the regimens described below.

- The *Dose-Adjusted EPOCH* regimen includes etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin plus rituximab and intrathecal methotrexate.
- The *Cancer and Leukemia Group B (CALGB) 10002 Regimen* includes any of the following combinations:
 - cyclophosphamide and prednisone followed by cycles containing either ifosfamide (Ifex) or cyclophosphamide
 - high-dose methotrexate, leucovorin, vincristine (Oncovin), dexamethasone, and doxorubicin (Doxil) or etoposide (Vepesid) or cytarabine (Cytosar-U)
 - intrathecal triple therapy (methotrexate, cytarabine, and hydrocortisone) plus rituximab

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- The *CODOX-M* regimen (original or modified) consists of cyclophosphamide, doxorubicin, and vincristine with intrathecal methotrexate and cytarabine, followed by high-dose systemic methotrexate with or without rituximab, for three cycles. This regimen is sometimes alternated with IVAC (ifosfamide, intrathecal methotrexate, etoposide, and high-dose cytarabine). *CODOX-M/IVAC* is one of the most commonly utilized regimens in the United States to treat adults with Burkitt lymphoma.
- The HyperCVAD regimen includes cyclophosphamide, vincristine, doxorubicin, and dexamethasone alternating with high-dose methotrexate and cytarabine plus rituximab. This regimen includes intrathecal therapy and may be given for a longer duration than the other regimens listed above.

Different combination chemotherapy regimens are used to treat Burkitt lymphoma in children and adolescents. Burkitt syndrome is one of the most common types of childhood lymphoma, and younger patients tend to have excellent responses to chemotherapy and particularly high cure rates. For this reason, the current trend in the treatment of children is focused on decreasing toxicity by reducing the overall amount of chemotherapy used to treat the disease.

Treatments Under Investigation

Ongoing clinical trials are investigating various combination therapy regimens, including new agents in combination with the agents mentioned above. The combination of brentuximab vedotin (Adcetris) plus rituximab is being studied in clinical trials as *front-line* (initial) therapy for patients with CD30+ and/or EBV+ lymphomas. New agents are also being investigated alone or as part of combination therapy in relapsed or *refractory* (disease does not respond to treatment) disease, including the following:

- Alisertib (MLN8237)
- Everolimus (Afinitor)
- Lenalidomide (Revlimid)
- Panobinostat (Farydak)
- Vorinostat (Zolinza)

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 the Lymphoma Research Foundation's (LRF's) website at www.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 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 computed tomography [CT] 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 effects resulting from treatment or potential disease recurrences.

Support

A lymphoma diagnosis often triggers a range of feelings and concerns. In addition, cancer treatment can cause physical discomfort. Support groups and online message boards can help patients connect with other people who have lymphoma. One-to-one peer support programs, such as LRF's Lymphoma Support Network, match lymphoma patients (or caregivers) with volunteers who have gone through similar experiences.

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 disease-specific websites, videos, and eNewsletters for current lymphoma information and treatment options. To learn more about any of these resources, visit our website at www.lymphoma.org, or contact the LRF Helpline at (800) 500-9976 or helpline@lymphoma.org.